Appendix P: Review of resource use and cost data to use in defining 'best supportive care' for NCGC economic model

P.1 Introduction **2**
P.2 Definition in technology appraisals **2**
P.3 Cohort studies of resource use **3**
P.3.1 Fonia and colleagues 2011[2] 3
P.3.2 Driessen and colleagues 2011[3] 4
P.3.3 Woods and colleagues 2008[4] 5
P.3.4 Department of Health (DoH) Hospital Episode Statistics (HES) data 5
P.4 GDG experience and opinion **6**
P.5 Best supportive care in the NCGC model **6**
P.5.1 Drug and other treatments 7
P.5.2 Health care resource use 7
P.5.2.1 Outpatient attendances 7
P.5.2.2 Drug monitoring and laboratory tests 7
P.5.2.3 Phototherapy 8
P.5.2.4 Day-care attendances 8
P.5.2.5 Inpatient admissions and length of stay 8
P.6 Summary of NCGC model assumptions **9**
P.7 References **10**

P.1 Introduction

This appendix is a review of resource use and cost data available in the published literature, which was used to estimate suitable parameters with which to populate the best supportive care arm of the NCGC model. For the purposes of this model the GDG sought to define 'best supportive care' (BSC) in terms of NHS resource use for the average patient for whom a second biologic is being considered.

The review has been structured to provide first a brief summary of assumptions about BSC that have been made in previous NICE guidance on biologic therapies in the treatment of moderate to severe psoriasis. Next, the review looks to recently published resource use studies of high-need psoriasis patients in the year before and the year of initiation of biologic therapy. Thirdly, some of the issues raised by the GDG in considering the evidence and population are highlighted. Finally, everything is brought together to provide a working definition of BSC to be used in the NCGC model.

P.2 Definition in technology appraisals

Woolacott and colleagues[1], authors of the original health technology appraisal of biologic therapy used in the treatment of psoriasis, were the first to define BSC in psoriasis. They used placebo response rates from the placebo-controlled trials of systemic and biologic therapies in order to define the benefits of BSC and used expert opinion to inform likely resources used. All subsequent technology appraisals appear to have used the same or very similar definitions for BSC.

The authors assumed that there were no significant additional treatment costs associated with BSC compared to older systemic treatments (methotrexate and ciclosporin). It was assumed that patients on BSC would have two outpatient visits annually. The cost of an outpatient appointment was based on the NHS Reference Cost category J10op ('Major dermatological conditions; other attendance without other investigation or procedure) and was £56.60[2].

The main additional cost with BSC in the model resulted from increased rate of hospitalisation due to a lower rate of PASI75 response. No published data were available to inform the rate of hospitalisation so estimates were based on a range of scenarios informed by expert opinion.

Length of stay for an inpatient hospital admission was based on Department of Health Hospital Episode Statistics (2002-03)[3] for psoriasis which gave a mean of 19.6 days. This statistic was supported by evidence from recent audits of two local hospitals (supplied to the authors from personal communication) which had an average length of stay of 22.3 and 22.7 days. In key scenario analyses, the authors assumed that patients would spend an average of 21 days in hospital per year. The cost of an inpatient day was based on the average of two NHS Reference Cost categories: elective inpatient J39 ('major dermatological conditions (>69 or w cc: aged over 69 or with co-morbidities or complications)') and J40 ('major dermatological conditions (<70 or w/o cc)'). Using the number of Finished Consultant Episodes to weight the costs, the resulting weighted average cost for an inpatient day was £248.31. Thus, the total annual cost for inpatient stays was £5,214.51.

The GDG discussed using a similar definition of BSC (i.e. 2 outpatient visits in a base case and 21 inpatient days per year in a scenario analysis), but argued that these estimates of resource use are likely to be an underestimate of what currently happens in clinical practice. They believed that the patients meeting the eligibility criteria for biologic therapy are generally high-need patients and utilise a lot of health care resources through inpatient admissions, lengthy hospital stays, frequent visits to day clinics for specialist-applied topical treatments and UVB and monitoring toxicity related to systemic treatments. Based on the GDG experience, the group of patients modelled by

Woolacott and colleagues would receive 'no treatment' only very rarely and would almost certainly require more care than 2 outpatient visits per year and likely more than 21 days in hospital.

When translating this information to build the NCGC model, which focuses on patients who are being considered for treatment with a second biologic, the GDG is certain that these resource use estimates are inadequate. In their opinion, the group of patients requiring a second biologic are likely to be even more high-need and resource intensive; therefore it would be inappropriate to assume the same assumptions about what comprises BSC.

P.3 Cohort studies of resource use

Two cohort studies have been published in response to a request for more research on the actual resource use of high-need psoriasis patients. One study[4] was undertaken at a tertiary dermatology unit in the UK and the other study[5] was undertaken at a tertiary dermatology unit in the Netherlands.

P.3.1 Fonia and colleagues 2011[4]

Fonia and colleagues investigated resource use in a cohort of 76 patients with severe psoriasis before and after the introduction of biologic therapy at St John's Institute of Dermatology. The primary objective of the retrospective observational study was to compare resource use and associated costs in patients with plaque psoriasis for a period of 12 months before and for up to 12 months immediately after starting biologic therapy. They also captured estimates of quality of life and disease severity during these before and after periods. Costs were estimated from an NHS perspective and used 2008 British pounds.

The relative proportions of patients on each biologic were:

- 7.9% on adalimumab
- 11.8% on efalizumab
- 71% on etanercept
- 31.6% on infliximab.

The pattern of biologic drug use observed reflects the availability of each drug during the time period of data collection (2003-08). Their data also indicate that in general etanercept is used continuously, rather than intermittently.

Patients were on a variety of conventional systemic drugs prior to initiation of biologic therapy: 47% were taking ciclosporin; 41% were taking methotrexate; 35% were taking fumarates; 24% were taking acitretin. Upon starting biologic therapy, half of people taking ciclosporin stopped taking it; all but one patient stopped taking acitretin; all but 3 patients stopped taking fumarates. The number of patients taking methotrexate reduced very slightly (31 to 27 patients) and the mean number of days on methotrexate reduced very slightly as well (104.3 days to 100.2 days).

Inpatient admissions were less frequent after initiation of biologic therapy (absolute values not reported) and length of stay was reduced (6.49 days to 1.55 days). There was no difference in outpatient attendances (3.22 vs 3.25 visits). Day ward admissions were more frequent upon initiation of biologic therapy (0.14 vs 1.16) with 91% attributable to infusion of infliximab.

Overall, mean hospital costs decreased by £1,682 in the year following initiation of biologic therapy. However, these savings are counterbalanced by the increase in drug costs, which amounted to £9,456. In the end, there was a significant increase in mean cost per patient of £7,774 in the period after biologic therapy was initiated.

The authors note that following initiation with biologic therapy, the mean PASI score fell by 8.9 points, from 18.7 to 9.8 which represents a mean PASI improvement of 48%. They point out that

'while the degree of improvement was less than that reported in randomised controlled trials, this may reflect a relatively treatment resistant group (failed prior systemic therapy) and/or differences between real life and highly controlled clinical trial settings.' They also highlight the fact that many patients will have switched to biologic from ciclosporin and/or methotrexate due to toxicities rather than to poor disease control, therefore improvement in PASI for these patients might not be reflected.

P.3.2 Driessen and colleagues 2011[5]

The authors investigated resource use in a cohort of 67 patients with severe psoriasis before and after the introduction of biologic therapy at Radbound University Nijmegen Medical Centre Department of Dermatology between February 2005 and February 2009. The objective of the retrospective cohort analysis was to compare resource use and associated costs in patients with plaque psoriasis for a period of 12 months before and for up to 12 months after starting initial biologic therapy.

The relative proportions of patients on each biologic were:

- 18% on adalimumab (18% at time of analysis)
- 30% on efalizumab (9% at time of analysis)
- 95% on etanercept (72% at time of analysis)
- 6% on infliximab (1% at time of analysis)

The pattern of biologic drug use observed reflects the availability of each drug during the time period of data collection (2005-09). 63% were treated with only one biologic (majority etanercept), 28% were treated with two biologics and 9% were treated with three or four biologics. The GDG believes that it is extremely improbable that a patient in the UK would be managed on any more than a single biologic at a time.

Patients were on a variety of conventional systemic drugs prior to initiation of biologic therapy: 85% were taking methotrexate; 51% were taking ciclosporin; 51% were taking acitretin; 37% were taking fumarates; 16% undergoing PUVA. Upon starting biologic therapy, three-quarters of people taking methotrexate, ciclosporin, acitretin and fumarates stopped taking them.

The authors separated the analysis of resource use by mean length of inpatient stay asserting that the yearly expenses for biologic treatment equals that of 30 hospital admission days. Therefore, they analysed resource use and costs for patients with mean length of stay less than 30 days and mean length of stay more than 30 days separately.

For the group with a mean length of stay less than 30 days (82% of the cohort), the number of days spent in day care per year reduced from 5.1 to 0.3 upon initiation of biologic therapy. Mean hospital inpatient days per year were reduced from and 14.9 to 5.4 days. There was little change in the mean number of outpatient consultations between the two periods (7.6 vs 7.0 visits). In this group, mean hospital costs (inpatient and day care) decreased by €5,621 in the year following initiation of biologic therapy. However, these savings in hospital costs are counterbalanced by the increase in drug costs, which amounted to €13,325. Looking at overall costs in this group, there was a significant increase in mean cost per patient of approximately €7,500 in the period after biologic therapy was initiated.

For the group with a mean length of stay longer than 30 days (18% of the cohort), the median inpatient length of stay was 53 days in the pre-biologic treatment period and 5.3 days upon introduction of biologic therapy.

In the overall patient group, the mean PASI at the start of biologic treatment was 19.0 and during treatment this decreased to 6.4, indicating a mean improvement of 66.4%. 73% of patients reached a PASI50 and 43% achieved a PASI75.

One key limitation of the analysis is that only patients that finished 12 months of biologic therapy were included; therefore, there are no estimates of resource use for patients who did not respond or were intolerant to biologic therapy.

P.3.3 Woods and colleagues 2008[6]

Woods and colleagues conducted a multicentre prospective service review in four specialist dermatology centres in the UK (Hope Hospital, Manchester; St John's Institute of Dermatology, London; Royal Victoria Infirmary, Newcastle upon Tyne; Royal Gwent Hospital, Newport) in 2004 and 2005. Two of the aims of their study of greatest interest to this guideline were to identify variables that might predict length of inpatients stay, including measures of disease severity, and investigate the effectiveness of inpatient stay as measured by the proportion achieving at least a PASI50 or PASI75.

The results of their review confirmed that length of stay increases with disease severity and that inpatient admission was effective, with 30% of patients achieving a PASI75 or above and 65% achieving a PASI50 or above at discharge from hospital. 58% also experienced at least a 50% reduction in their DLQI score and 27.4% had at least a 75% reduction. Woods and colleagues also reported the time taken to achieve a PASI50 in three groups of psoriasis severity, according to PASI at admission. These are presented in Table 1.

Table 1: Time taken to PASI50 based on disease severity

Disease severity at admission	Mean length of stay (days)	Percent of patients achieving PASI50	Mean length of stay (days) to achieve PASI50
PASI <10	15.8	52%	19.2
PASI 10 to 20	20.8	65%	20.7
PASI >20	23.7	83%	24.4

(a) Adapted from Woods and colleagues[6]

P.3.4 Department of Health (DoH) Hospital Episode Statistics (HES) data

Woolacott and colleagues used data from the 2002-03 DoH HES to estimate the length of stay for patients whose psoriasis remains uncontrolled. The data at the time could be expected to reflect care prior to the introduction of biologic therapy into the NHS. Table 2 shows how the mean length of stay for psoriasis appears to have decreased since then (19.6 days in 2002-03 to 12.1 days in 2010-11). As has been reflected in the two cohort studies, this might be explained by reductions in the length of stay for high-need patients upon initiation of biologic therapy.

Although mean length of stay has decreased, the total number of admissions has increased and the proportion of those admissions which are classified as day cases appears to have increased. These changes are thought to reflect changes to the service configuration over the last decade and the way in which infliximab infusions are coded for costing purposes. Historically, patients were admitted for lengthy periods for intensive treatment with dithranol, tar and/or UVB. Now, many of these admissions will have been converted into day centre attendances. Infliximab infusions are often coded as a day case procedure or a regular day/night admission; however, the relative proportion of the total biologic cohort receiving infliximab is quite small given the stricter NICE eligibility criteria.

Table 2: DoH HES data for diagnosis of psoriasis vulgaris (L40.0)

	2002-03	2004-05	2006-08	2008-10	2010-11
Total admissions	873	667	887	1008	1279

	2002-03	2004-05	2006-08	2008-10	2010-11
Mean length of stay	19.6 days	18.1 days	16.8 days	15.1 days	12.1 days
Number of day cases	341	135	347	505	860

P.4 GDG experience and opinion

The GDG has indicated that best supportive care is difficult to define because of the heterogeneous population and lack of clear clinical alternatives. The population is likely to have significant co-morbidities, many of which may have been induced by previous treatments for their psoriasis (liver fibrosis, hypertension, renal impairment) and have been the reason for initiating treatment with biologic therapy. The other significant co-morbidity is psoriatic arthritis, which may be found in more than half of psoriasis patients with moderate to severe disease. Biologic therapy has also been shown to be effective in the treatment of psoriatic arthritis. Biologic therapy is also initiated following non-response to methotrexate or following non-response, lost response and/or rapid relapse upon withdrawal of ciclosporin. It also follows on from a patient reaching a maximum cumulative exposure to PUVA, which has put them at increased risk of skin cancer. In summary, a variety of factors make it difficult to consider revisiting previously trialled therapies such as these.

NICE guidance states that treatment with a biologic should be discontinued if an adequate response (PASI75 or PASI50 and 5-point drop in DLQI) is not achieved within 10 to 16 weeks (exact time point depends on the biologic therapy). The clinicians on the GDG indicated that many patients will be maintained if they achieve a PASI50 regardless of a drop in DLQI, but their assumption is that DLQI will have improved and that for most patients a PASI50 is an acceptable improvement given the problems associated with the alternatives (i.e. conventional systemic therapies).

The GDG has also indicated that in current practice, if treatment with a second-line biologic is unavailable, then when a patient loses response (secondary non-responder) after some time, they may not necessarily discontinue treatment given the problems associated with alternative treatments (e.g. conventional systemic therapies). Instead they will follow one of several pathways:

1. Continue treatment, maintaining a suboptimal response (PASI50 or less)
2. Continue treatment, adding in methotrexate or, very rarely, ciclosporin (lower doses than when used as monotherapy) or UVB
3. Continue treatment and increase the dose (if etanercept or adalimumab) or decrease the interval between infusions (if infliximab)

The thought is that options 2 and 3 will not necessarily improve response very much, but may help to maintain at least a PASI50. The reason that clinicians give for continuing patients on marginally effective biologic therapy is that there are few safe and/or effective alternatives. As is clear from the data, some patients will have switched to biologic therapy due to ineffectiveness of other treatments, but many will also have switched due to the toxic adverse events associated with long term use of conventional systemic therapies.

P.5 Best supportive care in the NCGC model

Based on discussions within the GDG, evidence from two retrospective cohort studies and assumptions made in previous NICE technology appraisals, the following definition for best supportive care was used in the NCGC model. It is broken up into different resource categories and then summarised at the end in a single table (Table 4)

P.5.1 Drug and other treatments

As outlined in section P.4, there is recognition that at the point at which patients become eligible for a first biologic therapy, they must have exhausted treatment options such as conventional systemic therapy and phototherapy, including PUVA. Therefore, it may seem paradoxical to include these treatments as possible therapies post-biologic therapy. It was felt that although these therapies had either proved ineffective or given rise to certain toxicities, the patients for whom a second biologic was being considered were unlikely to go without treatment altogether. In the absence of a second biologic therapy, the likelihood is that they would be cycled through different modalities, accepting the associated risks. On this basis, the NCGC model has attempted to approach the treatments comprising 'best supportive care' in a pragmatic fashion, albeit with limitations.

Drugs included under 'best supportive care' and the proportions of patients receiving each were defined by the GDG in the following way:

- 45% of patients will be managed with ciclosporin for a maximum of 2 years
- 45% of patients will be managed with methotrexate
- 10% will be managed with no active pharmacological treatment (some patients will opt for no treatment given the possible risks associated with conventional systemic therapies)

These proportions were varied in sensitivity and scenario analyses.

According to both cohort studies, around 35% of patients have taken fumarates in the year prior to starting biologic therapy. The GDG has indicated that based on this, one could reasonably assume that 65% of patients failing a biologic could trial a course of fumarates. Unfortunately, fumarates are not licensed in the UK and are therefore outside the scope of the guideline.

P.5.2 Health care resource use

P.5.2.1 Outpatient attendances

Both cohort studies showed that there was no significant difference between the number of outpatient attendances during the pre-biologic period and during the first year of biologic therapy. The UK study[4] showed the mean number of outpatient visits to be around 3.2 and the Dutch study[5] showed the mean number to be around 7.2. Woolacott and colleagues[1] based their estimates on expert opinion and assumed that

- patients receiving ciclosporin would have 6-7 visits annually
- patients receiving methotrexate would have 4-5 visits annually
- patients receiving best supportive care (i.e. no active treatment) would have 2 visits annually

In the NCGC model we have assumed there to be no difference between outpatient attendances on best supportive care and biologic treatments and we will assume that there is no difference between ciclosporin and methotrexate under BSC. We have estimated the number of annual outpatient visits to be 4 (i.e. every 3 months). This is slightly higher than the estimate in the cohort study by Fonia and colleagues; however, the group of patients included in the NCGC model are likely to be even more high-need than those included in the cohort study given that they have already failed at least one biologic therapy.

P.5.2.2 Drug monitoring and laboratory tests

Patients undergoing pharmacological treatment with conventional systemic therapies (i.e. methotrexate or ciclosporin) are assumed to be monitored at regular intervals during treatment. Frequency of monitoring used in the model (Table 3) was informed by estimates used in Woolacott

and colleagues[1] and GDG experience. It was assumed that some of these tests will be undertaken as part of outpatient visits and the remainder will be performed outside of an outpatient visit.

Table 3: Resource use: outpatient and laboratory tests

	Ciclosporin	Methotrexate
Outpatient visits		
Annually (maintenance)	4	4
Laboratory tests (annual maintenance)		
FBC	4	4
LFT	4	4
Serum Creatinine	4	4
Urea & Electrolytes	4	4
PIIINP	-	4
Glomerular Filtration Rate	1	-
Liver biopsy	-	0.4 (a)

(a) Frequency of liver biopsy with methotrexate with concurrent use of PIIINP test was based on estimates from Chalmers and colleagues[7]

P.5.2.3 Phototherapy

We have assumed that 16% of patients will undergo one course of narrowband UVB each year (24 sessions). This is based on the estimated use of PUVA in the Driessen study[5] during the year prior to initiation of biologic therapy. Given the high probability of contraindication to PUVA in the hypothetical population of the NCGC model, a course of narrowband UVB was thought to me more realistic than further PUVA.

P.5.2.4 Day-care attendances

Fonia and colleagues[4] estimated day care attendances to be quite low in the pre-biologic period (0.14 per patient per year). Driessen and colleagues[5] estimated it to be higher at 5.1 attendances per year before biologics. The GDG indicated that if the service is available, the population included in the NCGC model (failed biologic therapy) is very likely to utilise such services. On this basis, the NCGC model has assumed that all patients receiving BSC will attend a day centre for specialist applied topicals or other specialist treatment 5 times per year.

P.5.2.5 Inpatient admissions and length of stay

Fonia and colleagues[4] estimated inpatient length of stay to be 6.49 days per year before biologics; Driessen and colleagues[5] estimated it to be 14.9 days per year for 82% of patients and 53.0 days per year for 18% of patients. Combining the subgroups in Driessen and colleagues would give a weighted mean of 21.8 days per year (0.82*14.9+0.18*53=21.8).

The observed length of stay from Fonia and colleagues seems low compared to HES data, length of stay listed in the relevant NHS reference costs (between 9 and 15 days per admission) and GDG opinion. It is difficult to know how applicable the observations from Driessen and colleagues are because they are from a Dutch health system perspective and there may be important differences in terms of service configuration and delivery of care.

For the NCGC model, we took the breakdown in high-need versus very high-need as observed in the Driessen cohort study (82% vs 18%) to inform a weighted average length of stay. In the base case, we assumed that high-need patients (82%) will require one hospital admission per year, which was assumed to correspond to a mean length of stay of 20.8 days (from Woods and colleagues, see

section P.3.3 and Table 1). This is much longer than the 6.5 days observed in Fonia and colleagues, but as this is likely to be a higher-need population than their cohort, the GDG considered this to be a reasonable assumption.

In the base case, we assumed that very high-need patients (18%) will require 2.55 hospital admissions per year, each also 20.8 days in length, which equals out to 53 inpatient days per year, the figure reported for this population in Driessen and colleagues[5].

Given that these variables are quite uncertain extensive sensitivity analyses were performed to explore how small and large changes might affect the cost-effectiveness of second line biologic therapy. In particular, the proportions of high- and very-high need patients and the number of annual admissions and mean length of stay per group were varied.

P.6 Summary of NCGC model assumptions

The working definition of best supportive care, in the context of patients with moderate to very severe plaque psoriasis who are being considered for further biologic therapy, is summarised in terms of resource use in Table 4. This is based on several different sources of information and supplemented by GDG experience and opinion. This defined package of services is expected to cost an annual £10,731. It is worth noting that previous NICE technology appraisals have estimated this cost to be at most £5,328 (based on 21 days in hospital plus 2 outpatient visits per annum). Due to substantial uncertainties in these model parameters, they were subject to extensive sensitivity analyses, each of which was considered by the GDG as they looked to make guideline recommendations that would represent an effective and cost-effective use of NHS resources.

Table 4: Assumed resource use for best supportive care

	Total annual cost			
Component	**Proportion receiving**	**Resource use components**		**Total Cost**
Drugs				
Methotrexate	45% (a)			£228
Ciclosporin (b)	45% (a)			£1,107
No drug	10% (a)	5 OP visits		£41
Other treatment				
Day centre care	100% (a)	5 visits		£1,813
NBUVB	16% (c)	1 course	24 sessions	£327
Inpatient care (g)				
High need	82% (d)	1 admission (a)	20.8 days per admission (f)	£4,625
Very high need	18% (d)	2.55 admissions (e)		£2,589
TOTAL				**£10,730 (h)**

(a) Based on GDG opinion
(b) Maximum treatment 2 years; after 2 years then no drug
(c) Based on proportion receiving PUVA in year before starting biological therapy in Driessen and colleagues[5]
(d) Based on split in Driessen and colleagues(under/over 30 days in hospital per annum)
(e) Calculated based on mean length of stay from Woods[6] (20.8) and mean in hospital days per annum in the very high need group in Driessen[5] (53.0).
(f) Based on mean length of stay for patients admitted with baseline PASI 10 to 20 in Woods[6]. 23.7 days used in sensitivity analysis.
(g) Weighted average length of stay equals 26.6 days per year per patient (20.8[0.82*1+0.18*2.55]=26.6) and weighted average cost equals £7,214 per patient.*
(h) Note: previous TAs[8-11] have estimated this cost to be approximately £5,327.71 (21 days in hospital + 2 outpatient visits per annum)

P.7 References

1 Woolacott N, Hawkins N, Mason A et al. Etanercept and efalizumab for the treatment of psoriasis: a systematic review. *Health Technol Assess.* 2006; 10(46):1-252.

2 Department of Health. *NHS reference costs 2003 and national tariff 2004 ('payment by results core tools 2004')*. Available from: http://www dh gov uk/PublicationsAndStatistics/Publications/PublicationsPolicyAndGuidance/PublicationsPolicyAndGuidanceArticle/fs/en?CONTENT_ID=4070195&chk=UzhHA3. Last accessed on: 2004 Nov. 23.

3 Department of Health. *Hospital episode statistics England: financial year 2002-03*. Available from: http://www dh gov uk/assetRoot/04/06/74/03/04067403 pdf. Last accessed on: 2004 Dec. 12.

4 Fonia A, Jackson K, Lereun C et al. A retrospective cohort study of the impact of biologic therapy initiation on medical resource use and costs in patients with moderate to severe psoriasis. *Br J Dermatol.* 2010; 163(4):807-816.

5 Driessen RJ, Bisschops LA, Adang EM et al. The economic impact of high-need psoriasis in daily clinical practice before and after the introduction of biologics. *Br J Dermatol.* 2010; 162(6):1324-1329.

6 Woods AL, Rutter KJ, Gardner LS et al. Inpatient management of psoriasis: a multicentre service review to establish national admission standards. *Br J Dermatol.* 2008; 158(2):266-272.

7 Chalmers R, Kirby B, Smith A et al. Replacement of routine liver biopsy by procollagen III aminopeptide for monitoring patients with psoriasis receiving long-term methotrexate: a multicentre audit and health economic analysis. *Br J Dermatol.* 2005; 152(3):444-450.

8 National Institute for Health and Clinical Excellence. *Etanercept and efalizumab for the treatment of adults with psoriasis. NICE technology appraisal 103.* London: National Institute for Health and Clinical Excellence, 2006. http://guidance.nice.org.uk/TA103

9 National Institute for Health and Clinical Excellence. *Infliximab for the treatment of adults with psoriasis. NICE technology appraisal 134.* London: National Institute for Health and Clinical Excellence, 2008. http://www.nice.org.uk/TA134

10 National Institute for Health and Clinical Excellence. *Adalimumab for the treatment of adults with psoriasis. NICE technology appraisal 146.* London: National Institute for Health and Clinical Excellence, 2008. http://guidance.nice.org.uk/TA146

11 National Institute for Health and Clinical Excellence. *Ustekinumab for the treatment of adults with moderate to severe psoriasis. NICE technology appraisal 180.* London: National Institute for Health and Clinical Excellence, 2009. http://guidance.nice.org.uk/TA180