National Institute for Health and Clinical Excellence

Comment 1: the draft scope

Section	Consultees	Comments	Action
Background information	British society of dermatologists	1) After "PUVA" add narrowband UVB (TLO1) phototherapy 2) Add "blood" before "monitoring" 3) Add "Quality of life studies in psoriasis reveal a negative impact on patients comparable with that seen in cancer, arthritis and heart disease" (taken from British Association of Dermatology Biologics guideline) Page 1 second line upper rather than top layer of skin is better 3rd line - progressive is not appropriate as not all cases progress. Chronic persistent severe condition is better. 3rd line unpredicatable preferred to erratic Page 2 3rd line add TL01 UVB phototherapy to second/3rd line treatments	Scope revised accordingly
	Serono Ltd	Fine	No action required
	Centre of evidence-based dermatology	Nil (comments from Prof Hywel Williams)	No action required
The technology/ intervention	British society of dermatologists, Centre of evidence-based dermatology	Yes	No action required
	Serono Ltd	Yes	No action required
Population	British society of dermatologists	yes, second question no	No action required

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	Centre of evidence-based dermatology	No - if you reallly restrict the population to "People with moderate to severe plaque psoriasis who have not responded to, or are intolerant to other systemic therapy including ciclosporin, methotrexate or PUVA or whom these treatments are contraindicated. ", then you will have virtually no patients from RCT data. I realise that this is the population group you may wish to resitrict infliximab to if it is approved, but very few of the trials (mostly placebo controlled) have included or adequately documented treatment resistant or intolerant patients. I would suggest it would be wiser to keep things a bit more open at this stage and look at all severe psoriasis patients (defining sever on the basis that they need systemic therapy), and then you can do sensitivity analyses to see if the effect are different for those who failed on other treatments.	This is based on the marketing authorisation
	Serono Ltd	Yes	No action required
Comparators	British society of dermatologists	Add: methotrexate; cyclosporin; PUVA/TLO1 phototherapy; acitretin; hydroxycarbamide to standard treatments. No single agent could be identified as best alternative care Consider adding adalimumab as comparator as this is expected to become licensed for psoriasis.	Covered by standard treatments without a TNF inhibitor or have been excluded by the marketing authorisation
	Centre of evidence-based dermatology	Not yet, and although recent guidance has approved etanercept lowe dose, supply is still very inequitable. I would suggest that methotrexate and phototherapy or cicosporin should also be used as standard comparators	Covered by standard treatments without a TNF inhibitor or have been excluded by the marketing authorisation
	Wyeth	Given the requirement to have not responded to, or be intolerent to standard systemic therapy in order to receive infliximab, the standard treatment without a TNF inhibitor or efalizumab is presumably best supportive care.	Included in standard care without TNF inhibitors
	Schering Plough	We note that alefacept is not included as a standard comparator and concur that this is appropriate since it does not have a UK license for psoriasis or any other therapeutic indication as far as we are aware. The comparators mentioned (standard care without TNF-inhibitor / efaluzimab, etanercept, afaluzimab) are appropriate.	No action required

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	Serono Ltd	Query standard treatments without anti-tnf-inhibitor or efalizumab as infliximab is to be used after these other therapies, ie where they do not work, so why compare to them? Also, what are the trials being put forward in terms of population groups-do they reflect eligibility criteria?	Standard care includes best supportive care
Outcomes	British society of dermatologists	Also should consider potential benefits for patients with psoriatic arthritis as well.	The institute has already issued guidance on infliximab for psoriatic arthritis TA104
	Centre of evidence-based dermatology	OK	No action required
	Wyeth	The Psoriasis Area and Severity Index (PASI) and the Dermatology Life Quality Index (DLQI) are respectively the appropriate measures of severity and quality of life as defined in the recent MTA (TA 103)	NICE does not usually specify a measurement scale.
	Schering Plough	Rather than 'severity of psoriasis', a more specific outcome measure might be mentioned such as treatment response, e.g. proportion of patients achieving a reduction in Psoriasis Area Severity Index of 75 per cent (i.e. PASI 75).	NICE does not usually specify a measurement scale.
	Serono Ltd	1) Assuming PASI 75 or 50 here? 2) Long term efficacy is important in a chronic condition such as psoriasis as efficacy which decreases over time is not acceptable. Short term studies would not suffice. Whilst Infliximab shows good short term efficacy, The Lancet study in 2005 showed Infliximab decreasing in efficacy out to one year 3) Relapse rates-will these be considered within the context of efficacy? 4) Long term safety in long term disease control of psoriasis is imperative. There are growing concerns associated with anti-tnf's as a class. Any safety data needs to be in Psoriasis patients not historical RA patients as these patients have different histologies Bongartz et al, JAMA May 17 2006, Vol 295, No 19, 2275-2285 discusses long term safety of anti tnf's in detail. Also, Scheinfeld et al 2004 and Listing et al 2004 5) DLQI as an outcome needs to be long term also	1 and 5 - NICE does not usually specify a measurement scale. 3 – Scope revised accordingly 2 and 4 – Comments noted

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Economic analysis	Centre of evidence-based dermatology	OK	No action required
	Wyeth	Reference should be made to the previous economic analysis of infliximab in the treatment of psoriasis, performed by the York Technology Assessment Group (Section 6.3.5 of the TA 103 Assessment Report and associated economic addendum)	This is the responsibility of the manufacturer when preparing their submission.
	British society of dermatologists	None	No action required
	Serono Ltd	Holistic costs incurred need to be assessed, clinic time, infusion time, healthcare profressional time, VAT ie all costs not just product Also, co prescribing of other medications eg methotrexate need to be considered Economic analysis needs to be coupled with outcomes analyisis and the long term data presented-these two cannot be seen in isolation or on different parameters To capture the chronic nature of the disease we would recommend a time horizon using the available 1 year data, coupled with all costs associated with rescue therapy for failing patients including in-patient care.	Comments noted please see reference case
Other considerations	British society of dermatologists	TA 104 infliximab for psoriatic arthritis is also relevant as comparator	This is outside the remit
	Centre of evidence-based dermatology	One thing that you could also consider when comparing these systemic treatments, is the spread of responses eg two treatments might have the same mean treatment effect across groups of patients, but one might have a bigger spread of dramatic responses than the other. This is my hunch with infliximab - some do incredibly well and hit the newspapers as "cured", and you could explore this by comparing the spread of treatment responses in the raw data. This is of practical significance - if indeed one treatment has the potential for spectacular results in a group of patients even though on average it is not much better than methotrexate, then that might be good news for patients, and certainly could increase patient choice.	Should be captured in existing health outcomes.

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	Serono Ltd	Class approaches to drug use is important-why go from one failing anti-tnf to another anti-tnf vs a change in class approach-it would not seem logical or indeed to be a good strategy for the benefit of patients Infusion clinics incur acute sector costs and management and the recognition of infliximab being used solely in the acute sector needs to be understood-as per license and against NHS White Paper of Jan 2006 pushing dermatology out to Primary Care	Where the evidence allows, sequencing of different drugs and the place of leflunomide in such a sequence should be considered. Costs will be considered from an NHS perspective and PSS
Questions for consultation	Centre of evidence-based dermatology	Already covered	No action required
	Wyeth	It is unclear how the resultant guidance from this STA will be placed in context with existing MTA guidance (TA 103).	Guidance on the MTA will be considered for review in July 2008
	Serono Ltd	Any decisions on sequencing the available products needs to be wholly transparent via available data In terms of overall quality of life, the 2 hour infusion and 2 hour observation themselves adversely affect quality of life	Where the evidence allows, sequencing of different drugs and the place of leflunomide in such a sequence should be considered. Should be captured by health related quality of life data
Additional comments on the draft scope.	Schering Plough	We note that the comprehensive scoping exercise for STAs as set out in the Institute's guidance document for the STA process has not been followed for this appraisal. This is of concern since there has therefore been no proper consultation on the appropriateness of the STA process for this appraisal, in contrast to other ongoing consultations for appraisals in the 13th wave.	This appraisal was referred as part if the 8th wave and the scoping process has followed the hybrid procedure

Comment 4: Regulatory issues

Section	Consultees	Comments	Action

Section	Consultees	Comments	Action
Remit			
Current or proposed marketing authorisation			

The following consultees/commentators indicated that they had no comments on the draft remit and/or the draft scope

DoH
Novartis Pharmaceuticals UK limited