NICE National Institute for Health and Care Excellence

NICE guidance

Golimumab for the treatment of psoriatic arthritis

Technology appraisal guidance
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Your responsibility

The recommendations in this guidance represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, health professionals are expected to take this guidance fully into account, alongside the individual needs, preferences and values of their patients. The application of the recommendations in this guidance is at the discretion of health professionals and their individual patients and do not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian.

All problems (adverse events) related to a medicine or medical device used for treatment or in a procedure should be reported to the Medicines and Healthcare products Regulatory Agency using the Yellow Card Scheme.

Commissioners and/or providers have a responsibility to provide the funding required to enable the guidance to be applied when individual health professionals and their patients wish to use it, in accordance with the NHS Constitution. They should do so in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.

Contents

1 Recommendations

1.1 Golimumab is recommended as an option for the treatment of active and progressive psoriatic arthritis in adults only if:

- it is used as described for other tumour necrosis factor (TNF) inhibitor treatments in NICE's technology appraisal guidance on etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis **and**
- the manufacturer provides the 100 mg dose of golimumab at the same cost as the 50 mg dose.

1.2 When using the Psoriatic Arthritis Response Criteria (PsARC; as set out in NICE's technology appraisal guidance on etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis), 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 The technology

2.1 Golimumab (Simponi, Schering-Plough/Centocor) is a human monoclonal antibody that prevents the binding of tumour necrosis factor (TNF) to its receptors, thereby neutralising its activity. Golimumab has a marketing authorisation for the treatment of active and progressive psoriatic arthritis (alone or in combination with methotrexate) in adults when the response to previous disease-modifying antirheumatic drug (DMARD) therapy has been inadequate. The summary of product characteristics (SPC) notes that golimumab has also been shown to improve physical function in this population.

2.2 Golimumab is contraindicated in people with moderate to severe heart failure, hereditary problems of fructose intolerance, active tuberculosis and other severe infections. Before initiating therapy, physicians should evaluate people for prior evidence of hepatitis B virus infection, and both active and inactive (latent) tuberculosis infection. The SPC states that the needle cover on the pre-filled golimumab injection pen contains latex and therefore may cause allergic reactions in people with latex sensitivity. The SPC reports that the most common adverse reactions are upper respiratory tract infections, including nasopharyngitis, pharyngitis, laryngitis and rhinitis. For full details of adverse effects, contraindications, special warnings and precautions for use, see the SPC.

2.3 Golimumab is injected subcutaneously via a pre-filled injection pen. The recommended dose is 50 mg given once a month, on the same date each month. The SPC states that in people who weigh more than 100 kg whose psoriatic arthritis does not show an adequate clinical response after 3 or 4 doses, the dose of golimumab may be increased to 100 mg once a month. The cost of golimumab is £774.58 for a 50 mg pre-filled injection pen (excluding VAT, 'MIMS' February 2011 edition), which is equivalent to an annual cost of £9,294.96 (based on the 50 mg dose). Costs may vary in different settings because of negotiated procurement discounts.

2.4 The manufacturer of golimumab has agreed a patient access scheme with the Department of Health, in which the 100 mg dose of golimumab will be available to the NHS at the same cost as the 50 mg dose. The Department of Health considered that this patient access scheme does not constitute an excessive

administrative burden on the NHS.

3 The manufacturer's submission

The Appraisal Committee considered evidence submitted by the manufacturer of golimumab and a review of this submission by the Evidence Review Group (ERG).

3.1 The main clinical effectiveness data were derived from a single phase 3 randomised controlled trial (RCT) – GO-REVEAL. The trial compared golimumab with placebo for the treatment of active and progressive psoriatic arthritis in people who had symptoms despite the use of current or previous DMARDs or non-steroidal anti-inflammatory drugs. Of the 405 trial participants, 113 were randomised to placebo, 146 were randomised to a 50 mg dose of golimumab and 146 were randomised to a 100 mg dose of golimumab. Randomisation was maintained for 24 weeks. Upward titration was allowed at week 16, such that the participants in the placebo group could switch to 50 mg golimumab and those in the 50 mg golimumab group could have their dose increased to 100 mg if their disease had failed to respond. In the placebo group 50% of participants crossed over to golimumab 50 mg treatment and in the golimumab 50 mg group 20% crossed over to golimumab 100 mg treatment. Outcomes were assessed at 14 and 24 weeks.

3.2 The primary outcomes in GO-REVEAL were American College of Rheumatology (ACR) 20 response at week 14 and the change from baseline in the psoriatic arthritis modified van der Heijde-Sharp (vdH-S) score at week 24. Secondary outcomes included ACR 20 response at week 24, Psoriatic Arthritis Response Criteria (PsARC) response at weeks 14 and 24, and Psoriasis Area and Severity Index (PASI) 75 improvement at week 14 in participants with psoriasis that affected 3% or more of their body surface area at baseline. Physical functional status was measured by Health Assessment Questionnaire (HAQ) score at week 24. Health-related quality of life was measured by the Short Form 36 Health Survey (SF-36) at week 14.

3.3 The week 14 results of GO-REVEAL indicated that, compared with placebo, golimumab showed a statistically significant improvement in joint disease. An ACR 20 response was seen in 50.7% of participants in the 50 mg treatment arm compared with 8.8% in the placebo arm (relative risk [RR] 5.727, 95% confidence interval [CI] 3.24 to 10.56). A PsARC response was seen in 73.3% of participants

in the 50 mg treatment arm compared with 21.2% in the placebo arm (RR 3.451, 95% CI 2.46 to 4.87). Golimumab also showed a statistically significant improvement in skin disease as measured by PASI 75 at both 14 and 24 weeks. A PASI 75 response was seen in 40.4% of participants in the 50 mg treatment arm compared with 2.5% in the placebo arm (RR 15.945, 95% CI 4.62 to 59.11) at 14 weeks, and in 55.9% of participants in the 50 mg treatment arm compared with 1.4% in the placebo arm (RR 40.794, 95% CI 7.86 to 232.88) at 24 weeks. There was also a statistically significant improvement in functional status (HAQ) at 24 weeks. A mean HAQ score change from baseline of 0.33 (standard deviation [SD] 0.55, $p<0.001$) was observed in the golimumab 50 mg arm compared with -0.01 (SD 0.49) in the placebo arm. Data on HAQ score change from baseline were not available for the 14-week time point.

3.4 The manufacturer reported that golimumab 50 mg produced a statistically significant reduction from baseline in vdH-S score of 0.16 ($p=0.01$) at 24 weeks compared with placebo. The reduction from baseline in vdH-S score was not statistically significant in the golimumab 100 mg group ($p=0.09$). The manufacturer did not report vdH-S scores at the 14-week time point.

3.5 The Evidence Review Group (ERG) reported that the main limitation of the efficacy evaluation of golimumab was that the analyses of efficacy outcomes were restricted to the GO-REVEAL trial, which had a limited sample size and was of limited duration (see section 3.1).

3.6 The manufacturer stated that the most frequently reported adverse events associated with golimumab therapy were infections and infestations, including upper respiratory tract infections and nasopharyngitis. The manufacturer reported that the safety profile of golimumab was comparable to that of the other TNF inhibitors adalimumab, etanercept and infliximab.

3.7 The ERG reported concerns about the adverse event data presented for golimumab. It noted that no long-term adverse event data had been presented, and that in its original submission the manufacturer had not included adverse event data on golimumab from controlled studies of its use in other conditions such as rheumatoid arthritis or ankylosing spondylitis. The ERG reported that the manufacturer's conclusion that golimumab has a safety profile comparable to that of the other TNF inhibitors may be premature.

3.8 Following consultation on the Appraisal Consultation Document, the manufacturer submitted evidence on the long-term safety of golimumab. These data included 104-week results from the GO-REVEAL extension study in addition to 52- and 104-week safety data in trial participants with psoriatic arthritis, rheumatoid arthritis and ankylosing spondylitis who had received treatment with golimumab across all of the original phase 3 studies. These data were marked as confidential and therefore cannot be reported.

3.9 In the absence of head-to-head comparisons between golimumab and the other TNF inhibitors, the manufacturer conducted a mixed treatment comparison. The mixed treatment comparison included 7 trials: the GO-REVEAL trial (golimumab versus placebo); 2 RCTs comparing etanercept with placebo (Mease 2000 and Mease 2004); 2 RCTs comparing infliximab with placebo (IMPACT and IMPACT 2); and 2 RCTs comparing adalimumab with placebo (ADEPT and Genovese 2007). All of the TNF inhibitors have marketing authorisations for the treatment of active and progressive psoriatic arthritis that has responded inadequately to previous DMARDs.

3.10 The trials included in the mixed treatment comparison were similar in terms of joint disease severity at baseline (for example, mean tender joint count and mean swollen joint count). There were differences, however, in the proportions of trial participants who could be evaluated for psoriasis endpoints at baseline. Most participants had received treatment with 1 prior DMARD, although no trial specified non-response to at least 2 DMARDs.

3.11 The outcomes included in the mixed treatment comparison analyses were PsARC response, change in HAQ score given PsARC response to treatment, change in HAQ score given no PsARC response, and change in PASI in people with psoriasis that affected 3% or more of their body surface area at baseline. The manufacturer selected absolute changes as the main outcomes, stating that these were the most appropriate outcomes for economic modelling. No analysis of the ACR outcomes was included in the mixed treatment comparison.

3.12 The results of the mixed treatment comparison indicated that of the 4 TNF inhibitors, golimumab was associated with the third highest PsARC response and absolute change in PASI from baseline. Of the 4 TNF inhibitors, golimumab had the lowest HAQ score change from baseline, both in people whose disease

responded to treatment based on PsARC score and in those whose disease did not respond. The numerical values for each outcome derived from the mixed treatment comparison were marked as confidential and therefore cannot be reported.

3.13 The ERG reported that the network of trials included in the mixed treatment comparison was appropriately constructed, but that there were differences among the trial populations in disease severity and number of previously tried DMARDs (with many participants having received only 1 previous DMARD). The ERG commented that the trial populations were not precisely representative of the population with active and progressive psoriatic arthritis for whom TNF inhibitors are recommended in current British Society for Rheumatology guidelines and in NICE's technology appraisal guidance on etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis (TA199).

3.14 The manufacturer developed its own economic evaluation, which comprised a patient cohort model. The model compared the effects of treatment with golimumab (50 mg) in adults with active and progressive psoriatic arthritis whose disease had responded inadequately to DMARDs with the effects of treatment with infliximab, adalimumab and etanercept and with palliative care. All people entered the model with the same baseline characteristics as participants in the GO-REVEAL trial and left the model at death, irrespective of the treatment regimen. The model used a 12-week cycle for the first 2 cycles and annual cycles thereafter. The model captured response to treatment using HAQ score (conditional on PsARC response) as the arthritis measure and PASI score as the psoriasis measure. If there was no response to treatment at 12 weeks (according to PsARC), treatment was discontinued. The price year used for costs was not reported in the manufacturer's submission. Costs and benefits were discounted at 3.5% per annum over 40 years.

3.15 The manufacturer reported that estimates of treatment effectiveness – including PsARC response, HAQ score changes from baseline for people whose disease had responded to treatment according to PsARC at 12 weeks, HAQ score changes from baseline for those whose disease had not responded to treatment according to PsARC at 12 weeks, and PASI change from baseline in people with measurable psoriasis – were derived from the mixed treatment comparison.

3.16 The model assumed that people who continue treatment with a TNF inhibitor maintain their initial improvement in HAQ score. The same ongoing rate of withdrawal from treatment was used for all the TNF inhibitors (16.5% per annum) and represented withdrawal because of treatment failure or adverse events.

3.17 The manufacturer combined data from IMPACT2 (a study of infliximab) and GO-REVEAL using the 'Gray' algorithm to estimate utility values. The Gray algorithm converts Short Form 36 (SF-36) data to EuroQol (EQ-5D) estimates and then to utilities. The disutility of adverse events was not modelled.

3.18 The manufacturer reported that resource use associated with treatment, administration and monitoring of infliximab, etanercept and adalimumab was taken from the Assessment Group's model for TA199. In the patient access scheme (as described in section 2.4) the manufacturer provides the 100 mg dose of golimumab at the same cost as the 50 mg dose. Therefore, only the cost of the 50 mg dose of golimumab (£774.58) was included in the model. The model contained an additional 4 hours of staff nurse costs for training people to self-administer subcutaneous TNF inhibitors. The costs of infliximab were initially calculated on the assumption that vial sharing was allowed (using an average of 3.5 vials per infusion, although this assumption was later removed following a request for clarification from the ERG). The costs associated with adverse events were not included.

3.19 The manufacturer revised its original base-case estimates in response to a request from the ERG for clarification about the way utilities were calculated and for the removal of the infliximab vial sharing assumption. The revised base-case results produced total costs, total quality-adjusted life years (QALYs) and incremental cost-effectiveness ratios (ICERs, pairwise comparisons with palliative care) as follows:

- palliative care: total costs of £62,224 and total QALYs of 6.61
- adalimumab: total costs of £86,410 and total QALYs of 7.89, resulting in an ICER of £18,824 per QALY gained
- golimumab: total costs of £94,151 and total QALYs of 8.21, resulting in an ICER of £19,993 per QALY gained
- etanercept: total costs of £94,578 and total QALYs of 8.49, resulting in an

ICER of £17,177 per QALY gained

- infliximab: total costs of £106,620 and total QALYs of 8.49, resulting in an ICER of £23,578 per QALY gained.

3.20 The ERG reported that the manufacturer had not provided an incremental analysis in which dominated and extendedly dominated options were excluded. An option is 'dominated' if there is another option that is less costly and more effective. An option is 'extendedly dominated' when its ICER is higher than that of the next, more effective, option when compared with a common baseline (that is, it is dominated by a combination of 2 other alternatives). The ERG recalculated the manufacturer's base-case results by incrementally comparing each treatment with the next, more effective, option and excluding those that were extendedly dominated. The recalculated base-case results showed that both adalimumab and golimumab were extendedly dominated by a combination of etanercept and palliative care. Etanercept in comparison with palliative care was associated with an incremental cost of £32,354 and an incremental QALY gain of 1.88, resulting in an ICER of £17,209. Infliximab was dominated by etanercept.

3.21 The manufacturer conducted 2 subgroup analyses: 1 of the population with 'predominantly' rheumatic disease and 1 of the population with 'significant' psoriasis. The ERG recalculated the results of these analyses as described in section 3.20. The results of the recalculated subgroup analyses show adalimumab and golimumab to be extendedly dominated by a combination of etanercept and palliative care. Etanercept in comparison with palliative care was associated with an incremental cost of £34,492 and an incremental QALY gain of 2.21, resulting in an ICER of £15,607 per QALY gained in the rheumatic disease subgroup. In the psoriasis subgroup, etanercept in comparison with palliative care was associated with an incremental cost of £31,564 and an incremental QALY gain of 2.25, resulting in an ICER of £14,028 per QALY gained. Infliximab was dominated by etanercept in the rheumatic disease subgroup, and was associated with an incremental cost of £5,702 and an incremental QALY gain of 0.01, resulting in an ICER of £570,200 per QALY gained in comparison with etanercept in the psoriasis subgroup.

3.22 The ERG commented that the model structure was reasonable. The ERG stated that the inclusion of costs to cover time for training in self-injection may have

been unnecessary, but reported that all other included costs were appropriate. The ERG considered that it may have been appropriate to account for the possibility of dose escalation to 100 mg (as per the marketing authorisation; see section 2.3). The ERG reported that the subgroup analyses were appropriate.

3.23 Full details of all the evidence are in the manufacturer's submission and the ERG report.

4 Consideration of the evidence

4.1 The Appraisal Committee reviewed the data available on the clinical and cost effectiveness of golimumab, having considered evidence on the nature of psoriatic arthritis and the value placed on the benefits of golimumab by people with the condition, those who represent them, and clinical specialists. It also took into account the effective use of NHS resources and the impact of the patient access scheme (see section 2.4).

4.2 The Committee understood that psoriatic arthritis can cause significant distress and psychological impact on the person's life, employment and social activities. The Committee heard from a patient expert that TNF inhibitors are valued options for the treatment of psoriatic arthritis and have a positive impact on quality of life. It understood that people with the condition may prefer the option of a treatment that is self-injectable and/or has a longer retreatment interval. The Committee understood that people value having a choice of TNF inhibitors and that another treatment option will always be welcome.

4.3 The Committee considered current clinical practice for the treatment of psoriatic arthritis. It understood that TA199 recommends adalimumab, etanercept and infliximab for the treatment of psoriatic arthritis in people who have peripheral arthritis with 3 or more tender joints and 3 or more swollen joints, and when the psoriatic arthritis has not responded to adequate trials of at least 2 standard DMARDs (administered either individually or in combination). The Committee also noted that TA199 specifies that treatment should be with the least expensive drug, taking into account drug administration costs, required dose and product price per dose. It heard from the clinical specialists that they considered there to be little demonstrable difference between the TNF inhibitors in terms of their clinical effectiveness. The clinical experts did, however, note slight differences among the TNF inhibitors in TA199 with regard to the subjective reduction in response to treatment in the skin and joint components of the disease. The Committee heard from the commissioning expert that subtle differences in cost and administration, particularly with regard to dose escalation (as included in the marketing authorisation for infliximab) and hospitalisation, can make a big cost difference. The Committee concluded that adalimumab, etanercept and infliximab were the appropriate comparators for golimumab.

4.4 The Committee heard from the clinical specialists and the patient expert that people often prefer a less frequent dosing schedule; that is, a longer time period between treatments. However, the Committee noted that the longer retreatment interval associated with golimumab could potentially result in more discomfort because of waning efficacy before retreatment. It understood that people with psoriatic arthritis and their clinicians may therefore value the once-monthly, self-injectable administration of golimumab. The Committee concluded that golimumab could, on balance, be a valued additional treatment option for people with psoriatic arthritis.

4.5 The Committee considered the evidence on the clinical effectiveness of golimumab. It understood that the main clinical effectiveness data were derived from a single phase 3 RCT. The Committee noted statistically significant outcomes for the 50 mg dose compared with placebo in terms of improvements in joint disease, skin disease and functional status (see sections 3.3 and 3.4). The Committee concluded that golimumab was clinically effective compared with placebo.

4.6 The Committee discussed the 100 mg dose of golimumab, which may be considered for people who weigh more than 100 kg and whose psoriatic arthritis has not responded after 3 or 4 doses of golimumab (as stated in the SPC). It noted that neither the 100 mg arm nor dose escalation to 100 mg in the 50 mg arm in the GO-REVEAL trial was limited to people who weighed more than 100 kg, and therefore the trial population did not reflect the population in the marketing authorisation for the 100 mg dose. The Committee heard from clinical specialists that they would be more likely to select a different TNF inhibitor than to increase the dose if the 50 mg dose of golimumab failed to produce a response. The Committee concluded that it was uncertain of the extent to which the 100 mg dose would be used in clinical practice.

4.7 The Committee noted that there had been no head-to-head trials of golimumab and any of the other TNF inhibitors, and that, as a result, the manufacturer had conducted a mixed treatment comparison. The Committee recognised the limitations of mixed treatment comparisons and was aware that the associated results would need to be interpreted with caution. It also noted the manufacturer's reservations about mixed treatment comparisons and the uncertainty associated with the use of such methodologies, but noted that no

alternative methods or data had been provided. Following the consultation on the Appraisal Consultation Document, the manufacturer suggested the removal of the Mease 2000 results (for etanercept) from the mixed treatment comparison, because this trial did not disaggregate HAQ scores in the same way as other trials, and showed better results for etanercept than Mease 2004 (the larger etanercept trial). The Committee had misgivings about the selective removal of individual trials, but heard from the ERG that extracting the Mease 2000 study from the mixed treatment comparison had little effect on the results. The Committee agreed it would bear this in mind when considering the results of the mixed treatment comparison.

4.8 The Committee carefully considered the results of the mixed treatment comparison. It noted that for PsARC response and absolute change in PASI from baseline, the results showed that golimumab was generally equivalent to the other TNF inhibitors. However, it also noted that golimumab had the lowest HAQ score change from baseline (both in participants whose disease responded to treatment based on PsARC score and those whose disease did not respond based on PsARC score) compared with the other TNF inhibitors.

4.9 The Committee further discussed the HAQ results from the mixed treatment comparison. The Committee understood from the clinical specialists and the patient expert that pain and disability caused by arthritis (as captured by HAQ score and reflected in the manufacturer's economic model) often have a significant impact on the person's quality of life. The Committee was concerned that, out of the 4 TNF inhibitors that were compared, golimumab had the lowest HAQ score change from baseline and that this might indicate inferiority of its anti-arthritic activity (see section 3.12); however, the Committee was also aware of the limitations of the mixed treatment comparison methodology. Therefore, the Committee also considered the radiographic progression data, which, together with the change in HAQ score, could be used to assess the effect of a treatment on disease progression. The Committee noted the statistically significant reduction from baseline in vdH-S score (a measure of radiographic progression) for golimumab compared with placebo at 24 weeks (-0.16 for 50 mg golimumab compared with 0.27 for placebo, p=0.01; see section 3.4). It noted that the change from baseline in vdH-S score at week 24 for golimumab was less than that for infliximab (-0.70 for 5 mg/kg infliximab compared with 0.82 for placebo, p<0.001), which was the other TNF inhibitor for which radiographic progression

was measured by vdH-S score in the trials included in the mixed treatment comparison. The Committee was aware, however, that this difference may be due to differences in the trial populations, as reflected by the respective changes from baseline with placebo. The Committee also understood that the absolute differences between the 2 changes from baseline were small. Although the evidence suggested that golimumab may be less effective in its anti-arthritic activity (based on the HAQ score results from the mixed treatment comparison and the data for radiographic progression), on balance the Committee concluded that the evidence was not robust enough to confirm clinically important differences in the effectiveness of golimumab compared with the other TNF inhibitors.

4.10 The Committee considered the evidence on the adverse event rates associated with the use of golimumab. It noted a number of reported 'serious' adverse events, but understood that GO-REVEAL was not powered to detect statistically significant differences in adverse event outcomes. The Committee considered the additional evidence submitted by the manufacturer on the long-term adverse event data for golimumab in people with psoriatic arthritis, and also for people with rheumatoid arthritis and ankylosing spondylitis. It concluded that although there remains uncertainty about golimumab's long-term adverse event profile, it had not been shown to be different from that of other TNF inhibitors.

4.11 The Committee considered the economic model presented by the manufacturer. The Committee noted that the model assumed people continuing on therapy maintained their initial improvement in HAQ score. The Committee considered the utility estimates incorporated in the model, and noted that the utility formula was derived from the HAQ score change and the PASI response. The HAQ score change had a greater effect on utility than the PASI response did, indicating that the calculated utility benefit was driven more by the reduction in joint symptoms than the reduction in skin disease. The Committee concluded that this was appropriate (see section 4.9).

4.12 The Committee considered the results of the manufacturer's base-case analysis, which compared each of the TNF inhibitors (including golimumab) with palliative care. The Committee heard from the ERG that the pair-wise comparisons with palliative care needed to be reworked into an incremental analysis comparing each treatment with the next most effective alternative. The ERG re-presented

these results. The Committee was aware that the acquisition costs of adalimumab, etanercept and golimumab (50 mg) were similar, and that the acquisition cost of infliximab was dependent on the person's weight and the amount of the drug required, with additional administration costs for infliximab (related to intravenous infusion). The Committee noted that all alternatives to etanercept were either dominated (infliximab was more expensive but no better than etanercept) or extendedly dominated (adalimumab and golimumab were, in effect, less cost effective than etanercept; see section 3.20). The Committee agreed that golimumab was, in effect, less cost effective than etanercept.

4.13 The Committee was aware, however, that TA199 recommends adalimumab and infliximab alongside etanercept. The Committee therefore also considered whether golimumab was at least as cost effective as adalimumab and infliximab. The Committee was aware that in the incremental analysis, both adalimumab and golimumab were extendedly dominated by etanercept. However, the Committee noted that the pairwise ICER of golimumab compared with adalimumab alone would be approximately £24,000 per QALY gained. The Committee similarly noted that the pairwise ICER for golimumab compared with infliximab would be approximately £45,000, aware that in this instance the ICER would represent a 'savings per QALY lost', as golimumab was associated with both lower costs and fewer QALYs compared with infliximab (see section 3.19). Given the weaknesses of the evidence suggesting lesser clinical effectiveness of golimumab compared with the other TNF inhibitors, and the estimates of golimumab's cost effectiveness compared with adalimumab and infliximab, the Committee concluded that the 50 mg dose of golimumab was acceptable when the criteria in TA199 are met; that is, the person has peripheral arthritis with 3 or more tender joints and 3 or more swollen joints, and the psoriatic arthritis has not responded to adequate trials of at least 2 standard disease-modifying antirheumatic drugs (DMARDs), administered either individually or in combination.

4.14 The Committee considered the 100 mg dose of golimumab. The Committee was aware that the SPC for golimumab states that for people who weigh more than 100 kg whose disease does not show an adequate clinical response after 3 or 4 doses, the dose of golimumab may be increased to 100 mg once a month. The Committee heard 2 different opinions about the proportion of people who would be eligible for the higher dose. The Committee agreed that this proportion was uncertain, but that it could be substantial. The Committee noted that the 100 mg

dose of golimumab was not considered in the economic model, but that, because of the patient access scheme (as described in section 2.4), the cost of the 100 mg dose would be equal to that of the 50 mg dose. In addition, the Committee acknowledged the comments from the clinical specialists that, in clinical practice, people would be more likely to be switched to a different TNF inhibitor if no response was observed with the 50 mg dose, than to have the dose increased (see section 4.6). The Committee also noted TA199 states that treatment choice should be based on cost (taking into account drug administration costs, required dose and product price per dose), with treatment initiated with the least expensive drug. Therefore, the Committee concluded that with the incorporation of the patient access scheme, golimumab would be considered an acceptable option for the treatment of psoriatic arthritis if used as described for other TNF inhibitors in TA199.

4.15 The Committee discussed the discontinuation of treatment with etanercept, infliximab and adalimumab in TA199. The Committee considered that the recommendation to discontinue treatment based on an inadequate PsARC response at 12 weeks included in TA199 was also appropriate for golimumab. The Committee was aware that no evidence had been provided by the manufacturer for the use of golimumab after the failure of other TNF inhibitors. The Committee was therefore unable to make recommendations about the use of golimumab following the failure of other TNF inhibitors.

4.16 The Committee was aware that there may be some circumstances that could affect a person's responses to components of the PsARC such as any physical, sensory or learning disabilities, or communication difficulties. The Committee concluded that in such cases, healthcare professionals should make any adjustments they consider appropriate.

4.17 The Committee was aware of registries that collect data on the long-term outcomes of treatment with TNF inhibitors for rheumatoid arthritis. The Committee noted the importance of registries in gathering data and supported the inclusion of outcomes specific to psoriatic arthritis in a suitable registry so that specific information about treatments and treatment-related adverse events in psoriatic arthritis can be collected.

4.18 In summary, the Committee considered the clinical and cost effectiveness of

golimumab in the light of the submitted evidence and the comments of the clinical specialists, the commissioning expert and the patient expert. The Committee noted that although the evidence suggested that golimumab may be less effective in its anti-arthritic activity (based on the HAQ score results from the mixed treatment comparison and the data for radiographic progression), the evidence was not robust enough to confirm clinically important differences in the effectiveness of golimumab compared with the other TNF inhibitors. The Committee further noted that golimumab was, in effect, not cost effective when compared with etanercept, but may be cost effective when compared with adalimumab and infliximab. The Committee was aware that the patient access scheme (as described in section 2.4) would provide the 100 mg dose of golimumab at the same cost as the 50 mg dose. The Committee concluded that, with the incorporation of the patient access scheme and if the criteria specified in TA199 were met, golimumab should be recommended as an option for the treatment of active and progressive psoriatic arthritis in adults, as described for other TNF inhibitor treatments in TA199.

5 Implementation

5.1 Section 7 of the National Institute for Health and Care Excellence (Constitution and Functions) and the Health and Social Care Information Centre (Functions) Regulations 2013 requires integrated care boards, NHS England and, with respect to their public health functions, local authorities to comply with the recommendations in this evaluation within 3 months of its date of publication.

5.2 The Welsh ministers have issued directions to the NHS in Wales on implementing NICE technology appraisal guidance. When a NICE technology appraisal guidance recommends the use of a drug or treatment, or other technology, the NHS in Wales must usually provide funding and resources for it within 2 months of the first publication of the final draft guidance.

5.3 When NICE recommends a treatment 'as an option', the NHS must make sure it is available within the period set out in the paragraphs above. This means that, if a patient has psoriatic arthritis and the healthcare professional responsible for their care thinks that golimumab is the right treatment, it should be available for use, in line with NICE's recommendations.

6 Recommendation 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 Appraisal Committee members and NICE project team

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 4 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 Kathryn Abel
Reader and Consultant Psychiatrist and Director of Centre for Women's Mental Health, University of Manchester

Dr David Black
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Dr Andrew Burnett
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Dr Mary Cooke

Lecturer, School of Nursing, Midwifery and Social Work, University of Manchester

Dr Chris Cooper
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Professor Peter Crome
Consultant Physician, Bucknall Hospital, Stoke-on-Trent

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Professor Cathy Jackson
Professor of Primary Care Medicine, University of St Andrews

Dr Peter Jackson
Clinical Pharmacologist, University of Sheffield

Professor Gary McVeigh
Professor of Cardiovascular Medicine, Queens University Belfast and Consultant Physician, Belfast City Hospital

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Dr Neil Myers
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Professor Paul Trueman
Health Economics Research Group, Brunel University

Dr Judith Wardle
Lay member

NICE project team

Each technology appraisal is assigned to a team consisting of 1 or more health technology analysts (who act as technical leads for the appraisal), a technical adviser and a project

manager.

Whitney Miller
Technical Lead

Helen Knight
Technical Adviser

Lori Farrar
Project Manager

8 Sources of evidence considered by the Committee

The Evidence Review Group (ERG) report for this appraisal was prepared by the NHS Centre for Reviews and Dissemination and Centre for Health Economics:

- Yang H, Epstein D, Bojke L, Craig D et al. (August 2010). Golimumab for the treatment of psoriatic arthritis. York: NHS Centre for Reviews and Dissemination and Centre for Health Economics, University of York.

The following organisations accepted the invitation to participate in this appraisal as consultees and commentators. They were invited to comment on the draft scope, the ERG report and the appraisal consultation document (ACD). Manufacturers or sponsors were also invited to make written submissions. Professional or specialist, patient or carer groups, and other consultees had the opportunity to give their expert views. Manufacturers or sponsors, professional or specialist, patient or carer groups, and other consultees also have the opportunity to appeal against the final appraisal determination.

Manufacturers or sponsors:

- Centocor/Schering-Plough

Professional or specialist, and patient or carer groups:

- Psoriasis and Psoriatic Arthritis Alliance
- Psoriasis Association
- British Association of Dermatologists
- British Health Professionals in Rheumatology
- British Society for Rheumatology
- Primary Care Rheumatology Society
- Royal College of Nursing
- Royal College of Pathologists

- Royal College of Physicians

Other consultees:

- Department of Health
- NHS Haringey
- NHS Havering
- Welsh Assembly Government

Commentator organisations (did not provide written evidence and without the right of appeal):

- British National Formulary
- Commissioning Support Appraisals Service
- Department of Health, Social Services and Public Safety for Northern Ireland
- NHS Quality Improvement Scotland
- Abbott (adalimumab)
- Pfizer (methotrexate, sulfasalazine)
- Sanofi-Aventis (leflunomide)
- National Institute for Health Research Health Technology Assessment Programme
- NHS Centre for Reviews & Dissemination and Centre for Health Economics – York

The following individuals were selected from clinical specialist and patient expert nominations from the non-manufacturer or sponsor consultees and commentators. They gave their expert personal view on golimumab for the treatment of psoriatic arthritis by attending the initial Committee discussion and providing written evidence to the Committee. They were also invited to comment on the ACD.

- Eleanor Korendowych, Consultant Rheumatologist, nominated by British Society for Rheumatology – clinical specialist
- Alex Anstey, Consultant Dermatologist, nominated by British Association of

Dermatologists – clinical specialist

- Philip Helliwell, nominated by British Society of Rheumatology – clinical specialist
- Jana James, nominated by Psoriasis and Psoriatic Arthritis Alliance – patient expert

The following individual was nominated as NHS Commissioning expert by the selected NHS trust allocated to this appraisal. She gave her NHS commissioning personal view on golimumab for the treatment of psoriatic arthritis by attending the initial Committee discussion and providing written evidence to the Committee. She was also invited to comment on the ACD.

- Sue Ashwell, Chief Pharmacist, NHS Cambridgeshire selected by NHS Havering – NHS Commissioning expert

Representatives from the following manufacturer or sponsor attended Committee meetings. They contributed only when asked by the Committee chair to clarify specific issues and comment on factual accuracy:

- Merck Sharp & Dohme (formerly Schering-Plough)

Update information

February 2014: Implementation section updated to clarify that golimumab is recommended as an option for treating psoriatic arthritis.

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