National Institute for Health and Clinical Excellence

Psoriasis
Guideline Consultation Comments Table
11th May 2012 - 26th June 2012

Type	Stakeholder	Order No	Document	Page No	Line No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
SH	Abbott Laboratories	26.0	Full	General		Abbott considers the draft guideline produced by the GDG to be a fully comprehensive guide to the management of psoriasis patients and welcomes that psoriasis has been recognised as a multi-faceted disease which can significantly impact a patient's quality of life. In particular, Abbott welcomes the recognition of the high prevalence of psoriatic arthritis (PsA) in patients with psoriasis and the need to treat these patients early in the progression of the disease. Comments made by Abbott, detailed below, are mainly for consistency and completeness.	Thank you for your comments.
SH	Abbott Laboratories	26.1	Full	15	2	The draft guideline makes reference to: *'distinctive nail changes …more common in those with arthritis'.* However this is the first time that arthritis is specifically mentioned in the document, although a reference to 'joint disease' is made (Page 15, line 2). Abbott believes that the incidence of	We agree that psoriatic arthritis is an important comorbidity in a proportion of people with psoriasis. Reference to psoriatic arthritis is made in the second line of the introduction. We have made this clearer and we think it does have marked prominence. The guideline specifically addresses identification and referral for psoriatic arthritis and also links are given to the NICE Technology Appraisals cited in

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						psoriatic arthritis and its associated burden should be described prominently early in the guideline. This would highlight the importance of the condition and would place other references to arthritis in this section into context, *e.g.* page 16, line 2 and page 16 line 42. In addition, in Abbott's view the importance of early identification and treatment of PsA should be highlighted prominently by reference to NICE TA199 [i], page 7 section 2.5. *'Aggressive treatment of early stage progressive psoriatic arthritis can help to improve prognosis.'* Abbott also considers that a statement to this effect should be added to the short guideline itself. In support of this recommendation, a study by Kimball et al. (2010)[ii] assessed the level of persistent functional impairment in patients with psoriasis and PsA from Abbott's Phase III RCT ADEPT[iii] and also assessed the impact of psoriasis disease duration on such functional impairment. The authors found that a 5 year increase in psoriasis disease duration was associated with 0.05 units greater persistent HAQ	relevant parts of the guideline and in association with relevant recommendations. We are not able to quote text from NICE Technology Appraisals that do not fall within a recommendation. The treatment of psoriatic arthritis is beyond the scope of the guideline and therefore specific recommendations on treatment cannot be included.

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						impairment (p=0.002) after adjusting for PsA duration, age, weight, baseline HAQ, and other patient characteristics. The authors concluded that longer psoriasis disease duration was independently associated with greater persistent functional impairment in patients with psoriasis and PsA who were responsive to adalimumab therapy. The authors added that such functional impairment may represent an irreversible dimension of the disease.	
SH	Abbott Laboratories	26.10	Full	688	24	Abbott recognises the difficulty encountered by the GDG in assessment of the benefits of Cognitive Behavioural Therapy specifically in psoriasis. However, Abbott believes that the strength of evidence supporting the use of CBT in depression associated with chronic physical illness as described in NICE Clinical Guideline 90[iv] supports the value of CBT in psoriasis and feels that a recommendation should be made on that basis in the psoriasis guideline.	The benefit of CBT needs to be consistently supported in psoriasis to be specifically recommended. There was insufficient evidence to support such a recommendation at this time. However, we have made a future research recommendation in this area (see Appendix R).
SH	Abbott Laboratories	26.11	Full	47	14-16	*"When offering treatments to a person with any type of psoriasis: take into account the age and individual circumstances of the person, disease phenotype, severity and impact, co-existing psoriatic arthritis, comorbidities and previous treatment history."*	Thank you for your comment. The GDG are aware of this literature however we are not aware of any robust evidence that nail disease is predictive of developing psoriatic arthritis or for tools to predict which patients who will go on to develop psoriatic arthritis.

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						Abbott suggests that the GDG considers adding "risk of developing psoriatic arthritis" as a factor to consider when offering treatments to psoriasis patients. This recommendation is based on the suggested use of nail disease as a predictive factor for PsA (see point 8)	Additionally, the prognostic relevance of nail disease on the development of psoriatic arthritis was not prioritised as an area for review. Therefore, the literature has not been reviewed and no recommendation can be made.
SH	Abbott Laboratories	26.12	Full	47	14-16	*"When offering treatments to a person with any type of psoriasis: take into account the age and individual circumstances of the person, disease phenotype, severity and impact, co-existing psoriatic arthritis, comorbidities and previous treatment history."* Abbott suggests that the GDG consider adding CV risk as an separate factor to consider when offering treatments to psoriasis patients. This suggestion is based on the principles outlined below relating to how the presence of CV risk factors may affect treatment choice (see recommendation 43).	Thank you for your comment. The term 'comorbidities' refers to and includes cardiovascular disease and risk factors for cardiovascular disease. Therefore it is already encompassed in the recommendation. It is not possible to list all the comorbidities individually.
SH	Abbott Laboratories	26.13	Full	47	14	Abbott welcomes the GDG recommendation that co-existing PsA be taken into account when offering treatments to psoriasis patients. However, it is Abbott's view that the significance of this should be highlighted further by reference to NICE TA199, page 7	We haven't specifically covered the management of psoriatic arthritis as it was not within the in the scope of the guideline. We have, however, highlighted the importance of identification and immediate referral to rheumatologists in the event of identification and this is included in the

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						section 2.5: *'Aggressive treatment of early stage progressive psoriatic arthritis can help to improve prognosis.'* As recommendations 18, 19 and 20 (page 49, lines 2,4 and 7) also refer to identification and management of psoriasis patients with concomitant PsA, Abbott believes that these should be brought under a single heading to illustrate that multiple recommendations are in place to ensure this at-risk patient group is adequately managed.	recommendations We have cross- referred to the technology appraisals in the chapters of the full guideline.
SH	Abbott Laboratories	26.14	Full	48	17	*"In specialist settings and if practical in non-specialist settings, use a validated tool to assess the impact of all types of psoriasis on physical, psychological and social wellbeing…"* Abbott considers there would be value in introducing DLQI questionnaires to patients diagnosed with psoriasis in a primary care setting in England. This suggestion is based on SIGN guidelines for psoriasis.[v] It is hoped that this will facilitate referral of patients in whom quality of life is significantly affected by their psoriasis despite topical therapy. These patients can	Thank you, the GDG (especially primary care members of the GDG) felt very strongly that this wording remain as it is. The GDG noted that the relative values of the different outcomes may change, depending on the health care setting and the purpose of using the tool. In primary care or other non-specialist settings, practicability was considered very important; use of complex, time consuming tools requiring training in use and interpretation is unlikely to be feasible, and may not be acceptable to patients.

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						then be further assessed by a specialist using the PASI and clinical judgement to optimise treatment. Harlow et al. (2000)[vi] examined the feasibility of using the DLQI in primary care amongst patients with a variety of skin conditions including psoriasis. The authors concluded that *"the DLQI was easy to use in general practice. It was acceptable to the patients, who found it quick and easy to complete. Scoring was also quick and simple…"* Abbott considers that implementation of this recommendation would not be resource intensive and will identify patients who need further clinical investigation using PASI in secondary care sooner than is currently being done. Abbott suggests that the guideline recommends that patients complete DLQI forms following a diagnosis of psoriasis in primary care and then again following assessment of response to 1st line topical therapies after 4-6 weeks of treatment. It is suggested a referral be made to specialist care if the patient has not responded to topical therapy after this period and they have a DLQI of >5, consistent with SIGN	

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						guidelines for psoriasis. Abbott considers this recommendation should also be included in the shortened NICE version of guidance and included in any patient flow diagrams.	
SH	Abbott Laboratories	26.15	Full	49	9	Page 49, line 9 in the full guideline states: *"Offer a cardiovascular risk assessment using a validated risk estimation tool to adults with severe psoriasis at presentation, and offer further assessments every 5 years, or more frequently if indicated following risk assessment. For further information see 'Lipid modification' (NICE clinical guideline 67)."* Abbott welcome this recommendation but argue that this CV assessment should be routine in patients psoriasis of **all** severities. Studies that have looked at patients with psoriasis compared to controls have found that both mild and (moderate-to-)severe psoriasis are associated with increased risk of CV events. In a prospective UK study, Gelfand et al. (2006)[vii] studied whether psoriasis is an independent risk factor for myocardial infarction (MI) when controlling for major cardiovascular risk factors. A total of 556,995 control patients and patients with mild (n = 127,139) and severe psoriasis (n = 3837) were identified. The incidences per	Thank you for your comment. The GDG reviewed the evidence and did not feel that a cardiovascular risk assessment for all people with psoriasis was appropriate. The absolute risk of cardiovascular events in people with mild disease was thought to be minimal and there was heterogeneity in the findings. When weighing the potential benefit of identifying CVD in a small minority of people with mild psoriasis against the potential harm of increased anxiety and stigmatisation the GDG did not believe it would be appropriate to recommend risk assessment to all people with psoriasis, although the GDG did recommend that preventative education be provided to all people with psoriasis when appropriate.

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						1000 person-years for control patients and patients with mild and severe psoriasis were 3.58 (95% confidence interval [CI], 3.52-3.65), 4.04 (95% CI, 3.88-4.21), and 5.13 (95% CI, 4.22-6.17), respectively. Patients with psoriasis had an increased adjusted relative risk (RR) for MI that varied by age. For example, for a 30-year-old patient with mild or severe psoriasis, the adjusted RR of having an MI is 1.29 (95% CI, 1.14-1.46) and 3.10 (95% CI, 1.98-4.86), respectively. The authors concluded that psoriasis may confer an independent risk of MI. A Danish cohort study by Ahlehoff et al. (2011)[viii] investigated the psoriasis-related risk of adverse cardiovascular events and mortality. The overall RRs for the composite endpoint were 1.20 (95% confidence interval [CI] 1.14-1.25) and 1.58 (95% CI 1.36-1.82) for mild and severe psoriasis, respectively. The corresponding RRs for cardiovascular death were 1.14 (95% CI 1.06-1.22) and 1.57 (95% CI1.27-1.94). The authors concluded that psoriasis is associated with increased risk of adverse cardiovascular events and all-cause mortality. Young age, severe skin affection and/or psoriatic arthritis carry the most risk. Patients with psoriasis may be candidates for early cardiovascular risk factor	

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						modification. These studies suggest that, whilst a more severe form of psoriasis may be associated with a higher CV risk including death, mild psoriasis also carries a statistically significantly higher risk than healthy control patients who do not have the disease. Abbott argues this milder group of psoriasis patients should not be excluded from regular CV monitoring given the evidence presented. Abbott suggests that the wording should be changed to reflect the CV risk in psoriasis patients of all severities and that a CV risk assessment must be made at presentation and every 5 years, or more frequently if indicated following risk assessment. Consider: *"Offer a cardiovascular risk assessment using a validated risk estimation tool to adults with all severities of psoriasis at presentation, and offer further assessments every 5 years, or more frequently if indicated following risk assessment. For further information see 'Lipid modification' (NICE clinical guideline 67)."*	
SH	Abbott Laboratories	26.16	Full	55	7-32	Abbott welcomes the recommendation made by the GDG to monitor patients on	Thank you for your comment. We hope that the implementation tools brought

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						systemic non-biologic therapies for safety and efficacy. This is an area in which Abbott considers there is great variation in practices occurring in the UK and a need exists to ensure implementation of the guideline. In particular, emphasis needs to be placed on PASI and DLQI scoring every 3 months for patients on methotrexate (MTX) and ciclosporin. Abbott considers that there are a number of psoriasis patients who are eligible for biologic therapy based on their disease severity but who are being sub-optimally managed with systemic non-biologic therapy for periods of time in excess of those currently recommended in the draft guideline. An example of this is with reference to treatment with methotrexate. The draft guideline suggests that response to methotrexate should be assessed every 3 months using PASI and DLQI. A recent analysis of 72 chronic plaque psoriasis patients from BADBIR (systemic control cohort, patients enrolled 27 Nov 2007 to 30 Jan 2012), who had been treated with MTX for >3months at registry entry, showed that 21 (29.2%) patients had a PASI **and** DLQI of greater than 10. The average time on MTX for this group of patients was 6.4 months and the group had a mean PASI of	out to aid the uptake of this guidance will improve this situation.

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						14.2 and a mean DLQI of 13.6. Abbott expects this practice to be confirmed by a number of audits looking at systemic therapy of psoriasis patients currently being conducted in regions throughout the UK. Abbott considers this to be the main reason for the delay in initiating patients on a biologic despite being eligible for biologic treatment. Additional analysis of BADBIR data further highlights this delay to biologic treatment. In this analysis, the mean PASI baseline score for patients being initiated on adalimumab in the adalimumab cohort of BADBIR was found to be 15.4 and the mean DLQI was 13.5 (patients enrolled 26 Nov 2007 to 30 Jan 2012, n=1024), both significantly higher than the NICE recommended scores for biologic consideration. When considered together, these analyses highlight that there is inadequate monitoring of clinical efficacy of patients on non-biologic systemic therapies in secondary care resulting in patients being considered for biologic therapy when they have higher PASI and DLQI scores and longer duration of disease. The latter analysis also reemphasises the need for earlier identification of patients who may warrant	

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						further clinical assessment of their psoriasis using PASI by means of using DLQI in primary care (see comment 15).	
SH	Abbott Laboratories	26.17	Full	54	38	For consistency with the statement relating to methotrexate and the monitoring the risk of liver toxicity, Abbott suggests that due to the potential side effect of nephrotoxicity associated with ciclosporin therapy that a baseline check for renal impairment and a recommendation or minimum frequency of measuring serum creatinine levels and blood pressure measurement during ciclosporin therapy should be introduced.	Thank you for your comment. There was insufficient evidence to make any specific recommendations about nephrotoxicity and we did not look for data on how best to monitor for nephrotoxicity or hypertension. However, the GDG were aware that all systemic treatments carry a risk for a range of adverse events and included recommendations 74 and 75 to take account of this. Please also note that appendix S summarises the available data of the risks and benefits of the interventions recommended, including nephrotoxicity and hypertension with ciclosporin.
SH	Abbott Laboratories	26.18	Full	55	33	*"Before and during methotrexate treatment, evaluate for potential hepatotoxicity."* Abbott considers that close monitoring of liver disease in psoriasis patients is essential given the association between the disease, alcohol consumption and obesity Abbott therefore welcomes this recommendation but suggests that guidance should be issued on the frequency of monitoring of hepatotoxicity whilst patients are on methotrexate treatment. The BAD guidelines suggest	Thank you for your comment. We were unable to find sufficient evidence to make a firm recommendation about the frequency of monitoring for hepatotoxicity.

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						that, given the potential for hepatotoxicity with treatment, patients are assessed monthly for the first 6 months of treatment followed by every 3 months as a minimum whilst on therapy.	
SH	Abbott Laboratories	26.19	Full	55	33	Abbott welcomes the GDG guidance on methotrexate and monitoring for hepatotoxicity (recommendations 91,92,93,94 and 95). However, it is Abbott's view that the detail afforded to recommendations regarding use of methotrexate is much greater than that given to ciclosporin and acitretin, which arguably have similarly complex considerations around contraindications and monitoring.[ix] In Abbott's view additional recommendations regarding toxicity and monitoring for ciclosporin and acitretin would improve the balance of the final guideline for the reader.	The GDG prioritised methotrexate and liver toxicity for review due to uncertainty and variation in clinical practice, hence the specific recommendations around this. The GDG were aware that all systemic treatments carry a risk for a range of adverse events and included recommendations 74 and 75 to take account of this. However, we agree that the current format may infer that other drugs do not require monitoring. Therefore, to remove the unintended implication that liver fibrosis is the main problem associated with methotrexate or that other systemic agents have preferable side effect profiles recommendation 81 has been moved to the section on methotrexate monitoring and toxicity, where the evidence for this side effect was examined in more detail.
SH	Abbott Laboratories	26.2	Full	15	29	Recent studies have suggested that the effect of psoriasis on patients lives is cumulative (Cumulative Life Course Impairment, CLCI). Kimball AB et al.	Thank you. The introduction emphasises the long-term nature of psoriasis and that it can

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						(2010)[x] proposed that psoriasis patients may be affected by the cumulative effect of physical and psychological burden caused by the condition affecting all facets of a patient's life including relationships, social activities, work and emotional wellbeing. It was reported by the authors that, in some cases, this cumulative burden lead to the failure to achieve "full life potential." Warren RB et al. (2011)[xi] looked retrospectively at the live's of four patients with psoriasis to assess whether or not their condition had affected lifetime achievements. Whilst the authors acknowledged that significant cumulative life course impairment is unlikely to occur in all patients with psoriasis, they reported that the case studies examined were supportive of the model of CLCI. In conclusion, the authors stated: *"Understanding the key risk factors for CLCI has the potential to help physicians identify patients who may be more vulnerable to the cumulative impact of psoriasis than others, allowing more appropriate treatment decisions earlier in the disease course."* Abbott considers that the GDG should acknowledge the important concept of CLCI in the disease impact section of the full	impact on all aspects of an individual's daily life (section 1.3). The background information provided is necessarily brief and so inevitably cannot comprehensively cover all aspects in detail.

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						guideline (p.15, line 29). This would underline the morbidity associated with psoriasis and emphasises the importance of early and effective management of psoriasis. Abbott considers that the concept also acknowledges the limitations of the PASI and DLQI measures in a chronic condition such as psoriasis which is characterized by flares and remission as they are only able to capture point-in-time measurements, *e.g* within the past 7 days for the DLQI. Abbott considers that the acknowledgment of the CLCI concept in psoriasis should also be made in the shortened NICE version of the guideline.	
SH	Abbott Laboratories	26.2	Full	15	2	*"It is associated with joint disease in a significant proportion of people (reported in one study at 13.8%)"* Abbott welcomes the reference to joint disease in the opening section of the guidelines, however, in Abbott's view there is insufficient information about psoriatic arthritis in this section and inclusion of the following additional pieces of information would signpost the reader to guidance specifically about PsA, and would place later recommendations into context: • PsA can be associated with progressive	Thank you for this comment. The importance of identification and referral of people with psoriasis who have psoriatic arthritis was prioritised by the GDG as an area for specific recommendations (see section on assessment and referral for psoriatic arthritis). The introduction to the whole guideline is necessarily a very brief overview of all the key points in the whole treatment pathway. However, the introduction to the specific section on the identification

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						joint damage which can cause disability similar to that seen in rheumatoid arthritis.[xii] • PsA treatment strategies (including use of licensed anti-TNF agents) demonstrate significant efficacy for people with PsA including improvement in symptoms, physical function, quality of life and reduction of joint damage. • The management of PsA with anti-TNF therapies licensed for use in this condition is covered by NICE TA199.i • Strategies for the early identification, referral and management of psoriatic arthritis in psoriasis patients are within the scope of this guideline.	and referral of people with psoriatic arthritis, is able to provide more detail on this topic area specifically and within this, the section on specialist referral for psoriatic arthritis outlines all the key points mentioned.
SH	Abbott Laboratories	26.20	Full	55	3	The BAD has published guidelines on the use of acitretin; recommended monitoring includes assessment of liver enzymes and fasting serum cholesterol and triglycerides every 2–4 weeks for the first 2 months of treatment, and then every 3 months.	Thank you for your comment. We are not able to link to guidance published by other organisations; however, we hope that recommendation 75 stating that people should be monitored in line with national and local policy should prompt health care practitioners to refer to BAD guidance as well as others.

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						Abbott suggests that these monitoring guidelines are included in the NICE guideline.	
SH	Abbott Laboratories	26.21	Full	55	10	For greater clarity, Abbott suggests that rather than using the wording *an example* of treatment response that using the wording *defined as* would be most consistent with the EU consensus statement.[xiii]	The GDG do not wish to alter this recommendation as to do so would limit its validity because PASI is not always an appropriate measure.
SH	Abbott Laboratories	26.22	Full	55	17	For greater clarity, Abbott suggests that rather than using the wording *an example* of treatment response that using the wording *defined as* would be most consistent with the EU consensus statement.[xiii]	The GDG do not wish to alter this recommendation as to do so would limit its validity because PASI is not always an appropriate measure.
SH	Abbott Laboratories	26.23	Full	55	89	For consistency, Abbott suggests that adding a similar treatment response wording for acitretin as mentioned for ciclosporin and methotrexate would be beneficial: "*less than a 75% decrease in PASI score or less than a 50% decrease in PASI score and less than 5 points in DLQI score"*	Thank you, we agree and have added an assessment time for response to acitretin in to the recommendation as follows: "Assess the treatment response after 4 months at the optimum dose of acitretin and stop treatment if the response is inadequate (for example, less than a 75% decrease in PASI score or less than a 50% decrease in PASI score and less than 5 points in DLQI score or not achieving clear or nearly clear on the PGA for pustular forms of psoriasis)." This was based on the evidence reviewed and the full rationale has been added to the linking evidence to recommendations table.

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SH	Abbott Laboratories	26.24	Full	482	12	Following a review conducted by SIGN, the SIGN group concluded that combination of methotrexate and ciclosporin has no significant effect on PsA and is not recommended for routine practice.[v] For clarity to the reader, it would be beneficial that this is stated within the NICE guideline.	Thank you for your comment. The introduction has been amended to reflect the intended meaning of the sentence.
SH	Abbott Laboratories	26.25	Full	482	14	Please complete the sentence after "BSA >10% was 5.25% of all people with…"	Thank you, the phrase has been completed.
SH	Abbott Laboratories	26.26	Full	482	31	For clarity to the reader, Abbott suggests outlining what is meant by co-morbidities such as depression and cardiovascular risk as these have significant impact on treatment decisions.	Thank you for your comment. However, the guideline is already very long and we do not want to add further to the extent of this document unnecessarily. Please note that the introduction is only scene setting and we believe that the text is sufficiently clear.
SH	Abbott Laboratories	26.27	Full	549	72	For clarity to the reader, Abbott suggests that additional information on term "specialist setting" is provided, for example healthcare professionals who are experienced in administering systemic therapies.	Thank you for your comment. We have now included a definition of specialist care in the glossary of the full guideline. This contains a link to the British Association of Dermatologists' Quality Standard where specialist settings are defined in more detail. The guideline does not stipulate who should deliver care, rather what should be provided. Psoriasis, as a quality standard topic, has been referred by the Department of Health, following advice from the National Quality Board. See

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							htt://www.nice.org.uk/guidance/qualitystandards/QualityStandardsLibrary.jsp The NICE psoriasis quality standard will include set of specific, concise statements and associated measures. They will set out aspirational, but achievable, markers of high-quality, cost-effective patient care, covering psoriasis.
SH	Abbott Laboratories	26.28	Full	549	73	For clarity for the reader, Abbott suggests that providing examples of appropriate therapy choices when tailoring the choice of therapy for example *"conception plans: avoid methotrexate and consider using ciclosporin as an alternative"*	The GDG considered that an explicit recommendation about the need to consider conception plans when planning treatment was an important element of care, hence the inclusion of conception plans within this recommendation. However, evaluating the risks and benefits of specific interventions in this context is beyond the scope of the guideline, and we did not formally review any relevant evidence. The GDG were therefore unable to give drug specific recommendations.
SH	Abbott Laboratories	26.29	Full	549	73	Abbott suggests that the statement on the optimal therapy choice when treating a patient with both psoriasis and psoriatic arthritis should be added from the economic consideration on page 555: *"considered methotrexate likely to be the optimal systemic non-biological therapy in the treatment of psoriasis patients with*	Thank you for your comment. In recommendation 79 we suggest that a rheumatologist be involved in the choice of systemic agent for those with active psoriatic arthritis and psoriasis. The GDG did not want to make a didactic recommendation for which agent to use in this group of people as there may be

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						concomitant psoriatic arthritis".	multiple factors to consider and seeking rheumatology advice was thought to be the best practice. The 'linking evidence to recommendation' section notes the GDG discussion pertaining to methotrexate. Lastly, we cannot make specific recommendations about how to treat psoriatic arthritis as this was outside our scope.
SH	Abbott Laboratories	26.3	Full	16	43	*'Setting aside psoriatic arthritis, there is no compelling evidence that any of the interventions have a disease modifying effect.'* Abbott welcomes the GDG recognition that disease modifying therapies such as TNF antagonists are available in psoriatic arthritis. Abbott further proposes that this point should also be recognised in the shortened NICE guideline, to increase emphasis on early identification and treatment of this at-risk patient group, and support the recommendations on the use of PEST and referral to rheumatology.	Thank you for your comment. It was outside of our scope to review the evidence for the management of psoriatic arthritis and so we are not able to include any recommendations specifically around interventions to manage joint disease associated with psoriasis. The NICE version of the guideline includes only the recommendations and the brief introduction and the GDG believes that the existing recommendations provide sufficient emphasis on the need for early identification and referral within the remit of the guideline.
SH	Abbott Laboratories	26.30	Full	549	74	For additional clarity to the reader, Abbott suggests that additional information should be provided related to the contraindications and adverse effects associated with systemic treatments particularly at risk	It is beyond the scope of the guideline to address all contraindications and there was insufficient evidence to make recommendations about the toxicity profiles. There is a recommendation in

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						population of hepatotoxicity such as type 2 diabetes and obesity.	the guideline to ensure that healthcare professionals prescribing systemic therapy will be aware of the risks and benefits and that they should refer to the BNF.
SH	Abbott Laboratories	26.31	Full	550	84	Due to the potential side effect of nephrotoxicity associated with ciclosporin therapy Abbott suggests a baseline check for renal impairment and a recommendation or minimum frequency of measuring serum creatinine levels and blood pressure measurement during ciclosporin therapy	Thank you for your comment. There was insufficient evidence to make any specific recommendations about nephrotoxicity and we did not look for data on how best to monitor for nephrotoxicity. However, the GDG were aware that all systemic treatments carry a risk for a range of adverse events and included recommendations to take account of this. Please also note that appendix S summarises the available data of the risks and benefits of the interventions recommended, including nephrotoxicity with ciclosporin.
SH	Abbott Laboratories	26.32	Full	551	85	For greater clarity, Abbott suggests that rather than using the wording *an example* of treatment response that using the wording *defined as* would be most consistent with the EU consensus statement.[xiii]	The GDG do not wish to alter this recommendation as to do so would limit its validity because PASI is not always an appropriate measure.
SH	Abbott Laboratories	26.33	Full	551	87	For greater clarity, Abbott suggests that rather than using the wording *an example* of treatment response that using the wording *defined as* would be most consistent with the EU consensus statement.[xiii]	The GDG do not wish to alter this recommendation as to do so would limit its validity because PASI is not always an appropriate measure.

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SH	Abbott Laboratories	26.34	Full	551	89	For consistency, Abbott suggests that adding a similar treatment response for acitretin as mentioned for ciclosporin and methotrexate: "*less than a 75% decrease in PASI score or less than a 50% decrease in PASI score and less than 5 points in DLQI score"*	Thank you, we agree and have added an assessment time for response to acitretin in to the recommendation as follows: "Assess the treatment response after 4 months at the optimum dose of acitretin and stop treatment if the response is inadequate (for example, less than a 75% decrease in PASI score or less than a 50% decrease in PASI score and less than 5 points in DLQI score or not achieving clear or nearly clear on the PGA for pustular forms of psoriasis)." This was based on the evidence reviewed and the full rationale has been added to the linking evidence to recommendations table.
SH	Abbott Laboratories	26.35	Full	551	89	To ensure the contraindication of pregnancy before, during and after acitretin therapy is clearly highlighted to the reader, Abbott suggests that incorporation of acitretin is highly teratogenic and must not be used by women who are pregnant. The same applies to women of childbearing potential unless strict contraception is practiced 4 weeks before, during and for 2 years after treatment.**Error! Bookmark not efined.** Please add this contraindication warning to p.55, line 24 and the shortened NICE guideline.	The GDG considered that an explicit recommendation about the need to consider conception plans when planning treatment was an important element of care, hence the inclusion of conception plans within this recommendation. However, evaluating the risks and benefits of specific interventions in this context is beyond the scope of the guideline, and we did not formally review any relevant evidence. The GDG were therefore unable to give drug specific recommendations.

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SH	Abbott Laboratories	26.36	Full	55	19	Abbott suggests the GDG state that patients who may be at risk of nephritic disease such as patients who have hypertension and/ or Type 2 diabetes are at a greater risk for nephrotoxicity associated with ciclosporin therapy.	Thank you for your comment. We did not look for data on risk groups for nephrotoxicity on ciclosporin and so we are not able to make such a recommendation. However, the GDG were aware that all systemic treatments carry a risk for a range of adverse events and included recommendations 74 and 75 to take account of this. Please also note that appendix S summarises the available data of the risks and benefits of the interventions recommended, including nephrotoxicity with ciclosporin.
SH	Abbott Laboratories	26.37	Full	56	6	Abbott considers that there should be explicit wording in the guideline relating to the initiation of biologic agents in psoriasis patients. At present, the only recommendation on systemic biologic therapy in the summary points is concerned with switching of primary or secondary non-responders. This is in contrast with the section on systemic non-biologic therapies (full guideline, p.46 line 24) which includes a list of criteria which resembles a treatment algorithm. Abbott considers that for consistency and completeness, a similar consideration is given to the use of systemic biologic therapies. Abbott suggests that this point is included in the "key priorities for implementation" and	Thank you for your comment. The scope excluded us from doing any work on first line biologics as this is covered in the NICE technology appraisals. All of the recommendations from TAs 103, 134, 146 and 180 have been quoted verbatim and form the current guidance for the use of biological agents for psoriasis, and cannot be amended in any way. We have added explanatory text and subheadings to make this clear.

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						that it precedes the recommendations made for the individual biologic agents (p.56, line 6, full guideline) and is replicated in the NICE version of the guideline.	
SH	Abbott Laboratories	26.38	Full	56	37-40	The draft guidance relating to the use of systemic biologic therapy in eligible psoriasis patients contains the following recommendation for the use of etanercept: *"It is recommended that the use of etanercept for psoriasis should be initiated and supervised only by specialist physicians experienced in the diagnosis and treatment of psoriasis. If a person has both psoriasis and psoriatic arthritis their treatment should be managed by collaboration between a rheumatologist and a dermatologist."* This reference to the integrated management of psoriasis patients who have psoriatic arthritis (PsA) between a dermatologist and rheumatologist is **not** mentioned in the recommendations for adalimumab nor infliximab both of which were licensed and subsequently recommended for treatment of the same psoriatic arthritis patient population as etanercept in NICE TA 199.i Abbott appreciates this statement has been taken directly from the original NICE technology appraisal (TA) 103, and that the wording is	Thank you. On this occasion we were able to undertake limited editing in collaboration and agreement with NICE and the TA team. We have modified the recommendation to make it clear that all biologics should be initiated and supervised by specialist physicians experienced in the diagnosis and treatment of psoriasis.

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						not present in TA 146 or TA 134 relating to the use of adalimumab and infliximab respectively, however, Abbott suggests that the GDG consider adding the same statement relating to adalimumab and infliximab as both technologies are licensed and recommended by NICE for use in active PsA following TA 199. The wording "specialist physicians" and "experienced in the diagnosis and treatment of psoriasis" in the above statement relating to etanercept use may also be misleading in suggesting that patients treated with etanercept are in some way different to patients treated with the other biologics. Consider adding the following as an additional bullet point following recommendation 98 on page 56 in the full guideline relating to the use of adalimumab: *"It is recommended that the use of **adalimumab** for psoriasis should be initiated and supervised only by specialist physicians experienced in the diagnosis and treatment of psoriasis. If a person has both psoriasis and psoriatic arthritis their treatment should be managed by collaboration between a rheumatologist and a dermatologist."* Abbott suggests that, for completeness, similar wording is also added to the section	

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						pertaining to infliximab's use in chronic plaque psoriasis.	
SH	Abbott Laboratories	26.39	Full	57	39	Abbott welcomes the recommendation that there should be integrated care between a dermatologist and rheumatologist for those patients who have psoriasis and psoriatic arthritis. However, Abbott considers there is a need to clarify which healthcare professional has overall care in the management of a psoriasis patient who also has psoriatic arthritis (PsA). This is relevant and important in the care of those patients considered for treatment with adalimumab given the different licensed dosing regimens at treatment initiation between the two indications. The recommended dose of adalimumab in adults with moderate to severe chronic, plaque psoriasis is 80mg at week 0 followed by 40mg every other week from week 1 (NICE TA 146). The recommended dose of adalimumab in adults with psoriatic arthritis is 40mg given every other week from week 0 (NICE TA 199). Peng et al. (2008)[xiv] looked at the benefits of a loading dose in an adalimumab therapeutic regimen for moderate to severe psoriasis. In this study, clinical trial simulations predicted that this 80mg loading dose is required to achieve rapid, therapeutic steady-state drug	Thank you for your comment. The use of a first biological agent was not within our scope and is covered by the NICE Technology Appraisals (TAs). We are only able to reproduce the recommendations directly from the TAs. As the text that you cited does not appear within a recommendation we are unable to include it in the guideline. We have provided a link to the relevant TAs where full details can be found.

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						concentrations . It was concluded that a single 80-mg loading dose of adalimumab may help patients with psoriasis achieve therapeutic steady-state drug concentrations substantially earlier (by Week 1 vs. Week 12) than without a loading dose. Consider adding the following in the adalimumab section: *"If a patient with psoriasis and psoriatic arthritis meets the eligibility criteria for an anti-TNF based on their psoriasis alone, the patient must be initiated on 80mg at week 0 followed by 40mg every other week from week 1. For more information see NICE TA 146"*	
SH	Abbott Laboratories	26.4	Full	22	40	'What this guideline covers' section: The guideline also covers biologic therapies for psoriasis. Abbott considers that the list of included topics should be updated to reflect this.	Thank you, we have not revised the list of key clinical issues covered as biological therapies are incorporated from the NICE Technology Appraisals. Please see section 3.6 'Relationship between the guideline and other NICE guidance'.
SH	Abbott Laboratories	26.40	Full	46 57	36-39 33-36	The GDG suggests the following relating to switching therapies between biologic agents: *"Consider changing to an alternative biological drug in adults with psoriasis in whom there is an inadequate response to a*	Thank you. We agree and have amended the recommendation.

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						first biological drug (either following the first 3 months of treatment [primary failure], or following an initially adequate response [secondary failure]), or if the first biological drug cannot be tolerated or becomes contraindicated." Abbott agrees with this recommendation made by the GDG but considers that patients should be assessed for primary non-response at the time of assessment recommended in NICE guidance for the particular biologic in question. For example, if a patient is treated with adalimumab, response to treatment should be assessed at 16 weeks, rather than at the suggested 3 months, in accordance with recommendations made in NICE technology appraisal 146.[xv] Making an assessment of response at 3 months in patients treated with adalimumab may disadvantage certain patients who may not have been given the recommended time on treatment to achieve the NICE specified endpoint(s). In a similar manner, it is suggested that response to etanercept treatment should be assessed at 12 weeks (NICE TA 103)[xvi], response to infliximab should be assessed at 10 weeks (NICE TA 134)[xvii] and response to ustekinumab should be assessed at 16 weeks (NICE TA 180)[xviii].	

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						Abbott suggests that wording reflecting the recommended time of assessment for response with each of the individual biologics (as stated in the original technology appraisals) should replace the current 3 month recommendation throughout the full guideline and shortened guideline.	
SH	Abbott Laboratories	26.41	Full	57	16-29	Abbott strongly considers that there should be some consistency between the NICE guideline and the BAD biologic guidelines[xix] on the use of IL-12/23 biologic agents in psoriasis. The BAD biologic guidelines state:- "*In light of limited patient exposure, ustekinumab should be reserved for use in patients with severe psoriasis who fulfil the stated disease severity criteria AND where TNF antagonist therapy has failed or is contraindicated."* While Abbott recognises that the safety experience with this class of biologic agents has advanced since the publication of the 2009 BAD biologic guidelines, Abbott believes that this issue has not yet been conclusively addressed: Two recent meta-analysis have analysed whether patients taking the IL-12/23 antagonists ustekinumab and briakinumab for psoriasis have a significantly increased risk of a	Thank you for your comment. The scope excluded us from doing any work on first line biologics as this is covered in the NICE technology appraisals, hence we were only able to look at a very specific aspect of the use of biologic drugs in psoriasis – namely the use of a second biologic agent. Therefore, we are unable to make any new recommendations about the safety of ustekinumab and to comply with the scope recommendations related to the first use of ustekinumab are quoted verbatim from NICE Technology Appraisal 180 and we are unable to amend them in any way.

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						Major Adverse Cardiovascular Event (MACE)[xx,xxi]. While one of these publications concluded that this risk was significant the other concluded that it was not significant. Ryan et al. (2011) found that, compared to placebo, there was no statistically significant difference between MACE rates in those treated with the IL-12/23 antagonists ustekinumab and briakinumab or anti-TNF agents. However, the authors commented: *"Until more definitive data become available, we believe that dermatologists should exercise heightened vigilance for cardiovascular risk factors when initiating anti–IL-12/23 agents in psoriasis patients."* Tzellos et al. (2011) re-evaluated the same RCT's reportedly using more powerful risk-difference methods than Ryan et al. (2011) and found that, compared to placebo, there was a statistically significant increased risk of MACE associated with the IL-12/23 antagonists ustekinumab and briakinumab when used in plaque psoriasis patients. In conclusion, the authors of this study stated: *"This meta-analysis of RCTs with the use of a more powerful statistical approach was able to detect a statistically significant*	

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						increase in MACEs associated with anti-IL-12/23 use. In the general population, patients with risk factors for cardiovascular morbidity may use these agents for a long period of time, and therefore the real rate of MACEs could be higher." Abbott understands that these studies are based on short-term trials which are designed primarily to assess efficacy of treatment nevertheless argues that, given the inconclusive results presented above, there is sufficient uncertainty around the increase in MACE following the use of IL-12/23 antagonist agents in psoriasis patients to suggest that patients should only be considered for treatment with IL-12/23 antagonist agents following anti-TNF failure. Given that ustekinumab is currently the only licensed IL-12/23 antagonist agent for use in chronic plaque psoriasis, consider adding: "*In light of inconclusive safety data, ustekinumab should be reserved for use in patients with severe psoriasis who fulfil the stated disease severity criteria AND where TNF antagonist therapy has failed or is contraindicated."*	

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						Abbott considers that this consistency between the two National guidelines would help to standardize practices throughout the UK relating to biologic use in psoriasis.	
SH	Abbott Laboratories	26.42	Full	56	6-23	Abbott recommends that the GDG are consistent with the BAD biologic guidelines on the choice of biologic drug to be used in rapid disease control and stable chronic plaque psoriasis. Whilst Abbott recognises that the draft guideline does not address the question of optimal sequencing of biologic therapy in psoriasis, Abbott considers it necessary to offer *some* guidance on 1st line choice of biologic agent to be used in psoriasis depending on the type of response required. Adalimumab is currently recommended as the only biologic for use in rapid disease control and stable chronic plaque psoriasis in the BAD biologic guidelines.	Thank you for your comment. Our scope excluded us from doing any work on first line biologics as this, as you acknowledge, is covered in the NICE technology appraisals (TAs). Section 3.6 (Relationships between the guideline and other NICE guidance) of the full guideline indicates which TAs have been incorporated into the psoriasis guideline. We looked at a very specific aspect of the use of biologic drugs in psoriasis only. We have now added more information in to the NICE guideline to set the scene for biologics.
SH	Abbott Laboratories	26.43	Full	56	24-40	*"Etanercept, within its licensed indications, administered at a dose not exceeding 25 mg twice weekly is recommended…"* Abbott welcomes the GDG comment on the NICE recommended dose of etanercept for use in adults with moderate to severe chronic plaque psoriasis.	Thank you for your comment. We are only able to reproduce the recommendations directly from the NICE technology appraisal. As the text that you cited does not appear within a recommendation we are unable to include it in the guideline.

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						However, Abbott considers that particular reference should be made to the NICE assessment that the 50mg twice weekly dose of etanercept after week 12 has **not** been deemed a cost-effective use of NHS resources (Technology Appraisal 103. Section 4.3.8 in TA 103). Abbott believe that the use of 50mg twice weekly in moderate to severe chronic plaque psoriasis patients routinely occurs in clinical practice in the UK **after** 12 weeks of treatment with etanercept. It is believed that the licensed dose of etanercept is sufficiently complex to warrant clarification within this guideline. Based on NICE guidance and comments above, Abbott recommends that a statement be added in the section detailing etanercept: *"Etanercept is not recommended for use at a dose of 50mg twice weekly after 12 weeks of treatment."*	We have provided a link to the relevant NICE technology appraisals where full details can be found.
SH	Abbott Laboratories	26.44	Full	57	40	*"If a person has both psoriasis and psoriatic arthritis, take into account both conditions before making changes to biological therapy and manage their treatment in consultation with a rheumatologist. For further information see 'Etanercept,*	Thank you for your comment. We agree and have amended the recommendation to reflect your suggestions.

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						infliximab and adalimumab for the treatment of psoriatic arthritis' (NICE technology appraisal guidance 199)." Abbott agrees with this recommendation but suggests that the wording should be amended to reflect the influence of PsA on any anti-TNF treatment decision at **initiation.** Consider the following wording to reflect the influence of PsA on any anti-TNF treatment decision at initiation: *"If a person has both psoriasis and psoriatic arthritis, take into account both conditions before **initiating and** making changes to biological therapy and manage their treatment in consultation with a rheumatologist. For further information see 'Etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis' (NICE technology appraisal guidance 199)."*	
SH	Abbott Laboratories	26.45	Full	65	1	Abbott considers that the Algorithm choice of drugs (systemic non-biological) diagram should be updated to include part of recommendation 88 (full guideline page 55, line 19). *'Do not use ciclosporin continuously for more than 1 year unless disease is severe or unstable and other treatment options*	Thank you this has now been included in the relevant algorithm.

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						cannot be used.'	
SH	Abbott Laboratories	26.46	Full	General		Abbott considers there would be value in using a simplified patient flow diagram in the full guideline and in the shortened version of the guideline as a quick visual reference guide for readers. Abbott suggest that this diagram includes key recommendations on how patients are managed in primary care, criteria for referral, key recommendations on systemic drug use and monitoring for safety and efficacy and key recommendations on biologic drug use and monitoring for safety and efficacy.	Thank you for your comment. NICE will include a simplified version of the patient pathway on their website with links to the recommendations.
SH	Abbott Laboratories	26.47	Full	45	2	Abbott considers that the "Key priorities for implementation" (section 5.1) should include some of the recommendations made in this response to draft. Some of the proposed changes are alterations to wording whilst others are suggested as **additional** recommendations to those already made under the 10 key priority headings which have been identified. These include: In the assessment tool for disease severity and impact section add: • *the impact of disease on physical, psychological and social wellbeing* ***using DLQI*** *(alteration)*	Thank you for your comments. The key priorities for recommendation are voted for by the guideline development group. The criteria used for selecting these recommendations are listed in detail in the NICE Guideline Manual.

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						• *scalp psoriasis has a major cosmetic impact (addition)* • *if their psoriasis has a significant impact on work productivity (addition)* • *Any facet of psoriasis, e.g. high impact sites such as genitalia, hands, feet, head and neck, is having a major impact on a person's physical, psychological or social wellbeing.(alteration)* In the assessment and referral for psoriatic arthritis section add: • *"Nail disease should be referred to a specialist for assessment and advice about planning their care." (addition)* • *Assess psoriasis patients yearly for development of psoriatic arthritis (addition)* In the identification of co-morbidities section, add: • *"Offer a cardiovascular risk assessment using a validated risk estimation tool to adults with **all severities of** psoriasis at presentation, and offer further assessments every 5 years, or more*	

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						frequently if indicated following risk assessment. For further information see 'Lipid modification' (NICE clinical guideline 67)." (addition) In the systemic therapy section add: • *"When offering treatments to a person with any type of psoriasis: take into account the age and individual circumstances of the person, disease phenotype, severity and impact, co-existing psoriatic arthritis,* ***risk of developing psoriatic arthritis****, comorbidities,* ***CV risk factors*** *and previous treatment history." (addition)* • *Assess the treatment response after 3 months at the target dose of methotrexate, ciclosporin and acitretin and stop treatment if the response is inadequate (****defined as*** *a decrease of less than 75% in PASI score or a decrease of less than 50% in PASI score and 5 points in DLQI score). (alteration)* In the systemic biologic therapy section: • Include a statement on the initiation of biologic therapy, *i.e* "Consider biologic therapy in patients with	

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						psoriasis if…" The list should then include criteria recommended by NICE to assess for biologic eligibility in chronic plaque psoriasis with reference to TA 103, 134, 146 and 180. (addition) • "*In light of inconclusive safety data, ustekinumab should be reserved for use in patients with severe psoriasis who fulfil the stated disease severity criteria and where TNF antagonist therapy has failed or is contraindicated." (addition)* • Change the time of assessment of response for consideration of switching biologic therapy in primary responders from 3 months to 10 weeks for infliximab, 12 weeks for etanercept, 16 weeks for adalimumab and 16 weeks for ustekinumab in line with NICE recommendations made in TA 134, 103, 146 and 180 respectively. (alteration) • Given the identified importance of early, effective treatment of PsA, Abbott suggests that the GDG include the recommendation on biologic use in psoriasis and PsA in this key implementation section *"If a person has both psoriasis and psoriatic arthritis, take into account*	

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						*both conditions **before initiating and** making changes to biological therapy and manage their treatment in consultation with a rheumatologist. For further information see 'Etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis' (NICE technology appraisal guidance 199)." (addition)*	
SH	Abbott Laboratories	26.5	Full	45	13-19	Abbott agrees with the referral recommendations made by the GDG but considers that scalp psoriasis has been omitted. Abbott considers the following bullet point should be added: • Scalp psoriasis which is having a major cosmetic impact	Thank you. The GDG believe that this is already encompassed within the last bullet point. We were keen to ensure that some flexibility is available for the clinician.
SH	Abbott Laboratories	26.7	Full	45	19	In Abbott's view the section on referral of patients to specialist care should more closely reflect the multifaceted nature of psoriasis *e.g*. by rewording the final bullet point: *Any facet of psoriasis, e.g. high impact sites such as genitalia, hands, feet, head and neck, is having a major impact on a person's physical, psychological or social wellbeing,.* This change should also be made in the full	Thank you. The GDG believe that this is already encompassed within the last bullet point. We were keen to ensure that some flexibility is available for the clinician.

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						recommendations list and the shortened NICE guideline version.	
SH	Abbott Laboratories	26.8	Full	45	21	Consider recommending that patients with nail disease should be referred to a specialist for advice and planning their care. Abbott considers that the GDG should examine evidence on the studied link between nail psoriasis and PsA and make recommendations for early referral and treatment of the affected patients based on this evidence. Ash et al. (2012)[xxii] studied whether psoriasis patients with nail disease have a greater magnitude of underlying systemic subclinical enthesopathy, a major feature of PsA, than those with normal nails. Forty-six patients with psoriasis (31 with nail disease) and 21 matched healthy controls (HC) were recruited from within the UK. 804 entheses of upper and lower limbs were scanned by an ultrasonographer blinded to clinical details. Results showed that psoriasis patients had higher enthesitis scores than HC (median (range) 21 (0-65) vs 11 (3-39), p=0.005). Enthesopathy scores were higher in patients with nail disease (23 (0-65)) than in patients without nail disease (15 (5-26), p=0.02) and HC (11 (3-39), p=0.003). Inflammation scores of patients with nail disease (13 (0-34)) were higher than	Thank you for your comment. The GDG are aware of this literature however we are not aware of any robust evidence that nail disease is predictive of developing psoriatic arthritis or for tools to predict which patients who will go on to develop psoriatic arthritis. Additionally, the prognostic relevance of nail disease on the development of psoriatic arthritis was not prioritised as an area for review. Therefore, the literature has not been reviewed and no recommendation can be made. The GDG debated at length the key priorities for implementation and based their decision on the criteria specified in the NICE technical manual.

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						patients without nail disease (8 (2-15), p=0.02) and HC (5 (0-19), p<0.001). Importantly, patients studied did not have PsA. The authors reported that no link between the PASI and enthesitis was found, highlighting that the conventional PASI may not be suitable in detecting the underlying changes which may be occurring in patients with psoriasis. In summary, this study found that enthesopathy was common in psoriasis patients without clinical arthritis. Moreover, subclinical enthesopathy was especially associated with nail psoriasis in the above cross-sectional analysis. These findings suggest that nail disease is in some way linked to the expression of either overt or subclinical enthesitis. The authors concluded: *"the link between nail disease and contemporaneous subclinical enthesopathy offers a novel anatomical basis for the predictive value of nail psoriasis for PsA evolution."* In 2009, McGonagle et al.xxv investigated the nail as a muscoskeletal appendage and implications this may have on the link between psoriasis and arthritis. In	

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						conclusion, the authors stated that the nail was an integral part of the enthesis organs around the DIP joint. It appeared that the nail had strong skeletal attachments and that this may be the unifying basis for the link between the skin and joint in PsA. The study also supported the emerging data where subclinical enthesitis is a feature of psoriasis patients without arthritis. These findings are similar to those in other published studies which look at the link between nail psoriasis and PsA in psoriatic patients.[xxiii,xxiv,xxv] In support of the above studies, Abbott conducted an analysis of 2066 psoriasis patients enrolled in the British Association of Dermatologists Biologic Interventions Register (BADBIR). BADBIR is a UK and Eire observational study which seeks to assess the long-term safety of biologic treatments for psoriasis. The patients analysed were from the adalimumab cohort (patients enrolled 26 Nov 2007 to 30 Jan 2012) and systemic control cohort (patients enrolled 01 Oct 2007 to 30 Jan 2012). The analysis showed that, of the 436 (21%) patients who had a diagnosis of PsA at registry entry, 248 (57%) had been identified with nail psoriasis. A statistically significant proportion of patients with nail psoriasis had PsA compared to those with no nail	

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						psoriasis (p=0.0008). There were no statistical differences between these two groups in terms of basic demographic characteristics including age and sex. Based on the evidence presented, Abbott considers that there is potential for nail psoriasis to be used as a predictive factor to identify patients who may go on and develop PsA. Abbott considers that this key recommendation should be included in the "key priorities for implementation" section.	
SH	Abbott Laboratories	26.9	Full	48	10	Abbott suggests that the GDG considers adding wording concerning the effect a patients psoriasis may be having on work productivity. Wu et al. (2009)[xxvi] studied the effect of psoriasis on work productivity. In a retrospective analysis of 40,730 patients, 1127 with psoriasis were matched with a cohort of non-psoriasis patients. Results showed that psoriasis patients were more likely to have missed work for health-related reasons ($p < 0.05$), had significantly more health-related work productivity impairment ($p < 0.001$), more overall work impairment ($p < 0.001$), and more impairment in activity other than work ($p < 0.001$) than non-psoriasis patients. The authors concluded that the results of this large-scale national survey suggest that psoriasis has a significant negative impact on overall work productivity.	Thank you for your comment. We believe that the effect of the patients psoriasis has on work productivity is included in the wording 'what aspects of daily living are affected'. We are not able to provide an exhaustive list of these aspects.

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						This concept may be examined further, in that work productivity loss has been shown to be correlated with Health Related Quality of Life rather than clinical severity assessment. Results from a cross-sectional study by Schmitt et al. (2006)[xxvii] found that indirect costs of productivity loss exceeded the total direct cost. In contrast to objective clinical disease severity, health-related quality of life (measured by the Dermatology Life Quality Index) was an independent predictor of work productivity. In order to highlight the effects of adalimumab treatment on work productivity in psoriasis patients, Kimball et al. (2012)[xxviii] analysed patients in Abbott's Phase III RCT REVEAL.[xxix] Greater improvements in total work productivity impairment and total activity impairment were observed with adalimumab treatment versus placebo (15.5 and 11.1 percentage points, respectively; P < .001). Unemployment rate, total work productivity impairment, and total activity impairment were significantly associated with greater baseline psoriasis severity. Changes in WPAI outcomes were significantly correlated with greater psoriasis severity. The Dermatology Life Quality Index had stronger associations with changes in WPAI outcomes compared with clinical severity	

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						measures (Psoriasis Area and Severity Index and Physician Global Assessment). The authors concluded that adalimumab reduced psoriasis-related work productivity and activity impairment in patients with moderate to severe psoriasis. Both of these studies illustrate the potential benefit of DLQI scoring in primary care as suggested below (comment 15). The GDG are urged to recognise this issue which may not be adequately captured in clinical indicators such as PASI scoring or condition specific quality of life assessment such as DLQI but which has the potential to cause considerable economic burden on individuals and society as a whole. In addition to work productivity impairment, Abbott considers it important to recognise the effect of psoriasis on daily activities including the impact of the disease in those who do not work. Lynde et al. (2009)[xxx] studied the burden of psoriasis in 500 Canadian patients with moderate to severe disease. Results showed that 35% (176 of 500) of respondents indicated that they considered psoriasis to be a substantial problem in their daily life and the authors concluded that psoriasis, PsA, and their associated comorbidities impose a severe	

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						burden on the daily lives of patients with a history of moderate to severe psoriasis. Consider adding (p.48, line 10): • ***if their psoriasis has a significant impact on work productivity and/or daily activities***	
SH	British Dermatology Nursing Group - BDNG	21.0	Full	61		Algorithm needs to be simplified; there are newer combinations/preparations that offer quicker clearance. Patient's concordance will decrease if they have to go back to twice daily treatments.	Thank you for your comments. We have revised the topical algorithm for trunk and limbs. However, the actual sequence and interventions recommended are based on the best available evidence and cost effectiveness. We agree that adherence is an important issue and was not adequately addressed in the original economic models. A sensitivity analysis has been performed to explore the impact of reduced adherence on twice daily treatments. In this sensitivity analysis, it was assumed that 40% of patients on twice daily treatment would only apply the topical once daily, thus reducing the strategies efficacy. The conclusions of the analysis and the recommendations so informed are insensitive to this reduction in adherence. We have added text in the full guideline to clarify this further and details of the assumptions and results of this sensitivity analysis are included in

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							section M3.2.3 of Appendix M.
SH	British Dermatology Nursing Group - BDNG	21.1	Full	62		Scalp psoriasis, .The low cost preparations tend to be runny and difficult to apply so compliance fails again.: Offer a potent corticosteroid for 8 weeks (any vehicle the patients chooses) or a short contact very potent corticosteroid for 4 weeks or combined product daily for up to 8 weeks. Along side a tar based shampoo.	Thank you for your comment, we agree that for scalp psoriasis the formulation is very important, particularly as this is a high impact site and that application is difficult. We have now removed this line. We believe that other recommendations adequately cover the importance of formulation and patient preference. However, the evidence does not support the use of tar-based shampoo for severe scalp psoriasis.
SH	British Dermatology Nursing Group - BDNG	21.2	Full	63		Flexural psoriasis – add in guidance with using combined products +/- anti-infective agents.	Thank you. The GDG did not prioritise this area and we did not look at the evidence for anti-infective agents. Therefore, we are unable to make a specific recommendation.
SH	Department of Health	10.0				No substantive comments to make regarding this consultation	Thank you for your comment.
SH	Dermal Laboratories	8.0	Full	General		Whilst the full guideline recognises that most patients benefit from an emollient to relieve pruritus and scaliness this has not been included in the NICE guideline. Although the GDG accept that the use of emollients in psoriasis is widespread and of accepted value this is not reflected in the actual NICE guideline and this omission could result in the misconception that emollients should not be offered to	Thank you for your comments. The Guideline Development Group (GDG) agrees that emollients are an accepted important component of treatment for psoriasis. However, the GDG was unable to cover every aspect of psoriasis management and had to prioritise areas where practice is variable or unsafe and where recommendations are likely to be

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						psoriasis patients. Also the assumption that, when appropriate, emollients have already been prescribed in the treatment pathway and are therefore not included in the NICE guideline could lead to emollients being overlooked as an adjunctive therapeutic option. Our previous comments submitted about the draft scope also addressed the point that emollients have an important role to play in the management of psoriasis (supported by recommendations of professional dermatology bodies and reviews) and **should be included within the NICE guideline**. This should be done even if recommendations on specific emollients are not possible – the application of an emollient should be the cornerstone of psoriasis treatment, as recommended by the BAD and Primary Care Dermatology Society (PCDS).	informed by a robust evidence base. The GDG were aware that there is little or no formal evidence for emollients compared to no treatment. In defining the scope the GDG therefore opted to begin the topical pathway after emollients. The GDG noted stakeholders concerns that without an explicit statement about emollients this component of management might be omitted. The NICE Guideline has therefore been amended to include the following wording: *The treatment pathway in this guideline begins with active topical therapies. The GDG acknowledged that the use of emollients in psoriasis was already widespread and hence the evidence review was limited to active topical therapies in psoriasis. Please refer to the BNF and the cBNF for guidance on use of emollients'.* This wording has also been included within the algorithms for topical therapy.
SH	Dermal Laboratories	8.1	Full	23	1.3.3.6	The Capasal Therapeutic Shampoo MHRA approved current SPC states that Capasal **can** be used alone for the treatment of plaque-type scalp psoriasis. Indeed, the	Thank you. The evidence for effectiveness of tar based shampoo in the network meta-analysis indicated that its effect was no better than placebo.

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						product is licensed for use as a shampoo in the treatment of dry, scaly scalp conditions such as psoriasis. The evidence cited in the draft guideline does not support the statement 1.3.3.6 – Do not offer coal tar-based shampoos alone for the treatment of plaque-type psoriasis. Based on the cost efficacy model the conclusion that coal tar shampoos are not cost effective is based on the assumption that there are secondary care referral costs associated with coal tar shampoos. Is there data to support this statement? In general practice it is highly unlikely that failure to respond to a coal tar-based shampoo alone would result in an immediate secondary care referral. Surely the addition of a further topical treatment, like calcipotriol, would be more likely, with the patients remaining in primary care? Finally the full guideline commented originally on the cost-effectiveness and efficacy of Capasal Shampoo, however this statement was subsequently removed from the main body of the full guideline in the Corrigendum. As this forms the basis for the above statement, and taking into account the points raised above, the recommendation of not offering coal tar shampoos alone for scalp psoriasis should **not** remain in the NICE guideline.	This is clearly documented in the 'linking evidence to recommendation' section of the full guideline. The economic model placed coal tar-based shampoos into a range of topical sequences and referral to secondary care was only assumed to follow failure of two or three treatments, which might include coal tar shampoo. The GDG felt that psoriasis of the scalp is a high impact site and of importance to patients. If scalp psoriasis is having an impact on quality of life and is unresponsive to three different cycles of treatment, patients should be offered referral. The recommendation has been edited.

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SH	IMPACT – University of Manchester	24.0	FULL	58	2-17	Research Recommendations Given that psoriasis is a condition with significant psychological and social impact the recommendations have not prioritised as a key research goal studies which aim to develop appropriate and effective modes of psychological and social support for people affected with the condition and which go beyond CBT or structured 'self-management' support. This would include research to develop: • interventions to help people manage low mood/ emotions such as anger • arousal reduction interventions • lifestyle behaviour change interventions • interventions specifically aimed at young people • interventions tailored to people of different cultures / ethnicities • interventions specifically aimed at parents/carers of people with psoriasis • interventions for practitioners to support mood/emotional management and lifestyle behaviour management	Thank you for your comment. However, we are not able to make research recommendations in areas where we did not review the evidence.

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SH	Janssen	19.0	Full	632	5	We suggest a minor amendment to this line: "...the IL12/23 monoclonal antibody (ustekinumab) are licensed..."	Thank you for your comments. We have made this change.
SH	Janssen	19.1	Full	632	18-20	"Some studies have suggested that response rates to a second biological drug may be lower than that to the first, and also that even in those who do respond, the duration of response may be shortened." We suggest this statement be referenced so that a reader can understand which studies have shown such results. Also, it may be more appropriate to state that "...response rates to a second biological drug in the same class may be lower than that to the first..." because Gniadecki (2011) found that patient retention in anti-TNF therapy was reduced in patients who have previously failed another TNF blocker. (Gniadecki, R et al. Comparison of drug survival rates for adalimumab, etanercept and infliximab in patients with psoriasis vulgaris, British Association of Dermatologists 2011 164, pp1091–1096)	Thank you for your comment. All of the discussion and the recommendations were based on the evidence that was reviewed according to a strict review protocol. We agree that based on the evidence reviewed "There are some data to suggest a slightly better response in those with no prior exposure to biological therapy." and refer you to the linking evidence to recommendations table where this is stated. Based on the available evidence there was no suggestion that response rates to a second biological drug in the same class may be lower than if an agent from a different class was offered and so we cannot add this statement. The study that you cited was ordered in full but excluded from the review as it did not meet the protocol criteria (please see appendix F).
SH	Janssen	19.10	Full	647		Clear/nearly clear (PASI90; week 52) / PHOENIX2 - We suggest the data in this row (i.e. 86/148 (58.1%), 276/389 (71%)) be double-checked. We do not recognise these figures, and numbers of subjects appear too high given the design of the trial. For the data we provided, please refer to	These data are accurate according to the November 2011 submission which the call for evidence relates to. Janssen confirmed on 6th July 2012 that the comment submitted was an error.

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						our response to a call for evidence in Sep 2011.	
SH	Janssen	19.11	Full	648		Clear/nearly clear (PGA; week 52) / PHOENIX2 - We suggest the data in this row (i.e. 98/148 (66.2%), 291/389 (74.8%)) be double-checked. We do not recognise these figures, and numbers of subjects appear too high given the design of the trial. For the data we provided, please refer to our response to a call for evidence in Sep 2011.	These data are accurate according to the November 2011 submission which the call for evidence relates to. Janssen confirmed on 6th July 2012 that the comment submitted was an error.
SH	Janssen	19.12	Full	650		PASI75 (week 52) / PHOENIX2 - We suggest the data in this row (i.e. 127/148 (85.8%), 360/389 (92.5%)) be double-checked. We do not recognise these figures, and numbers of subjects appear too high given the design of the trial. For the data we provided, please refer to our response to a call for evidence in Sep 2011.	These data are accurate according to the November 2011 submission which the call for evidence relates to. Janssen confirmed on 6th July 2012 that the comment submitted was an error.
SH	Janssen	19.13	Full	651		PASI50 (week 52) / PHOENIX2 - We suggest the data in this row (i.e. 146/148 (98.6%), 386/389 (99.2%)) be double-checked. We do not recognise these figures, and numbers of subjects appear too high given the design of the trial. For the data we provided, please refer to our response to a call for evidence in Sep 2011.	These data are accurate according to the November 2011 submission which the call for evidence relates to. Janssen confirmed on 6th July 2012 that the comment submitted was an error.
SH	Janssen	19.14	Full	651-3		For % improvement in PASI and change in DLQI, it seems that numbers of subjects are quoted, instead of the clinical outcomes data. For the data we provided, please refer to our response to a call for evidence in	Thank you for your comment. You are correct that the number of participants is given in the table. This is the standard format of a GRADE table row for a continuous outcome and the data in the

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						Sep 2011.	mean difference (MD) column reflect the data from your submission. This is also reflected in the relevant forest plot in appendix J.
SH	Janssen	19.15	Full	654	5	We suggest removing the sentence "Prior biological drugs included alefacept and efalizumab (proportions unclear)". In our response to a call for evidence, we submitted data from the PHOENIX 1 and PHOENIX 2 trials, and defined a prior biologic therapy as etanercept, infliximab or adalimumab. Alefacept and efalizumab were excluded from the analyses submitted in Sep 2011.	Thank you for this clarification. The footnote has been removed as requested.
SH	Janssen	19.16	Full	665		For % improvement in PASI and change in DLQI, it seems that numbers of subjects are quoted, instead of the clinical outcomes data. For the data we provided, please refer to our response to a call for evidence in Sep 2011.	Thank you for your comment. You are correct that the number of participants is given in the table. This is the standard format of a GRADE table row for a continuous outcome and the data in the mean difference (MD) column reflect the data from your submission. This is also reflected in the relevant forest plot in appendix J.
SH	Janssen	19.17	Full	665	6	We suggest removing the sentence "Prior biological drugs included alefacept and efalizumab (proportions unclear)". In our response to a call for evidence, we submitted data from the PHOENIX 1 and PHOENIX 2 trials, and defined a prior biologic therapy as etanercept, infliximab or adalimumab. Alefacept and efalizumab were excluded from the analyses submitted	Thank you for this clarification. The footnote has been removed as requested.

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						in Sep 2011.	
SH	Janssen	19.18	Full	667		For % improvement in PASI, it seems that numbers of subjects are quoted, instead of the clinical outcomes data. For the data we provided, please refer to our response to a call for evidence in Sep 2011.	Thank you for your comment. You are correct that the number of participants is given in the table. This is the standard format of a GRADE table row for a continuous outcome and the data in the mean difference (MD) column reflect the data from your submission. This is also reflected in the relevant forest plot in appendix J.
SH	Janssen	19.19	Full	667	3	We suggest removing the sentence "Prior biological drugs included alefacept and efalizumab (proportions unclear)". In our response to a call for evidence, we submitted week 12 data from the ACCEPT trial, and defined a prior biologic therapy as infliximab or adalimumab. Alefacept and efalizumab were excluded from the analyses submitted in Sep 2011.	Thank you for this clarification. The footnote has been removed as requested.
SH	Janssen	19.2	Full	635		Table 173 Row 3 (GRIFFITHS 2010) Column 6 (Treatment) - We suggest amending a sentence "in the group who received ustekinumab in the first phase of the trial 10.4% had also received a previous biological therapy" to "… 11.2% had also...". According to Table 1 in the Griffiths 2010 paper (ref. no. 413 in the full version), 62 (=26+36) out of 556 (=209+347) subjects in the ustekinumab group had received biologic agents.	Thank you for the suggested correction. The table has been amended accordingly.

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SH	Janssen	19.20	Full	677		We suggest a statement "The harms are reduced efficacy of a second biological drug compared to a first" (at the bottom of page 677) be changed to "The harms are reduced efficacy of a second biological drug in the same class compared to a first". Please see our comment on page 632 lines 18-20 for further information.	It is not possible to make this statement based on the evidence reviewed. Although the data showed that a second biologic was marginally less effective than the first, there was no evidence to show that switching to a different class was preferable to switching within a class.
SH	Janssen	19.21	Full	680		"Some participants were under- and some over-dosed in the ACCEPT, PHOENIX1 and PHOENIX-II trials as participants were randomised to 40 or 90 mg of ustekinumab…" should be amended to "...randomised to 45 or 90 mg of ustekinumab…"	Thank you for your correction. The text has been amended accordingly.
SH	Janssen	19.22	Full	680		A statement "There was no compelling evidence to suggest that switching from one particular biological drug to another particular biological drug is beneficial" may be misinterpreted as a reason not to prescribe any second biological drug. We feel it is worth reiterating the overall recommendation at this point. For example, the statement could be amended to "While there is a clinical and economic benefit of a second biological drug (as discussed in "Trade off between clinical benefits and harms" and "Economic consideration" sections), there was no compelling evidence to suggest that switching from one particular biological drug to another particular biological drug is beneficial."	Thank you for your comment. We agree that it is important not to allow misinterpretation and have amended the text accordingly.

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SH	Janssen	19.23	Full	681		A sentence just above 'Other considerations' ("Future research needed on cost and clinical effectiveness of") seems incomplete.	Thank you for your observation. The missing text has been re-inserted.
SH	Janssen	19.24	Full	682		We suggest the sentence "The mechanisms underlying loss of response to biological drugs are poorly understood but may relate to development of drug antibodies" be amended to "… but may relate to development of anti-drug antibodies."	Thank you. We have amended according to your suggestion.
SH	Janssen	19.3	Full	635		Table 173 Row 4 (JANSSENCILAG2011) - We suggest removing this row because it seems to discuss the same study as in the row above (i.e. GRIFFITHS 2010, ACCEPT trial).	Thank you for your comment. The two rows do discuss the same study but the data sources are different. One is the published evidence, the results of which are included only as an appendix, and one is the unpublished data that you kindly submitted during the call for evidence. They are included separately as the comparative data available are different. A footnote has been added to the table to clarify this and the column heading changed from study to data source.
SH	Janssen	19.4	Full	635		Table 173 Row 5 (JANSSENCILAG2011A) - We suggest changing the heading of this row to "LEONARDI 2008" because this row describes the PHOENIX 1 trial (ref. no. 417).	Thank you for your comment. The data used in the review were derived from that submitted during the call for evidence. In order to distinguish this from the published data (from LEONARDI 2008) a different reference identification number has been used.

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SH	Janssen	19.5	Full	635		Table 173 Row 5 (JANSSENCILAG2011A) Column 5 (Prior biologic therapy) - We suggest adding etanercept to the list of biological therapies. Please refer to Table 1 of the Leonardi 2008 paper.	Thank you for your correction. The table has been amended accordingly.
SH	Janssen	19.6	Full	635		Table 173 Row 6 (JANSSENCILAG2011B) - We suggest changing the heading of this row to "PAPP 2008" because this row describes the PHOENIX 2 trial (ref. no. 410). Also, "Ustekinumab (subcutaneously) 40 or 90mg..." should be amended to "Ustekinumab (subcutaneously) 45 or 90mg..."	Thank you for your comment. The data used in the review were derived from that submitted during the call for evidence. In order to distinguish this from the published data (from PAPP 2008) a different reference identification number has been used. The dose information has been corrected in accordance with your comment.
SH	Janssen	19.7	Full	636		Table 173 Row 6 (PAPP 2008) - "Ustekinumab (subcutaneously) 40 or 90mg..." should be amended to "Ustekinumab (subcutaneously) 45 or 90mg..."	Thank you for your correction. The table has been amended accordingly.
SH	Janssen	19.8	Full	640		% improvement in PASI (week 12) at the top of the page - 27 and 311 are a number of subjects for biologic ever used and biologic never used, respectively. Mean percentage changes in PASI from baseline at week 12 are 65.55% and 72.59% for 'ever used' and 'never used' groups, respectively.	This is correct – giving a MD of -7.04 as reported in the table.
SH	Janssen	19.9	Full	640	4	We suggest removing the sentence "Prior biological drugs included alefacept and efalizumab (proportions unclear)". In our	Thank you for this clarification. The footnote has been removed as requested.

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						response to a call for evidence, we submitted week 12 data from the ACCEPT trial, and defined a prior biologic therapy as infliximab or adalimumab. Alefacept and efalizumab were excluded from the analyses submitted in Sep 2011.	
SH	Leo Pharma UK	25.0	Full	General		LEO Pharma UK welcomes the opportunity to comment on the draft psoriasis guideline. We are encouraged to see the guidelines' focus on supporting the patients with their care and recommending that health care professionals should • take into account patients' needs and preferences when considering treatment and care options • assess the impact a patient's psoriasis has on their physical, psychological and social wellbeing, and • support people to adhere to treatment in line with the NICE 'Medicines Adherence' clinical guideline.	Thank you for your comments.
SH	Leo Pharma UK	25.1	Full	19	18	The GDG has justified in the Full Guideline its reason for not evaluating the role of emollients in the treatment of psoriasis however, LEO Pharma believe a general recommendation in section 1.3.1 would be useful to guideline users who do not refer to the Full guideline.	Thank you for your comment. The Guideline Development Group (GDG) agree that emollients are an accepted important component of treatment for psoriasis. However, the GDG was unable to cover every aspect of psoriasis management and had to prioritise areas where practice is variable or unsafe and where recommendations are likely to be informed by a robust evidence base.

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							The GDG were aware that there is little or no formal evidence for emollients compared to no treatment. In defining the scope the GDG therefore opted to begin the topical pathway after emollients. Thank you for acknowledging that we have justified this in the NCIE guideline. Without reviewing the evidence we are unable to formulate a specific recommendation. However, the GDG noted stakeholders concerns that without an explicit statement about emollients this component of management might be omitted. The NICE Guideline has therefore been amended to include the following wording: *The treatment pathway in this guideline begins with active topical therapies. The GDG acknowledged that the use of emollients in psoriasis was already widespread and hence the evidence review was limited to active topical therapies in psoriasis. Please refer to the BNF and the cBNF for guidance on use of emollients'.* This wording has also been included within the algorithms for topical therapy.

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SH	Leo Pharma UK	25.10	Appendix M	4		The model structure does not capture all treatment options available to treat a patient with psoriasis (as listed on page 16, line 15 – 23 of the Full guideline) and nor does it capture all costs associated with treatment (such as time off work to attend phototherapy sessions). Inclusion of these would affect the downstream costs associated with initial topical treatment and therefore give more meaningful and relevant values of cost effectiveness of initial topical treatments.	Thank you for your comment. The model only considers the treatment of mild to moderate psoriasis and therefore we have not included treatments for more severe psoriasis. We did include the costs of phototherapy. We are also mindful of the fact that we have identified and referred those with severe disease to directly to secondary care
SH	Leo Pharma UK	25.11	Appendix M	4		The model is based on a patient not responding to their treatment visiting their primary care based healthcare professional three times and receiving three different topical treatments before being referred to a specialist. The Bottomley paper (2007) was based on two topical treatment cycles before referral and we believe this to be more reflective of UK clinical practice.	Thank you. This was debated at the GDG and they felt that 3 cycles was more reflective of current UK practice. The guideline analysis included strategies of two treatments followed by referral and these were shown to be less cost-effective than 3-treatment sequence strategies.
SH	Leo Pharma UK	25.12	Appendix M	16		NHS Reference Costs 2010 – 2011 are published and give the most up to date costs (i.e. unit cost of phototherapy in 2010 – 2011 was £90 vs. unit cost in 2009 – 2010 of £81).	Thank you for your comment. We endeavour to use the most up to date costs, but as modelling is undertaken throughout guideline development some models are built prior to publication of the newest Reference Costs. In our review of the 2010-11 reference costs (NHS Trusts and PCTs combined) we found that the unit cost for phototherapy as an outpatient procedure (JC29Z) was just

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							£83 compared to £82 in 2009-10. We also checked similarity between 2009-10 costs and 2010-11 costs for consultant and non-consultant led outpatient visits and day case admissions for intensive topical therapies. None were substantially different and therefore we do not expect these to have any impact on the conclusions of the analysis.
SH	Leo Pharma UK	25.13	Appendix M	23		Table 14 - It is not clear to the average guideline user how the figures in this table have been calculated.	Thank you. Table 14 in Appendix M presents total costs broken down by type of resource use (i.e. topical, GP visits, etc). They were calculated as part of the deterministic implementation of the model and therefore the totals may not match exactly to the mean values generated in the probabilistic analysis presented in Table 12 and Table 13; however, totals should be similar. Text has now been added to help the reader interpret these figures.
SH	Leo Pharma UK	25.14	Appendix M	30		Another limitation of the model is that it does not factor in the effect of adherence and therefore the cost of non-adherence in terms of patient outcomes and financial cost to the NHS and patient is not considered. Patient adherence is seen as one of the biggest issues in psoriasis treatment with 66% of UK physicians citing it as one of the	Thank you for your comment. We agree that adherence is an important issue and was not adequately addressed. A sensitivity analysis has been performed to explore the impact of reduced adherence on twice daily treatments. In this sensitivity analysis, it was assumed that 40% of patients on twice daily treatment would only apply the topical once daily, thus reducing the

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						biggest challenges[1]. In addition, up to 40% of patients are estimated to be non-compliant with their treatment regimes thereby adversely affecting clinical outcomes[2]. 97% of healthcare professionals believe that improved compliance would lead to a reduction in inappropriate referrals[3]. References: 1 LEO Pharma. Data on file (European Psoriasis Study. Jan 2010) 2 Richards HL et al. J Eur Acad Dermatol Venereol 2006; 20:370-379 3 LEO Pharma. Data on file (Psoriasis HCP Questionnaire. BAD 2010 Conference)	strategies efficacy. The conclusions of the analysis are relatively insensitive to this reduced adherence. The assumptions and results of this sensitivity analysis are included in section M3.2.3 of Appendix M.
SH	Leo Pharma UK	25.15	Appendix N	4		The model considers patients with only scalp psoriasis. It does not capture patients who have psoriasis on multiple locations. For example, a significant proportion (50-80%)[1] of patients with body psoriasis will report scalp psoriasis, or have concomitant psoriasis of the scalp and body. For patients such as these, treatments licenced for use on both body and scalp would be appropriate but as the model has been built to consider patients with only scalp psoriasis it is not possible to know the true cost effectiveness of these treatments. In addition, the model does not capture all the options available to HCPs and patients after unsuccessful topical treatment.	Thank you. The GDG discussed this issue and highlighted it under section N4.3 in Appendix N. The separation of the analysis is driven by the evidence, which does not evaluate treatments across different sites. The GDG feels that the recommendations sufficiently covers how health care professionals and patients can discuss what formulations may work best for them by taking into account preferences, cosmetic acceptability, practical aspects of application and site(s) and extent of psoriasis.

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						Reference: 1 Papp K et al. J Eur Acad Dermatol Venereol 2007; 21:1151-1160	
SH	Leo Pharma UK	25.2	Full	47	31	A significant proportion (50-80%)[1] of patients with body psoriasis will report scalp psoriasis, or have concomitant psoriasis of the scalp and body. Therefore a recommendation advising healthcare professionals to assess the extent of psoriasis is advised. Reference: 1 Papp K et al. J Eur Acad Dermatol Venereol 2007; 21:1151-1160	Thank you, we believe that this is already sufficiently covered in the subsequent recommendations in this section relating to assessment.
SH	Leo Pharma UK	25.3	Full	50	14	The list of formulations is not inclusive of all formulations available to healthcare professionals for treating widespread psoriasis. For completeness the list should include 'ointment' and 'gel'.	Thank you for your comment. The list of formulations is not intended to be fully comprehensive. However, the GDG believe that gel may be appropriate for widespread psoriasis and so this has been added to the recommendation
v	Leo Pharma UK	25.4	Full	50	21	As recommended in the SIGN Psoriasis guideline[1], we believe all patients with psoriasis should be offered a review at least annually, not just those using a potent or very potent corticosteroid. Reference: 1 SIGN guideline - Diagnosis and management of psoriasis and psoriatic arthritis in adults. October 2010	Thank you for your comment. The annual review recommendation relates specifically to use of corticosteroids. The evidence indicates that safety data on topical corticosteroids is only available up to a year. The GDG were mindful that both local and systemic side effects represent potential risks with use of topical

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							corticosteroid. Given the paucity of evidence on what the actual risks of these side effects are in the psoriasis population beyond a year, and that the introduction of potent corticosteroid as a first line treatment for psoriasis is likely to be a significant shift in practice, annual review is justified. The GDG discussed the benefits outweighing (in terms of avoidance of corticosteroid side effects) the potential (unknown) harm associated with this (cost, inconvenience, medicalisation). In addition, it is important to ensure that the annual review recommendation remains specifically linked to the need to review for adverse effects of topical corticosteroids. A general recommendation around annual review for all patients risks losing this focus. The GDG did not specifically address the question 'how often should patients with psoriasis be reviewed' and so we do not know of the risks and benefits of a more generic 'annual review' recommendation.

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							The guideline includes recommendations that will provide additional opportunities for reassessment and review of psoriasis patients.
SH	Leo Pharma UK	25.5	NICE	11	1.1.1.2	We do not believe that the recommendations in sections 1.3.2. and 1.3.3 support the principles of care. According to the recommendations in 1.3.2 patients will have to visit their healthcare professional (HCP) a number of times before being offered what the guideline development group (GDG) considers to be "the most effective treatment strategy (starting with once daily combined product containing calcipotriol monohydrate and betamethasone dipropionate)". Similarly with recommendation 1.3.3, patients will have to visit their HCP a number of times before being offered the most effective treatment. This will not only cause inconvenience to the patient (time off work, transport costs) but will also be stressful, possibly leading to patients' loss of adherence and confidence in their treatment as well as their HCP while continuing to deal with the ongoing symptoms of their psoriasis. Research shows that 41% of psoriasis patients don't go back to their GP for an alternative prescription if their treatment doesn't work[1].	Thank you for your comment. The sequence of treatment was informed by original health economic modelling, which clearly indicated that once daily combined product containing calcipotriol monohydrate and betamethasone dipropionate would not be cost effective except possibly as a third-line option. The slightly greater efficacy of the two compound product did not offset the significantly higher cost compared with other topical treatments and only a minority of patients would be expected not to respond to the first or second topical treatment options based on the data reviewed. We agree that patients should be involved in treatment decisions and have highlighted this in the recommendations.

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						Making assumptions about patient preference should be avoided[2]. Patients should be given the opportunity to be involved in making decisions about prescribed medicines[2]. Consultations that ignore patient's perspective would be more likely to lead to treatment decisions that were not 'agreed' by the patient resulting in an increased risk of non-compliance[3]. Clinicians can achieve this by communicating the benefits, adverse effects, necessity and instructions for using the medication[4]. References: 1 LEO Pharma. Data on file (Psoriasis Perceptions 2010) 2 NICE Adherence Guideline 3 Report for the National Co-ordinating Centre for NHS Service Delivery and Organisation R&D. December 2005 4 Storm et al. J Am Acad Dermatol. December 2008	
SH	Leo Pharma UK	25.6	NICE	20	1.3.2	On reviewing this section we believe the interest of the patient has not been fully considered. The guideline development group recognise that adherence to topical therapy regimens may be the greatest barrier to effective disease control and that attention to cosmetic acceptability, formulation, local	Thank you. The sequence of treatment was informed by original health economic modelling, which clearly indicated that once daily combined product containing calcipotriol monohydrate and betamethasone dipropionate would not be cost effective except possibly as a third-line option. The slightly greater efficacy of the two

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						side effect profiles, and practicalities of application is important. Additionally, the results of the cost effectiveness analysis identify "the most effective treatment strategy as starting with once daily combined product containing calcipotriol monohydrate and betamethasone dipropionate". Despite this, the section (1.3.2) recommends the most effective strategy as a 4th line option after 1st, 2nd and 3rd line treatments that are less effective and include a twice daily regimen. As noted in our comment about Appendix M, page 30, the cost effectiveness model did not factor in adherence rates for the different treatments. Adherence to treatment not only affects patient outcomes but also the cost of the treatment and future costs related to referrals, phototherapy and possible systemic therapies. 97% of healthcare professionals believe that improved compliance would lead to a reduction in inappropriate referrals[1]. Further evidence suggests that patient compliance is seen as one of the biggest issues in psoriasis treatment with 66% of UK physicians citing it as one of the biggest challenges[2] and up to 40% of patients are estimated to be non-compliant with their treatment regimes thereby adversely	compound product did not offset the significantly higher cost compared with other topical treatments. We agree that adherence is an important issue and was not adequately addressed in the original economic models. A sensitivity analysis has been performed to explore the impact of reduced adherence on twice daily treatments. In this sensitivity analysis, it was assumed that 40% of patients on twice daily treatment would only apply to the topical once daily, thus reducing the strategies efficacy. The conclusions of the analysis and the recommendations are insensitive to this reduction in adherence. We have clarified this in the full guideline and details of the assumptions and results of this sensitivity analysis are in Appendix M. Regarding formulation, the GDG feel that the recommendations already cover patient preference in relation to formulations, Gels are among the formulations listed.

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						affecting clinical outcomes[3]. For these reasons it is important that adherence is given significant consideration (in addition to the cost effectiveness analysis) when making decisions relating to psoriasis treatment strategies. Although there may be a proportion of patients whose psoriasis will be effectively managed with the 1st, 2nd and 3rd line recommended treatments, there will be patients with body and scalp psoriasis and/or patients with known issues with adherence who should be offered a combined product containing calcipotriol monohydrate and betamethasone dipropionate as a 1st line option. Minimising the number and frequency of daily treatments will help improve adherence[4]. This in turn will improve factors such as treatment outcomes and cost to the NHS and patient. In general, newly developed vehicles which do not leave a greasy residue and are easy to apply are preferred by patients over traditional ointments and creams[5]. We therefore suggest that combined calcipotriol monohydrate and betamethasone dipropionate gel is included as an alternative option in recommendation 1.3.2.1. (in line with the PCDS guideline[6]).	

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						References: 1 LEO Pharma. Data on file (Psoriasis HCP Questionnaire. BAD 2010 Conference) 2 LEO Pharma. Data on file (European Psoriasis Study. Jan 2010) 3 Richards HL et al. J Eur Acad Dermatol Venereol 2006; 20:370-379 4 SIGN guideline - Diagnosis and management of psoriasis and psoriatic arthritis in adults. October 2010 5 Papp K et al. J Eur Acad Dermatol Venereol 2007; 21:1151-1160 6 PCDS guideline 2010. http://www.pcds.org.uk/image-atlas/a-z-of-diagnosis/50-image-atlas-detailed-articles/151-psoriasis	
v	Leo Pharma UK	25.7	NICE	22	1.3.3	We believe that scalp psoriasis has significant psychological impact on patients and therefore they need to be offered an effective treatment immediately. Psoriasis lesions located on visible body parts are significantly correlated with aspects of quality of life[1]. The guideline development group recognise that adherence to topical therapy regimens may be the greatest barrier to effective disease control and that attention to cosmetic acceptability, formulation, local side effect profiles, and practicalities of application is important.	Thank you. The recommendation was based on clinical evidence and health economic evaluation. Thank you for your comment. We agree that adherence is an important issue and this was inadequately addressed in the original economic modelling. A sensitivity analysis has been performed to explore the impact of reduced adherence on twice daily treatments. In this sensitivity analysis, it was assumed that 40% of patients on twice daily treatment would only apply

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						The 1st and 2nd line treatments recommended in this section can be less effective due to reduced patient adherence as a result of patient inconvenience, messiness and lack of cosmetic acceptability. Patients with scalp (and body) psoriasis and/or patients with known issues with adherence should be offered a combined product containing calcipotriol monohydrate and betamethasone dipropionate gel as a 1st line option. Minimising the number of daily treatments will help improve adherence[2]. This in turn will improve factors such as treatment outcomes and cost to the NHS and patient. We therefore suggest that combined calcipotriol monohydrate and betamethasone dipropionate gel is included as an alternative option in recommendation 1.3.3.1. References: 1 Heydendael V et al. J Investig Dermatol Symp Proc 9:131-135. 2004 2 SIGN guideline - Diagnosis and management of psoriasis and psoriatic arthritis in adults. October 2010	the topical once daily, thus reducing the strategies efficacy. The conclusions of the analysis and the recommendations are largely insensitive to reduced adherence. The assumptions and results of this sensitivity analysis are summarised in the full guideline and detailed in Appendix N.

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SH	Leo Pharma UK	25.8	Appendix M	2		A one year time horizon seems too short especially when taking into consideration the chronic nature of the disease and multiple treatment options available to patients after topical treatments. Phototherapy is not the last treatment option for patients suffering from mild to moderate psoriasis as suggested in the model structure and in fact phototherapy, as highlighted in Appendix A, 3.2.c, is not available for all patients. If the model were to take into account additional treatment options, such as methotrexate, cyclosporine and in some cases biologic treatments then a longer time horizon, such as 2 – 3 years would be more suitable. This approach would likely have a significant impact to the model output highlighting the positive impact of increased efficacy early in the treatment pathway.	Thank you. Data for most topical therapies were limited to 8 weeks of treatment, occasionally 12 weeks. Given the dearth of longer term data, it was felt that extrapolation of this evidence beyond 1 year would be inappropriate. The time horizon was extended in deterministic sensitivity analyses (presented in Appendix M.3.2.8) and the conclusions of the base case were shown to be insensitive to this structural assumption.
SH	Leo Pharma UK	25.9	Appendix M	2		It is recognised amongst health economists that EQ-5D does not capture the burden of dermatological diseases. In order to overcome this challenge the EuroQoL group are working on a psoriasis specific bolt-on questionnaire (EQ-5D Psoriasis). Work is still ongoing and in the meantime we would encourage the GDG to look at other factors that affect the effective treatment of psoriasis (such as adherence) and not just the ICER based on QALY improvement. This comment also applies to	Thank you for your comment. We agree that some potential problems have been identified with regard to the content validity of the EQ-5D in psoriasis and so have now added this to our discussion of the potential limitations of our analyses. But we note that even using a £30,000 per QALY threshold rather than £20,000 would not change the conclusions of our analyses. Therefore only if the EQ-5D is under-estimating health gain of one treatment

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						Appendix N, page 2.	compared to another by a considerable extent, could this pose a serious limitation. We also agree that adherence is an important issue and it was not adequately addressed. A sensitivity analysis has been performed to explore the impact of reduced adherence on twice daily treatments. In this sensitivity analysis, it was assumed that 40% of patients on twice daily treatment would only apply the topical once daily, thus reducing the strategies efficacy. The conclusions of the analysis are relatively insensitive to this reduced adherence. The assumptions and results of this sensitivity analysis are included in section M3.2.3 of Appendix M.
SH	Lilly UK	17.0	General	General	General	We thank the CDG and NICE for the considerable amount of work that has gone into developing this resource. We support the review of this guideline in 3 years when additional data will be available to guide clinical decision making in psoriasis.	Thank you for your comments.
SH	Lilly UK	17.1	NICE	7	17	We ask the CDG to consider whether it would be appropriate if, following assessment in a non-specialist setting, healthcare professionals also offer referral when: • There is any involvement of high-	Thank you. The GDG believe that this is already encompassed within the last bullet point. We were keen to ensure that some flexibility is available for the clinician.

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						impact or difficult-to-treat sites (for example, the face, scalp, palms, soles, flexures and genitals) Please note this is consistent with the guidance on psoriasis that involves difficult-to-treat sites and the wording used throughout the rest of the NICE document.	
SH	Lilly UK	17.10	NICE	28	2	The guidelines recommend that systemic therapy only be used in specialist settings. Our understanding is that currently some patients with stable disease may be managed in primary care. Could the CDG consider whether the wording could be changed to "Systemic therapy should be initiated in a specialist setting"? And consider whether any guidance could be given for management once control is established.	Patients may be managed under 'shared care' arrangements ie between specialist and primary care settings but rarely exclusively in primary care. The GDG considered that patients requiring systemic therapy should remain under specialist supervision. The recommendation has been amended to reflect this as follows: *'Responsibility for use of systemic therapy should be in specialist settings only. Certain aspects of supervision and monitoring may be delegated to other healthcare professionals and completed in non-specialist settings, in which case, such arrangements should be formalised.'*
SH	Lilly UK	17.11	NICE	29	4	We believe systemic therapy should be offered to people with psoriasis if difficult-to-treat areas are affected. As such we suggest adding this to the 2nd sub bullet of the 3rd bullet in this paragraph ("*psoriasis is localised and associated with significant functional impairment and/or high levels of distress and/or difficult-to-treat areas*") This is in line with the wording used	The GDG do not agree that psoriasis at difficult to treat sites is a reason to use a systemic therapy if psoriasis at that site is not causing distress or functional impact. The examples given in the 2nd sub bullet of the 3rd bullet in this paragraph include all potentially difficult to treat sites.

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						throughout the rest of the NICE document.	
SH	Lilly UK	17.12	NICE	30	8	Please note a typo – "*fulfils*". It should be "*fulfil*".	Thank you, we have made this change.
SH	Lilly UK	17.13	NICE	31	26	We suggest that information on the additional monitoring required with ciclosporin be added to this section, as per the ciclosporin SPC.	Thank you for your comment. There was insufficient evidence to make any specific recommendations about nephrotoxicity and we did not look for data on how best to monitor for nephrotoxicity. However, the GDG were aware that all systemic treatments carry a risk for a range of adverse events and included recommendations 74 and 75 to take account of this. Please also note that appendix S summarises the available data of the risks and benefits of the interventions recommended, including nephrotoxicity with ciclosporin. The GDG expect that health care professionals will consult the SPC and BNF when appropriate.
SH	Lilly UK	17.14	NICE	33	11	Section 1.8 is titled Systemic biological therapy. Currently this section appears to be taken directly from the technology appraisals of the individual biological therapies, and as such reflects the guidance, but is not a guideline on when to use the biologics, or which to choose. We would like to request that an introductory paragraph or section be added	Thank you for your comment. We have amended the headings of the sections in the NICE guideline to ensure it is clear which recommendations relate to non-biological and which recommendations relate to biological systemic therapy. We have now added more information in to the NICE guideline to set the scene

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						that discusses systemic biological therapy in general, to include information as listed below: • When systemic biological therapy should be offered. • Recommendations on initiation and supervision by specialist physicians; while all SPCs include information on initiation and supervision, this information is currently only included in the section on etanercept. • Whether there is any guidance on which drug to choose first, or if there is insufficient evidence to provide guidance this should be stated. • Any important differences between options, for example, infliximab has an IV route of administration and is administered in hospital; infliximab is recommended for different criteria than the other compounds in this section i.e. where disease is very severe. We would also like to request that some rationale for the order of the compounds be given (eg. order of preference, alphabetical, mode of action). The way it's currently written could be open to different interpretations. In addition, we also believe this section	for biologics and explain which recommendations are taken directly from the TAs. The compounds are listed in alphabetical order. We have added a sentence at the top of the section to clarify this. The wording has been matched to the wording in Final Appraisal Determination on ustekinumab. The systemic therapy section does provide some general principles, but the specific detail is outside of the scope of the guideline. We can only incorporate the recommendations as they have been published in the NICE Technology Appraisal.

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						would benefit from having consistent formatting. Currently there are many variations in the format of the sections taken from the different technology appraisals; the language for this section could be made consistent across the paragraphs within this section and with the rest of the document.	
SH	Lilly UK	17.15	NICE	37	1	We believe it would be useful for the CDG to consider adding some recommendations on the order of cycling through biological therapies (which to use first-line, second-line etc). If this is not considered appropriate because of inconclusive evidence on such an order we still believe this would add value and a note adding that there is insufficient evidence to recommend an order could be added.	Thank you for your comment. Our scope excluded us from doing any work on first line biologics as this is covered in the NICE technology appraisals. All of the recommendations from TAs 103, 134, 146 and 180 have been quoted verbatim and form the current guidance for the use of biological agents for psoriasis, and cannot be amended. We state in the linking evidence to recommendations table in the Systemic (Biological Therapy) chapter that there is no robust evidence to recommend using biologic drugs in a particular order and that we have listed in alphabetical order by drug..
SH	Lilly UK	17.16	NICE	37	7	Section 1.8.1.14 addresses what to do if a patient has an inadequate response to a second biological drug. The wording here is a little confusing – "supra-specialist" doesn't seem to be a common phrase – does this mean referral from secondary to tertiary care? In addition, we question what this guidance is based on – what evidence is	The term supra-specialist is derived from the BAD standards document and is defined in the psoriasis full guideline glossary as level 4 care. This usually takes place entirely within an acute hospital and is carried out by: • consultant dermatologists • a range of other healthcare

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						this recommendation linked to and what evidence suggests that requiring a 3rd biological agent is a reason to go to a tertiary centre? In addition, we would like to know what advice the psoriasis clinical guideline offers to these supra-specialists on management of the disease.	professionals with special skills in the management of complex and/or rare skin disorders). It equates to tertiary care. The recommendation was based on expert opinion of the guideline group. The GDG consensus was that patients failing a second biologic should be referred to a supra specialist service, given this group are likely to be very high need, form a minority of those receiving biologics, and therefore benefit from expert opinion and management. No specific recommendations are provided given that the evidence for use of a third biologic was not available due to paucity of data; it is expected that such centres will become part of the proposed 'Specialised dermatology rare disease network in development.
SH	Lilly UK	17.17	Full	37	10	We would ask the CDG to consider adding a note around take into account effectiveness of treatments in both psoriasis and psoriatic arthritis before making changes to therapy.	Thank you. The GDG believe that the recommendation adequately covers the considerations to be made, which will include the effectiveness of treatments in both the skin and joint compartments.
SH	Lilly UK	17.18	Full	65	1	While algorithms are provided for Assessment, topical, phototherapy and systemic non-biological treatments, none is provided for systemic biological treatments.	Thank you, following advice from NICE we have included the relevant web link into the non-biologic system treatment algorithm

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						We question the rationale for this especially as a NICE algorithm already exists for biological agents for psoriasis (dated January 2011, NICE guidance implementation tool). We believe the omission of this algorithm limits the guidance provided and should be included at page 66 of the full guidance.	
SH	Lilly UK	17.19	Full	670	18	We strongly support the inclusion of PASI 75–90 and PASI >90 in the analyses and the goal of reaching higher levels of PASI response with treatments.	Thank you for your comment
SH	Lilly UK	17.2	NICE	8	13	In line with the section on systemic therapy, we suggest adding a sentence to the section on topical therapy as follows: "*Be aware of the benefits or, contraindications to and adverse effects or risks associated with continuous use of potent or very potent corticosteroids which may cause: irreversible skin atrophy and striae; psoriasis to become unstable; systemic side effects when applied continuously to extensive psoriasis. Explain the risks of these side effects to people undergoing treatment and discuss how to avoid them.*"	Thank you. We do not think that it would be helpful to make this change as it results in the main message being confused, which is to do with the specific adverse effects of steroids and that they can be avoided. As we already have a general recommendation that says benefits and risks should be discussed we do not believe it would be helpful to reword this recommendation.
SH	Lilly UK	17.3	NICE	10	1	While the previous sections on systemic non-biological therapy and phototherapy include information on when to offer these treatment options, there is no guidance provided on when to offer systemic biological therapy. Instead the guideline	Thank you for your comment. We have now added more information in to the NICE guideline to set the scene for biologics. Our scope excluded us from doing any work on first line biologics as this is covered in the NICE Technology

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						only addresses when to consider changing to a second biological drug. In order for the guideline to be comprehensive we believe the guideline should also include information as to when to offer patients systemic biological therapy.	Appraisals, hence were only able to look at a very specific aspect of the use of biologic drugs.
SH	Lilly UK	17.4	NICE	11	10	We believe NICE guidance acts to encourage aspirational, world class standards of care and as such in the section Principles of care we ask the CDG to consider whether a statement around the ultimate goals of care could be added. The Mrowietz 2011 European consensus paper states that "the goal of psoriasis treatment is to achieve complete clearance of skin symptoms." Mrowietz U, Kragballe K, Reich K, et al. Definition of treatment goals for moderate to severe psoriasis: a European consensus. Arch Dermatol Res 2011;303(1):1-10.2.	Defining what constitutes 'goals of care' in psoriasis was not included in the scope of the guideline and therefore a specific recommendation is not possible. However, we agree that the goals of treatment must be considered central in the treatment of patients with psoriasis, which gave rise to a specific recommendation. In addition, all the recommendations on treatment are derived from an evidence base that considered outcomes PASI 75, PASI 90, clear/nearly clear as well as patient-reported outcome measures and quality of life (DLQI). The GDG are aware of the paper quoted which includes many of the above outcomes, although note that this was a consensus based rather than evidence based definition of treatment goals and did not include any patient representatives in the group.
SH	Lilly UK	17.5	NICE	11	23	In light of the importance of patient adherence in achieving optimal treatment	Thank you, we think that the recommendation already adequately

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						outcomes, and the link between patient adherence and patient expectations, we would suggest the guideline highlight the importance of including expectations of treatment in discussions with patients to improve adherence and treatment satisfaction.	highlights the importance of ensuring the individual's treatment expectations are discussed. We have now cross referred to the medicines adherence guideline within this recommendation and added a specific bullet point about highlighting the importance of adherence to treatment in discussion with the patient. Note that we also have a recommendation which encourages health care professionals to support people to adhere to topical treatment in line with the NICE medical adherence guideline.
SH	Lilly UK	17.6	NICE	14	1	The PASI tool is the key tool used to assess severity of disease. While the wording in this section around what tool to use in children is clear, it is less so in adults. As such we suggest the wording here should be revised to: "*In specialist settings, use a validated tool to assess severity. Use the PASI with adults and the PGA with young children.*"	The important aspect of this recommendation is that the tool used should be a validated tool. We have added the 'for example' in order to 'future proof' the recommendation so that if other tools are published in the future which superseded the PASI then these could be used.
SH	Lilly UK	17.7	NICE	15	10	As per our comment above, we feel the following wording should be included for referral: • There is any involvement of high-impact or difficult-to-treat sites (for example, the face, scalp, palms, soles, flexures and genitals) This is consistent with the guidance on	Thank you. The GDG believe that this is already encompassed within the last bullet point. We were keen to ensure that some flexibility is available for the clinician.

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						psoriasis that involves difficult-to-treat sites and the wording used throughout the rest of the NICE document.	
SH	Lilly UK	17.8	NICE	18	9	We ask the CDG to consider adding some text to the General recommendations section to clarify and reinforce the meaning of severe disease, perhaps as follows: "*Offer people with psoriasis topical therapy as first-line treatment and escalate to second-line treatment (that is, phototherapy or systemic non-biological therapy) or third-line treatment (systemic biological therapy) if psoriasis is extensive and/or has significant psychological impact and/or is unresolved in high-impact or difficult-to-treat sites*"	Thank you for your comment. We have reworded this recommendation to clarify that escalation would be recommended when topical therapy alone is unlikely to adequately control psoriasis, for example extensive disease, 'moderate' on PGA or at sites such as the nail. However, the point of this recommendation is that people with extensive or moderate disease are unlikely to be adequately managed with topical therapy alone (ie monotherapy) and therefore active consideration of other treatment modalities is necessary at the time of presentation. This is not the same as providing an indication of who should be given systemics/phototherapy. This detail is provided in separate recommendations in the relevant sections. Therefore, the wording suggested would not be appropriate.
SH	Lilly UK	17.9	NICE	24	19	In the section on psoriasis of the face, flexures and genitals the guideline states that very potent corticosteroids should not be used in children. However, the section previously indicates that short-term mild or moderate potency corticosteroids should be	Thank you for your comment. We have reorganised the recommendations in line with your suggestion to move this recommendation to the section on topicals for the face, flexures and genital sites as well as having an

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						used on the face, flexures and genitals, with calcineurin inhibitors in those that show an unsatisfactory response, as such very potent corticosteroids are not recommended in any patient, and the guidance with the current wording is a little ambiguous and could be confusing. In the "Topical therapy - general recommendations" section 1.3.1.5 of the NICE guideline, it does state: "Do not use potent or very potent corticosteroids on the face or flexures, including genital sites". If this were included in the section on psoriasis of the face, flexures and genitals, this might be clearer.	overarching recommendation in the general section on topical therapies that very potent steroids should not be used in children and young people. We have removed the duplication of this recommendation in the scalp section.
SH	**medac GmbH**	23.0	Full	484	27	We would propose that the following be added at the beginning of this statement, with the addition of a following paragraph: Which agent to choose and **method of administration** is influenced by multiple factors and must be tailored to the needs of the individual. The type and pattern of psoriasis, extent of involvement and whether or not rapid control is necessary are important. For example, stable chronic plaque psoriasis requires a very different treatment strategy to generalised pustular psoriasis. The presence of psoriatic arthritis, co-morbidities, age, conception plans, preferences of patient and clinician, logistical issues around safe drug	Thank you for your comments. Please note that the introduction is only scene setting and cannot comprehensively cover all aspects of treatment. The guideline is already very long and we do not want to add further to the extent of this document unnecessarily. The GDG are aware of this work and the recommendations do not preclude the subcutaneous route being used if appropriate. We believe that HCPs using systemic therapy need to be familiar with all options- hence the recommendations that it should only be provided in specialist settings and the need to be aware of benefits and contraindications.

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						administration and monitoring as well as many other factors also need to be taken into account. Nevertheless, it is useful to review the evidence on the relative efficacy and safety of the available agents to inform the decision-making process. **Methotrexate can be administered orally or subcutaneously.[xxxi] The subcutaneous route has been shown to have improved bioavailability over the oral route, which can enhance efficacy and clinical outcome.[xxxii] This has been demonstrated in other inflammatory conditions where methotrexate is a first-line therapy.[xxxiii,xxxiv] Along with the improved tolerability concerning gastrointestinal side effects, subcutaneous methotrexate has become the preferred method of administration in many countries.[xxxi,xxxv] European and German guidelines on the use of systemic non-biological therapy in psoriasis both emphasise that subcutaneous methotrexate is a valid treatment option.**xxxi,[xxxv] **Correct use of methotrexate in psoriasis also reduces the incidence of vascular disease which can be associated with chronic inflammatory conditions, such as psoriasis.[xxxvi]**	

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SH	**medac GmbH**	23.1	Full	496	11	We would propose that the following be added at the end of this statement: Heterogeneity was present for the outcomes of clear or nearly clear, PASI75, final PASI and withdrawal due to toxicity between three studies. This was thought to be due to the different dosing regimens of methotrexate used in the included studies, as the estimate of efficacy moved towards favouring methotrexate compared with ciclosporin as the dose of methotrexate used increased (while the dose of ciclosporin was similar among the studies). Conversely, there were relatively more withdrawals due to toxicity with higher dose methotrexate compared with ciclosporin. However, it is also possible that the differences were caused or contributed to by the differences in the use of folic acid. The Flytstrom study, which also used the lowest dosing schedule, was the only one to have administered folic acid which may have reduced the efficacy of methotrexate while also making it more tolerable. **In patients receiving oral methotrexate where there is a poor therapeutic response following adequate dosage escalation and duration of treatment, a switch to subcutaneous methotrexate may be an appropriate choice of**	Thank you for this comment and data. The GDG were aware of this information however, did not deem it to be relevant to include in the guideline.

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						therapy. Bioavailability has been shown to be enhanced by the subcutaneous route of administration, and this may increase efficacy.xxxii,[xxxvii] **The bioavailability of a higher oral dose of methotrexate in adult patients is highly variable, and on average is only two-thirds that of the subcutaneous administration.**xxxii **Furthermore, subcutaneous administration may also be an option for patients experiencing toxicity on oral therapy, particularly gastrointestinal side effects.**[xxxviii]	
SH	**medac GmbH**	23.2	Full	626	6	Please consider revising the statement regarding liver biopsy in patients *without* risk factors. No other international guidance produced would recommend a liver biopsy in patients without risk factors for liver disease. We propose that this be changed to: **A retrospective cohort review analysis of 119 rheumatoid arthritis patients and 690 psoriasis patients who had received at least one dose of methotrexate showed that there was no significant difference between the two groups concerning hepatotoxicity related to methotrexate.**[xxxix] **Advanced hepatic fibrosis with methotrexate therapy in psoriasis is now recognised to be much less frequent than previously**	Thank you for your comment. This section of text cites the monitoring strategies evaluated by Chalmers and colleagues in a published paper which informed the health economic modelling for monitoring using P3P. The suggested strategy not that recommended by the guideline. The full version of the guideline has emboldened the text as follows '**The monitoring strategies evaluated by Chalmers and colleagues were defined as follows:'** In addition, the two suggested strategies have been numbered for clarity.

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						reported.[xl,xli,xlii] **A liver biopsy should only be considered in patients with the following risk factors for liver damage:[xliii]** **⇒ Positive HBV or HCV serology** **⇒ Current history of excess alcohol intake** **⇒ Family history of liver disease** **⇒ Persistently abnormal liver function tests** **⇒ Diabetes mellitus** **⇒ Obesity** **⇒ Previous exposure to hepatotoxic drugs or chemicals** **⇒ Lack of folate supplementation** **⇒ Hyperlipidaemia** **The first biopsy in patients with risk factors for liver damage may be considered before commencing treatment and thereafter at cumulative methotrexate doses of 1.0 g – 1.5 g. If at any point during treatment, hepatoxicity is apparent on serological monitoring in any patient (such as raised ALT, AST or PIINP), a liver biopsy should be carried out.[xliii]**	
SH	MSD Ltd	20.0	NICE version	16		Section 1.2.2.3 – We believe this section should emphasize the importance of shared care – dermatology and rheumatology	Thank you for your comments. We believe that this is already included in a subsequent recommendation which

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						should work closely together to manage patients with severe joint and skin disease.	refers to 'multidisciplinary working and communication between specialities and, if needed, interdisciplinary team working'.
SH	MSD Ltd	20.1	NICE version	10		Systemic biological therapy This section refers only to a situation where a patient needs to be switched to an alternative biological drug. It would be beneficial to have detail in this section on how biological drugs should be used for the treatment of psoriasis.	Thank you for your comment. We have now added more information in to the NICE guideline to set the scene for biologics. Our scope excluded us from doing any work on first line biologics as this is covered in the NICE technology appraisals, hence were only able to look at a very specific aspect of the use of biologic drugs in psoriasis. The recommendations from TAs 103, 134, 146 and 180 have been quoted verbatim and form the current guidance for the use of biological agents for psoriasis. The new recommendations on when to switch to an alternative biologic agent supplement this guidance.
SH	MSD Ltd	20.2	NICE version	30		Section 1.7.1.4 should also reference NICE technology appraisal guidance TA220 – Golimumab for the treatment of psoriatic arthritis	Thank you we agree and have added the reference to TA220.
SH	NHS Direct	12.0	Full			NHS Direct welcome the guideline and have no comments on the content as part of the consultation.	Thank you for your comment.
SH	Novartis Pharmaceuticals UK Ltd	27.0	NICE	11	N/A	Recommendation 1.1.1.1. We suggest an additional bullet point to state "risks and benefits of all suitable treatment options" as it is important for patients to confidently	Thank you for your comments. We agree with this point but feel that this is already explicitly covered by recommendations already.

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						understand risks and benefits in reaching agreement with their clinician about the most appropriate treatment strategy.	
SH	Novartis Pharmaceuticals UK Ltd	27.1	NICE	13	N/A	Recommendation 1.2.1.3. We suggest that disease severity is assessed in all patients using the PASI and DLQI in order to guide management strategies.	Thank you. The GDG discussed the practicalities of using these tools in primary care at length. This is included in the link between evidence and recommendations in the full guidelines.
SH	Novartis Pharmaceuticals UK Ltd	27.2	NICE	31	N/A	Recommendations 1.7.2.1 & 1.7.2.3 for methotrexate and ciclopsporin respectively. We suggest deleting the words "for example". This would ensure that there is no ambiguity around the choice of response definition and would ensure consistency with mentions of response definitions elsewhere in the guideline (i.e. decrease of less than 75% in PASI score or decrease of less than 50% in PASI score and 5 points in DLQI).	The GDG do not wish to alter this recommendation as to do so would limit its validity because PASI is not always an appropriate measure and more sensitive tools may become available.
sH	Novartis Pharmaceuticals UK Ltd	27.3	NICE	37	N/A	Recommendations 1.8.1.13 & 1.8.1.14. We support the guideline recommendations that consideration should be given to changing to an alternative biological therapy in patients for whom there is primary or secondary failure to a first or second biological therapy. Given that these are key recommendations in the draft guideline, it would be beneficial for the guideline to restate the specific PASI/DLQI response criteria and timing of response assessment for each of the biological therapies, perhaps as bullet points underneath the	Thank you for your comment. The response criteria were established by the existing NICE technology appraisals (TAs). We have quoted their recommendations verbatim in compliance with our scope and are unable to edit them or incorporate them in to new recommendations as we did not review the evidence for this. We did not have sufficient data specifically for secondary failure to recommend a time-frame for review but

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						recommendations. This would ensure that the conditions for switching therapies are clear to anyone reading these bullet points in isolation. Regarding secondary failure, the guideline recommendations should also make it clear how frequently response should be measured in order to determine if secondary failure is an issue e.g. reassessment of response every 3 months. We note the requirement in point 1.8.1.14 that 'supra-specialist' advice should be sought from a clinician with expertise in biological therapy. Clearer definition of the term 'supra-specialist' would be desirable and may permit more consistent implementation of this recommendation. We recognise the relative lack of evidence to inform the guideline recommendations on switching between biological therapies. However, it is often good clinical practice in many therapeutic areas to consider switching to therapies with a different mechanism of action after primary or secondary failure of a first therapy (rather than switching to another agent with the same mechanism of action). As not all biological therapies have the same mechanism of action, we feel that the	given that biologics are only administered by specialists we hope that their expertise would be sufficient to guide appropriate practice. Additionally, the TAs were also unable to recommend a frequency of reassessment for a first biologic. However, we have added a recommendation to clarify that timing of assessment for primary failure of a second biologic should be in line with that in the TAs for a first biologic. The term supra-specialist is defined in the glossary. The term is derived from the BAD standards document and is defined in the glossary as level 4 care, which usually takes place entirely within an acute hospital and is carried out by: • consultant dermatologists • a range of other healthcare professionals with special skills in the management of complex and/or rare skin disorders). It equates to tertiary care. There was no robust evidence to suggest that switching to a different class of biologic was better than switching to another agent of the same class from the clinical review. Additionally, in the health economic

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						recommendations should at least mention this as a consideration with regard to clinician and patient choice. Similarly, there may be specific considerations from a patient choice perspective with regard to the route of administration and administration frequency of an alterative biological therapy. Again, we suggest that the NICE guideline at least acknowledges this issue.	analysis a class effect was assumed so it was not possible to model different sequences of treatment.
SH	Pfizer Limited	9.0	Full	General		Pfizer welcomes the development of the guideline for the management of Psoriasis. We think that it offers a good framework for improving the care of people with Psoriasis.	Thank you for your comments.
SH	Pfizer Limited	9.1	Full	General		Pfizer welcomes that the guideline addresses the need to increase assessment of psoriasis patients for the presence of psoriatic arthritis and subsequent access to rheumatology services as soon as psoriatic arthritis is suspected.	Thank you for your comment.
SH	Pfizer Limited	9.2	Full	632	33	Within the methodological introduction section it states "The population was limited to adults with chronic plaque psoriasis because biological treatments are currently only licensed for use among this subset of people with psoriasis." Please note that Etanercept has the	Thank you for your comment. The methods section has been amended to accurately reflect the licensing of etanercept. We limited the review to use in adults because we were only able to address the use of a second biological agent and the NICE Technology Appraisals only addresses use in adults. Therefore,

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						following licensed indication in children: *Treatment of chronic severe plaque psoriasis in children and adolescents from the age of 6 years who are inadequately controlled by, or are intolerant to, other systemic therapies or phototherapies.* We feel it is important to amend the guideline wording accordingly to acknowledge etanercept's paediatric licence although we are aware treatment of paediatric psoriasis does not fall within the scope of the guidelines.	although paediatric psoriasis does fall within the scope of the guideline, the protocol for this question was limited.
SH	Primary Care Dermatology Society	13.0	Full	20		We are disappointed to see no recommendation for the use of emollients as a primary treatment for hyperkeratotic plaque psoriasis.	Thank you for your comments. The Guideline Development Group (GDG) agree that emollients are an accepted important component of treatment for psoriasis. However, the GDG was unable to cover every aspect of psoriasis management and had to prioritise areas where practice is variable or unsafe and where recommendations are likely to be informed by a robust evidence base. The GDG were aware that there is little or no formal evidence for emollients compared to no treatment. In defining the scope the GDG therefore opted to begin the topical pathway after emollients. Without reviewing the

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							evidence we are unable to formulate a specific recommendation. However, the GDG noted stakeholders concerns that without an explicit statement about emollients this component of management might be omitted. The NICE Guideline has therefore been amended to include the following wording: *The treatment pathway in this guideline begins with active topical therapies. The GDG acknowledged that the use of emollients in psoriasis was already widespread and hence the evidence review was limited to active topical therapies in psoriasis. Please refer to the BNF and the cBNF for guidance on use of emollients'.* This wording has also been included within the algorithms for topical therapy.
SH	Primary Care Dermatology Society	13.1	Full	General		General approval of the guidance	Thank you for your comment.
SH	Psoriasis and Psoriatic Arthritis Alliance	15.0	Full	General		**As a stakeholder charity representing people affected by psoriasis and psoriatic arthritis, we are grateful for the opportunity to comment on these guidelines. We have confined ourselves to commenting on the main recommendations, where we feel it is**	Thank you for your comments.

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						appropriate to do so. **Our overall view of the guidelines is that they have taken into consideration current practice and the evidence available (although it is obvious that some of those data are of low quality), and applied a pragmatic approach to the treatment pathway for psoriasis.** **It will be useful for patients to know that there is a clear pathway for treating psoriasis, which is based on evidence.** **Hopefully the publication of the guideline will change some current poor treatment practices, and people affected by psoriasis and to some extent psoriatic arthritis will benefit.**	
SH	Psoriasis and Psoriatic Arthritis Alliance	15.1	Full	17	30	***Typo*** *'children'*	Thank you, we have made this change.
SH	Psoriasis and Psoriatic Arthritis Alliance	15.10	Full	48	29	***Recommendation 14*****.** *Following assessment in a non-specialist setting, offer referral for dermatology specialist advice if:* **We welcome the recommendation to refer under the circumstance listed, particularly when a body service area is >10%, as many people complain to PAPAA that they are often denied referral even when they see their psoriasis spread.**	Thank you for your comment.

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SH	Psoriasis and Psoriatic Arthritis Alliance	15.11	Full	49	2	***Recommendation 18***. *Offer annual assessment for psoriatic arthritis to people with any type of psoriasis. Assessment is especially important within the first 10 years of onset of psoriasis.* We particularly pleased to see this **recommendation, as we have campaigned for many years to get psoriatic arthritis recognised in the primary care setting.**	Thank you for your comment.
SH	Psoriasis and Psoriatic Arthritis Alliance	15.12	Full	49	7	***Recommendation 20*****.** *As soon as psoriatic arthritis is suspected, refer the person to a rheumatologist for assessment and advice about planning their care*. **As with our previous comment above, we welcome this recommendation, as early intervention for joint disease will help many people avoid disability**	Thank you for your comment.
SH	Psoriasis and Psoriatic Arthritis Alliance	15.13	Full	49	13	***Recommendation 22*****.** *Discuss risk factors for co morbidities with people who have psoriasis of all severities. Explain that they are at higher risk of hypertension, diabetes, obesity and hyperlipidaemia than people without psoriasis. Offer preventative advice and healthy lifestyle information in line with the following NICE guidance:* **We welcome any recommendation that improves health, but would like to caution against stigmatising people with psoriasis. It would be helpful for this advice to be expressed in terms of absolute risk in comparison with the**	Thank you for your comment. We agree. The recommendation was based on discussion about both the absolute and relative risks and so this has been taken into account. We have presented absolute risks within the appendices of the full guideline for further information. In addition in the section relating to general principles of care we have cross referred to the patient experience guideline (CG138) where it is very clear healthcare professional should talk about risk with patients. We have also reworded the

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						general population.	recommendation to prevent unnecessary anxiety being caused by information being provided on a blanket basis, when it may not be appropriate to all people with psoriasis.
SH	Psoriasis and Psoriatic Arthritis Alliance	15.14	Full	49	40	***Recommendation 26*****.** *Offer practical support and advice about the use and application of topical treatments. Advice should be provided by healthcare professionals who are trained and competent in the use of topical therapies*. **We welcome this recommendation as there is often confusion about the safe application of topical of topical treatments, especially when steroids are used. This may result in patients not achieving optimal results and moving on to more aggressive treatment options too soon.**	Thank you for your comment.
SH	Psoriasis and Psoriatic Arthritis Alliance	15.15	Full	50	11	***Recommendation 32*** *When offering topical agents take into account patient preference, cosmetic acceptability, practical aspects of application and the site(s) and extent of psoriasis to be treated. Discuss the variety of formulations available and use:* **This is very important recommendation for patients as this could have an impact of the use of a product.**	Thank you for your comment.
SH	Psoriasis and Psoriatic Arthritis Alliance	15.16	Full	50	30	***Recommendation 36*** *Offer people with psoriasis* ***keep*** *a supply of their topical treatment to keep at home for the self-management of their condition.*	Thank you for your comment. We agree that patients need to be aware of the dangers of over treatment and the GDG believe that this is adequately covered

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						We welcome this recommendation, which would make earlier treatment much easier for patients when their psoriasis flares-up. The only caveat is that patients need to be aware of the dangers of over-treatment, especially where steroids are concerned.	by the existing recommendations around safe use of steroids.
SH	Psoriasis and Psoriatic Arthritis Alliance	15.17	Full	General		**With regard to phototherapy, make patients aware of the number of visits needed as this might prove to be inconvenient or unacceptable for those in employment or full-time education.**	Thank you for your comment. We agree that it is important that people are aware of the number of visits required, which is why we included in first recommendation in the phototherapy section the information that narrowband UVB phototherapy may be given 3 or 2 times a week depending on patient preference. It is not possible to state the total number of visits required as this will vary depending on disease severity and other factors.
SH	Psoriasis and Psoriatic Arthritis Alliance	15.18	Full	54	28	***Recommendation 79*** *In people with both active psoriatic arthritis and psoriasis that fulfils the criteria for systemic therapy (see recommendation 78) consider the choice of systemic agent in consultation with a rheumatologist. For further information see 'Etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis' (NICE technology appraisal guidance 199).* **We welcome this recommendation to a combined approach for those with both psoriasis and psoriatic arthritis.**	Thank you for your comment.

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SH	Psoriasis and Psoriatic Arthritis Alliance	15.19	Full	57	39	***Recommendation 110.*** *If a person has both psoriasis and psoriatic arthritis, take into account both conditions before making changes to biological therapy and manage their treatment in consultation with a rheumatologist. For further information see 'Etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis' (NICE technology appraisal guidance 199).* **As with previous comments, we welcome this recommendation for a combined approach to treatment in those with both psoriasis and psoriatic arthritis.**	Thank you for your comment.
SH	Psoriasis and Psoriatic Arthritis Alliance	15.2	Full	47	1	***Recommendation 1.*** *Offer people with all types of psoriasis support and information tailored to suit their individual needs and circumstances, in a range of different formats so they can confidently understand*: **We welcome this recommendation, but would like to see some form or process that demonstrates the information is appropriate and/or sourced from recognised organisations that follow principles, such as plain English or the Information Standard rules, in order that patients can trust the information provided.**	Thank you for your comment. We have listed some resources, and linked to some patient organisations, in the 'Understanding NICE Guidance' version of the guideline. We are unable to endorse other sources that we haven't reviewed.

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SH	Psoriasis and Psoriatic Arthritis Alliance	15.20	Full	58	16	***Key research recommendations*** *Do structured psoriasis focussed educational programmes improve patient confidence, well-being and disease control as compared to standard care?* **We welcome this recommendation. As a charity we believe that education and empowering patients improves their understanding and ability to self mange their disease better. It would be useful to understand which element of education has the most impact and particularly, at which point in the patient pathway such interventions are most effective.**	Thank you for your comment.
SH	Psoriasis and Psoriatic Arthritis Alliance	15.3	Full	47	17	***Recommendation 2.*** *When offering treatments to a person with any type of psoriasis**:** discuss the risks and benefits of treatment options with the person and where possible include use of absolute risk and natural frequency.* **We agree with this recommendation as an important part of treatment decision making and to provide patients with risks and benefits' It might also be useful to explain that lower treatment risk might mean accepting lower treatment benefit, which might be acceptable to those wary of long-term side-effects.**	Thank you for your comment. We agree that each individual has different needs and we have highlighted the need to explore these expectations in the principles of care. We have also included a table of absolute risks in the appendices of the guideline which may help healthcare practitioners provide more accurate information. We have added your comment about lower treatment risks and lower treatment benefits in the link between evidence and recommendations in the full guideline.

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SH	Psoriasis and Psoriatic Arthritis Alliance	15,.4	Full	47	19	***Recommendation 3.*** *Assess whether support and information needs updating or revising at every review or interaction with the person affected, in particular during transition from children's services to adult services, when new interventions become available, and when the person's disease severity or circumstances change.* **We welcome this recommendation, as psoriasis is unlike other conditions and therefore moving from children's services to adult can prove traumatic.**	Thank you for your comment.
SH	Psoriasis and Psoriatic Arthritis Alliance	15.5	Full	47	23	***Recommendation 4*** *Provide a single point of contact to help people with all types of psoriasis access appropriate information and advice about their condition and the services available at each stage of the care pathway* **We welcome this recommendation as people with psoriasis often have to repeat endlessly symptoms and previous outcomes at each point of care.**	Thank you for your comment.
SH	Psoriasis and Psoriatic Arthritis Alliance	15.6	Full	47	33	***Recommendation 6*** *Assess people with all types of psoriasis for **:** the impact of disease on physical, psychological and social wellbeing.* **We believe this is very import recommendation as mild disease could have greater impact than extensive disease. Members of PAPAA, often cite lack of compassion, particular amongst the medical profession, for disease**	Thank you for your comment.

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						affecting small areas such as the hands or nails.	
SH	Psoriasis and Psoriatic Arthritis Alliance	15.7	Full	48	1	*Record high impact areas,* **We agree should be considered for disease severity and are an important consideration of overall impact on patients.**	Thank you for your comment.
SH	Psoriasis and Psoriatic Arthritis Alliance	15.8	Full	48	12	*Asking what aspects of their daily living is affected by the person's psoriasis.* **It should also take in consideration spouse, children siblings etc, as the impact on domestic life could have a considerable influence on treatment outcomes.**	Thank you for your comment. We believe that these factors are included in the wording 'what aspects of daily living are affected'. We are not able to provide an exhaustive list of these aspects.
SH	Psoriasis and Psoriatic Arthritis Alliance	15.9	Full	48	21	***Recommendation 12*** *Assess whether people with any type of psoriasis are depressed when assessing disease severity and impact, and when escalating therapy. If appropriate offer information, advice and support in line with ...* **We welcome this recommendation, but would caution against a blanket default of assuming that if an individual has psoriasis they will be depressed. Many of our members have commented that they feel 'down' but are not depressed and often feel reluctant to mention this because of the negative impact the diagnosis might have on their future employment.**	Thank you for this comment. Healthcare professionals assessing an individual for depression should do this in a sensitive manner, mindful of the potential concern about the stigma attached. In addition, the assessment should be able to discriminate between 'low mood' and depression. The evidence review indicated that depression is an important comorbidity in a clinically relevant proportion [the excess risk attributable to psoriasis was one case of depression for every 39 severe psoriasis patients per year (or per 87 patients per year with mild psoriasis)] and as per the linking evidence to recommendations table, felt that the any risk of labelling or

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							stigmatising people with psoriasis would be outweighed by the benefit of early recognition and management of depression.
SH	Royal College of Nursing		NICE	1.3.1.2	18	There is some concern that with regard to topical therapies. The document recommends that patients should be advised on how to use topical agents by healthcare professionals trained and competent in the use of topical therapies. This needs to be addressed by Primary Care providers; currently it seems they have no financial motivation to provide any education to dermatology patients, as is currently in Wales and there is lack of training into management of skin disease by nurses. Education provides better healthcare outcomes for patients and makes economic sense through more effective use of topical therapies.	Thank you for your comment. This aspect is outside of the remit of the scope of the guideline. The following link provides more information about the educational element of the NICE Implementation programme http://www.nice.org.uk/usingguidance/education/Education.jsp
SH	Royal College of Nursing	22.0	All	General		The Royal College of Nursing welcomes this document. It is comprehensive and timely.	Thank you for your comments.
SH	Royal College of Nursing	22.1	NICE	1.3.2.6	21	One of the recommendations is that treatment is given in a day care setting for topical treatment. This may be appropriate for a specialized city centre dermatology unit but it is not available in many District General Hospitals and it is inappropriate for patients to be referred to secondary care for	Thank you. The recommendation for provision in a day care setting only relates to the use of dithranol due to specific practicality and safety issues. Additionally, the role of the guideline is to recommend the most appropriate treatment but not to specify who should

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						topical therapies. This again goes back to the point made earlier about education/training.	undertake it.
SH	Royal College of Nursing	22.2	NICE	1.3.2	20	When looking at trunk psoriasis, first line treatment is application of steroid and vitamin D in two separate applications - nurses aim to encourage concordance but patients find it very difficult to apply creams twice daily. This should not be recommended on cost basis only compared to combined Steroid/ Vitamin D therapy which is more expensive but better tolerated and accepted by patients making it more cost effective.	Thank you for your comment. The GDG debated this at length and the recommendations were not made solely on a cost basis. This is discussed in link between evidence and recommendation section. Furthermore, a sensitivity analysis has been performed to explore the impact of reduced adherence on twice daily treatments. In this sensitivity analysis, it was assumed that 40% of patients on twice daily treatment would only apply the topical once daily, thus reducing the strategies efficacy. The conclusions of the analysis and the recommended sequences so informed were insensitive to reduced adherence. We have added text in the full guideline to clarify this further. Details on the assumptions and results of this sensitivity analysis are included in Appendix M.
SH	Royal College of Nursing	22.3	NICE	1.3.4	24	The guidelines also suggest using low cost preparation of topical steroid for face /flexures – vehicle of therapy for psoriasis site and cosmetic acceptability are a priority	The GDG agree that formulation is vey important and believe that this is covered by the recommendations. Reference to low cost has been deleted.

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						over cost.	
SH	Royal College of Nursing	22.4	NICE	General		We also have some concern that consultation time in clinics will need to be increased greatly to take into account all the advice needed with regard to risk factors. Some of these need to be the responsibility of primary care providers.	Thank you for your comment. We understand the implementation concerns. The guideline aims to look at what should be done rather than who should do it or where it should be done. The GDG discussed the practical aspects of implementing the recommendations and it was felt that many of the risk assessments, for example assessing cardiovascular risk, were standard practice in primary care and would probably occur here.
SH	Skin Care Campaign	14.0	Full	47	7	The term 'safe monitoring' is difficult to interpret. I presume it means 'monitoring for safety'. As it is in the context of minimising the risks of side effects I wonder if it would be better to say 'appropriate monitoring for safety'?	Thank you for your comments. We agree and have changed the wording to read 'monitoring for safety'.
SH	Skin Care Campaign	14.1	Full	47	41	It seems a pity not to include the patient's assessment of overall severity too. This would provide valuable information and is another way of ensuring that the patient is genuinely involved in his/her management.	Thank you. The GDG agreed with your comment and a bullet point has been added to indicate that the patient assessment of severity should also be recorded.
SH	Skin Care Campaign	14.2	Full	48	12-15	This section seems rather weak – especially line 15 which is a closed question inviting a yes/no answer. Would it be possible to recommend the use of visual analogue scale to assess the overall impact of psoriasis on physical, psychological and	Thank you for your comment. This recommendation is representative of the evidence found. The GDG didn't find any evidence to assess the validity of the visual analogue scale to assess impact and so were unable to

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						social wellbeing? This would have the advantage of providing a way of tracking impact over time, monitoring the impact of interventions etc.	recommend its use. We have included in our research recommendations that there is a need to develop these tools. The GDG felt it was important to use simple questions for ease of use in primary care, where the GDG were aware that this aspect of assessment was not always even considered. Although we accept the shortfalls of the DLQI we have suggested it is used to track the response to second and third line treatment. The GDG were aware that formal tools in primary care weren't always practical.
SH	Skin Care Campaign	14.3	Full	50	7	Could we add 'of appropriate potency' at the end of the line to avoid confusion?	Thank you for your comment. We have reworded the recommendation to avoid misinterpretation.
SH	Skin Care Campaign	14.4	Full	50	38	I see from the cost-effectiveness analysis (Appx M) that the combination product (calcipotriol/betamethasone) is the most clinically effective option but not the most cost-effective because it would cost an additional £192 per year. This seems a small cost for the convenience of once-daily treatment with a single product. The additional prescription costs (to the patient) of using two products should also be taken into account here. It is unfortunate that the guideline as written does not allow prescribing of the combination product for several weeks (could be up to 24 weeks). It might be better to offer it as an option at the	Thank you for your comment. We do not agree that it is a small cost, particularly when multiplied across the entire population receiving topical therapies for the treatment of their psoriasis. Costs to the patient are not included in analyses for NICE because an NHS and Personal Social Costs (PSS) costing perspective is used.

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						outset.	
SH	Skin Care Campaign	14.5	Full	50	38	There is no mention of the role of emollients in psoriasis management at all. Although there is no trial evidence of effectiveness as far as I am aware, expert opinion favours their use to help to control itching and scaling and to improve appearance and reduce cracking. Could some acknowledgment of this role be made?	Thank you for your comment. The Guideline Development Group (GDG) agree that emollients are an accepted important component of treatment for psoriasis. However, the GDG was unable to cover every aspect of psoriasis management and had to prioritise areas where practice is variable or unsafe and where recommendations are likely to be informed by a robust evidence base. The GDG were aware that there is little or no formal evidence for emollients compared to no treatment. In defining the scope the GDG therefore opted to begin the topical pathway after emollients. Without reviewing the evidence we are unable to formulate a specific recommendation. However, the GDG noted stakeholders concerns that without an explicit statement about emollients this component of management might be omitted. The NICE Guideline has therefore been amended to include the following wording: *The treatment pathway in this guideline begins with active topical therapies. The GDG acknowledged that the use of emollients in psoriasis was already*

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							widespread and hence the evidence review was limited to active topical therapies in psoriasis. Please refer to the BNF and the cBNF for guidance on use of emollients'. This wording has also been included within the algorithms for topical therapy.
SH	Skin Care Campaign	14.6	Full	51	32	It might be better to offer the topical agents to soften and loosen scale at the beginning rather that waiting 4 weeks for treatment to fail	Thank you**.** The recommendation was based on the evidence which showed that potent steroids were effective treatments even when descalers were not used, as they were not included in the study protocols of the trials reviewed. The evidence reviewed included trials involving patients with more severe scalp psoriasis where one would expect some of the patients to have adherent scale. Therefore, the recommendation was based on the effect size of monotherapy with potent steroid without descalers with the comparison intervention. Additionally, when developing the recommendation, the GDG aimed to balance simplicity and adherence.
SH	Skin Care Campaign	14.7	Full	51	37	It is not clear whether this is intended instead of the topical steroid treatment or in addition to it	Thank you, we have amended the wording of the recommendation. Please also refer to the algorithms to clarify the treatment pathway.

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SH	Skin Care Campaign	14.8	Full	52	9	This appears to be inconsistent with line 37, p51	Thank you, we agree that more detail is required to ensure consistency. Therefore, we have added some qualifying text to the recommendation.
SH	Skin Care Campaign	14.9	Full	54	35	The only risk of methotrexate treatment mentioned is liver fibrosis but there is no mention of the risk of bone marrow suppression or pulmonary fibrosis or the measure that patients need to take to monitor for these conditions – this would be helpful. Also- the risks associated with once weekly (vs daily) treatment should be mentioned even if only by reference to the NPSA guidance	Thank you for your comment. The GDG were aware that all systemic treatments carry a risk for a range of adverse events and included recommendations to take account of this. There was insufficient evidence from the review of systemic therapies to make any specific recommendations except for liver fibrosis with methotrexate, although long term data were sought for a range of toxicities for all of the non-biological systemic drugs reviewed. However, to remove the unintended implication that liver fibrosis is the main problem associated with methotrexate or that other systemic agents have preferable side effect profiles, the recommendation regarding risk of liver damage has been moved to the section on methotrexate monitoring and toxicity, where the evidence for this side effect was examined in more detail.
SH	The British Association of Skin Camouflage	11.0	Full	General		BASC consider there is no need for amendment to the draft document	Thank you for your comment.

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SH	The British Psychological Society	18.0	Full	General		The BPS is encouraged to note the high level of recognition of the degree of psychological distress and social interference associated with psoriasis throughout the guideline.	Thank you for your comments.
SH	The British Psychological Society	18.1	Full	General		The guideline identifies the need to assess psychosocial wellbeing, information and support needs at each interaction. We make additional comments linked to the first research recommendation (Points 12, 20 and 27) about the need to develop assessment tools to ensure assessments can be used to identify appropriate treatment pathways.	Thank you for your comment. Please see responses to your specific points in the relevant rows.
SH	The British Psychological Society	18.10	Full	46 49	1 42	The BPS welcomes the inclusion of the reference to the National Institute for Health & Clinical Excellence clinical guideline 76 on Medicine Adherence, which is strongly informed by psychological theory and evidence-based approaches (NICE, 2009). However, one challenge for supporting adherence in psoriasis is that there are no tools available which assess adherence to topical treatments. Given that the vast majority of people with psoriasis use only topical treatments this is a very important step in supporting effective self-care. Whilst tools such as the Medication Adherence Report Scale (MARS; Horne & Weinman, 1999) or the Morisky scale	Thank you. As we did not explicitly search for evidence on adherence to topical therapies or how this is measured we are unable to make a recommendation for future research in this area.

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						(Morisky *et al.*, 1986) are suitable for many types of treatment (such as tablet taking), they are unsuitable for assessing adherence to topical treatments. The BPS recommends that the development of a brief, valid and reliable adherence measure for topical treatments should be a research priority, particularly given the strong emphasis on treatment response as a criterion for changing to other, stronger topical or systemic therapies. *References:* Horne, R. & Weinman, J. (1999). Patients' Beliefs About Prescribed Medicines and Their Role in Adherence to Treatment in Chronic Physical Illness. *Journal of Psychosomatic Research*, *47(6)*, 555-567. Morisky, D.E., Green, L.W. & Levine, D.M. (1986). Concurrent and Predictive Validity of a Self-Reported Measure of Medication Adherence. *Medical Care*, *24(1)*, 67–74. NICE (2009). CG76 Medicines Adherence: NICE Guideline. London: National Institute for Health & Clinical Excellence. Available from: www.nice.org.uk/guidance/CG76/NICEGuidance. Accessed 21 June 2012.	

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SH	The British Psychological Society	18.11	Full	47	40	*Recommendation 8:* The BPS suggests that, when assessing disease severity, as well as the physician global assessment, it is also important to ask patients their views of psoriasis severity, which is relatively quick and easy to do. Assessment of self perceived severity has been consistently associated with psychological distress. Disparity between physician and patient assessments quickly provides clinicians with an indicator of potential disease-related distress (Fortune *et al*., 2000). Furthermore, self-assessed severity is associated with both psychological distress and suicide risk (e.g. Gupta *et al*., 1993). *References:* Fortune, D. G., H. L. Richards, Main, C.J. & Griffiths, C.E.M. (2000). Pathological Worrying, Illness Perceptions and Disease Severity in Patients with Psoriasis. *British Journal of Health Psychology*, *5(1)*, 71-82. Gupta, M.A., Schork, N.J., Gupta, A.K., Kirby, S. & Ellis, C.N. (1993). Suicidal Ideation in Psoriasis. *International Journal of Dermatology*, *32*, 188-190.	Thank you. The GDG agreed with your comment and a bullet point has been added to indicate that the patient assessment of severity should also be recorded.
SH	The British Psychological Society	18.12	Full	48	21	Given the potential risk of suicide (Kurd *et al*., 2010), it would be helpful to formally recommend conducting risk assessments in situations where low mood is identified.	Thank you, we have cross referred to the NICE depression guideline which provides guidance on identifying suicide risk and appropriate management.

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						Reference: Kurd, S.K., Troxel, A.B., Crits-Christoph, P. & Gelfand, J.M. (2010). The Risk of Depression, Anxiety, and Suicidality in Patients with Psoriasis. *Archives of Dermatology*, *146*, 891-895.	The GDG did not believe that low mood in people with psoriasis should be managed differently from any other patient populations and so specific guidance was not thought to be necessary.
SH	The British Psychological Society	18.13	Full	49	13	The BPS welcomes the recognition of lifestyle factors in relation to risk reduction for co-morbidities. People with psoriasis are more likely to engage in problematic lifestyle behaviours (Favato, 2008; Herron *et al*., 2005; Kirby *et al*. 2008: Naldi & Mercuri, 2009) and be overweight (Lebwohl & Callen, 2006). Whilst offering advice and healthy lifestyle information is important, however, this is not sufficient for behavioural change. We recommend offering support with behavioural change, such as *referral* to smoking cessation services, is the minimum for those assessed as needing this intervention. Therefore, we would recommend changing the wording of this section from "*Offer preventative advice and healthy lifestyle information*" to "*Offer to support lifestyle behavioural changes in line with the following NICE guideline*" There are specific barriers for people with disfiguring conditions that can limit	Thank you. We have edited the recommendation to: *'Discuss risk factors for cardiovascular comorbidities with people who have any type of psoriasis (and their families or carers). Where appropriate offer preventative advice, healthy lifestyle information and to support lifestyle behavioural change tailored to meet the needs of the individual in line with the following NICE guidance…'*

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						opportunities for exercise. People with psoriasis have often experienced negative comments from other individuals in gyms, swimming pools which reduce the likelihood of use of these facilities (Ginsburg & Link, 1993; Vardy *et al*., 2002). Thus, services may need tailoring for people with psoriasis. The BPS therefore views the identification of effective and tailored lifestyle behavioural change support for people with psoriasis, as an important research recommendation, particularly given the GDG's emphasis upon risk reduction for comorbid conditions. *(cont'd/…)* *References:* Favato, G. (2008). High Incidence of Smoking Habit in Psoriatic Patients. *The American Journal of Medicine*, *121(4)*, e17. Ginsburg, I.H. & Link, B.G. (1993). Psychosocial Consequences of Rejection and Stigma Feelings in Psoriasis Patients. *International Journal of Dermatology*, *32*, 587-91. Herron, M.D., Hinckley, M., Hoffman, M.S., Papenfuss, J., Hansen, C.B., Callis, K.P. *et al*. (2005). Impact of Obesity and Smoking on Psoriasis Presentation and Management. *Archives of Dermatology*,*141(12)*,1527-34.	

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						Kirby, B., Richards, H.L., Mason, D.L., Fortune, D.G., Main, C.J. & Griffiths, C.E.M. (2008). Alcohol Consumption and Psychological Distress in Patients with Psoriasis. *British Journal of Dermatology*,*158(1)*,138-40. Lebwohl, M. & Callen, J.P. (2006). Obesity, Smoking, and Psoriasis. *Journal of the American Medical Association*, *295*, 208-10. Naldi, L. & Mercuri, S.R. (2009). Smoking and Psoriasis: From epidemiology to pathomechanisms. *Journal of Investigative Dermatology*,*129(12)*, 2741-43. Vardy, D., Besser, A., Amir, M., Gesthalter, B., Biton, A. & Buskila, D. (2002). Experiences of Stigmatization Play a Role in Mediating the Impact of Disease Severity on Quality of Life in Psoriasis Patients. *British Journal of Dermatology*, *147*, 736-42.	
SH	The British Psychological Society	18.14	Full	49	13	The evidence for association between obesity and psoriasis is growing. The impact upon psoriasis severity of significant weight loss via dietary restriction or bariatric surgery (e.g. Farias *et al*., 2012), plus an indication that treatment response is associated with obesity (Bardazzi *et al*., 2010; Gisondi *et al*., 2008), give a strong steer to the need to develop effective	Thank you for your comment. The GDG are aware of this literature but it was not prioritised for evidence based review. However, we have amended the recommendation to include that the advice and support given should be tailored to the needs of the individual.

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						interventions to improve diet and reduce obesity for this population. Whilst the draft guideline suggests following existing NICE guidance on obesity, the BPS would welcome a recommendation that interventions are tailored to this population. Psychological factors such as mood (Markowitz *et al*., 2008) (prevalent in psoriasis population and known to be associated with binge eating - e.g. Linde *et al*., 2004), self-efficacy and motivation will all play a role in effective weight loss and weight maintenance interventions. Interventions tailored to address the specific behavioural and emotional challenges faced by people with psoriasis are worthy of further investigation. Commercial weight management programmes may not be accessed by those whose visible appearance makes them reluctant to engage in activities which bring them into contact with other people. *(cont'd/…)* *References:* Bardazzi, F., Balestri, R., Balde, E., Antonucci, A., De Tommaso, S. & Patrizi, A. (2010). Correlation Between BMI and PASI in Patients Affected by Moderate to Severe Psoriasis Undergoing Biological Therapy. *Dermatology & Therapy*, *23(Suppl. 1*), S14–	

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						S19. Farias, M.M., Achurra, P., Boza, C., Vega, A., de la Cruz, C. (2012). Psoriasis Following Bariatric Surgery: Clinical evolution and impact on quality of life on 10 patients. *Obesity Surgery*, *22*, 877-80. Gisondi, P., Del Giglio, M., Di Francesco, V., Zamboni, M. & Girolomoni, G. (2008). Weight Loss Improves the Response of Obese Patients with Moderate-to-Severe Chronic Plaque Psoriasis to Low-Dose Cyclosporine Therapy: A randomized, controlled, investigator-blinded clinical trial. *American Journal of Clinical Nutrition*, *88*, 1242–1247. Linde, J.A., Jeffrey, R.W., Levy, R.L., Sherwood, N.E., Utter, J., Pronk, N.P., et al. (2004). Binge Eating Disorder, Weight Control, Self-Efficacy, and Depression in Overweight Men and Women. *International Journal of Obesity*, *28*, 418–425. Markowitz, S., Friedman, M.A. & Arent, S.M. (2008). Understanding the Relation Between Obesity and Depression: Causal mechanisms and implications for treatment. *Clinical Psychology: Science and Practice*, *15(1)*, 1-20.	
SH	The British Psychological Society	18.15	Full	49	27	Many people with psoriasis use multiple medications, such as medication for co-morbid cardiovascular disease, pain or	Thank you for your comment. We understand your concerns and have now added a bullet to a

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						depression. There is evidence to suggest that medication self-management for people with co-morbid conditions is complex and adherence may be suboptimal because individuals prioritise one condition over another (Stack *et al*., 2008; 2011). In order to support optimal self-management in those managing co-morbid conditions, the BPS therefore recommends that interventions for this group should take account of co-morbid conditions. We therefore suggest the following wording: "For people with multiple comorbidities and any type of psoriasis needing second or third-line therapy, ensure multidisciplinary team working and communication between specialties and, if needed, interdisciplinary team working (for example when both skin and joints are significantly affected). • Offer specific support with multiple medications adherence in line with existing NICE guideline 76 (NICE, 2009)". *(cont'd/…)* *<u>References:</u>* NICE (2009). CG76 Medicines Adherence: NICE Guideline. London: National Institute	recommendation in the principles of care section which cross refers to the medicines adherence guideline (CG76).

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						for Health & Clinical Excellence. Available from: www.nice.org.uk/guidance/CG76/NICEGuidance. Accessed 21 June 2012. Stack, R.J., Bundy, C., Elliott, R.A., New, J.P., Gibson, J.M. *et al.* (2011) Patient Perceptions of Treatment and Illness When Prescribed Multiple Medicines for Co-Morbid Type 2 Diabetes. *Diabetes, Metabolic Syndrome & Obesity*, *4*, 127 – 135. Stack, R.J., Elliott, R.A., Noyce, P.R. & Bundy, C. (2008). A Qualitative Exploration of Multiple Medicines Beliefs in Co-Morbid Diabetes and Cardiovascular Disease. *Diabetic Medicine*, *25*, 1204–1210.	
SH	The British Psychological Society	18.16	Full	55	41	The draft guideline reads: "*Provide advice on modifiable risk factors for liver disease prior to and during therapy including alcohol intake and weight reduction if appropriate*". As in Point 14 above, advice alone is unlikely to lead to behavioural changes that reduce risk. The BPS therefore recommends that the wording be revised to read as follows: "*Offer interventions which support appropriate behavioural changes to reduce risk factors for liver disease prior to and during therapy including alcohol intake and weight reduction if appropriate.*"	Thank you for your comment. We are unable to directly recommend that interventions be offered as we have not reviewed the evidence for their effectiveness. We believe that both informing the patient about the modifiable risks, and helping them do something about it are both are relevant and important. Therefore, we have added a sentence to the recommendation advising that people should refer to *NICE Public Health Guidance PH6 for further advice on how to support attitude and behavioural*

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						This would make the guideline consistent with NICE guidance on behavioural change (NICE 2007). *Reference:* NICE (2007). PH6 Behaviour Change: Guidance. London: National Institute for Health & Clinical Excellence. Available from: http://guidance.nice.org.uk/PH6/Guidance/pdf/English. Accessed 21 June 2012.	*change.*
SH	The British Psychological Society	18.17	Full	57	10	Recommendations about the Dermatology Life Quality Index (DLQI; Finlay & Khan, 1994) need to be viewed in a context which recognises, first, that it does not adequately measure the specific psychological impact of psoriasis on mood, and second, that is does not capture well-being or coping, all of which could be useful to promote as part of a patient self-management programme. The BPS agrees with research recommendation R.1 – that there is a need for a broader wellbeing measure that includes full ranges of experiences such as coping responses associated with psoriasis (for example, an increased use of alcohol). *(cont'd/…)* *References:*	Thank you for your comment. Please note that we have removed duplication in the recommendations quoted from the NICE Technology Appraisals for biologics relating to the DLQI. However, to comply with the scope we are unable to amend the wording of the recommendation, which is quoted verbatim from NICE Technology Appraisal 180. . However, we do comment on the limitations of the DLQI in the linking evidence to recommendations table in chapter 7 and have added more detail to this section in line with your comment.

Type	Stakeholder	Order No	Document	Page No	Line No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
						Finlay, A.Y. & Khan, G.K. (1994). Dermatology Life Quality Index (DLQI): A simple practical measure for routine clinical use. *Clinical and Experimental Dermatology*, *19*, 210-216.	
SH	The British Psychological Society	18.18	Full	66 – 80		The BPS agrees that research in this area is generally of poor methodological quality and that, as a result, the impact of self-management interventions in this population remains unclear. Due to the failure of authors to identify the target of change in interventions, only limited conclusions can be drawn about which components had a significant impact on the outcomes reported.	Thank you for your comment.
SH	The British Psychological Society	18.19	Full	106		The BPS welcomes the clear coverage of assessment of patients' well-being however, we feel more detail could usefully be included regarding the specific assessment of appearance-related issues and levels of appearance-related distress (including social anxiety). This could be addressed as part of Research Recommendation R.1	Thank you, we found no extensive or robust evidence relating to these factors in the tools in our reviews. We have now added this to our future research recommendation.
SH	The British Psychological Society	18.2	Full	General		The BPS recommends that more detail be given to the specific psychosocial impact of psoriasis amongst young people and the provision of appropriate psychosocial support to meet their particular needs, particularly those around altered	Thank you for your comment. We have amended the introduction to include specific reference to issues around body image during adolescence and the need to provide appropriate support.

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						appearance/ disfigurement which can be especially challenging during adolescence when issues around body image and appearance are particularly salient. The majority of individuals are diagnosed with psoriasis in young adulthood with 25% being diagnosed before the age of 18 years (Lebwohl, 2003). *References:* Lebwohl M. (2003). Psoriasis. *Lancet*, *361(9364)*,1197-204.	
SH	The British Psychological Society	18.20	Full	558	28	Although excessive alcohol consumption is considered a relative contraindication for methotrexate in recent treatment guidelines, there is a lack of literature on specific alcohol consumption guidelines; some physicians' recommend complete abstinence while others permit a daily alcohol intake (Menter *et al*., 2009). In a recent survey it was reported that dermatologists were more conservative than rheumatologists in their advice regarding alcohol and methotrexate (complete abstinence recommended by 53% vs. 24%, respectively). (Taylor *et al*., 2008). For those who did not recommend abstinence, there was wide variation on the amount of alcohol permitted. Future research is therefore necessary in	Thank you for this comment and we agree. We specifically looked for evidence in order to inform recommendations in this area but were unable to identify robust data. Therefore, the GDG made a research recommendation.

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						order to understand alcohol as a contraindication for methotrexate. If such research were to conclude that alcohol is a contraindication, then specific alcohol guidelines and lifestyle behaviour change support would need to be developed. *References:* Menter, A., Korman, N.J., Elmets, C.A., Feldman, S.R, Gelfand, J.M., Gordon, K.B.. et al. (2009). Guidelines of Care for the Management of Psoriasis and Psoriatic Arthritis: Section 3. Guidelines of care for the treatment of psoriasis with traditional systemic agents. *Journal of the American Academy of Dermatology*, *61*, 451-485. Taylor, W.J., Korendowych, E., Nash, P., Helliwell, P.S., Choy, E. & Krueger, G.G. (2008). Drug Use and Toxicity in Psoriatic Disease: Focus on methotrexate. *The Journal of Rheumatology*, *35*, 1454-1457.	
SH	The British Psychological Society	18.21	Full	683	1	It is disappointing to see that only cognitive behavioural therapy was examined as an intervention. The BPS believes that it would have been helpful to include other forms of psychological intervention in addition to CBT in the search; for example, arousal reducing approaches, such as relaxation therapy and meditation, have shown some benefits, and there are a	The GDG prioritised CBT for review as it was thought to be the best studied psychological intervention in psoriasis so the GDG believed that the evidence quality would be better and more likely to support a recommendation on CBT compared with other psychological interventions, which have not been studies in psoriasis with the same rigor

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						number of studies that warrant inclusion (e.g. Gaston, 1991; Kabit-Zinn *et al*., 1998). *References:* Gaston, L., Crombez, J., Lassonde, M., Lassonde, M., Bernier-Buzzanga, J. & Hodgins, S. (1991). Psychological Stress and Psoriasis: Experimental and prospective correlation studies. *Acta Dermato-Venereologica*, *156*, *37-43.* Kabat-Zinn, J., Wheeler, E., Light, T., Skillings, A., Scharf, M.J., Cropley, T.G. *et al.* (1998). Influence of a Mindfulness Meditation-Based Stress Reduction Intervention on Rates of Skin Clearing in Patients with Moderate to Severe Psoriasis Undergoing Phototherapy (UVB) and Photochemotherapy (PUVA). *Psychosomatic Medicine*, *60*, *625-32.*	as CBT. For example, the evidence base on mindfulness is in its infancy and the Kabat-Zinn study in this field has not been replicated. It was also known that access to CBT is problematic and demand outstrips supply with long waiting times. This rationale has been added to the methods section of the chapter discussing the evidence for CBT to improve transparency.
SH	The British Psychological Society	18.22		689		Under "quality of evidence" in the table, the report read "*The GDG noted that CBT improved HADS score and distress, but felt the improvement in PASI was unconvincing*." Whilst this statement may be factually correct, we feel it was unfortunate that it was used as a statement to assess quality of the study. As it is written here, it could be taken to imply that psychological symptoms such as depression or distress are of less	Thank you, we agree with this comment. Therefore, we have reworded the comment and moved it to the trade-off between clinical benefits and harms section.

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						importance than psoriasis severity. The BPS would recommend that this sentence is reworded to avoid this implied meaning.	
SH	The British Psychological Society	18.23	Full	690		The need for more research to assess the effectiveness of CBT/psychological interventions with patients with psoriasis is stated page 690 but should also be included in the specific recommendations for future research. In some places the guideline content appears to imply that clinical assessment of severity of the condition is directly associated with psychological distress; however, we know from previous research that level of distress is not directly proportional to the clinical severity of the condition (Fortune *et al.*, 2000), for example the guideline states. "*The GDG agreed to make future research recommendations on whether CBT is of value and identifying which individuals are most likely to benefit from CBT. Future research should take into account disease severity which should be controlled at baseline*." (page 690). The BPS therefore recommends that the focus for the evaluation of all psychological interventions (i.e. not just CBT) should also include specific measures of appearance-	Thank you for your comment. A formatting error occurred in the full guideline that was posted for consultation. The research recommendations relating to chapter 13 were duplicated in chapter 14. This has now been corrected and the research recommendation agreed by the GDG in relation to CBT now reads as follows: "Does a psoriasis-specific cognitive behavioural therapy intervention improve distress, quality of life and psoriasis severity compared with standard care?" In concordance with the NICE Guideline Manual the developers are only able to make future research recommendations for areas that they have performed literature searches for and full reviewed the evidence. We did not directly review the evidence for a stepped care approach, although this is suggested in the criteria in Appendix R as an element to be considered in relation to this

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						related distress (such as the Derriford Appearance Scale – Carr et al, 2000) rather than disease severity, as a control at baseline. We suggest the following amendment: "*The GDG agreed to make future research recommendations on whether CBT is of value and identifying which individuals are most likely to benefit from CBT. Future research should take into account appearance related distress which should be controlled at baseline"* *<u>References:</u>* Carr, T., Harris, D. & James, C. (2000), The Derriford Appearance Scale (DAS-59): A new scale to measure individual responses to living with problems of appearance. *British Journal of Health Psychology*, *5*, 201–215. doi: 10.1348/135910700168865 Fortune, D.G., Richards, H.L., Main, C.J. & Griffiths, C.E.M. (2000). Pathological Worrying, Illness Perceptions and Disease Severity in Patients with Psoriasis. *British Journal of Health Psychology*, *5*, 71-82.	research, which has been categorised as high priority. The GDG did not think it would be appropriate to limit the considerations specifically to appearance-related distress.
v	The British Psychological Society	18.24	Appendix R	1	1	The BPS welcomes the call to develop validated tools to look at severity and impact; however, the guidance fails to be	Thank you for your comment. The GDG agree that there is a need for a measure

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						explicit in stating that there is a need to examine (and develop) measures that identify broader measures of psychological wellbeing that include mood and coping.	that is sensitive to mood as well as quality of life. However, the future research recommendations do not aim to provide an exhaustive list of points. Instead they seek to provide broad suggestions for research bearing in mind the apparent gaps in the literature. The future research recommendation has now been reworded following your comments. We have incorporated the impact on psychological wellbeing.
SH	The British Psychological Society	18.25	Appendix R	2		Research Recommendation 1.1. This recommendation appears to accept that the relationship between CVD and psoriasis is firmly established. As several studies now indicate that these relationships, and in particular the risks, are unclear (Nijsten & Wakkee, 2009; Stern & Huibregtse, 2011; Stern & Nijsten, 2012; Wakkee *et al*., 2009), some have argued that the high levels of CVD can be explained as a consequence of detection biases. Hence, work to establish the nature of the relationships between these conditions should remain a key research recommendation. There is a danger that unnecessary anxiety may be caused through CVD risk assessments or communication with those patients for whom these are unnecessary.	Thank you for your comment. We agree that there is still uncertainty around the exact relationship between CVD and psoriasis, particularly for those with mild disease. We also accept that unnecessary anxiety may be caused by the communication of CVD risk to those with mild psoriasis, although the absolute increase in risk (particularly for mortality from CVD) in those with severe disease was found to be compelling after taking in to account the possible biases. Based upon the many stakeholder comments received pertaining to the future research recommendations we

Type	Stakeholder	Order No	Document	Page No	Line No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
						References: Nijsten, T. & M. Wakkee (2009). Complexity of the Association Between Psoriasis and Comorbidities. *Journal of Investigative Dermatology*, *129(7)*, *1601-1603.* Stern, R.S. & T. Nijsten (2012). Going Beyond Associative Studies of Psoriasis and Cardiovascular Disease. *Journal of Investigative Dermatology*, *132(3)*, 499-501. *(cont'd/…)* Stern, R.S. & Huibregtse, A. (2011). Very Severe Psoriasis is Associated with Increased Noncardiovascular Mortality But Not With Increased Cardiovascular Risk. *Journal of Investigative Dermatology*, *131(5),*1159-1166. Wakkee, M., Meijer, W., Neumann, H.A., Herings, R.M., Nijsten, T. (2010). Psoriasis May Not Be an Independent Predictor for the Use of Cardiovascular and Anti-Diabetic Drugs: A 5-Year Prevalence Study. *Acta Dermato-Venereologica*, *89(5)*, 476-483.	have deprioritised this particular research recommendation (but retained it on the list of research recommendations).
SH	The British Psychological Society	18.26	Appendix R	2	7	Whilst it is clear that there is high co-morbidity with psychological conditions, the nature of the relationship between specific types of psychological condition/ distress (such as social anxiety, shame, and depression) and psoriasis requires further investigation. Understanding the	Thank you for your comment. We did not look at the evidence for the association between different types of psychological presentation and psoriasis – depression was the only psychological comorbidity addressed.

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						relationship between specific types of psychological presentation and psoriasis has important implications for ascertaining which types of psychological treatment to pursue.	Given this we are unable to make a research recommendation around this issue.
SH	The British Psychological Society	18.27	Appendix R	5		Appendix R includes the following recommendation on "*Do structured psoriasis-focused educational programmes improve patient confidence, well-being and disease control compared with standard care*?" This research recommendation was an extremely disappointing aspect of this draft guideline. There is no evidence that programmes with educational elements alone improve outcomes or behaviours associated with self-management. The reviewed evidence base for nurse-led interventions in psoriasis was found to be generally poor, with no direct evidence for impact on either adherence or psychological well-being (Full guideline, page 78). The phrase a "psoriasis-focused educational programme" does not provide a steer to the type of intervention anticipated. Nurse-/clinician-led information provision has not been effective and yet this recommendation appears to reflect an	Thank you for your comment. We agree that educational interventions alone may not be effective and have edited the research recommendation to the broad umbrella term of 'self-management'. The text underpinning the future research recommendation has been expanded. The research recommendations aim to provide a broad steer, it is expected that researchers provide detail within a research protocol.

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						assumption that information alone will improve self-management. Please also see Points 31 and 32, below.	
SH	The British Psychological Society	18.28	Appendix R	5		Key psychological factors such as self-efficacy (confidence) and low mood, as well as patient perceptions of psoriasis and treatments, all impact upon ability to manage the condition and treatments. The BPS suggests that Appendix R should include a recommendation that these factors be investigated further to provide pointers for the development of new interventions.	Thank you for your comment. As we did not seek evidence on how psychological factors impact upon treatment outcomes as a prognostic review we are unable to make a future research recommendation in this area.
SH	The British Psychological Society	18.29	Appendix R	5	10	There is a need for tailored programmes; however, it is essential that educational programmes be distinguished from psychological interventions. *(cont'd/…)* Optimum self-management in psoriasis can be difficult to achieve, as shown by low levels of adherence to treatment impaired quality of life, poor psychological well-being and high prevalence of unhelpful lifestyle behaviours. We would argue that self-management or self-care programmes need to be informed by psychological considerations and with likely mechanisms of action specified and fully described (Craig et al, 2008b; Michie et al, 2009). The development of theoretically informed,	Thank you for your comment. The primary focus of the research recommendation pertains to self-management and exploring the concepts that underpin self-management. As you acknowledge psychological interventions are one of many elements regarded as important for exploration. In relation to models, we did not directly search for 'stepped care' models and hence did not wish to change the focus of the future research recommendations.

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						evidence-based, self-management interventions is required. Self-management interventions based upon accessing and addressing patients' beliefs about their condition and treatment, emotional states, and the interaction between cognitions and emotions, have been shown to be effective across a number of long-term conditions (Cameron & Jago, 2008; McAndrew *et al*., 2010; Wearden & Peters, 2008). The BPS therefore recommends alternative wording which incorporate these additional elements: "*Do tailored psoriasis-focused combined programmes containing psychological and educational elements improve patient confidence, well-being and disease control compared with standard care*?" <u>In addition</u>, the BPS recommends the inclusion of the option of integrated specialist psychological interventions to address psychological distress that cannot be managed by dermatology staff alone. There is an urgent need to develop psychological interventions that can be applied at different points in a stepped care model (Thompson, 2009). Indeed, as	We have retained the words 'self-management' as a broad umbrella term within the research recommendation. The research recommendations aim to provide a broad steer, it is expected that researchers provide detail within a research protocol and this may include all or any of the specific elements you have highlighted. Please refer to the revised Appendix R.

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						management of psychological need is a key focus of the guidance it is surprising that there are not any research recommendations specifically relating to this. The BPS believes that the development of self-management programmes (and psychological interventions) should follow the outline for the development of interventions recommended by the Medical Research Council (Craig et al, 2008a). The current research recommendations are premature in so far as they suggest that it is possible to progress straight to a trial phase, whereas there is clearly a need for research to further identify predictive relationships, develop theory, and address accessibility, usability, and feasibility. For example, it is crucial to first investigate determinants of good self-care or adherence using robust, longitudinal study designs before testing new interventions. *(cont'd/…)* There is significant evidence from other areas of behaviour change that self-management based on psychological theory produces larger effects, and consequently the development of both self-management and psychological interventions require careful development	

Type	Stakeholder	Order No	Docu ment	Page No	Line No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
						underpinned by psychological theory. *References:* Cameron, L.D. & Jago, L. (2008). Emotion Regulation Interventions: A common-sense model approach. *British Journal of Health Psychology*, *13*, 215-21. Craig, P., Dieppe, P., Macintyre, S., Michie, S., Nazareth, I., Petticrew, M. (2008a). Developing and Evaluating Complex Interventions: New guidance. London: Medical Research Council. Available from: www.mrc.ac.uk/Utilities/Documentrecord/index.htm?d=MRC004871. Accessed 21 June 2012. Craig, P., Dieppe, P., Macintyre, S., Michie, S., Nazareth, I., Petticrew, M. (2008b). Developing and Evaluating Complex Interventions: The new Medical Research Council guidance. *British Medical Journal*, *337*, *a1655.* McAndrew, L.M., Musumeci-Szabó, T.J., Mora, P.A., Vileikyte, L., Burns, E., Halm, E. A. *et al.* (2008). Using the Common Sense Model to Design Interventions for the Prevention and Management of Chronic Illness Threats: From description to process. *British Journal of Health Psychology*, *13*, 195–204. Michie, S., Fixsen, D.M., Grimshaw, J. &	

Type	Stakeholder	Order No	Document	Page No	Line No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
						Eccles, M.P. (2009). Specifying and Reporting Complex Behaviour Change Interventions: The need for a scientific method. *Implementation Science*, *4*,*40.* Thompson, A.R. (2009). Managing the Psychosocial Impact of Skin Conditions: Theory and the nursing role. *Dermatological Nursing*, *8*, 43-48. Wearden, A. & Peters, S. (2008). Therapeutic Techniques for Interventions Based on Leventhal's Common Sense Model. *British Journal of Health Psychology*, *13*, 189–193.	
SH	The British Psychological Society	18.3	Full	General		The BPS welcomes the recognition of the importance of good communication by health professionals. Within Section 1.8 "Aims of the Guideline" the authors write, "*Evidence indicates that a substantial proportion of people with psoriasis are currently dissatisfied with treatment*". This was identified in recent qualitative studies (Uhlenhake *et al*., 2010) and one in which patients identified dissatisfaction as a reason for opting out of care from their primary care practitioners (Nelson *et al*., under submission). This issue presents a potential challenge to the aim of maintaining good discussion and channels of communication, and recognition of this would be useful in the background to the	Thank you for your comment and the two references. In addition the background section (section 1.8) of the guideline includes discussion of the importance of good communication. The background aims to be brief and act as scene setting and hence cannot comprehensively cover all aspects and references in detail.

Type	Stakeholder	Order No	Docu ment	Page No	Line No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
						guideline. *References:* Nelson P, Chew-Graham, C., Griffiths, C.E.M., Cordingley, L. (under submission, June 2012, *British Journal of Dermatology*) Recognising distress in health care consultations: a qualitative study of people with psoriasis. Uhlenhake, E.E., Kurkowski, D. & Feldman, S.R. (2010). Conversations on Psoriasis - What Patients Want and What Physicians Can Provide: A qualitative look at patient and physician expectations. *Journal of Dermatological Treatment*, *21*, 6-12.	
SH	The British Psychological Society	18.30	Appen dix R	gene ral		Throughout the draft guideline, psychological distress is highlighted and is correctly identified as prevalent in this population. It was therefore surprising that this area did not become a major research recommendation. This is in contrast to other recommendations which focus on physical outcomes, including comorbid CVD. Given that the evidence for high levels of psychological distress is significant, especially when compared to CVD, this seems a significant oversight on the part of the GDG. To rectify this we recommend additional research recommendations to address this area. Research into a range of	Thank you. We did not directly review the evidence for psychological distress, management of psoriasis related distress, social anxiety or stepped care approaches. The GDG did not prioritise questions in these areas. As such we are unable to formulate a future search recommendation without a full and direct review of the literature to establish the research gap. In relation to your point about physical outcomes e.g. CVD we have deprioritised this as a key future research recommendation (but retained

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						psychological interventions is needed to manage psoriasis-related distress including social anxiety and depression at increasing levels of severity. A stepped approach should also be explored, from lower intensity interventions such as guided self-help up to more intensive complex psychological therapies for intervening with persistent/serious psychological distress (an area which has been particularly neglected – Thompson, 2009). Again, the BPS recommends that the development of such interventions should be theory driven and follow recognised recommendations for the development of interventions such as those laid down by the MRC (Craig *et al*., 2008b). *References:* Craig, P., Dieppe, P., Macintyre, S., Michie, S., Nazareth, I., Petticrew, M. (2008b). Developing and Evaluating Complex Interventions: The new Medical Research Council guidance*. British Medical Journal*, *337*, *a1655.* Thompson, A.R. (2009). Managing the Psychosocial Impact of Skin Conditions: Theory and the nursing role. *Dermatological Nursing*, *8*, 43-48.	it on the list of research recommendations).

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SH	The British Psychological Society	18.31	Appendix R	General		There is growing awareness of the relationship between stress and psoriasis severity, with some studies identifying stress as a trigger for psoriasis flares (Verhoeven, 2009). Whilst this is a good reason for exploring interventions such as arousal-reduction (see Point 22, above) there is also the need for basic psychophysiological research which investigates mechanisms that may account for this relationship. The field of psychoneuroimmunology is growing and the nature of psoriasis as an immune-mediated condition lends itself to further research in this area (e.g. Steptoe *et al*., 2007). In addition, given the increasing understanding of the relationships between exercise and inflammation (e.g. Hamer & Steptoe, 2009), this could provide further information on the potential of lifestyle factors to reduce psoriasis severity. *References:* Hamer, M. & Steptoe A. (2009). Prospective Study of Physical Fitness, Adiposity, and Inflammatory Markers in Healthy Middle-Aged Men and Women. *The American Journal of Clinical Nutrition*, *89(1)*, 85-89.	Thank you for your comment. However, this line of research was beyond the scope of the guideline and so we are not able to make any research recommendations.

Type	Stakeholder	Order No	Document	Page No	Line No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
						Steptoe, A., Hamer, M., Chida, Y. (2007). The Effects of Acute Psychological Stress on Circulating Inflammatory Factors in Humans: A review and meta-analysis. *Brain, Behavior & Immunity*, *21(7)*, 901-912. *(cont'd/…)* Verhoeven, E.W.M., Kraaimaat, F.W., de Jong E.M.G.J., Schalkwijk, J., van der Kerkhof, P.C.M. & Evers, A.W.M. (2009). Individual Differences in the Effect of Daily Stressors on Psoriasis: A prospective study. *British Journal of Dermatology*,*161(2)*,295-99.	
SH	The British Psychological Society	18.4	Full	General		The BPS welcomes the fact that psychological interventions, such as cognitive behaviour therapy (CBT), have been assessed by the guideline development group (GSG). However we believe that it is important to recognise the broader role that psychological interventions play in terms of patient benefit including support for improved medication, self-management and healthy lifestyles (see points 14-16 and 30-32) and therefore to broaden the scope of the evidence considered. We believe that further research is needed to underpin the development of	Thank you for your comment. Although we agree that CBT is an evidence based approach in other conditions, the evidence base in psoriasis is limited and there have been no replications of the Fortune et al studies. Therefore, the GDG made a future research recommendation around CBT and self management and cross referenced to the NICE guideline on depression in adults with a chronic physical health problem (CG91), which endorses the stepped care approach.

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						interventions to populate the following tiered approach to the provision of psychological care. The BPS recommends research into the following stepped care provision of appropriate psychological interventions for people with psoriasis (in line with the recommendation already in the report for stepped care for the physical symptoms): • The lowest level of psychological intervention to be offered to all would be regular assessment of well-being (as is identified by the guideline, page 48, line 10) plus provision of tailored resources on how to tackle common difficulties. • The next level would be interventions to support self-management (see points 30-31). • The highest level of psychological intervention (such as CBT) would be delivered 1:1 by a specialist as part of a multidisciplinary dermatology team. This model offers patients the full range of interventions as recommended by Thompson, 2012.	We are not able to make specific research recommendations in areas that have not been reviewed and so cannot directly recommend research into the stepped care provision of psychological interventions, although this is suggested in the criteria in Appendix R as an element to be considered in relation to this research, which has been categorised as high priority. Population level interventions are also beyond the scope of the guideline.

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						In addition, research into population level interventions to improve public understanding of psoriasis and reduce stigma towards those affected could also be beneficial, given the degree of stigmatisation experienced in social situations, including the workplace (Kimball *et al*., 2005). *References:* Kimball, A.B., Jacobson, C., Weiss, S., Vreeland, M.G. & Wu, Y. (2005). The Psychosocial Burden of Psoriasis. *American Journal of Clinical Dermatology*, *6(6)*, 383-92. *(cont'd/…)* Thompson, A.R. (2012). *Skin conditions.* In Cash, T.F (Ed.). *The Encyclopedia of Body Image and Human Appearance.* London, UK & San Diego, CA: Academic Press (Elsevier).	
SH	The British Psychological Society	18.5	Full	16	5	The draft guideline cites research indicating that psoriasis is associated with cardiovascular disease (CVD) (e.g. Gelfand *et al*., 2006). However, Stern (2010) argues that even if psoriasis is an independent risk factor for CVD risk, it is unlikely to be a clinically useful one. Psoriasis itself is unlikely to provide important prognostic information for the risk	Thank you for this additional general information. The paragraph that you refer to is general background information. In the link between evidence and recommendations in the full guideline, the risks and benefits of providing the cardiovascular disease risk assessment are discussed. The GDG did not assess the evidence for

Type	Stakeholder	Order No	Document	Page No	Line No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
						of CVD, compared with other traditional risk factors, many of which are more prevalent in psoriasis. Indeed, unhelpful lifestyle behaviours have also been shown to be more prevalent in psoriasis than in the general population, including excessive alcohol consumption (Poikolainen *et al.*, 1990) and smoking (Poikolainen *et al.*, 1994). There are also greater rates of obesity (Neimann *et al.*, 2006). Reasons for these increased risk factors are unclear but likely to be associated with psychological distress and/or unhelpful coping strategies. As well as being risk factors in themselves, these lifestyle factors increase the likelihood of flares. Thus further research into the links between distress and problematic coping responses for people with psoriasis is warranted. *References:* Gelfand, J.M., Neimann, A.L., Shin, D.B., Wang, X., Margolis, D.J. & Troxel, A.B. (2006). Risk of Myocardial Infarction in Patients with Psoriasis. *The Journal of the American Medical Association*, *296*, 1735-41. Neimann, A.L., Shin, D.B., Wang, X., Margolis, D.J., Troxel, A.B. & Gelfand, J.M. (2006). Prevalence of Cardiovascular Risk Factors in Patients with Psoriasis. *Journal*	the prognostic value of distress in predicting problematic lifestyle behaviours and so are unable to make a future research recommendation in this area.

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						of the American Academy of Dermatology, *55*, 829-35. Poikolainen, K., Reunala, T., Karvonen, J., Lauharanta, J. & Karkkainen, P. (1990). Alcohol Intake: A risk factor for psoriasis in young and middle aged men? *British Medical Journal*, *300*, 780-3. Poikolainen, K., Reunala, T. & Karvonen, J. (1994). Smoking, Alcohol and Life Events Related to Psoriasis Among Women. *British Journal of Dermatology*, *130*, 473-7. Stern, R.S. (2010). Psoriasis is Not a Useful Independent Risk Factor for Cardiovascular Disease. *Journal of Investigative Dermatology*, *130*, 917-919.	
SH	The British Psychological Society	18.6	Full	16	30	Although the methodological quality of many studies of adherence to medication in psoriasis limits the drawing of firm conclusions, there is research evidence to suggest that adherence may also be suboptimal in those using phototherapy (Evers *et al.*, 2010), oral therapy (Zaghloul & Goodfield, 2004) and biologic therapy (Bhosle *et al.*, 2006). Adherence difficulties are a significant problem in psoriasis management. However, there is clearly a strong need for further high quality research in this area before firm recommendations and conclusions about adherence in relation to treatment type can be drawn.	Thank you for your comment. We accept that adherence to therapy is a generic to all treatments (although some more so than others) and have deleted the phrase 'Adherence to topical therapy regimens may be the greatest barrier to effective disease control'

Type	Stakeholder	Order No	Document	Page No	Line No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
						References: Bhosle, M.J., Feldman, S.R., Camacho, F.T., Whitmire, J., Nahata, M.C. & Balkrishnan, R. (2006). Medication Adherence and Health Care Costs Associated with Biologics in Medicaid-Enrolled Patients with Psoriasis. *Journal of Dermatological Treatment*, *17*, 294-301. Evers, A.W., Kleinpenning, M.M., Smits, T., Boezeman, J., van de Kerkhof, P.C., Kraaimaat, F.W. & Gerritsen, M.J.(2010) Treatment Nonadherence and Long-Term Effects of Narrowband UV-B Therapy in Patients with Psoriasis. *Archive of Dermatology*, *146*, 198-9. Zaghloul S.S. & Goodfield, M.J.D. (2004). Objective Assessment of Compliance with Psoriasis Treatment. *Archives of Dermatology*, *140*, 408-14.	
SH	The British Psychological Society	18.7	Full	16	31	The statement in line 31 suggests that treatment factors such as cosmetic side-effects, adverse effects and practical aspects of application may have important implications for adherence. However, it is important to note that the majority of these factors have not been investigated systematically whilst controlling for other potential confounding factors, thus it is not yet possible to estimate accurately the	Thank you for your comment. We accept that adherence is not simply related to treatment factors, and have amended the text to address this in the general introduction as follows: "In common with many long term conditions, poor adherence to prescribed treatment can prevent optimal outcomes, and is influenced by multiple factors including those related

Type	Stakeholder	Order No	Document	Page No	Line No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
						independent contribution of each of these predictors. Two studies have examined psychological distress and adherence in psoriasis, both of which reported psychological distress to be associated with lower levels of adherence (Kulkarni *et al*., 2004; Renzi *et al*., 2002). This implies that effective self-care interventions should incorporate assessment and management of distress as a core component and, therefore, that they should be more than "educational programmes". This issue is further discussed under Points 31 and 32, below. *References:* Kulkarni, A.S., Balkrishnan, R., Camacho, F.T., Anderson, R.T. & Feldman, S.R. (2004). Medication and Health Care Service Utilization Related to Depressive Symptoms in Older Adults with Psoriasis. *Journal of Drugs in Dermatology*, *3*, 661-6. Renzi ,C., Picardi, A., Abeni, D. Agostini, E., Baliva, G., Pasquini, P. et al. (2002). Association of Dissatisfaction with Care and Psychiatric Morbidity with Poor Treatment Compliance. *Archives of Dermatology*, *138*, 337-42.	to the treatment itself (for example complex, cosmetically unacceptable topical regimens), quality of communication between clinician and patient, as well as beliefs and perceptions of the individual affected." Please also note the factors you highlight are further discussed in chapters about principles of care and cognitive behaviour therapy.
SH	The British	18.8	Full	18	45	The draft guideline reads, "*Good*	Thank you for this comment. The

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	Psychological Society					*communication between healthcare professionals and patients is essential*". Most people with psoriasis are treated in primary care. However, studies have indicated high levels of dissatisfaction with primary care consultations, citing: poor recognition of the levels of distress caused by the condition (Nelson *et al*., under submission); low levels of knowledge of general practitioners (GPs); and concerns about appropriate referral to secondary care services (Gillard & Finlay, 2005; Griffiths *et al*., 2006). These factors leads to significant numbers of people with psoriasis actively deciding not to consult primary care physicians (Beresford, 2002). Thus, consultation rates should not necessarily be viewed as an indicator of need as low rates of consultation may in fact illustrate high levels of dissatisfaction as opposed to low need for care. The BPS suggests that this background is acknowledged in the guideline as a context within which improved communication is recommended. There are also significant associated implications for the training of medical and nursing practitioners. *References:* Beresford, A. (2002). Psoriasis Association Members Questionnaire: Report prepared	paragraph that you refer to is general background information. We have tried to strike a balance between providing scene setting information and a detailed review of the relevant background literature. Whilst we acknowledge this point we feel that this is too much information for this section. Particularly in view of balancing other stakeholders comments on the length of the guideline.

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						by independent market researcher. Northampton, UK. *Psoriasis Association, 22.* Gillard, S.E. & Finlay, A.Y. (2005). Current Management of Psoriasis in the United Kingdom: Patterns of prescribing and resource use in primary care. *International Journal of Clinical Practice*, *59(11*), 1260-1267. Griffiths, C. E. M., Taylor, H., Collins, S.I., Hobson, J.E., Collier, P.A., Chalmers, R.J.G. et al. (2006). The Impact of Psoriasis Guidelines on Appropriateness of Referral from Primary to Secondary Care: A randomized controlled trial. *British Journal of Dermatology*, *155(2)*, 393-400. Nelson P, Chew-Graham C, Griffiths CEM, Cordingley L. *(under submission June 2012, British Journal of Dermatology)*. Recognising distress in health care consultations: a qualitative study of people with psoriasis.	
SH	The British Psychological Society	18.9	Full	20	7	There are several qualitative studies that have explored the experience of living with psoriasis and this section currently does not refer to any of this literature. Reference to this literature would be useful as it has the potential to inform clinicians of some of the nuances of the experience of living with the condition and therefore has both	Thank you. This section of the guideline was written by the patient members of the guideline development group and seeks to give a 'lived experience' view. We have edited this section of the guideline to include a short sentence to this effect.

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						educational and training benefits. For example, Wahl *et al*.(2002) describe the social vulnerability that can be associated with psoriasis. *(cont'd/…)* *<u>Reference:</u>* Wahl, A.K., Gjengedal, E. & Hanestad, B.R. (2002). The Bodily Suffering of Living with Severe Psoriasis: In-Depth Interviews with 22 Hospitalized Patients with Psoriasis. *Qualitative Health Research*, *12*, 250-261.	
SH	The Psoriasis Association	7.0	Full	General		**<u>The Principles of care</u>** The Psoriasis Association welcomes and supports the principles of care outlined in the Guidelines. We welcome in particular the recognition, founded on both clinical and research evidence and patient experience, that psoriasis and its treatment can be a physically, psychologically and socially challenging long term condition. We do have doubts however concerning the existence of a sound evidential basis for the suggestion that there are "consequent reduced levels of employment and income". Research is needed in this area. The character and extent of this Psoriasis morbidity is well documented. The symptoms are distressing and it is crucial to	Thank you for your comments. We have responded using the same subheadings as in your comments **<u>The Principles of Care</u>** Regarding the first point about the impact on employment, there are a number of studies which have evaluated surrogate indicators of the impact of psoriasis on employment and income which support the statement in the background introduction. Furthermore, there is also evidence from intervention studies that improvements in health-related quality of life that occur with effective treatment are associated with reduced impact on work productivity. The relationship between psoriasis and

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						understand the interplay between the physical manifestation of the disease and its visibility and obtrusiveness, and anticipated threat of social judgement, rejection, and stigmatisation. With reference to symptoms we note the passing reference to "chronic itch". This can be an important part of patient experience, and indeed there is also some research evidence that it is a highly relevant factor in patient assessment of disease severity/seriousness. But it is disappointing to find little or no attention to its management in the body of the Guidelines. We are also pleased to see the detailed attention given to the increased risk of potentially serious co-morbidities, notably among those affected by severe Psoriasis, and the essential need to address the issue. We are surprised and puzzled, given the assumption that emollients are "widely prescribed" (page 19), to find no reference to the relevance of their use in first line topical therapy, beyond passing mention in relation to Scalp Psoriasis. It is a widespread and much valued component of therapy, though GPs do not in fact universally recognise its value. It is nonetheless always prominent in the guidance on self-care given by specialist nurses. It is also a conventional adjunct to	employment and income is complex, and does not directly relate to objective measures of disease severity and we agree with this comment that it is an area that deserves further research. Relevant references in this area include 1. Schmitt JM, Ford DE. Work limitations and productivity loss are associated with health-related quality of life but not with clinical severity in patients with psoriasis. Dermatology 2006; 213:102-10. 2. Pearce DJ, Singh S, Balkrishnan R, Kulkarni A, Fleischer AB, Feldman SR. The negative impact of psoriasis on the work- place. J Dermatolog Treat 2006;17:24-8. 3. Fowler JF, Duh MS, Rovba L, Buteau S, Pinheiro L, Lobo F, et al. The impact of psoriasis on health care costs and patient work loss. J Am Acad Dermatol 2008;59:772-80. Regarding the management of itch, this was not prioritised as a key outcome to assess treatment efficacy, partly because it is rarely reported in the trials. Therefore, we cannot give any specific recommendations on which interventions might best address this important symptom. However, this underlines the already

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						ultra-violet therapy. We would be greatly disappointed if, on the basis of the assumption that they are widely prescribed, omission from the Guidelines were to lead to the withdrawal of NHS-funded provision for the prescription of emollients for use in the management of the condition. Patient experience confirms the evidence of the UK Audit that there are significant variations in management practice, in both primary and secondary care. We would emphasise that here is widespread disappointment and dissatisfaction among patients with the level of knowledge and understanding among General Practitioners. It is serious because most Psoriasis patients receive service in General Practice for most of the time, in some cases for a disease course lasting decades. Improvement in this area is long overdue. In any care setting the provision of specialist nurse support is limited, and access to psychological services even more so. This is again confirmed by the UK Audit data. **Patient-centred care** We welcome the principle that that treatment and care should be "culturally appropriate", but note that to date the research literature offers little evidence of direct relevance.	highlighted need to develop tools that properly evaluate the disease severity and impact, including patient-reported outcome measures, hence our research recommendation in this area. Additionally, the revised recommendations now include a specific enquiry on the patients assessment of their disease severity which we hope will also highlight when itch is a problem. We have also added some text to explain how itch impacts the patient experience of psoriasis in the introductory section in chapter 2. The Guideline Development Group (GDG) agrees that emollients are an accepted important component of treatment for psoriasis. However, the GDG was unable to cover every aspect of psoriasis management and had to prioritise areas where practice is variable or unsafe and where recommendations are likely to be informed by a robust evidence base. The GDG were aware that there is little or no formal evidence for emollients compared to no treatment. In defining the scope the GDG therefore opted to begin the topical pathway after emollients.

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						We note and applaud the reference to the specific needs of children and young people, and the importance of good management of the transition process. We would wish to see similar explicit consideration to be given to the potentially very difficult circumstances and needs of elderly Psoriasis patients or people with complex care needs, and the challenges faced by those caring for them. We are unhappy to find no specific attention given to the problem in the Guidelines. This no doubt reflects their almost complete absence from both clinical reports and the research literature (in the UK at least).This is a matter requiring urgent attention. **Key Priorities** We welcome the priorities laid out in the Guidelines **Topical therapy:** Regarding topical therapy, we note the reference to the need to support people in their medication use and the indication of the relevance of NICE Clinical Guideline 76: 'Medicines adherence' and welcome a review appointment at four weeks after starting a new topical treatment strategy to evaluate tolerability, toxicity and initial response to treatment (5.3.34). However, very little of the research evidence available relates to long term *topical* medication and	The GDG noted stakeholders concerns that without an explicit statement about emollients this component of management might be omitted. The NICE Guideline has therefore been amended to include the following wording: *The treatment pathway in this guideline begins with active topical therapies. The GDG acknowledged that the use of emollients in psoriasis was already widespread and hence the evidence review was limited to active topical therapies in psoriasis. Please refer to the BNF and cBNF for guidance on use of emollients'.* This wording has also been included within the algorithms for topical therapy. **Patient-centred Care** Regarding the elderly and those with complex care needs we have added text to relevant recommendations that, when appropriate, families and carers should be involved in treatment decisions, which we hope will capture their support needs. **Topical Therapy** We also agree about the clear need for more robust evidence on the long term

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						its use, and further attention should be given to its specific features in the management of Psoriasis. We are concerned to see the guidance to "choose a low cost preparation" when offering a corticosteroid, and would ask that the entirely understandable concern for "low cost" should be expressed alongside clinical judgement and patient preference founded on personal experience. The reference to low cost is repeated in relation to Scalp Psoriasis. We have noted (see above) the crucial importance emollients/moisturisers and their availability on NHS prescription. **Systemic therapy:** With reference to systemic therapies we are concerned for the care and access to appropriate treatments for those whose disease severity falls between BSA 3% and 10%. The Guidelines give examples of BSA >10% / PASI 10 before systemic non-biological therapies are considered, yet state those with "<3% BSA can be managed with topical therapies alone". **Assessment of disease severity and impact** We strongly welcome the suggestion that there must be better validated tools to aid in the assessment of severity and impact, and	use of topicals, which is why we have formulated future research recommendations in this area. Regarding the wording around choosing the lowest cost steroid, we have deleted this wording and highlighted the importance of patient preference and formulation **Systemic Therapy** Regarding the definitions of disease severity, the figures quoted relate to background information only and the GDG were careful not to stipulate 'absolute' boundaries for disease severity or impact in order to qualify or be considered for a particular intervention (above and beyond those for the biologics which are prespecified according to the relevant NICE technology appraisals). The GDG agreed that Body Surface Area (BSA)>10% should be given as an example of 'extensive' disease only. BSA >10% is only one indicator for consideration of systemic therapy and the GDG felt it important to emphasise right at the outset of the patient journey that those with extensive disease (for example BSA >10%) are likely to require additional treatment apart from

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						we would ourselves emphasise that patient experience and perspectives should be prominent in the relevant research. We have real doubts concerning the potential value of teledermatology and "remote monitoring" of disease activity, which can be founded on a simplistic and misleading assumption that "extensiveness" is the factor of overwhelming relevance in the assessment of severity. **General comments on (5) Guideline Summary:** **(5.1) Key priorities for implementation** **Assessment tool for disease severity and impact** Regrettably, the evidence of patient experience is that the level of knowledge and understanding of Psoriasis and the appreciation of its impact among General Practitioners is low. Given that their crucial role in making assessments as a basis for either primary care management/self-care or referral for dermatological specialist advice, it is crucial that attention is given to more and better training and support, and supervision by a specialist dermatologist. **Topical Therapy** See above: Currently, patient experience shows that non-specialist primary care practitioners are generally not adequately trained and competent in the use of topical	self administered topical therapy. However as per the recommendations within the systemic non-biological section of the guideline, systemic therapy would also be indicated in psoriasis that is localised and associated with significant functional impairment and/or high levels of distress (for example severe nail disease or involvement at high-impact sites) or in those for whom phototherapy has been ineffective, cannot be used or has resulted in rapid relapse. These instances are irrespective of BSA. Finally, whilst 3% is mentioned in the introduction, this figure is not mentioned anywhere in the recommendations. **Assessment of disease severity and impact** We agree with your views about teledermatology and have not recommended its use. **General Comments on (5) Guideline Summary** Regarding training and support for primary care the GDG is aware that the level of knowledge and understanding is low amongst some primary care practitioners. The NICE guideline implementation team are aware of this

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						therapies, nor capable of providing appropriate support for medicines use. The factors impacting on long term use of topical therapies are in any case poorly appreciated and understood. More and better research is needed, followed up by appropriate training and support. The Guidelines are silent on the recent introduction of so-called "patient support" programmes introduced by pharmaceutical companies designed in large part to enhance patient adherence and persistence with topical products, which can also involve a role for community pharmacists (who may in the process "lock in" patients to their own pharmacies). Pharmacists are not always fully appreciative of the issues surrounding the beliefs, preferences and behaviour of Psoriasis patients. Improvements in training in issues surrounding dermatological care, and support and supervision of their professional involvement in the management of the condition are essential. Pharmaceutical companies are moreover introducing *e-messaging* as a way of securing stricter patient adherence. The potential implications, both positive and negative, for patients and indeed the NHS should receive independent consideration. There is a need for independent research and monitoring of this growing feature,	gap in knowledge, and will be developing various educational/learning tools. Also the quality standard, which will be developed after guideline publication, should help to highlight gaps in care so that appropriate provision of necessary training and support can be further targeted. **<u>Topical Therapy</u>** Regarding patient support programmes, we performed a systematic review to look for evidence for the effectiveness of interventions aimed at improving treatment outcomes with therapy by improving self- management support but unfortunately the evidence base was very limited. Thank you for your additional comments around patient support programmes. However, we do not feel this would be appropriate for inclusion into the introduction, which is a necessarily brief scene setting section only. Although the GDG were aware of a number of commercially available programmes, discussion of these is beyond the remit of the introduction, which must not pre-empt the evidence. The GDG agree that the programmes you quoted are important and due to the paucity of evidence in this area a future research recommendation for self

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						especially if it is to be a widely used component of self-care within a framework for non-specialist community management of Psoriasis. (The NICE Clinical Guideline 76 gives no recognition to these developments.) **(5.2) Full list of recommendations** (5.2.1 and 5.2.4) With reference to assessment, support and information tailored to individual needs and circumstances, see the comments above about the need for greatly improved training for primary care practitioners. Declaring an interest, The Psoriasis Association would draw attention to its own potential for contributing to the provision of both information and support for patients and all concerned in Psoriasis care, noting that we have been awarded the Information Standard Certificate (i.e. certified membership) confirming the trustworthiness, accuracy and reliability of what we offer. It is not clear where a "single point of contact" (5.2.4) to offer information advice about the condition and services would be located. We would wish "age-appropriate" questions about impact on both patients and carers to be directed not only towards children and young people (5.2.10 and 5.2.16), but also towards elderly patients. Assessment tools	management has been designated as high priority. Please see appendix R for more details. **Full list of recommendations** Regarding information provision and support the guideline is not able to endorse specific organisations without reviewing the evidence. The Understanding NICE guidance (UNG) does however make some reference to support available. Regarding the single point of contact, we are not able to specify who should deliver care, but focus on what the standard of care should be. As a general principle, NICE clinical guidelines give information on what should be provided rather than by whom. We know this may be challenging to deliver, but it is emphasised by patients and in other Department of Health guidance on long term conditions as being critical to providing high quality care and support to patients. We agree that the elderly should be considered for additional support with topical therapy and have amended the relevant recommendation to clarify that

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						must be sensitive to the circumstances and needs of the latter, and currently they are less than satisfactory in that respect. (5.2.33) should also include specific reference to elderly patients, including those who are dependent on others for therapeutic care and support. With reference to practical support (5.2.26) see the reference above to the training and competence of health care professionals, and to adherence support. (5.2.32) Emollients and moisturisers are well recognised, widely used components of continuing care. They are essential to the wellbeing of huge numbers of patients, perhaps the vast majority of long-term patients engaged in self-care supported by GP management. The Guidelines ought in our view to be explicit in this respect. It would represent a significant problem if these invaluable products were to be no longer prescribed as integral to NHS Psoriasis care.	people of all ages should be offered advice and practical support. The recommendation about assessment tools already state that age should be taken in to account.
SH	Therapy & Guidelines sub-committee, British Association of Dermatologists	28.0	Full	General		The T& G committee generally felt this was a very thorough, well thought out and well written guideline, however, the main overall comment was that the extreme length of the guideline makes it unworkable. It is suggested that a much shorter summary version be made available, as otherwise we had concerns about whether it could ever	Thank you for your comments. We appreciate the guideline is long but it is a complex area with many different stages to the assessment and treatment process. We have had to balance your comment against other stakeholder comments requesting more information be added. There is a separate NICE

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						practically be used. There were also comments about frequent typos and the need for proofreading. Some judicious editing might help, as the tone especially in the introductory sections is conversational and this adds more length. Some of the sections, e.g. the very detailed methodology/statistics, might be better served in the final version as an appendix.	guideline which summarises the recommendations and NICE will also develop an 'Understanding NICE guidance' document, which is a patient version of the guideline. The full guideline has been written so that healthcare professionals with particular interest in one of the areas covered can immediately identify the evidence that has been reviewed and the justification for the recommendation developed. The methodology is integral to the guideline development and as such it is important that it resides within the main document. We hope we have now corrected the formatting and typing errors you have identified.
SH	Therapy & Guidelines sub-committee, British Association of Dermatologists	28.1	Full	81-203		110 steps in the pathway of a patient with psoriasis are a lot to expect for any health professional managing this condition.	Thank you for your comment, we appreciate that there are a lot of steps but it is a complex area. It is not expected that every patient will go through each of the steps. We have tried to clarify and simplify these steps in the algorithm which can be printed out as a reference guide.
SH	Therapy & Guidelines sub-committee, British Association of Dermatologists	28.10	full	440		The word "at" is missing from the 6th line at the bottom of the page beginning "patients".	Thank you, we have made this change.

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SH	Therapy & Guidelines sub-committee, British Association of Dermatologists	28.11	full	558-631		This section is well written and there are no specific comments other than the content reflects what most dermatologists know and already do with their psoriasis patients treated with methotrexate.	Thank you for your comment.
SH	Therapy & Guidelines sub-committee, British Association of Dermatologists	28.12	full	632-682		There was an element of repetition regarding the mention of insufficient evidence and poor quality studies, however, the conclusion that it is cost effective to try a second biologic treatment when patients have failed on a first one was fair.	Thank you for your comment. The references to evidence quality and quantity are consistent with the evaluation and commentary throughout the guideline and reflect the discussions by the GDG. We do not believe there is any unnecessary repetition. We have followed the NICE ascribed process and methodology.
SH	Therapy & Guidelines sub-committee, British Association of Dermatologists	28.2	Full	204-357		Comments were that there is far too much emphasis on the use of topical corticosteroids. Opinions differ around the country over this matter and that there are already many caveats in the document over their use, but, the use of very potent topical corticosteroids is contraindicated in the management of chronic plaque psoriasis. Reliance on topical corticosteroids as sole therapy, except perhaps in flexures, should be greatly discouraged. Further comments were that the basis of managing any patient with psoriasis is to identify the specific problems that patient has in the context of any compounding factors and arriving at a joint decision on the best way forward. The didactic way of	Thank you. We have fully complied with the scope and these are evidence based guidelines. The GDG debated at length the benefit and risk profile of topical steroids based on a thorough review of the clinical and economic evidence and their extensive clinical experience before arriving at the recommendations. There was felt to be good evidence of efficacy, although, as discussed in the linking evidence to recommendations table, the data available were largely short term for both efficacy and safety. The evidence also suggested that non-

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						recommending treatments both topical and systemic in one particular order in these guidelines is not necessarily compatible with the needs of individuals. A better approach would be to highlight the pros and cons of each treatment and recommend that the clinician arrives at a joint decision with the patient as to the best way forward. For instance, in some patient it may be more appropriate to start with a tar or dithranol preparation rather than a topical steroid/vitamin D analogue. Likewise, depending on the individual patient and the distribution of disease, acitretin may be a more appropriate first-line systemic therapy than methotrexate. It would be difficult to state the "correct order" of treatments for the population of psoriasis patients as a whole – it has to be bespoke and the guidelines should emphasise this.	steroid based treatments (e.g tazarotene, coal tar and vitamin D analogues) were ineffective in comparison to corticosteroids. The recommendations regarding treatment pathways represent the best approach for the majority of patients based on the available evidence, which the GDG believe will be more helpful and appropriate than suggesting that every treatment option may be considered in any order. We agree that patient evaluation is a complex process. The guidelines aim to provide an evidence based pathway of care, which is a requirement of the scope. Additionally, the guideline covers all psoriasis, in all healthcare settings and the topical section is aimed predominately at those in primary care, who would benefit from clear guidance. We agree that clinicians and patients should arrive at mutually agreeable joint decisions and believe that this is adequately supported by the recommendations in the principles of care section.

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SH	Therapy & Guidelines sub-committee, British Association of Dermatologists	28.3	Full	204		Irritation rather than burning.	Thank you. We have edited the wording. .
SH	Therapy & Guidelines sub-committee, British Association of Dermatologists	28.4	full	273		Dithranol studies include only short contact dithranol, not treatment regimes, e.g. Ingrams using dithranol for a longer contact time.	Thank you. Although monotherapy with dithranol in this chapter was not limited to short-contact use no other data were available. We specifically looked for data regarding Ingram's regimen in section 9.5 (Dithranol, coal tar and vitamin D or vitamin D analogues combined with UVB.
SH	Therapy & Guidelines sub-committee, British Association of Dermatologists	28.5	full	292		Agree with these concerns as studies have a short-term (e.g. 4 weeks duration) to look at adverse reactions of skin atrophy etc., and this may take years to occur but if potent topical steroids are proposed as first-line treatment, this may become a significant problem.	Thank you for your comment.
SH	Therapy & Guidelines sub-committee, British Association of Dermatologists	28.6	full	343		Grammar; unacceptability of coal tar.	Thank you, we have made this change.
SH	Therapy & Guidelines sub-committee, British Association of Dermatologists	28.7	full	357		This may be the correct conclusion from published studies but does not individualise treatment for patients, e.g. in a patient with thick scale, a de-scaling agent should be used from the start. This does not come out in studies where the 'standard' patient is	These are evidence based guidelines. Evaluation of any patient is a complex process but the guidelines aim to provide a pathway of care, which is a requirement of our scope.

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						used.	The GDG also believe that providing a pathway is helpful and appropriate, particularly for primary care physicians who will largely be responsible for administering topical treatments. However, we agree that clinicians should arrive at a joint decision with the patient and believe that this is adequately supported by the recommendation included in the principles of care section. Regarding your example of descalers for more severe scalp psoriasis, the recommendation was based on the evidence which showed that potent steroids were effective treatments even when descalers were not used, as they were not included in the study protocols of the trials reviewed. The evidence reviewed included trials involving patients with more severe scalp psoriasis where one would expect some of the patients to have adherent scale. Therefore, the recommendation was based on the effect size of monotherapy with potent steroid without descalers with the comparison intervention.
SH	Therapy & Guidelines sub-committee, British	28.8	full	367-481		Comments were that this is a reasonable section except that the suggestion that	Thank you for your comment.

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	Association of Dermatologists					PUVA should not be tried on patients who fail with narrow-band UVB except in exceptional cases. With appropriate discussion with the patient PUVA is often tried as a next step. There is confusion in these recommendations between the number of treatments and the cumulative UV dose. It is now normally the number of treatments that is taken into account although both are recorded. The cumulative UVA dose depends on skin type/MPD testing. Twenty years ago recommended PUVA maximums were based on cumulative UVA dose but now numbers of treatments/exposures are used. Might be worth consulting the British Photodermatology Group on this. There are some papers in the literature comparing bath PUVA vs. oral PUVA (Collins P et al., BJD 1992; volume 127: 392-395) even if not the desired quality of evidence may be worth reviewing. We contend the mentioning of specific costs in relation to removing BCC and SCC in primary care, as these are likely to be inaccurate. SCC should not knowingly be removed in primary care according to NICE guidelines.	The recommendations for PUVA in the treatment of psoriasis were informed by a comprehensive review of the evidence on efficacy and safety. The recommendations do indicate that PUVA may be tried in people after appropriate discussion, and consideration of other options. The GDG do not believe that this is overly restrictive based on the evidence reviewed. Regarding the inconsistent terminology we have now corrected the text in the linking evidence to recommendations table to refer to the number of treatments in accordance with your comment. The recommendations are also consistent regarding reference to number of exposures rather than dose and the GDG have recommended that the total number of UV exposures should be documented. Regarding the evidence for bath vs oral PUVA, this comparison was not prioritised for inclusion in the review protocol and so the evidence was not considered by the GDG.

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						Is the stated relative risk of relapse with PUVA vs. narrow-band UVB correct at 1.55? Surely the RR should be less than 1, as relapse is less likely with PUVA than narrow-band UVB – has this been accidentally reversed? Lindelof and Goeckermann are spelt in a variable way in the text.	You are correct that the NICE guidance is explicit that SCC should not be removed in primary care. All suspect skin cancers (ie BCC and SCC) are referred for secondary care review. We have made changes to the guideline to clarify that this is done as an outpatient procedure. Regarding the relative risk of relapse, as this is a negative outcome a relative risk >1 implies that the control group (PUVA) is favoured so the relative risk is correct. Thank you for indentifying the typing errors. We have ensured accuracy in spelling these terms throughout the document.
SH	Therapy & Guidelines sub-committee, British Association of Dermatologists	28.9	full	406		The word "and" is missing from the first complete sentence after pigmentosum.	Thank you, we have made this change.
SH	United Kingdom Clinical Pharmacy Association (UKCPA)	16.0	Full	47	7	The term 'safe monitoring' is difficult to interpret. I presume it means 'monitoring for safety'. As it is in the context of minimising the risks of side effects I wonder if it would be better to say 'appropriate monitoring for safety'?	Thank you, we agree and have changed the wording to read 'monitoring for safety'.
SH	United Kingdom Clinical Pharmacy	16.1	Full	47	41	It seems a pity not to include the patient's assessment of overall severity too. This	Thank you. The GDG agreed with your comment and a bullet point has been

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	Association (UKCPA)					would provide valuable information and is another way of ensuring that the patient is genuinely involved in his/her management.	added to indicate that the patient assessment of severity should also be recorded.
SH	United Kingdom Clinical Pharmacy Association (UKCPA)	16.2	Full	48	12-15	This section seems rather weak – especially line 15 which is a closed question inviting a yes/no answer. Would it be possible to recommend the use of visual analogue scale to assess the overall impact of psoriasis on physical, psychological and social wellbeing? This would have the advantage of providing a way of tracking impact over time, monitoring the impact of interventions etc.	Thank you for your comment. This recommendation is representative of the evidence found. The GDG didn't find any evidence to assess the validity of the visual analogue scale to assess impact and so were unable to recommend its use. We have included in our research recommendations that there is a need to develop these tools. The GDG felt it was important to use simple questions for ease of use in primary care, where the GDG were aware that this aspect of assessment was not always even considered. Although we accept the shortfalls of the DLQI we have suggested it is used to track the response to second and third line treatment. The GDG were aware that formal tools in primary care weren't always practical.
SH	United Kingdom Clinical Pharmacy Association (UKCPA)	16.3	Full	50	7	Could we add 'of appropriate potency' at the end of the line to avoid confusion?	Thank you for your comment. We have reworded the recommendation to avoid misinterpretation.
SH	United Kingdom Clinical Pharmacy Association (UKCPA)	16.4	Full	50	38	I see from the cost-effectiveness analysis (Appx M) that the combination product (calcipotriol/betamethasone) is the most clinically effective option but not the most cost-effective because it would cost an additional £192 per year. This seems a	Thank you for your comment. We do not agree that it is a small cost, particularly when multiplied across the entire population receiving topical therapies for the treatment of their psoriasis. Costs to the patient are not

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						small cost for the convenience of once-daily treatment with a single product. The additional prescription costs (to the patient) of using two products should also be taken into account here. It is unfortunate that the guideline as written does not allow prescribing of the combination product for several weeks (could be up to 24 weeks). It might be better to offer it as an option at the outset.	included in analyses for NICE because an NHS and Personal Social Costs (PSS) costing perspective is used.
SH	United Kingdom Clinical Pharmacy Association (UKCPA)	16.5	Full	50	38	There is no mention of the role of emollients in psoriasis management at all. Although there is no trial evidence of effectiveness as far as I am aware, expert opinion favours their use to help to control itching and scaling and to improve appearance and reduce cracking. Could some acknowledgment of this role be made?	Thank you for your comment. The Guideline Development Group (GDG) agree that emollients are an accepted important component of treatment for psoriasis. However, the GDG was unable to cover every aspect of psoriasis management and had to prioritise areas where practice is variable or unsafe and where recommendations are likely to be informed by a robust evidence base. The GDG were aware that there is little or no formal evidence for emollients compared to no treatment. In defining the scope the GDG therefore opted to begin the topical pathway after emollients. Without reviewing the evidence we are unable to formulate a specific recommendation. However, the GDG noted stakeholders concerns that without an explicit statement about emollients this

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							component of management might be omitted. The NICE Guideline has therefore been amended to include the following wording: *The treatment pathway in this guideline begins with active topical therapies. The GDG acknowledged that the use of emollients in psoriasis was already widespread and hence the evidence review was limited to active topical therapies in psoriasis. Please refer to the BNF and the cBNF for guidance on use of emollients'.* This wording has also been included within the algorithms for topical therapy.
SH	United Kingdom Clinical Pharmacy Association (UKCPA)	16.6	Full	51	32	It might be better to offer the topical agents to soften and loosen scale at the beginning rather that waiting 4 weeks for treatment to fail	Thank you**.** The recommendation was based on the evidence which showed that potent steroids were effective treatments even when descalers were not used, as they were not included in the study protocols of the trials reviewed. The evidence reviewed included trials involving patients with more severe scalp psoriasis where one would expect some of the patients to have adherent scale. Therefore, the recommendation was based on the effect size of monotherapy with potent steroid without descalers with the comparison intervention.

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							Additionally, when developing the recommendation, the GDG aimed to balance simplicity and adherence.
SH	United Kingdom Clinical Pharmacy Association (UKCPA)	16.7	Full	51	37	It is not clear whether this is intended instead of the topical steroid treatment or in addition to it	Thank you, we have amended the wording of the recommendation. Please also refer to the algorithms to clarify the treatment pathway.
SH	United Kingdom Clinical Pharmacy Association (UKCPA)	16.8	Full	52	9	This appears to be inconsistent with line 37, p51	Thank you, we agree that more detail is required to ensure consistency. Therefore, we have added some qualifying text to the recommendation.
SH	United Kingdom Clinical Pharmacy Association (UKCPA)	16.9	Full	54	35	The only risk of methotrexate treatment mentioned is liver fibrosis but there is no mention of the risk of bone marrow suppression or pulmonary fibrosis or the measure that patients need to take to monitor for these conditions – this would be helpful. Also- the risks associated with once weekly (vs daily) treatment should be mentioned even if only by reference to the NPSA guidance	Thank you for your comment. The GDG were aware that all systemic treatments carry a risk for a range of adverse events and included recommendations to take account of this. There was insufficient evidence from the review of systemic therapies to make any specific recommendations except for liver fibrosis with methotrexate, although long term data were sought for a range of toxicities for all of the non-biological systemic drugs reviewed. However, to remove the unintended implication that liver fibrosis is the main problem associated with methotrexate or that other systemic agents have preferable side effect profiles, the recommendation regarding risk of liver

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							damage has been moved to the section on methotrexate monitoring and toxicity, where the evidence for this side effect was examined in more detail.

These organisations were approached but did not respond:

Alder Hey Children's NHS Foundation Trust
Alliance Pharmaceuticals
Amgen UK
Arthritis and Musculoskeletal Alliance
Association of Anaesthetists of Great Britain and Ireland
Autistic Rights Movement UK, The
Bard Limited
Barnsley Hospital NHS Foundation Trust
Bradford District Care Trust

British Association of Skin Camouflage

British Dietetic Association
British Medical Association
British Medical Journal
British National Formulary

British Society for Immunology
Cambridge University Hospitals NHS Foundation Trust
Camden Link
Capsulation PPS

Care Quality Commission (CQC)
Central & North West London NHS Foundation Trust
Central London Community Healthcare
Changing Faces
Cochrane Skin Group
Coeliac UK
Department for Communities and Local Government

Department of Health, Social Services and Public Safety - Northern Ireland

Dorset Primary Care Trust
East and North Hertfordshire NHS Trust
Epsom & St Helier University Hospitals NHS Trust
Faculty of Occupational Medicine
Faculty of Sport and Exercise Medicine
Forest Laboratories UK Ltd
Galderma
George Eliot Hospital NHS Trust
Gloucestershire Hospitals NHS Foundation Trust
Gloucestershire LINk
Great Western Hospitals NHS Foundation Trust
Guy's and St Thomas' NHS Foundation Trust

H & R Healthcare Limited
Hammersmith and Fulham Primary Care Trust
Healing Honey International Ltd
Health Protection Agency
Health Quality Improvement Partnership
Healthcare Improvement Scotland
Hermal

Hindu Council UK
Independent Healthcare Advisory Services

Lambeth Community Health
Lancashire Care NHS Foundation Trust
Leeds Community Healthcare NHS Trust
Leeds Primary Care Trust (aka NHS Leeds)

Liverpool Community Health
Liverpool Primary Care Trust
Luton and Dunstable Hospital NHS Trust

Medicines and Healthcare products Regulatory Agency
Medway Community Centre
Ministry of Defence
National Clinical Guideline Centre
National Collaborating Centre for Cancer
National Collaborating Centre for Mental Health
National Collaborating Centre for Women's and Children's Health
National Institute for Health Research Health Technology Assessment Programme
National Patient Safety Agency
National Public Health Service for Wales
National Treatment Agency for Substance Misuse
NHS Bournemouth and Poole
NHS Clinical Knowledge Summaries
NHS Connecting for Health

NHS Nottinghamshire County
NHS Plus
NHS Sheffield

NHS Warwickshire Primary Care Trust
North Lancashire PCT

PERIGON Healthcare Ltd

Pharmametrics GmbH

Psoriasis Help Organisation
Public Health Wales NHS Trust
RioMed Ltd.
Roche Products
Royal Berkshire NHS Foundation Trust
Royal College of Anaesthetists
Royal College of General Practitioners
Royal College of General Practitioners in Wales
Royal College of Midwives

Royal College of Obstetricians and Gynaecologists
Royal College of Paediatrics and Child Health
Royal College of Paediatrics and Child Health , Gastroenetrology, Hepatology and Nutrition
Royal College of Pathologists
Royal College of Physicians
Royal College of Psychiatrists
Royal College of Radiologists
Royal College of Surgeons of England
Royal National Institute of Blind People
Royal Pharmaceutical Society
Royal Society of Medicine
Sandoz Ltd
Schering-Plough Ltd
Scottish Intercollegiate Guidelines Network

Sheffield Teaching Hospitals NHS Foundation Trust

SNDRi
Social Care Institute for Excellence
Social Exclusion Task Force
Society of Chiropodists & Podiatrists
Solent Healthcare
Solvay
South Asian Health Foundation
South Tees Hospitals NHS Trust
South West Yorkshire Partnership NHS Foundation Trust
Spectranetics Corporation
Stiefel Laboratories
Substance Misuse Management in General Practice
The Rotherham NHS Foundation Trust
The Whittington Hospital NHS Trust

University Hospital Birmingham NHS Foundation Trust
University of Bristol

Warwickshire County Council

Welsh Government
Welsh Scientific Advisory Committee
West Midlands Ambulance Service NHS Trust
Western Cheshire Primary Care Trust
Western Health and Social Care Trust
Westminster Local Involvement Network
Wirral University Teaching Hospital NHS Foundation Trust
York Hospitals NHS Foundation Trust

Please note the references below for the medac submission

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