NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Infliximab for the treatment of adults with psoriasis

Premeeting briefing

This briefing presents major issues arising from the manufacturer's submission (MS), Evidence Review Group (ERG) report and statements made by consultees and their nominated clinical specialists and patient experts. Please note that although condensed summary information is included for ease of reference, this briefing should be read in conjunction with the full supporting documents.

The manufacturer was asked to provide clarification on the search strategies used, the clinical and cost effectiveness data and the indirect treatment comparison.

Abbreviations

BSA	Body surface area	PASI	Psoriasis area and severity index
BNF	'British national formulary'	PGA	Physician's global assessment
CI	Confidence interval	PUVA	Psoralen and long-wave ultraviolet radiation
DLQI	Dermatology life quality index	QALY	Quality-adjusted life year
EQ-5D	Euro quality of life questionnaire	RR	Relative risk
ERG	Evidence Review Group	SF-36	Short form (version 36)
HRG	Healthcare Resource Group	SF-6D	Short form six dimensions
ICER	Incremental cost-effectiveness ratio	SHTAC	Southampton Health Technology Assessment Centre
		TA	Technology appraisal
NAPSI	Nail psoriasis severity index		

Licensed indication

Infliximab (Remicade, Schering-Plough) is indicated for the treatment of moderate to severe plaque psoriasis in adults who failed to respond to, or who have a contraindication to, or are intolerant to other systemic therapy including ciclosporin, methotrexate or psoralen and long-wave ultraviolet radiation (PUVA).

Key issues for consideration

- What are the implications of the concerns raised over the indirect comparison of infliximab with etanercept and efalizumab via the common comparator of placebo?
- When comparing infliximab with etanercept, is it more appropriate to consider etanercept given intermittently or continuously?
- What are the most appropriate criteria for assessment of response for infliximab? Should they include reference to dermatology life quality index (DLQI)?
- Do the fourth quartile DLQI utilities represent the disease severity of the population of interest?

- What impact would using short form version 36 (SF-36) scores directly from the trial to estimate utilities have on the incremental cost-effectiveness ratio (ICER)?
- What are the most appropriate estimates to be assigned to key parameters in the model, including utility values, length of stay, estimates of inpatient costs, and withdrawal rates?
- Does the Committee consider infliximab to be:
  - a replacement for etanercept (as recommended in current NICE guidance)
  - an alternative, equivalent treatment option to etanercept
  - an alternative only when etanercept cannot be used by reason of intolerance or contraindications?

1 Decision problem

1.1 Decision problem approach in the manufacturer's submission

Population	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 for whom these treatments are contraindicated. The manufacturer has indicated that infliximab should be recommended as a treatment option for use in patients who have failed to respond to systemic therapies, or are intolerant to these treatments and have a psoriasis area and severity index (PASI) ≥ 10 and DLQI > 10.
Intervention	Infliximab 5 mg/kg by intravenous infusion
Comparators	Etanercept 25–50 mg administered twice weekly until remission and only reinitiated after relapse (intermittent treatment). Etanercept 25 mg administered twice weekly continuously (continuous treatment). Efalizumab: initial stage dose of 0.7 mg/kg, weekly injections of 1.0 mg/kg body weight. Supportive care: includes inpatient stay and clinic visits for symptom management.
Outcomes	Severity of psoriasis – defined by PASI and DLQI scores. Remission and relapse rates. Health-related quality of life.
Economic evaluation	Modelling based on report from Woolacott and colleagues (Woolacott et al. 2006) for technology appraisal (TA)103. Data obtained from Bayesian hierarchal model for indirect comparison.

Previous NICE guidance

'Etanercept and efalizumab for the treatment of adults with psoriasis' (NICE technology appraisal guidance 103). More details on this guidance are included in Appendix B.

1.2 Evidence Review Group comments

1.2.1 Population

The manufacturer did not provide a definition of moderate psoriasis or any inclusion and exclusion criteria for rating the severity of psoriasis to confirm that the patient's condition was moderate to severe. The participants in the infliximab trials included in the manufacturer's submission were predominantly people with severe psoriasis. The proportion of trial participants that had previously been treated with systemic therapy was unclear to the ERG. It is therefore uncertain whether the participants included in the trials reflect those in the scope.

1.2.2 Comparators

The ERG noted the clinical opinion reported in the manufacturer's submission that current standard clinical practice in the NHS is to give etanercept continuously. However, NICE guidance recommends that etanercept be given intermittently.

1.2.3 Outcomes

The ERG reports that, while the PASI is not an ideal measure of the severity of psoriasis, it is an appropriate clinical measure to use. This is because it is regularly used as an assessment or outcome measure in clinical trials and other studies of psoriasis.

1.3 Statements from professional/patient groups and nominated experts

There was consensus among the experts that severe psoriasis is managed principally in secondary care, but there is a variation in treatment across the country. They considered that infliximab should be administered in hospital where infusion can be monitored. Treatment with biological therapies (etanercept, infliximab and efalizumab) begins after the failure of, or when there is a contraindication to, standard therapies such as phototherapy,

methotrexate, ciclosporin and acitretin. These standard treatments are often considered inappropriate for the long-term management of psoriasis, because they are inconvenient and associated with adverse events.

2 Clinical effectiveness evidence

2.1 Clinical effectiveness in the manufacturer's submission

The manufacturer presented data from four placebo-controlled trials comparing infliximab with placebo in adults with psoriasis (n = 1495). The duration of the trials ranged from 10 weeks to 50 weeks. Secondary outcomes include: PASI 90; PASI 50 at 10 weeks; DLQI change from baseline; change in SF-36 scores; PGA (that the psoriasis is minimal or cleared); PASI change from baseline; and NAPSI score. Summary details are presented in table 1

Table 1: Summary of infliximab trials

Trial name	Design and duration	Participants	Intervention and comparator (n =)	Primary outcome
SPIRIT (Gottlieb et al.)	Phase 2 USA 10 weeks 50-week follow-up[a]	Clinically stable plaque psoriasis > 10% BSA; baseline PASI ≥ 12	Infliximab 3 mg/kg (n = 99); Infliximab 5 mg/kg (n = 99) Placebo (n = 51)	% patients with PASI 75 at week 10
Chaudhari et al.	Phase 3 USA 10 weeks	Clinically stable plaque psoriasis > 5%	Infliximab 5 mg/kg (n = 11); Infliximab 10 mg/kg (n = 11) Placebo (n = 11)	% patients with PGA of minimal or cleared at week 10
EXPRESS (Reich et al.)	Phase 3 multicentre 10 weeks 50-week follow-up[a]	Clinically stable plaque psoriasis > 10% BSA; baseline PASI ≥ 12	Infliximab 5 mg/kg (n = 301) Placebo (n = 77)	% patients with PASI 75 at week 10
EXPRESS II (Menter et al.)	Phase 3 Multi-centre Induction 14 weeks 36-week follow-up[a]	Clinically stable plaque psoriasis > 10% BSA; baseline PASI ≥ 12	Infliximab 3 mg/kg (n = 313); Infliximab 5 mg/kg (n = 314) Placebo (n = 208)	% patients with PASI 75 at week 10

[a]Open label extensions.
BSA, body surface area; PASI, Psoriasis area and severity index.

At week 10, patients taking infliximab were significantly more likely to have a PASI 75 compared with patients taking placebo (range 75–88% versus 2–18% respectively; all four trials). There was also a statistically significant difference at 10 weeks in favour of infliximab for the proportion of patients achieving a PASI 50 and 90 (SPIRIT, EXPRESS and EXPRESS II).

In terms of secondary outcomes, there were statistically significant differences between infliximab and placebo in PGA score, quality of life, DLQI and NAPSI. The incidence of serious adverse events – for example squamous cell carcinoma, cholecystitis and cholelithiasis – was slightly higher in patients receiving infliximab compared with those receiving placebo.

Subgroup analysis by prior treatment history in EXPRESS and EXPRESS II demonstrated that previous treatment history did not have an impact on the PASI 75 response achieved.

There were no published randomised controlled trials that compared infliximab directly with any of the comparator drugs (etanercept or efalizumab). The manufacturer carried out an indirect comparison of infliximab with etanercept and efalizumab, with the common comparator being placebo or supportive care. The manufacturer included four randomised controlled trials comparing etanercept with placebo, and four randomised controlled trials comparing efalizumab with placebo. A random effects model was used to synthesise the efficacy data, which were incorporated into the Bayesian hierarchical model using a probit model.

The results of this analysis, taken from the manufacturer's submission, are presented in table 2.

Table 2. Likelihood of achieving PASI 50, 75, 90 goals at 10 to 12 weeks by indirect comparisons according to a random-effects model

Treatment	Probability of a response			RR		
		95% CI			95% CI	
	Mean	Lower	Upper	Mean	Lower	Upper
Response = PASI 50						
Placebo/supportive care	0.143	0.1219	0.1669	1.0	1.0	1.0
Etanercept 25 mg BIW	0.6258	0.5552	0.6958	4.34	3.74	5.19
Etanercept 50 mg BIW	0.7525	0.6986	0.8048	5.29	4.58	6.12
Efalizumab 1mg/kg	0.556	0.498	0.6107	3.91	3.36	4.50
Infliximab 5 mg/kg	0.9406	0.9172	0.9604	6.62	5.65	7.69
Response = PASI 75						
Placebo/supportive care	0.04001	0.03189	0.05001	1.0	1.0	1.0
Etanercept 25 mg BIW	0.3592	0.2928	0.4317	9.06	7.03	11.53
Etanercept 50 mg BIW	0.5001	0.4348	0.5691	12.362	10.22	15.55
Efalizumab 1 mg/kg	0.2939	0.2452	0.3435	7.41	5.96	9.09
Infliximab 5 mg/kg	0.8102	0.7592	0.8567	20.49	16.28	25.37
Response = PASI 90						
Placebo/supportive care	0.005815	0.004139	0.008012	1.0	1.0	1.0
Etanercept 25 mg BIW	0.1289	0.09218	0.1732	22.58	15.58	31.87
Etanercept 50 mg BIW	0.2202	0.1729	0.2754	38.62	28.21	52.51
Efalizumab 1 mg/kg	0.09438	0.07069	0.1213	16.50	12.08	21.93
Infliximab 5 mg/kg	0.5427	0.4721	0.6164	95.74	67.74	131.30

CI, confidence interval; PASI, Psoriasis area and severity index; RR, relative risk.

The manufacturer concluded that, in comparison with etanercept and efalizumab, infliximab was more likely to achieve a response assessed as PASI 50, 75 and 90.

2.2 Evidence Review Group comments

Overall, the ERG considered that the manufacturer presented an unbiased estimate of treatment efficacy for infliximab, etanercept and efalizumab based on the results of their placebo-controlled comparisons. However, the ERG identified a number of areas of uncertainty. These included:

- The short intervention period of 10 weeks provides limited information about the longer-term effectiveness of infliximab.
- The ERG considered combining the four infliximab trials in a meta-analysis to be inappropriate given the statistically significant heterogeneity between studies. Pooling data for the indirect

comparison was also considered inappropriate given the known heterogeneity. The ERG stated that the resulting pooled mean values should therefore be treated with caution.

- The ERG had difficultly checking the methodology of the indirect comparison. The descriptions of the principles and assumptions, as well as the data sources, were unclear to the ERG. The ERG was uncertain as to which trials had been included in the indirect comparison or which placebo groups were included in the pooled estimates, and attempted to clarify these issues with the manufacturer. However the methodology adopted by the manufacturer was the one used in the monograph by Woolacott and colleagues (Woolacott et al. 2006) and the ERG had difficulty understanding this from the details provided in the report. As a consequence of these factors, a comprehensive critique of the analysis was not possible.

2.3 Statements from professional and patient groups and nominated experts

The experts considered infliximab to be an effective treatment for psoriasis, especially when rapid control of symptoms is required since trial evidence suggests that it achieves remission at a faster rate than other treatments. This was supported by case series of using infliximab. In addition, one clinical expert suggested that it can provide benefit in patients in whom several systemic therapies have failed. The patient group emphasised the effect of psoriasis on health-related quality of life, including anxiety and discomfort.

The risks that were highlighted by the experts included opportunistic infection during infusion, malignancies, heart disease and tuberculosis. However, even though the SPC is clear that these risks exist, there is not a clear clinical reason for this, and the effect of infliximab has not been determined.

3 Cost effectiveness

3.1 Cost effectiveness in the manufacturer's submission

The manufacturer's cost effectiveness analysis was based on the monograph by Woolacott and colleagues (Woolacott et al. 2006) (referred to here as the York report) on efalizumab and etanercept. The differences between the approaches were in the analytical approach and formulas used in calculating costs and benefits. In addition to an analysis of the sequence of treatments, the manufacturer also carried out an additional standard comparative analysis. The economic analysis included comparisons with intermittent and continuous etanercept 25 mg, etanercept 50 mg, efalizumab and supportive care. The manufacturer presents clinical opinion from dermatologists that continuous etanercept best represents current practice. However, since current NICE guidance recommends intermittent use this is included in the analysis.

The model uses a 10-year time horizon and includes a trial period after which the patient receives best supportive care if their psoriasis does not respond (defined as not achieving PASI 75). Use of the DLQI measurement instrument is not included in the modelling. The manufacturer altered the original model so that efalizumab could be added as second-line therapy to take into account NICE technology appraisal guidance 103. The trial period to assess response was 12 weeks for etanercept and efalizumab, in line with this NICE guidance, and 10 weeks for infliximab. The manufacturer stated that there were very little data to inform the choice of a 10-week assessment period for infliximab, and it is uncertain whether this is the most appropriate period. On the basis of trial evidence, the manufacturer suggests that the response could be assessed as early as 6 weeks. Adverse events were not included in the modelling; the manufacturer states this was because the evidence base on which to model them was unclear.

3.1.1 Resource use and utilities

The cost and resource use data was obtained from the York report, Healthcare Resource Group (HRG) NHS reference costs and the 'British national formulary' (BNF 53, 2007). This was supported by data the manufacturer has on file and clinical opinion. The main component of the supportive care costs is the total length of inpatient admissions for non-responders per annum. This was assumed to be 21 days and was supported by Department of Health hospital episode statistics (Department of Health, 2004/05) for psoriasis of 18.1 days. The choice of 21 days is also supported by clinical opinion, which the manufacturer obtained from dermatologists across the UK. The dermatologists also stated that patients on supportive care would require 18 clinic visits annually.

The utilities for the model were taken from the York report. These were calculated from three etanercept trials involving patients in the fourth quartile DLQI who were assigned to four PASI response groups. The average DLQI change for each of these PASI responses was calculated and a linear formula was used to transform the results of DLQI into EQ-5D scores. In this way, EQ-5D calculated utilities were attached to PASI responses. These can then be used to provide an average utility change associated with changes in PASI score (e.g. PASI 75).

3.1.2 Results

The base case results demonstrated that, compared with continuous etanercept, the ICER for infliximab was £26,095 with a 10% probability of being cost effective at a willingness to pay of £20,000/quality-adjusted life year (QALY) or 73% at a willingness to pay of £30,000/QALY. The full results are presented in tables 3 and 4.

Table 3 Manufacturer's base case

	Mean QALYs[a]	Mean costs[a]	ICER
Continuous etanercept 25 mg twice weekly	0.089	£1531	-
Infliximab 5 mg/kg	0.205	£4562	-
Difference	0.116	£3031	£26,095

Table 4 Manufacturer's ICERs against supportive care

	Mean incremental QALYs	Mean incremental costs	ICER against supportive care
Supportive care	0	0	0
Intermittent etanercept 25 mg twice weekly (PASI 75)	0.089	£716	£8044
Efalizumab 1 mg/kg (PASI 75)	0.073	£1269	£17,467
Continuous etanercept 25 mg twice weekly (PASI 75)	0.089	£1531	£17,208
Etanercept 50 mg twice weekly (PASI 75)	0.124	£4439	£35,652
Infliximab 5 mg/kg (PASI 75)	0.205	£4562	£22,240

Results rounded for clarity
ICER, incremental cost-effectiveness ratio; PASI, Psoriasis area and severity index; QALY, quality-adjusted life year.

The sensitivity analysis demonstrates that the main drivers of cost effectiveness in the model are the range of utility values used, reducing the length of inpatient stay for non-responders to 10 days and assuming no additional clinic visits for non-responders. A worst case analysis was presented of £251,565/QALY and a best case of £11,657/QALY.

3.2 Evidence Review Group comments

The ERG considered that the manufacturer's reporting of the modelling was not fully transparent. Alternative estimates of parameters such as utility values

used, withdrawal rates from treatment, costs of administration and inpatient costs could significantly affect the cost-effectiveness analysis.

3.2.1 Utilities

The ERG commented that the derivation of the utilities used by the manufacturer, in particular the definition of fourth quartile DLQI, was not clear. The York report stated that the trials used to calculate the utilities had an inclusion criterion for patients of PASI ≥ 10 and affected body surface area (BSA) > 10. Therefore many of these patients correspond to NICE's definition of severe psoriasis (PASI ≥ 10 and DLQI > 10) and the manufacturer's inclusion criteria for their trials. It is unclear what severity of psoriasis the fourth quartile DLQI group represents. It could be argued that the utilities derived for all patients (regardless of DLQI) should have been used. In addition, even though SF-36 data were collected for the EXPRESS II trial, they were not used in the economic model. The ERG considered that the manufacturer could have used the short form six dimensions (SF-6D) to convert the SF-36 data into utilities and examine its effect in a sensitivity analysis. As a minimum, the ERG would expect the manufacturer to explore the relationship between changes in PASI and SF-36 in a sensitivity analysis. In clarification, the manufacturer stated the reason for their decision was the apparent preference NICE has for EQ-5D over SF-36.

3.2.2 Drop-out rates

The ERG considered that the assumed drop-out rate of 20% in the model might be an underestimate. The figure of 20% was based on the number of patients whose psoriasis responded to PASI 75 and PASI 90. EXPRESS II demonstrated that there is a 30% reduction in PASI 75 responders in 6 months; there were a similar number in EXPRESS (26%). If the number of responders continued to fall at this rate, the annual drop-out rate would be 60%. Consequently the ERG suggests that the drop-out rate could be as high as 50% per year.

3.2.3 Cost of inpatient stay

The ERG noted that the manufacturer had used elective inpatient HRG codes (major-dermatological conditions (J 39 and J40)) to calculate the cost of inpatient stays. The ERG stated that it was unclear why only elective codes were used given that there are nearly three times as many non-elective admissions as elective admissions under these codes. In addition, the average length of stay for a finished consultant episode for these codes varies between 10 and 12 days for elective admissions (and 4–7 days for non-elective). The ERG is unsure whether an average cost per day calculated from these figures would be appropriate. NHS reference costs provide excess bed days costs which are generally lower. The ERG recalculated the cost of a stay using the HRG cost for an episode plus excess bed days for the difference between 21 days and the average length of that episode. This resulted in a cost of either £5091 or £5488 depending upon whether only elective or both elective and emergency admissions were included. This is lower than the manufacturer's value of £6189. However, the previous assessment report used a method similar to the one used by the manufacturer.

3.2.4 Extra ERG analysis

The ERG updated the manufacturer's sensitivity analysis. Where evidence was not available, the ERG used arbitrary ranges. A summary of the major results is presented in table 5; the base case is £26,095 per QALY. The ERG calculated that if inpatient costs were reduced to £5091 from £6194, this increased the ICER to £30,379.

Table 5: ERG one way sensitivity analysis – base case £26,095 per QALY

Variable	Base case	Inputs		CE ratios		CE right minus left
		Left	Right	Left	Right	
Patient weight, kg	70	50	90	4984	47,205	42,221
Utility gain for responders, e.g. PASI ≥ 90%[a]	0.41	0.59	0.23	18,524	44,133	25,609
Best case response for etanercept vs worst for infliximab[a], e.g. PASI 90	0.129 = E 0.543 = I	0.092 = E 0.616 = I	0.173 = E 0.472 = I	22,601	32,633	10,032
Annual drop out rates	20%	10%	50%	24,191	36,886	12,695
Trial period for infliximab, weeks	12	18	6	22,199	28,195	5996
Inpatient stay for non-responders, days per year	21	25	10	21,513	38,694	17,181
Outpatients visits for non-responders per year	18	25	10	24,327	28,115	3788
Cost of inpatient stay per day (+/- 20%)	£294.96	£353.95	£235.97	21,284	30,906	9622
Cost of infliximab per vial (+/- 20%)	£419.62	£335.70	£503.54	9206	42,984	33,777

[a]Ranges for sensitivity analysis taken from lower and upper 95% confidence limits

CE, cost effectiveness; ERG, Evidence Review Group; E, etanercept; I, infliximab; PASI, psoriasis area and severity index; QALY, quality-adjusted life year; vs, versus.

The ERG carried out scenario analysis, which is shown in table 6. This analysis demonstrates the incremental effect of each change. Therefore, the effect of increasing the drop-out rate and reducing inpatient costs results in the ICER increasing from £26,095 to £41,229 per QALY. If all patients' utility is used, this increases the ICER to £76,961/QALY

Table 6 ERG scenario analysis for base case with cumulative effect of assumption for key parameters

	Incremental cost	Incremental QALY	ICER
Base case	£3031	0.116	£26,095
Drop-out rate of 50% per year	£4224	0.115	£36,886
Inpatient cost of £5091	£4722	0.115	£41,229
All patients	£4722	0.062	£76,961

ERG, Evidence Review Group; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life year.

Finally, the ERG carried out additional probabilistic sensitivity analyses, which are shown in table 7. These take into account variables that were not included in the manufacturer's sensitivity analysis.

Table 7 ERG probabilistic sensitivity analysis

Parameter	Mean	Standard deviation	Distribution	ICER	Pr(ICER < 30K)
Annual drop out rate	35%	a = 0.2, b = 0.5	Uniform	£36.9K	10%
Cost of infliximab per vial	£419.62	40	Gamma	£26.9K	64%
Length of inpatient stay (days)	21	2.3	Gamma	£26.9K	68%
Number of outpatient visits	18	2	Gamma	£26.5K	73%
All of the above				£33.2K	38%

ICER, incremental cost-effectiveness ratio; Pr, percent.

The ERG considered that the overall approach to the modelling was reasonable, but that the ICER is very sensitive to the above variables.

4 Authors

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Appendix A: Sources of evidence considered in the preparation of the premeeting briefing

A. The evidence review group (ERG) report for this appraisal was prepared by Southampton Health Technology Assessment Centre (SHTAC), University of Southampton:

    - Clegg A, Cooper K, Hartwell D et al, infliximab for the treatment of psoriasis, July 2007

B. The following organisations accepted the invitation to participate in this appraisal. Organisations listed in I were invited to make written submissions. Organisations listed in II gave their expert views on infliximab for the treatment of psoriasis by providing a written statement to the Committee.

    I Manufacturer/sponsor:

    - Schering-Plough Ltd

    II Professional/specialist and patient/carer groups:

    - British Association of Dermatologists
    - British Dermatological Nursing Group
    - Primary Care Dermatology Society
    - Royal College of General Practitioners
    - Royal College of Nursing
    - Royal College of Physicians
    - Psoriatic Arthropathy Alliance
    - Psoriasis Association

C. Additional references used:

Chaudhari U, Romano P, Mulcahy LD, Dooley LT, Baker DG, Gottlieb AB. Efficacy and safety of infliximab monotherapy for plaque-type psoriasis: a randomised trial. The Lancet 2001; 357:1842-47.

Gottlieb AB, Evans R, Li S, Dooley LT, Guzzo CA, Baker D et al. Infliximab induction therapy for patients with severe plaque-type psoriasis: A randomised, double-blind, placebo-controlled trial. J Am Acad Dermatol 2004; 51:534-42.

Menter A, Feldman SR, Weinstein GD, Papp K, Evans R, Guzzo C et al. A randomised comparison of continuous vs. intermittent infliximab maintenance regimens over 1 year in the treatment of moderate-to-severe plaque psoriasis. J Am Acad Dermatol 2006; 56:e1-15.

Reich K, Nestle FO, Papp K, Ortonne J-P, Evans R, Guzzo CA et al. Infliximab induction and maintenance therapy for moderate-to-severe psoriasis: a phase III, multicentre, double-blind trial. The Lancet 2005; 366:1367-74.

Woolacott N, Hawkins N, Mason A, Kainth A, Khadiesari Z, Bravo Vergel Y et al. Etanercept and efalizumab for the treatment of psoriasis: a systematic review. Health Tech Assess 2006; 10(46).

Appendix B: 'Etanercept and efalizumab for the treatment of adults with psoriasis' (NICE technology appraisal guidance 103)

1.1 Etanercept, within its licensed indications, administered at a dose not exceeding 25 mg twice weekly is recommended for the treatment of adults with plaque psoriasis only when the following criteria are met:

- The disease is severe as defined by a total PASI of 10 or more and a DLQI of more than 10.
- The psoriasis has failed to respond to standard systemic therapies including ciclosporin, methotrexate and PUVA; or the person is intolerant to, or has contraindication to, these treatments.

1.2 Etanercept treatment should be discontinued in patients whose psoriasis has not responded adequately at 12 weeks. Further treatment cycles are not recommended in these patients. An adequate response is defined as either:

- a 75% reduction in the PASI score from when treatment started (PASI 75) or
- a 50% reduction in the PASI score (PASI 50) and a five point reduction in DLQI from when treatment started.

1.3 Efalizumab, within its licensed indications, is recommended for the treatment of adults with plaque psoriasis under the circumstances detailed in section 1.1 only if their psoriasis has failed to respond to etanercept or they are shown to be intolerant of, or have contraindication to, treatment with etanercept.

1.4 Further treatment with efalizumab is not recommended in patients unless their psoriasis has responded adequately at 12 weeks as defined in section 1.2.

1.5 It is recommended that the use of etanercept and efalizumab 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.