NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Final appraisal determination

Etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis (review of technology appraisal guidance 104 and 125)

1 Guidance

1.1 Etanercept, infliximab and adalimumab are recommended for the treatment of adults with active and progressive psoriatic arthritis when the following criteria are met.

- The person has peripheral arthritis with three or more tender joints and three or more swollen joints, **and**
- The psoriatic arthritis has not responded to adequate trials of at least two standard disease-modifying antirheumatic drugs (DMARDs), administered either individually or in combination.

1.2 Treatment as described in 1.1 should normally be started with the least expensive drug (taking into account drug administration costs, required dose and product price per dose). This may need to be varied for individual patients because of differences in the method of administration and treatment schedules.

1.3 Etanercept, adalimumab or infliximab treatment should be discontinued in people whose psoriatic arthritis has not shown an adequate response using the Psoriatic Arthritis Response Criteria (PsARC) at 12 weeks. An adequate response is defined as an improvement in at least two of the four PsARC criteria, (one of which has to be joint tenderness or swelling score) with no worsening in any of the four criteria. People whose disease has a Psoriasis Area and Severity Index (PASI) 75 response at 12 weeks

but whose PsARC response does not justify continuation of treatment should be assessed by a dermatologist to determine whether continuing treatment is appropriate on the basis of skin response (see 'Etanercept and efalizumab for the treatment of adults with psoriasis' [NICE technology appraisal guidance 103], 'Infliximab for the treatment of adults with psoriasis' [NICE technology appraisal guidance 134] and 'Adalimumab for the treatment of adults with psoriasis' [NICE technology appraisal guidance 146] for guidance on the use of tumour necrosis factor [TNF] inhibitors in psoriasis).

1.4 When using the PsARC healthcare professionals should take into account any physical, sensory or learning disabilities, or communication difficulties that could affect a person's responses to components of the PsARC and make any adjustments they consider appropriate.

2 Clinical need and practice

2.1 Psoriatic arthritis is an inflammatory arthritis affecting the joints and connective tissue and is associated with psoriasis of the skin or nails. The prevalence of psoriasis in the general population is estimated at 2–3%. The prevalence of inflammatory arthritis in people with psoriasis is estimated at up to 30%. At least 20% of people with psoriasis have severe psoriatic arthritis with progressive joint lesions. Psoriatic arthritis is a progressive disorder ranging from mild synovitis to severe progressive erosive arthropathy. People with psoriatic arthritis presenting with oligoarticular disease progress to polyarticular disease and a large percentage develop joint lesions and deformities, which progress over time. Despite clinical improvement with current DMARD treatment, joint damage has been shown radiologically in up to 47% of people with psoriatic arthritis at a median interval of 2 years.

2.2 Psoriatic arthritis can affect people's ability to work and carry out daily activities, which can have a substantial impact on quality of life. The impact of severe psoriasis on health-related quality of life is considered to be similar to that of other major medical conditions including diabetes, heart disease and cancer. People with psoriatic arthritis have a higher self-rated disease severity than those with psoriasis only. People with psoriatic arthritis have a 60% higher risk of mortality than the general population and their life expectancy is estimated to be approximately 3 years shorter.

2.3 Most people with psoriatic arthritis develop skin symptoms before joint symptoms, although joint symptoms may appear first or simultaneously. Psoriatic arthritis usually develops within 10 years of a diagnosis of psoriasis. The rheumatic characteristics of psoriatic arthritis include joint stiffness, pain and swelling, and tenderness of the joints and surrounding ligaments and tendons. Symptoms can range from mild to very severe.

2.4 Assessing the effectiveness of treatments for psoriatic arthritis relies on outcome measures that accurately and sensitively measure disease activity. Outcomes of effectiveness are based on measures of the anti-inflammatory response (such as the PsARC, and the American College of Rheumatology response criteria [ACR 20/50/70]), measures of psoriatic skin lesions (PASI), functional measures (Health Assessment Questionnaire [HAQ]) and radiological assessments (Total Sharp Score, van der Heijde-Sharp Score) of disease progression, quality of life and overall global assessments. Overall response criteria have not yet been clearly defined.

2.5 The aim of psoriatic arthritis treatment is to relieve symptoms, slow disease progression and maintain quality of life. To effectively manage psoriatic arthritis, any associated skin disease also needs to be effectively treated. Non-steroidal anti-inflammatory drugs

(NSAIDs) and local corticosteroid injections are widely used. Disease that is unresponsive to NSAIDs, in particular polyarticular disease, is treated with DMARDs (currently, methotrexate and sulfasalazine are considered the DMARDs of choice) to reduce joint damage and prevent disability. Aggressive treatment of early stage progressive psoriatic arthritis can help to improve prognosis.

3 The technologies

Etanercept

3.1 Etanercept (Enbrel, Wyeth Pharmaceuticals) is a human TNF receptor fusion protein that inhibits TNF-α binding to cell surface TNF receptors. Etanercept is licensed for the treatment of active and progressive psoriatic arthritis in adults whose disease has not responded adequately to previous DMARD therapy.

3.2 The most common adverse events reported in the trials were infections (including upper respiratory tract infections, bronchitis, cystitis and skin infections), injection site reactions (including bleeding, bruising, erythema, itching, pain and swelling), and allergic reactions, such as pruritus. For full details of undesirable effects and contraindications, see the summary of product characteristics.

3.3 The acquisition cost of etanercept is £89.38 per 25-mg prefilled syringe or 25-mg vial with powder for reconstitution (with solvent), and £178.75 per 50-mg prefilled syringe (excluding VAT; British national formulary [BNF] edition 58). The annual cost of etanercept using either 50-mg once-weekly doses (52 doses per year) or 25-mg twice-weekly doses (104 doses per year) is £9295. Costs may vary in different settings because of negotiated procurement discounts.

Infliximab

3.4 Infliximab (Remicade, Schering-Plough) is a chimeric human-murine monoclonal antibody that inhibits the functional activity of TNF-α. Infliximab is licensed for the treatment of active and progressive psoriatic arthritis in adults when the disease has not responded adequately to previous DMARD therapy. Infliximab should be administered:

- in combination with methotrexate, **or**
- alone in people who show intolerance to methotrexate or for whom methotrexate is contraindicated.

3.5 The most common reported adverse events in the trials were infusion reactions and hypersensitivity, infections (tuberculosis, bacterial infections – including sepsis and pneumonia – invasive fungal infections, and other opportunistic infections), hepatitis B reactivation and heart failure. For full details of undesirable effects and contraindications, see the summary of product characteristics.

3.6 The acquisition cost of infliximab is £419.62 per 100-mg vial with powder for reconstitution (excluding VAT; BNF edition 58). The drug cost differs between individuals because the dose is adjusted to each person's body weight. For example, for an adult weighing 75 kg, if it is assumed that vials are not shared between patients, each infusion of 5 mg/kg requires four 100-mg vials at a cost of £1678. The three initial infusions are given at weeks 0, 2 and 6, at a cost of £5035. The subsequent annual cost following the loading doses is £10,910 per year based on infusions repeated every 8 weeks (average 6.5 doses per year). Costs may vary in different settings because of negotiated procurement discounts.

Adalimumab

3.7 Adalimumab (Humira, Abbott Laboratories) is a recombinant human monoclonal antibody that binds specifically to TNF and

neutralises its function. Adalimumab is licensed for the treatment of active and progressive psoriatic arthritis in adults when the disease has not responded adequately to previous DMARD therapy.

3.8 The most common reported adverse events in the trials were infections (including sepsis due to bacterial, mycobacterial, invasive fungal, parasitic, viral, or other opportunistic infections such as listeriosis and pneumocystis), tuberculosis, hepatitis B reactivation, formation of autoimmune antibodies and congestive heart failure. For full details of undesirable effects and contraindications, see the summary of product characteristics.

3.9 The acquisition cost of adalimumab is £357.50 per 40-mg prefilled pen or prefilled syringe (excluding VAT; BNF edition 58). An initial dose of 80 mg is given followed by a 40-mg dose 1 week later. The subsequent annual cost of adalimumab based on 40-mg doses given every 2 weeks is £9295 (26 doses per year). Costs may vary in different settings because of negotiated procurement discounts.

4 Evidence and interpretation

The Appraisal Committee (appendix A) considered evidence from a number of sources (appendix B).

4.1 *Clinical effectiveness*

4.1.1 The Assessment Group identified six double-blind, placebo-controlled, randomised controlled trials (RCTs) in people with psoriatic arthritis for the technologies: two for etanercept, two for infliximab and two for adalimumab.

Etanercept

4.1.2 The two double-blind, placebo-controlled RCTs of etanercept in adults with active psoriatic arthritis were Mease 2000 (n = 60; follow-up 12 weeks) and Mease 2004 (n = 205; follow-up

24 weeks). In both trials 25 mg etanercept was administered by subcutaneous injection twice a week. The inclusion criteria for both trials were active psoriatic arthritis (defined as more than three swollen joints and more than three tender or painful joints, although only the more recent trial specified stable plaque psoriasis), and psoriatic arthritis that had not responded adequately to NSAIDs. The primary outcome variable in the Mease 2000 trial was PsARC and in Mease 2004 it was ACR 20. Data for PASI at week 12 were available from Mease 2000 only.

4.1.3 The Assessment Group conducted a meta-analysis of the outcomes for etanercept at 12 weeks and the pooled estimates from both trials showed that etanercept was statistically significantly more effective than placebo for all outcomes (PsARC, ACR 20, ACR 50, ACR 70, and HAQ percentage change from baseline). For PsARC the pooled relative risk (RR) estimate was 2.60 (95% confidence interval [CI] 1.96 to 3.45), with some evidence of statistical heterogeneity (I^2 = 34%) between the two studies' estimates. For PASI 50, the results from the Mease 2000 trial at 12 weeks showed that etanercept was more effective than placebo (RR = 2.00 [95% CI 0.72 to 5.53]) although this was not statistically significant. For PASI 75 the results showed that etanercept was statistically significantly more effective than placebo (RR = 11.00 [95% CI 0.65 to 186.02]; p = 0.0154).

4.1.4 At 24 weeks the treatment effect for all joint disease outcome measures was statistically significantly greater for etanercept than for placebo, though these data were available only for one trial, Mease 2004. At 24 weeks, the annualised rate of progression as measured radiologically using the Total Sharp Score was statistically significantly lower in people treated with etanercept than in people treated with placebo (Total Sharp Score −0.56; 95% CI −0.86 to −0.26).

4.1.5 At 24 weeks the treatment effect on psoriasis favoured etanercept with RRs for PASI 75 of 7.05 (95% CI 1.68 to 29.56), PASI 50 of 2.65 (95% CI 1.46 to 4.80) and PASI 90 of 1.88 (95% CI 0.36 to 9.90). At 1 year the mean annualised rate of progression on the Total Sharp Score for all people was −0.03 (standard deviation [SD] 0.87), indicating that on average there was no clinically significant progression of joint erosion based on uncontrolled follow-up data.

Infliximab

4.1.6 The two double-blind, placebo-controlled RCTs of infliximab for the treatment of psoriatic arthritis were IMPACT and IMPACT 2. In the IMPACT trial, participants (n = 104) were randomised to receive infusions of infliximab (5 mg/kg) or placebo at weeks 0, 2, 6 and 14 with follow-up at week 16. In IMPACT 2, people (n = 200) were randomised to receive infusions of placebo or infliximab 5 mg/kg at weeks 0, 2, 6, 14 and 22, with assessments at weeks 14 and 24. In both RCTs the inclusion criteria required that participants' psoriatic arthritis should have five or more swollen/tender joints, and that their disease had an inadequate response to at least one DMARD. IMPACT 2 also required people to have active plaque psoriasis with at least one qualifying target lesion (2 cm or more in diameter).

4.1.7 The Assessment Group conducted a meta-analysis of the outcomes for infliximab at 14 weeks and the results for both trials reported a statistically significant improvement in PsARC for people receiving infliximab, relative to those receiving placebo (pooled RR 3.44, 95% CI 2.53 to 4.69). There was some evidence of statistical heterogeneity (I^2 = 68%) between the two study estimates. Infliximab was statistically significantly more effective than placebo for all pooled estimates for outcomes of joint response (ACR 20, ACR 50 and ACR 70) as well as the pooled percentage change

from baseline in HAQ score with infliximab compared with placebo (mean difference −60.37 [95% CI −75.28 to –45.46]).

4.1.8 The Assessment Group also presented pooled estimates for the outcomes of the skin component of psoriatic arthritis over 14–16 weeks and the results showed that infliximab was statistically significantly more effective than placebo.

4.1.9 The IMPACT 2 trial was randomised for 24 weeks followed by an open-label period. The data for all measures of joint disease, psoriasis and HAQ were similar to those at the 14-week follow-up, suggesting that infliximab's benefits were maintained for up to 24 weeks of treatment and for longer-term follow-up (50 weeks for IMPACT and 54 weeks for IMPACT 2) although the data for the longer-term follow-up were uncontrolled.

4.1.10 In terms of radiographic assessment, there was no statistically significant change from baseline in the total modified van der Heijde-Sharp Score for infliximab-treated people followed up at 50 weeks in the IMPACT trial (n = 70: −1.72 [5.82]) or 54 weeks in the IMPACT 2 trial (infliximab/infliximab −0.94 [3.4]; placebo/infliximab 0.53 [2.6]), suggesting infliximab may inhibit progression of joint damage. However, as with other outcomes measured after week 24, there was no placebo group for comparison.

Adalimumab

4.1.11 The two double-blind, placebo-controlled RCTs of adalimumab in adults with active psoriatic arthritis were ADEPT (n = 313, follow-up of 24 weeks) and Genovese 2007 (n = 100, follow-up of 12 weeks). In both trials adults were randomised to adalimumab (40 mg every other week) or placebo. The inclusion criteria for both RCTs required people to have active psoriatic arthritis (defined in both trials as more than three swollen joints and more than three tender

or painful joints, with active psoriatic skin lesions or a documented history of psoriasis). Overall, the baseline characteristics demonstrated that the trial populations were indistinguishable and represented people who required DMARDs or therapy with TNF inhibitors.

4.1.12 The Assessment Group conducted a meta-analysis of the outcomes for adalimumab at 12 weeks and the results from both trials showed a statistically significant improvement for adalimumab compared with placebo for all outcome measures. The pooled RR for PsARC was 2.24 (95% CI 1.74 to 2.88) and the pooled RR for ACR 20 was 3.65 (95% CI 2.57 to 5.17). The pooled RRs for ACR 50 and ACR 70 also favoured adalimumab, although their related CIs were wide. Regarding the associated skin disease, 12-week PASI response measures were reported by only one trial (ADEPT), and the response was statistically significantly greater for adalimumab than placebo at all three PASI thresholds: PASI 50 RR = 5.00 (95% CI 2.77 to 9.03); PASI 75 RR = 11.33 (95% CI 3.65 to 35.17)]; and PASI 90 RR = 43.00 (95% CI 2.66 to 696.04) The CIs, especially for PASI 75 and PASI 90, were wide.

4.1.13 The ADEPT trial was randomised for 24 weeks. The data for all measures of joint disease, psoriasis and HAQ were similar to those at 12-week follow-up. In addition, this trial also reported a statistically significant difference in mean change in Total Sharp Score from baseline (−0.2 versus 0.1, $p < 0.001$) favouring adalimumab over placebo in terms of delayed progression of joint disease, although this duration of follow-up is short.

Indirect comparison performed by the Assessment Group

4.1.14 In the absence of head-to-head RCTs on the relative efficacy of the three TNF inhibitors, an indirect comparison was undertaken by the Assessment Group using placebo as the common comparator. The

results were expressed as the probability of each of the TNF inhibitors achieving a response for the outcome measures PsARC, HAQ, PASI and ACR. Infliximab was associated with the highest probability of achieving a response for all of the outcomes measured. The probability of response in joint disease (PsARC and ACR) was higher with etanercept than with adalimumab, and the probability of response in skin disease (PASI) was higher with adalimumab than with etanercept.

Adverse events

4.1.15 There were no RCTs that directly compared the three drugs. To evaluate the adverse events of the three TNF inhibitors the Assessment Group reviewed a range of study types including RCTs, open-label extensions of trials and observational studies.

4.1.16 The Assessment Group provided a range of estimates for serious adverse event and withdrawal rates across non-randomised studies and large RCTs. These comprised serious infections, cancer, activation of latent tuberculosis, mortality and withdrawals from treatment because of adverse events.

4.1.17 The Assessment Group acknowledged that the adverse event data were primarily from people with rheumatoid arthritis or other indications, so it is unclear to what extent these can be generalised to psoriatic arthritis. Overall, the limited evidence prevented them from drawing firm conclusions from the systematic review about the comparative adverse event profile of the three TNF inhibitors.

4.2 *Cost effectiveness*

Published economic evaluations

4.2.1 The Assessment Group performed a systematic review of published literature and identified three studies (Bansback et al. 2007; Bravo Vergel 2006; and Olivieri et al. 2008) that met the inclusion criteria for the cost-effectiveness review.

4.2.2 The study by Olivieri et al. (2008) was difficult to compare with the other studies because in this study all TNF inhibitors were considered as a group compared with DMARDs. There were no model results. The economic evaluation was made using before-and-after studies and the effectiveness evidence was based on a single trial. This produced an incremental cost-effectiveness ratio (ICER) of around €40,000 (£34,700) per quality-adjusted life year (QALY) gained for TNF inhibitors.

4.2.3 The study by Bansback et al. (2007) compared etanercept with ciclosporin and leflunomide. The economic model focused on response according to PsARC and associated HAQ score, with changes in HAQ and further withdrawals modelled over 10 years. Mease 2004 was the source of evidence for response rates and HAQ. The base-case results showed an ICER of around £28,000 per QALY gained for etanercept compared with ciclosporin and £38,000 per QALY gained for etanercept compared with leflunomide.

4.2.4 The study by Bravo Vergel (2006) compared etanercept with infliximab and palliative care. The model included response according to PsARC and associated HAQ score. Changes in HAQ and further withdrawals were modelled over 40 and 10 years. Evidence from Mease 2000, Mease 2004 and IMPACT was used to model the PsARC response. The ICER for etanercept was between £26,361 and £30,628 per QALY gained compared with palliative care depending on the assumptions made about the deterioration in HAQ score at treatment withdrawal (rebound). Infliximab was the most effective strategy, and generated the highest number of QALYs.

Manufacturer's submission on the cost effectiveness of etanercept

4.2.5 A published cost-effectiveness model originally used to support a submission to NICE in 2004 was adapted to incorporate additional

effectiveness evidence and new comparators. The adjusted model compared the costs and benefits associated with etanercept, infliximab, adalimumab and best supportive care over a lifetime horizon. Best supportive care was assumed to be ciclosporin because the population considered in the model were assumed to have already tried other DMARDs (leflunomide, sulfasalazine and methotrexate).

4.2.6 The base-case results showed that the costs for best supportive care were £53,860 with QALYs of 5.96, and for etanercept the costs were £65,650 with QALYs of 6.90. This resulted in an ICER of £12,480 per QALY gained for etanercept when compared with best supportive care. Adalimumab was extendedly dominated by a combination of etanercept and palliative care (that is, additional QALYs could be generated with etanercept relative to adalimumab at a lower cost per QALY gained than is generated by adalimumab relative to palliative care). Infliximab was dominated by adalimumab (that is, infliximab was more costly and less effective than adalimumab).

Manufacturer's submission on the cost effectiveness of infliximab

4.2.7 In the economic analysis submitted by the manufacturer of infliximab four treatment alternatives were compared over a lifetime horizon. These included maintenance treatment with a TNF inhibitor (infliximab, adalimumab or etanercept) followed by a sequence of DMARDs. The comparator was palliative care with DMARDs. For the health-economic model, the incremental treatment effects for the comparative treatments were estimated for infliximab, etanercept and adalimumab. The direct drug costs for the TNF inhibitors were obtained from BNF edition 56.

4.2.8 The manufacturer presented base-case results for three different scenarios: people weighing 60 kg, 70 kg with vial optimisation for infliximab treatment (that is, making local arrangements so that

vials can be shared between patients who are being treated with infliximab, reducing wastage) and 80 kg. For people weighing 60 kg the base-case results showed that infliximab produced an ICER of £16,942 per QALY gained when compared with palliative care. For people weighing 70 kg, and accounting for vial optimisation, infliximab produced an ICER of £19,982 per QALY gained versus palliative care. For people weighing 80 kg infliximab produced an ICER of £23,022 per QALY gained when compared with palliative care.

Manufacturer's submission on the cost effectiveness of adalimumab

4.2.9 The manufacturer of adalimumab used an individual sampling model to simulate the disease progression of a cohort of people with psoriatic arthritis over a lifetime horizon under different treatment sequences. A 3-month cycle was used. Baseline characteristics from the ADEPT trial for people for whom two previous DMARDs had failed were used in the base-case analysis. The cost of all drugs used in the analysis was calculated based on the recommended dosages and vial prices given in the Monthly Index of Medical Specialties. The model assumed that four 100 mg vials of infliximab were required per infusion, based on an average person weighing 80 kg.

4.2.10 The base-case results showed that adalimumab, with a mean cost of £73,072 and QALYs of 8.33, was the most cost-effective treatment strategy when compared with a DMARD (mean costs of £47,537 and QALYs of 7.47), resulting in an ICER of £29,827 per QALY gained. Etanercept was more costly and had the same mean QALYs gained as adalimumab (8.33). Infliximab was more costly and more effective than adalimumab, which resulted in an ICER of £199,596 per QALY gained compared with adalimumab.

Assessment Group's economic assessment

4.2.11 The Assessment Group updated the economic model developed for 'Etanercept and infliximab for the treatment of adults with psoriatic arthritis' (NICE technology appraisal 104). This model allowed the three TNF inhibitors to be compared with each other. A probabilistic decision analytic model was developed to estimate the incremental costs and incremental QALYs of the three TNF inhibitors compared with palliative care over a lifetime horizon (40 years), only. The price year was 2008/2009 and costs and benefits were discounted at a rate of 3.5%.

4.2.12 The decision analytical model followed a cohort of people that represented the average characteristics of participants in the RCTs and had a Markov structure. People in the cohort were assumed to be 47 years old, had been diagnosed with psoriatic arthritis 7 years previously, were assumed to weigh 60–80 kg, and had psoriatic arthritis that had inadequately responded to at least two DMARDS. People in the treatment arm received etanercept, infliximab or adalimumab and people in the control arm received palliative care. The disease's response to treatment was assessed between 12 and 16 weeks. It was assumed that people whose disease had responded to treatment stayed in the treatment arm, while treatment was discontinued in people whose psoriatic arthritis failed to adequately respond to treatment – these people were assumed to go on to receive palliative care.

4.2.13 The following assumptions were included in the Assessment Group's model: people in the initial 3-month trial period had some improvement in HAQ (even if they did not reach the PsARC threshold); people who had a PASI 75 response would gain at least a 75% improvement in psoriasis compared with baseline PASI; people continuing on TNF inhibitors maintained their initial improvement in HAQ; and the same ongoing risk of withdrawal

from treatment was used for all TNF inhibitors (withdrawal because of reduction in efficacy, adverse events or other reasons).

4.2.14 The base-case analysis in the Assessment Group's model assumed a lifetime (40-year) time horizon for costs and QALYs, a baseline HAQ of 1.05, a baseline PASI of 7.5, rebound equal to gain, and incorporate the correlation between PsARC and PASI 75 outcomes. Health utility was measured as a function of HAQ and PASI based on linear regressions of EQ5D utility versus HAQ and PASI provided by the manufacturers based on RCT evidence. The total lifetime discounted health associated with palliative care was about 5.2 QALYs because the base case assumed that utility declined fairly rapidly in people with uncontrolled arthritis, and may have been less than 0 (representing a health state worse than death) in later years.

4.2.15 The base-case model assumed that people's psoriatic arthritis had failed to respond to treatment with at least two DMARDS but they had not received previous treatment with TNF inhibitors. The Assessment Group also modelled the cost effectiveness of sequencing TNF inhibitor therapies after people's psoriatic arthritis failed to respond to a first-line TNF inhibitor. The base-case analysis reported the lifetime costs and QALYs of the three TNF inhibitors in people with mild-to-moderate psoriatic arthritis, which was presented as an incremental analysis ranking the alternative strategies by mean cost.

4.2.16 Following comments made by NICE consultees on the Technology Assessment Report and model of December 2009, the Assessment Group revised the cost-effectiveness analysis results. The Assessment Group took into account the manufacturer of adalimumab's revised estimates from their RCTs of the effect of adalimumab on HAQ change for PsARC responders and non-responders. The Assessment Group corrected a standard error

calculation when extracting data for the evidence synthesis and used the correct calculation of the costs of adalimumab and etanercept. The results for the base case showed that infliximab was the most effective treatment taking into account both joint and skin effects (QALYs of 7.3), followed by etanercept (QALYs of 7.0), then adalimumab (QALYs of 6.6). Infliximab was also the most costly treatment (£88,442), followed by etanercept (£74,841), then adalimumab (£68,638). The ICER of etanercept compared with palliative care was £17,853 per QALY gained. The ICER for infliximab compared with etanercept was £44,326 per QALY gained. Adalimumab was extendedly dominated by a combination of etanercept and palliative care (that is, additional QALYs could be generated with etanercept relative to adalimumab at a lower cost per QALY gained than the ICER of adalimumab relative to palliative care, adalimumab was therefore excluded from the incremental analysis). Etanercept had the highest probability of being cost effective with probabilities of being cost effective of 44% if the maximum acceptable amount to pay for an additional QALY was £20,000 and 48% if the maximum acceptable amount to pay for an additional QALY was £30,000.

4.2.17 The Assessment Group conducted several univariate sensitivity analyses using different sets of assumptions. The Assessment Group presented the results according to whether the ICER was less than £20,000 per QALY gained, between £20,000 and £30,000 per QALY gained or greater than £30,000 per QALY gained.

4.2.18 The results of these analyses suggested that the ICER of etanercept increased to above £20,000 per QALY gained or was dominated by other strategies when the following assumptions were used and all other variables take mean values as in the base case:

- A patient whose psoriatic arthritis does not achieve a PASI 75 response is admitted to hospital for treatment of psoriasis (annual treatment). The base case assumed these patients are offered ultraviolet (UV) light therapy.
- The HAQ rebounds after withdrawal from TNF inhibitors to natural history rather than to initial gain.
- Treatment with TNF inhibitors becomes ineffective (relative to no treatment) after 10 years.
- Infliximab requires three vials rather than four vials per administration.
- All responders to PsARC have the same change in HAQ at 3 months, regardless of the TNF inhibitor used.

4.2.19 For most sensitivity analyses performed by the Assessment Group, the ICER for infliximab was greater than £30,000 per QALY gained. The ICER of infliximab fell below £30,000 per QALY gained, when the following assumptions were used and all other variables take mean values as in the base case:

- A patient whose psoriatic arthritis does not achieve a PASI 75 response is admitted to hospital for treatment of psoriasis (annual treatment). The base case assumed these patients are offered UV light therapy.
- Infliximab requires three vials rather than four vials per administration.
- If the manufacturer of infliximab's estimates of the cost of treating psoriasis with UV light therapy are used in the Assessment Group's model.
- HAQ improves while on biological therapy. The base case assumes no change after the first 3 months.

4.2.20 The ICER of adalimumab fell below £20,000 per QALY gained and was no longer dominated by other strategies, when the following

assumptions were used and all other variables take mean values as in the base case:

- All responders to PsARC have the same change in HAQ at 3 months, regardless of the TNF inhibitor used.
- A patient whose psoriatic arthritis does not achieve a PASI 75 response is admitted to hospital for treatment of psoriasis (annual treatment). The base case assumed these patients are offered UV light therapy.
- If the manufacturer of infliximab's estimates of the cost of treating psoriasis with UV light therapy are used in the Assessment Group's model.

4.2.21 The Assessment Group performed a sensitivity analysis assuming all TNF inhibitors had the same change in HAQ benefit at 3 months for a PsARC responder. The Assessment Group calculated that the ICERs per QALY gained were £17,717 for adalimumab compared with palliative care, £22,056 for etanercept compared with adalimumab and £50,806 for infliximab compared with etanercept.

4.2.22 The Assessment Group also provided cost-effectiveness results for subgroups with different patient characteristics. For a cohort in which baseline PASI was moderate to severe (PASI of 12.5 instead of 7.5 as in the base-case) the ICER of adalimumab versus palliative care was £16,310 per QALY gained, the ICER of etanercept versus adalimumab was £19,319 per QALY gained and the ICER of infliximab versus etanercept was £27,778 per QALY gained. For a cohort of people with negligible baseline psoriasis etanercept was the most cost-effective strategy with an ICER of £18,512 per QALY gained compared with palliative care, the ICER of infliximab compared with etanercept was £64,744 per QALY gained and adalimumab was extendedly dominated by a combination of etanercept and palliative care. For a cohort of

people with moderate-to-severe psoriasis (baseline PASI of 12.5) whose disease did not achieve a PASI 75 response and are assumed to be admitted to hospital for treatment of psoriasis (annual treatment) instead of annual UV light therapy, the ICER for adalimumab compared with palliative care was £7901 per QALY gained, the ICER for infliximab compared with adalimumab was £10,636 per QALY gained and etanercept was dominated by (that is, was more costly and generated less QALYs than) infliximab.

4.2.23 The Assessment Group presented an additional analysis in which people were assumed to continue on biological treatment after 3 months if their disease had either an adequate PsARC or a PASI 75 response (base case: PsARC only). For etanercept compared with palliative care the ICER was £17,859 per QALY gained, the ICER for infliximab compared with etanercept was £38,194 per QALY gained and adalimumab was extendedly dominated by a combination of etanercept and palliative care (that is, additional QALYs could be generated with etanercept relative to adalimumab at a lower cost per QALY gained than the ICER of adalimumab relative to palliative care).

4.2.24 The Assessment Group presented an analysis that compared the sequencing of the different TNF inhibitors in people with mild-to-moderate skin disease if a first TNF inhibitor has failed. The ICERs depended on which drug was used as first-line therapy, and was therefore ineligible for use as second-line therapy. The Assessment Group noted that the ICERs were broadly similar for people whose psoriatic arthritis failed to respond to first-line therapy because of adverse effects and those whose disease failed first-line therapy because of inefficacy.

4.2.25 An additional sensitivity analysis was performed by the Assessment Group at the Committee meeting and subsequently confirmed by running the model probabilistically. This analysis assumed that

adalimumab and etanercept were equally effective while the PsARC responses for infliximab remained the same as in the original analysis (that is, infliximab was assumed to be more effective than adalimumab and etanercept). The ICER for both adalimumab and etanercept compared with palliative care was £18,296 per QALY gained and the ICER for infliximab compared with adalimumab and etanercept was £45,557 per QALY gained.

4.3 *Consideration of the evidence*

4.3.1 The Appraisal Committee reviewed the data available for the clinical and cost effectiveness of etanercept, infliximab and adalimumab, having considered evidence on the nature of psoriatic arthritis and the value placed on the benefits of etanercept, infliximab and adalimumab by people with the condition, those who represent them, and clinical specialists. It also took into account the effective use of NHS resources.

4.3.2 The Committee considered the clinical effectiveness evidence for etanercept, infliximab and adalimumab. The Committee noted that there were no head-to-head RCTs comparing the TNF inhibitors and so indirect methods of comparison had to be used. The Committee also noted that the RCTs were powered primarily to detect statistically significant differences in the effectiveness of TNF inhibitors compared with placebo on joint disease and only secondarily on any associated skin disease. Nevertheless, the Committee concluded that the RCT evidence was sufficient to appraise the clinical effectiveness of TNF inhibitors.

4.3.3 The Committee considered the clinical-effectiveness data presented by the manufacturers and noted that etanercept, infliximab and adalimumab all showed a statistically significant response in the joint disease (PsARC, ACR) and skin disease (PASI) criteria at 12-week and 24-week follow-up compared with

placebo. Clinical specialists confirmed that in clinical practice improvement in psoriatic arthritis was maintained beyond 24 months, and that some people had been treated with TNF inhibitors for up to 10 years. The Committee heard from a patient expert that TNF inhibitors are effective and valued options for the treatment of psoriatic arthritis and have an appreciable impact on quality of life. The Committee heard from the clinical specialists that there was no theoretical reason to believe that the TNF inhibitors would differ in their efficacy in treating psoriatic arthritis. It heard that etanercept, infliximab and adalimumab were similarly effective in the treatment of psoriatic arthritis in clinical practice, and were used interchangeably. Although the indirect comparison conducted by the Assessment Group suggested that infliximab is the most effective treatment overall, taking into account both skin and joint disease, the Committee concluded that there was not enough evidence to indicate clinically important differences in the effectiveness of individual TNF inhibitors in the treatment of psoriatic arthritis.

4.3.4 The Committee considered the evidence on the adverse event rates associated with the TNF inhibitors, including the reactivation of tuberculosis and the rate of serious infections reported in RCTs, and noted that these data were mainly for people with rheumatoid arthritis. The Committee heard from clinical specialists that the adverse event profile of TNF inhibitors was comparable to that of conventional DMARDs. It also heard that adverse events could result in a break from treatment, for example, by stopping treatment while an infection is resolved, then restarting. The Committee concluded that the tolerability profile of the three TNF inhibitors was comparable.

4.3.5 The Committee then considered the economic models presented by the manufacturers and the Assessment Group. The Committee

noted that the Assessment Group updated the economic model submitted for 'Etanercept and infliximab for the treatment of psoriatic arthritis' (NICE technology appraisal 104) by taking into account the beneficial effect of TNF inhibitors on the skin disease as well as the joint disease. The Committee considered the utility estimates incorporated in the Assessment Group model and noted that the utility formula was derived from the PASI and HAQ. The HAQ response had a greater effect on utility than the PASI, indicating that the calculated utility benefit was mainly driven by the response in joint symptoms rather than skin disease. The Committee accepted that the Assessment Group's approach represented the best means of estimating utility for the purposes of the economic analysis given the available data.

4.3.6 The Committee considered the results of the Assessment Group's base-case model, which incrementally ranked the costs and QALYs associated with the different TNF inhibitors compared with palliative care. The Committee was aware that the acquisition costs of adalimumab and etanercept were similar, and the acquisition cost of infliximab was dependent on the patient's weight and the number of vials required, with additional administration costs (related to intravenous infusion) when compared with etanercept and adalimumab. The results of the model indicated that infliximab was the most effective treatment with an ICER of £44,000 per QALY gained compared with etanercept, while etanercept had an ICER of £18,000 per QALY gained compared with palliative care. The Committee noted that adalimumab was extendedly dominated by a combination of etanercept and palliative care (that is, additional QALYs could be generated with etanercept relative to adalimumab at a lower cost per QALY gained than the ICER of adalimumab relative to palliative care), and had therefore been excluded from the incremental analysis. However, the Committee noted that the estimate of relative effectiveness was based on indirect comparison

only and noted the comments of the clinical experts that the TNF inhibitors were used interchangeably in clinical practice. The Committee therefore concluded that treatment should be initiated with the least expensive drug.

4.3.7 The Committee considered the results of the univariate sensitivity analysis performed by the Assessment Group. The Committee noted that the model was most sensitive to assumptions around the cost of treating uncontrolled skin disease associated with psoriatic arthritis, differences in the relative improvements measured by HAQ score and the cost of infliximab (depending on the average number of vials required to treat people with psoriatic arthritis). The Committee took account of evidence from consultees that vial sharing arrangements for infliximab are available in some clinical settings and may reduce drug wastage by up to 50%. The Committee considered various ways of incorporating vial sharing but concluded that there were insufficient data to incorporate it into the economic model. The Committee accepted the clinical specialists' view that there was no robust evidence that etanercept, infliximab and adalimumab differ in their effectiveness for the treatment of psoriatic arthritis in clinical practice and agreed that the sensitivity analyses performed by the Assessment Group were comprehensive and robust. It noted that the calculated cost-effectiveness ratios of the TNF inhibitors varied depending on the assumptions used. The Committee concluded that, given the lack of conclusive evidence of difference between the TNF inhibitors, treatment choice should be based on cost, taking into account any local discounting agreements and/or vial-sharing arrangements.

4.3.8 The Committee considered the evidence for adalimumab, etanercept and infliximab in the context of clinical practice. The Committee considered that the criteria for recommending etanercept and infliximab (in NICE technology appraisal guidance

104) and adalimumab (in NICE technology appraisal guidance 125) remained valid. The Committee therefore concluded that etanercept, infliximab and adalimumab should be recommended for people with active and progressive psoriatic arthritis when the person has peripheral arthritis with three or more tender joints and three or more swollen joints and whose psoriatic arthritis has not responded to adequate trials of at least two standard DMARDs, administered either individually or in combination.

4.3.9 The Committee considered the recommendations on discontinuing treatment with etanercept and infliximab (in NICE technology appraisal 104) and with adalimumab (in NICE technology appraisal 125). The Committee considered that the recommendations to discontinue treatment based on an inadequate PsARC response at 12 weeks remained valid. The Committee noted that in the Assessment Group scenario analysis, the TNF inhibitors might be equally cost effective in people whose skin disease has a PASI 75 response but whose psoriatic arthritis does not have a PsARC response. The Committee noted that the trial evidence was less robust for PASI response because the degree of skin disease at randomisation was not consistent across the trials. The Committee was aware that previous NICE guidance had recommended the TNF inhibitors for people with severe or very severe plaque psoriasis (see 'Etanercept and efalizumab for the treatment of adults with psoriasis' [NICE technology appraisal guidance 103], 'Infliximab for the treatment of adults with psoriasis' [NICE technology appraisal guidance 134] and 'Adalimumab for the treatment of adults with psoriasis' [NICE technology appraisal guidance 146] for guidance on the use of tumour necrosis factor [TNF] inhibitors in psoriasis). It concluded that people whose skin disease achieves a PASI 75 response but whose psoriatic arthritis does not achieve an adequate PsARC response should be assessed by a dermatologist to determine whether the criteria for

continued treatment with etanercept, adalimumab or infliximab are met for the treatment of the psoriatic component of the condition alone. The Committee also noted the comments from clinical specialists about the benefits of having combined input from rheumatologists and dermatologists in managing this multisystem disease.

4.3.10 The Committee considered the evidence presented by the Assessment Group on the cost effectiveness for the sequencing of TNF inhibitor treatments. The Committee heard from the clinical experts that very limited data were available for the response rate for second-line treatment with TNF inhibitors. These were derived either from trials for people with rheumatoid arthritis or from registry data, which were uncontrolled and comprised predominantly people with rheumatoid arthritis. The Committee concluded that there were insufficient data to make a recommendation on the sequential use of TNF inhibitors in psoriatic arthritis.

4.3.11 The Committee was aware of registries that collect data for the long-term outcomes of treatment with TNF inhibitors for rheumatoid arthritis and psoriasis. The Committee noted the importance of registries in collecting data and supported including outcomes specific to psoriatic arthritis in a suitable registry so that specific information about these treatments in psoriatic arthritis can be captured.

4.3.12 In summary, the Committee considered the clinical and cost effectiveness of etanercept, infliximab and adalimumab in the light of clinical specialists' and patient experts' comments. It considered that there was insufficient evidence of superiority of any one agent over the others. On balance, considering the RCT data, modelling assumptions, modelling results and sensitivity analyses, together with expert opinion, the Committee concluded that etanercept, infliximab and adalimumab were similarly effective. The Committee

considered the higher treatment cost with infliximab compared with adalimumab and etanercept in the base-case model and the possibility of locally arranged discounts for infliximab. The Committee therefore concluded that etanercept, infliximab and adalimumab should be recommended as treatment options for people with psoriatic arthritis with three or more affected joints whose disease had inadequately responded to at least two conventional DMARDs and that the choice of treatment should be based on cost, taking into account acquisition and administration costs and any local discounting agreements and/or vial-sharing arrangements.

Summary of the Appraisal Committee's key conclusions

TA XXX (MTA): Etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis (review of technology appraisal guidance 104 and 125)		**FAD section**
Key conclusion		
Etanercept, infliximab and adalimumab are recommended for the treatment of adults with active and progressive psoriatic arthritis in specific circumstances (see section 1.1) and treatment should normally be started with the least expensive drug (taking into account drug administration costs, required dose and product price per dose). Treatment should be discontinued in people whose psoriatic arthritis has not shown an adequate response using the Psoriatic Arthritis Response Criteria (PsARC) at 12 weeks. People whose disease has a Psoriasis Area and Severity Index (PASI) 75 response at 12 weeks but whose PsARC response does not justify continuation of treatment should be assessed by a dermatologist to determine whether continuing treatment is appropriate on the basis of skin response (see 'Etanercept and efalizumab for the treatment of adults with psoriasis' [NICE technology appraisal guidance 103], 'Infliximab for the treatment of adults with psoriasis' [NICE technology appraisal guidance 134] and 'Adalimumab for the treatment of adults with psoriasis' [NICE technology appraisal guidance 146] for guidance on the use of tumour necrosis factor [TNF] inhibitors in psoriasis).		1
Current practice		
Clinical need of patients including the availability of alternative treatments	Psoriatic arthritis can affect people's ability to work and carry out daily activities, which can have a substantial impact on quality of life. People with psoriatic arthritis have a 60% higher risk of mortality than the general population and their life expectancy is estimated to be approximately 3 years shorter.	2.2
	The aim of psoriatic arthritis treatment is to relieve symptoms, slow disease progression and maintain quality of life. Non-steroidal anti-inflammatory drugs (NSAIDs) and local corticosteroid injections are widely used. Disease that is unresponsive to NSAIDs, in particular polyarticular disease, is treated with disease modifying antirheumatic drugs (DMARDs) to reduce joint damage and prevent disability.	2.5

The technology		
Proposed benefits of the technology How innovative is the technology in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition?)	The Committee heard from a patient expert that tumour necrosis factor (TNF) inhibitors are effective and valued options for the treatment of psoriatic arthritis and have an appreciable impact on quality of life.	4.3.3
What is the position of the treatment in the pathway of care for the condition?	The Committee considered that the criteria for recommending etanercept and infliximab (in NICE technology appraisal guidance 104) and adalimumab (in NICE technology appraisal guidance 125) remained valid.	4.3.8
Adverse effects	The Committee considered the tolerability profile of the three TNF inhibitors to be comparable.	4.3.4
Evidence for clinical effectiveness		
Availability, nature and quality of evidence	There were no head-to-head randomised controlled trials (RCTs) comparing the TNF inhibitors and so indirect methods of comparison had to be used. RCTs were powered primarily to detect statistically significant differences in the effectiveness of TNF inhibitors compared with placebo on joint disease and only secondarily on any associated skin disease. The Committee considered the evidence to be sufficient to appraise the clinical effectiveness of TNF inhibitors.	4.3.2
Relevance to general clinical practice in the NHS	The Committee considered the evidence for adalimumab, etanercept and infliximab in the context of NICE technology appraisal guidance 104 and 125.	4.3.8
Uncertainties generated by the evidence	The Committee concluded that there was not enough evidence to indicate clinically important differences in the effectiveness of individual TNF inhibitors in the treatment of psoriatic arthritis.	4.3.3
Are there any clinically relevant subgroups for which there is evidence of differential effectiveness	The Committee considered the subgroup of people whose skin disease has a PASI 75 response at 12 weeks but whose psoriatic arthritis does not have an adequate PsARC response, indicating treatment should be discontinued. The Committee was aware that previous NICE guidance had recommended the TNF inhibitors for people with severe or very severe plaque psoriasis (see 'Etanercept and efalizumab for the treatment of adults with psoriasis' [NICE technology appraisal guidance 103], 'Infliximab for the treatment of adults with psoriasis' [NICE technology appraisal guidance 134] and 'Adalimumab for the treatment of adults with psoriasis' [NICE technology appraisal guidance 146] for guidance on the use of tumour necrosis factor [TNF] inhibitors in psoriasis). The Committee considered that these people should be referred to a dermatologist to determine whether the criteria for continued treatment with etanercept, adalimumab or infliximab are met for the treatment of the psoriatic component of the condition alone..	4.3.9

Estimate of the size of the clinical effectiveness including strength of supporting evidence	The Committee accepted the clinical specialists' view that there was no robust evidence that etanercept, infliximab and adalimumab differ in their effectiveness for the treatment of psoriatic arthritis in clinical practice.	4.3.7
Evidence for cost effectiveness		
Availability and nature of evidence	The Committee noted that the Assessment Group updated the economic model submitted for 'Etanercept and infliximab for the treatment of psoriatic arthritis' (NICE technology appraisal 104) by including the effectiveness of the TNF inhibitors treatment on the skin disease as well as the joint disease.	4.3.5
Uncertainties around and plausibility of assumptions and inputs in the economic model	The Committee noted that the model was most sensitive to assumptions around the cost of treating uncontrolled psoriasis, differences in the relative HAQ score and the cost of infliximab (depending on the average number of vials required to treat people with psoriatic arthritis).	4.3.7
Incorporation of health-related quality of life benefits and utility values Have any potential significant and substantial health-related benefits been identified that were not included in the quality-adjusted life year (QALY) calculation? How have these been separately evaluated and what is the impact (if any) on the judgement of the most plausible incremental cost-effectiveness ratio) ICER?	The utility was driven by the patients' joint disease response (the Health Assessment Questionnaire [HAQ] response) rather than the skin response (PASI). The Committee considered that the model (updated from NICE technology appraisal 104) took into account the beneficial effects of TNF inhibitors on the skin disease as well as the joint disease. The Committee accepted that the Assessment Group's approach represented the best means of estimating utility for the purposes of the economic analysis given the available data.	4.3.5
Are there specific groups of people for whom the technology is particularly cost effective?	The Committee considered a subgroup of people whose disease achieved a response to PASI but not PsARC. They considered that they should be referred to a dermatologist to determine whether continued treatment is indicated for the symptoms of psoriasis alone.	4.3.9
What are the key drivers of cost effectiveness?	The relative effectiveness of the TNF inhibitors on skin disease and vial sharing arrangements for infliximab.	4.3.7
Most likely cost-effectiveness estimate (given as an ICER)	The Assessment Group base-case analysis found that infliximab was the most effective treatment with an ICER of £44,000 per QALY gained compared with etanercept, while etanercept had an ICER of £18,000 per QALY gained compared with palliative care. The Committee noted that adalimumab was extendedly dominated by a combination of etanercept and palliative care (that is, additional QALYs could be generated with etanercept relative to adalimumab at a lower cost per QALY gained than the ICER of adalimumab relative to palliative care), and had therefore been excluded from the incremental analysis. The Committee took account of evidence from consultees that vial sharing arrangements for infliximab are available in some clinical settings and may reduce drug wastage by up to 50%. The Committee concluded that, given the lack of conclusive evidence of difference between the TNF inhibitors, treatment choice should be based on cost, taking into account any local discounting agreements and/or vial-sharing arrangements.	4.3.6 4.3.7

Additional factors taken into account		
Patient access schemes (Pharmaceutical Price Regulation Programme)	No patient access scheme was submitted for any of the technologies under appraised.	
End-of-life considerations	The end-of-life criteria were not applicable for this population.	
Equalities considerations, Social Value Judgement	No equalities issues were raised.	

5 Implementation

5.1 The Secretary of State and the Welsh Assembly Minister for Health and Social Services have issued directions to the NHS on implementing NICE technology appraisal guidance. When a NICE technology appraisal recommends use of a drug or treatment, or other technology, the NHS must provide funding and resources for it within 3 months of the guidance being published. If the Department of Health issues a variation to the 3-month funding direction, details will be available on the NICE website. The NHS is not required to fund treatments that are not recommended by NICE.

5.2 NICE has developed tools to help organisations put this guidance into practice (listed below). These are available on our website (www.nice.org.uk/guidance/TAXXX). [NICE to amend list as needed at time of publication]

- Slides highlighting key messages for local discussion.
- Costing report and costing template to estimate the savings and costs associated with implementation.
- Implementation advice on how to put the guidance into practice and national initiatives that support this locally.
- A costing statement explaining the resource impact of this guidance.
- Audit support for monitoring local practice.

6 Recommendations for further research

6.1 The Committee highlighted the importance of collecting further data within registries of patients receiving biological treatments for psoriatic arthritis to obtain information on long-term outcomes including adverse events.

7 Review of guidance

7.1 The guidance on this technology will be considered for review in June 2013. The Guidance Executive will decide whether the technology should be reviewed based on information gathered by NICE, and in consultation with consultees and commentators.

Jane Adam
Chair, Appraisal Committee
February 2010

Appendix A: Appraisal Committee members, guideline representatives and NICE project team

A Appraisal Committee members

The Appraisal Committees are standing advisory committees of NICE. Members are appointed for a 3-year term. A list of the Committee members who took part in the discussions for this appraisal appears below. There are four Appraisal Committees, each with a chair and vice chair. Each Appraisal Committee meets once a month, except in December when there are no meetings. Each Committee considers its own list of technologies, and ongoing topics are not moved between Committees.

Committee members are asked to declare any interests in the technology to be appraised. If it is considered there is a conflict of interest, the member is excluded from participating further in that appraisal.

The minutes of each Appraisal Committee meeting, which include the names of the members who attended and their declarations of interests, are posted on the NICE website.

Dr Jane Adam (Chair)

Department of Diagnostic Radiology, St George's Hospital

Professor A E Ades

Professor of Public Health Science, Department of Community Based Medicine, University of Bristol

Elizabeth Brain

Lay Member

Dr Fiona Duncan

Clinical Nurse Specialist, Anaesthetic Department, Blackpool Victoria Hospital, Blackpool

Christopher Earl

Surgical Care Practitioner, Renal Transplant Unit, Manchester Royal Infirmary

John Goulston

Chief Executive, Barking, Havering and Redbridge Hospitals NHS Trust

Dr Peter Heywood

Consultant Neurologist, Frenchay Hospital

Professor Philip Home (Vice Chair)

Professor of Diabetes Medicine, Newcastle University

Dr Terry John

General Practitioner, The Firs, London

Dr Ian Lewin

Consultant Endocrinologist, North Devon District Hospital

Dr Louise Longworth

Reader in Health Economics, Health Economics Research Group, Brunel University

Dr Alec Miners

Lecturer in Health Economics, London School of Hygiene and Tropical Medicine

Dr James Moon

Consultant Cardiologist and Senior Lecturer, University College London Hospital (UCLH) and UCL

Dr Nick Murray

Senior Lecturer and Consultant in Medical Oncology, University of Southampton

Dr David Newsham

Lecturer (Orthoptics), University of Liverpool

Dr Ann Richardson

Lay Member

Angela Schofield

Chairman, Bournemouth and Poole Teaching Primary Care Trust (PCT)

Mike Spencer

General Manager, Cardiff and Vale University Health Board – Facilities and Clinical Support Services

Professor Iain Squire

Consultant Physician, University Hospitals of Leicester

David Thomson

Lay Member

William Turner

Consultant Urologist, Addenbrooke's Hospital

Dr Luke Twelves

General Practitioner, Ramsey Health Centre, Cambridgeshire

Dr John Watkins

Clinical Senior Lecturer/Consultant in Public Health Medicine, Cardiff University and National Public Health Service Wales

Dr Anthony S Wierzbicki

Consultant in Metabolic Medicine/Chemical Pathology, Guy's and St Thomas' Hospitals NHS Trust

Dr Olivia Wu

Reader in Health Economics, University of Glasgow

B NICE project team

Each technology appraisal is assigned to a team consisting of one or more health technology analysts (who act as technical leads for the appraisal), a technical adviser and a project manager.

João Vieira
Technical Lead

Eleanor Donegan
Technical Adviser

Bijal Joshi
Project Manager

Appendix B: Sources of evidence considered by the Committee

A The assessment report for this appraisal was prepared by:

CRD/CHE Technology Assessment Group (Centre for Reviews and Dissemination/Centre for Health Economics), University of York

- Rodgers M, Research, Epstein D, et al. Etanercept, Infliximab and adalimumab for the treatment of psoriatic arthritis (November 2009)

B The following organisations accepted the invitation to participate in this appraisal as consultees and commentators. They were invited to comment on the draft scope, assessment report and the appraisal consultation document (ACD). Organisations listed in I, II and III were also invited to make written submissions and have the opportunity to appeal against the final appraisal determination.

I Manufacturers/sponsors:

- Abbott Laboratories
- Schering-Plough
- Wyeth Pharmaceuticals

II Professional/specialist and patient/carer groups:

- Arthritis & Musculoskeletal Alliance
- Arthritis Care
- British Dermatological Nursing Group
- British Association of Dermatologists
- British Society for Rheumatology
- Primary Care Dermatology Society
- Primary Care Rheumatology Society
- Psoriasis and Psoriatic Arthritis Alliance
- Royal College of Physicians
- Skin Care Campaign

III Other consultees:

- Hull Primary Care Trust

IV Commentator organisations (without the right of appeal):

- Cochrane Skin Group – Centre of Evidence-based Dermatology
- Department of Health, Social Services and Public Safety for Northern Ireland
- Pfizer
- Sanofi-Aventis
- Schering Plough
- Scottish Intercollegiate Guidelines Network
- Wyeth Pharmaceuticals

C The following individuals were selected from clinical specialist and patient expert nominations from the non-manufacturer/sponsor consultees and commentators. They participated in the Appraisal Committee discussions and provided evidence to inform the Appraisal Committee's deliberations. They gave their expert personal view on etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis by attending the initial Committee discussion and/or providing written evidence to the Committee. They were also invited to comment on the ACD.

- Dr Philip Helliwell, Senior Lecturer in Rheumatology, nominated by the British Society for Rheumatology – clinical specialist
- Dr Eleanor Korendowych, Consultant Rheumatologist and Honorary Senior Lecturer – clinical specialist
- Professor Alex Anstey, Consultant Dermatologist/Professor, nominated by the British Association for Dermatologists.
- Denise Morris, nominated by the Psoriatic and Psoriatic Arthritis Alliance – patient expert.

D Representatives from the following manufacturers/sponsors attended Committee meetings. They contributed only when asked by the Committee chair to clarify specific issues and comment on factual accuracy.

- Abbott Laboratories
- Schering Plough
- Wyeth Pharmaceuticals