NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Appraisal consultation document

Certolizumab pegol for treating moderate to severe plaque psoriasis

The Department of Health and Social Care has asked the National Institute for Health and Care Excellence (NICE) to produce guidance on using certolizumab pegol in the NHS in England. The appraisal committee has considered the evidence submitted by the company and the views of non-company consultees and commentators, clinical experts and patient experts.

This document has been prepared for consultation with the consultees. It summarises the evidence and views that have been considered, and sets out the recommendations made by the committee. NICE invites comments from the consultees and commentators for this appraisal and the public. This document should be read along with the evidence (see the committee papers).

The appraisal committee is interested in receiving comments on the following:

- Has all of the relevant evidence been taken into account?
- Are the summaries of clinical and cost effectiveness reasonable interpretations of the evidence?
- Are the recommendations sound and a suitable basis for guidance to the NHS?
- Are there any aspects of the recommendations that need particular consideration to ensure we avoid unlawful discrimination against any group of people on the grounds of race, gender, disability, religion or belief, sexual orientation, age, gender reassignment, pregnancy and maternity?

Issue date: [month year]

Note that this document is not NICE's final guidance on this technology. The recommendations in section 1 may change after consultation.

After consultation:

- The appraisal committee will meet again to consider the evidence, this appraisal consultation document and comments from the consultees.
- At that meeting, the committee will also consider comments made by people who are not consultees.
- After considering these comments, the committee will prepare the final appraisal document.
- Subject to any appeal by consultees, the final appraisal document may be used as the basis for NICE's guidance on using certolizumab pegol in the NHS in England.

For further details, see NICE's guide to the processes of technology appraisal.

The key dates for this appraisal are:

Closing date for comments: 4 January 2019

Second appraisal committee meeting: 22 January 2019

Details of membership of the appraisal committee are given in section 6.

1 Recommendations

1.1 Certolizumab pegol (200 mg) is recommended as an option for treating plaque psoriasis in adults, only if:

- the disease is severe, as defined by a total Psoriasis Area and Severity Index (PASI) of 10 or more and a Dermatology Life Quality Index (DLQI) of more than 10 and
- the disease has not responded to other systemic treatments, including ciclosporin, methotrexate and PUVA (psoralen and long-wave ultraviolet A radiation), or these options are contraindicated or not tolerated and
- the company provides the drug according to the commercial arrangement (see section 2).

1.2 Stop certolizumab pegol at 16 weeks if the psoriasis has not responded adequately. An adequate response is defined as:

- a 75% reduction in the PASI score (PASI 75) from when treatment started or
- a 50% reduction in the PASI score (PASI 50) and a 5-point reduction in DLQI from when treatment started.

1.3 When using the PASI, healthcare professionals should take into account skin colour and how this could affect the PASI score, and make the clinical adjustments they consider appropriate.

1.4 When using the DLQI, healthcare professionals should take into account any physical, psychological, sensory or learning disabilities, or communication difficulties that could affect the responses to the DLQI and make any adjustments they consider appropriate.

1.5 The choice between certolizumab pegol or another biological treatment should be made after discussion between the patient and their healthcare professional about the advantages and disadvantages of the treatments

available. If more than 1 treatment is suitable, the least expensive should be chosen (taking into account administration costs, dosage, price per dose and commercial arrangements).

1.6 These recommendations are not intended to affect treatment with certolizumab pegol that was started in the NHS before this guidance was published. People having treatment outside these recommendations may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS clinician consider it appropriate to stop.

Why the committee made these recommendations

Certolizumab pegol is proposed as an alternative to other biological treatments already recommended by NICE for treating severe plaque psoriasis in adults. It is also proposed as an alternative to systemic non-biological treatments such as methotrexate, ciclosporin and acitretin in adults who have not had systemic treatment.

Clinical trial results show that certolizumab pegol improves severe plaque psoriasis more than either placebo or etanercept. When compared indirectly, it appears to be as effective as other biologicals for the condition, and also appears to be more effective than non-biological treatments.

Cost-effectiveness estimates for certolizumab pegol show that:

- in people who have not had previous systemic non-biological treatments, the lowest licensed dose (200 mg) is not cost effective compared with systemic non-biological treatments
- in people who have had systemic non-biological treatments and whose psoriasis has not responded, the lowest licensed dose (200 mg) has a similar cost effectiveness to other biologicals
- in people whose psoriasis has partially responded to the lowest licensed dose, increasing to the highest licensed dose (400 mg) is not cost effective compared with switching to an alternative biological.

Therefore, certolizumab pegol at its lowest licensed dose (200 mg) is recommended as an option for use in the NHS for severe psoriasis that has not responded to systemic non-biological treatment, or if these are contraindicated or not tolerated.

2 Information about certolizumab pegol

Marketing authorisation indication	Certolizumab pegol (Cimzia; UCB Pharma Limited) is indicated 'for the treatment of moderate to severe plaque psoriasis in adults who are candidates for systemic therapy'.
Dosage in the marketing authorisation	Loading dosage The recommended starting dosage of certolizumab pegol for adults is 400 mg (given as 2 subcutaneous injections of 200 mg each) at weeks 0, 2 and 4. Maintenance dosage The maintenance dosage of certolizumab pegol for adults is 200 mg every 2 weeks. A dosage of 400 mg every 2 weeks can be considered when there is an insufficient response. Available data in adults with plaque psoriasis suggest that there is usually a clinical response within 16 weeks of treatment. Continued treatment should be carefully reconsidered in people whose psoriasis shows no evidence of therapeutic benefit within the first 16 weeks of treatment. Sometimes, when there is an initial partial response, it may subsequently improve with continued treatment beyond 16 weeks.
Price	£357.50 per 200 mg pre-filled pen or syringe (excluding VAT, British National Formulary online; accessed November 2018). The company has a commercial arrangement (complex patient access scheme). This provides the first 12 weeks of certolizumab pegol free of charge.

3 Committee discussion

The appraisal committee (section 6) considered evidence submitted by UCB and a review of this submission by the evidence review group (ERG). See the committee papers for full details of the evidence.

Experience of people with psoriasis

Psoriasis is a lifelong condition that affects all aspects of a person's life

3.1 Psoriasis at any level of severity can be distressing and debilitating, affecting all aspects of life (physical, psychological, social and financial), and it is a lifelong condition. The committee noted that having treatments with few or manageable side effects, and which are effective for psoriasis on the face, hands, feet and genitals, is especially important to people with psoriasis, as is having a choice of treatments.

Clinical management

Psoriasis can be treated with topical therapies, phototherapy, and systemic non-biological and biological treatments

3.2 People with plaque psoriasis may have topical therapies first line, followed by phototherapy second line. If these do not control the psoriasis, people may have systemic conventional non-biological treatments third line (such as methotrexate, ciclosporin or acitretin). If the disease does not respond to these, people may have fourth-line treatment including systemic biological treatments (such as adalimumab, brodalumab, etanercept, guselkumab, ixekizumab, infliximab, secukinumab or ustekinumab), or apremilast or dimethyl fumarate. Biosimilar versions of some biologicals are also available. The drugs are used for as long as they continue to work. If the disease no longer responds to 1 biological, people will be offered another biological. This pattern is likely to be repeated over their lifetime. However, 1 clinical expert explained that switching treatments is likely to affect the effectiveness of subsequent drugs, although there is uncertainty about the degree to which this occurs. For people whose disease does not respond to multiple biologicals, apremilast or dimethyl fumarate, the only remaining treatment option is best supportive care, which usually consists of topical agents and bandaging.

Treatment pathway

Certolizumab pegol is most likely to be used as an alternative to other systemic biological treatments

3.3 The marketing authorisation for certolizumab is for 'adults who are candidates for systemic therapy'. In its submission, the company positioned certolizumab pegol as an alternative to: systemic non-biological treatments such as methotrexate, ciclosporin and acitretin, and following topical therapy and phototherapy; or biological treatments. The committee was aware that previous appraisals had only considered biologicals in the latter setting, and that current recommendations for biologicals reflected this positioning. The clinical experts explained that biologicals would be unlikely to be considered at the earlier position because of their higher cost compared with the non-biological treatments used in this setting. One clinical expert stated that, if cost was not an issue, some people may prefer to have a biological at this point in the pathway and that this approach may sometimes be reasonable. The committee agreed that certolizumab pegol is more likely to be used at the same position as alternative biologicals, but recognised there was some interest in using it earlier. It concluded that it would consider the cost effectiveness of certolizumab pegol in both positions.

Clinical evidence

The CIMPASI and CIMPACT trials provide the key clinical evidence for certolizumab pegol

3.4 The main evidence for certolizumab pegol came from the CIMPASI trials 1 and 2, and the CIMPACT trial. These were double-blind randomised controlled trials that included a total of 1,020 patients with plaque psoriasis. They compared 2 doses of certolizumab pegol (200 mg or 400 mg) with placebo (all trials) and etanercept (CIMPACT only). The primary outcomes were the Psoriasis Area and Severity Index (PASI) and the static Physician Global Assessment (sPGA). They were assessed at

the end of the induction period (16 weeks in the CIMPASI trials and 12 weeks in CIMPACT) as follows:

- In the CIMPASI trials, the co-primary outcomes were the proportion of patients with:
  - a 75% reduction in the PASI score from when treatment started (PASI 75) and
  - a rating of 'clear' (score of 0) or 'almost clear' (score of 1) on the sPGA.
- In the CIMPACT trial, the primary outcome was a PASI 75.

Patients in all 3 trials were followed up in open-label extension studies. The company presented open-label follow-up data up to 48 weeks (the trials are scheduled to follow-up patients for 144 weeks in total).

The populations in the CIMPASI trials and CIMPACT are similar to patients in the NHS who may have certolizumab pegol

3.5 The committee considered whether patients in the CIMPASI trials and in CIMPACT were similar to those in NHS clinical practice for:

- Severity of disease: CIMPASI and CIMPACT included patients with 'moderate to severe' psoriasis with a PASI score of 12 or more. No minimum Dermatology Life Quality Index (DLQI) score was included. Previous NICE technology appraisals defined 'severe' and 'very severe' psoriasis based on the PASI and DLQI; the PASI threshold for 'severe' is 10 or more.
- Previous treatment: the committee noted that about 28% to 30% of patients in the CIMPASI and CIMPACT trials had not had any previous systemic treatment or phototherapy. This is inconsistent with the current positioning of biological treatments in the NHS (see section 3.3). One clinical expert explained that international trials may include patients who have not had previous treatment because of different prescribing practices across countries. The committee was

aware that only a small number of patients were recruited in the UK, and that these patients were all recruited for the CIMPACT trial. The company stated that, in the CIMPASI and CIMPACT trials, similar PASI 75 response rates were reported in subgroups of patients who had previously had systemic treatment or phototherapy compared with those who had not. The committee noted that the subgroup of patients who had not had systemic non-biological treatment reflected the company's proposed positioning of certolizumab pegol at an earlier setting than that for biologicals in the NHS. The exception was that none of the patients in the clinical trials had previously had phototherapy.

The committee noted that the results from the overall CIMPASI and CIMPACT population may have overestimated the clinical effectiveness of certolizumab pegol for patients in the setting in which certolizumab pegol would most likely be used in the NHS (as an alternative to other biologicals, after non-biological treatment). This was because some patients in the trials had not had previous systemic treatment or phototherapy. Nevertheless, it concluded that the patients in the trials generally reflected those who would have treatment with certolizumab pegol in NHS clinical practice.

Certolizumab pegol is more clinically effective than placebo and etanercept

3.6 The committee noted that patients randomised to certolizumab pegol were clinically and statistically significantly more likely to have a PASI 75 and sPGA 0 or 1 response rates at week 16 compared with placebo, and a PASI 75 at week 12 compared with etanercept. The committee concluded that certolizumab pegol was more clinically effective than placebo and etanercept.

A PASI 75 response is more likely with certolizumab pegol than with adalimumab or etanercept, and as likely as with other biological treatments

3.7 The company's base-case network meta-analysis indirectly compared certolizumab pegol with other biological treatments (adalimumab, brodalumab, etanercept, guselkumab, infliximab, ixekizumab, secukinumab and ustekinumab) using data from 65 trials. It showed that certolizumab pegol resulted in PASI 75 response rates that were:

- higher (but not statistically significantly so) than the biologicals with the same mechanism of action (that is, the TNF-alpha inhibitors, adalimumab and etanercept)
- statistically significantly higher than etanercept
- similar to the interleukin inhibitors (brodalumab, ixekizumab, guselkumab, secukinumab and ustekinumab), shown by overlapping 95% confidence intervals.

There is no clinical evidence directly comparing certolizumab pegol with the non-biological treatments used earlier in the treatment pathway

3.8 The company presented clinical evidence comparing certolizumab pegol with placebo for the subgroup of patients who had not had previous systemic treatment. This showed a statistically significant and clinically meaningful increase in response rates for certolizumab pegol compared with placebo. The clinical experts explained that the relevant comparators in people who have not had previous systemic treatment are systemic non-biological treatments (methotrexate, ciclosporin and acitretin). The committee noted that there was no clinical trial evidence directly comparing certolizumab pegol with systemic non-biological treatments.

The company's network meta-analysis suggests that a PASI 75 response is more likely with certolizumab pegol than with non-biological treatments

3.9 The company's base-case network meta-analysis (see section 3.7) also included trials in which patients had non-biological treatments (methotrexate, acitretin and ciclosporin). The results showed that treatment with certolizumab pegol resulted in statistically significantly

improved PASI 75 response rates compared with all of the non-biological treatments.

When there is not a PASI 75 response to the 200 mg certolizumab pegol dose, there may be a response to an increased dose

3.10 The committee noted that a dose escalation strategy from 200 mg to 400 mg is within the marketing authorisation of certolizumab pegol. The company presented clinical evidence showing that, if there is not a PASI 75 response after 16 weeks of treatment with a dosage of certolizumab pegol 200 mg every 2 weeks, there may be a response if this is increased to 400 mg every 2 weeks. The committee noted that the trials did not compare the efficacy of increasing the dose of certolizumab pegol with either placebo or another active treatment. One clinical expert stated that dose escalation may be considered for some people, for example, those who also have psoriatic arthritis that is responding to treatment but whose psoriasis does not improve. The committee concluded that it was appropriate to consider the cost effectiveness of increasing the dosage to 400 mg every 2 weeks.

Certolizumab pegol can be used during pregnancy and breastfeeding; some people would value this additional treatment option

3.11 The summary of product characteristics for certolizumab pegol states that it can be used during pregnancy and breastfeeding. The evidence for this was based on 2 clinical studies (CRIB and CRADLE) and safety registry data collected on certolizumab pegol across its licensed indications. The clinical experts stated that these data were consistent with the structure of certolizumab pegol, which would not be anticipated to cross the placenta. They considered certolizumab pegol could be used in pregnancy if needed and while breastfeeding. The only other biological treatment with a summary of product characteristics stating that it can be used in pregnancy and breastfeeding is adalimumab, while infliximab's summary of product characteristics states that it can be used during in breastfeeding. The patient experts explained that people who are

pregnant or who are considering pregnancy would welcome further effective treatment options for plaque psoriasis that do not need to be stopped before and during pregnancy, or while breastfeeding.

Company's economic model

The model has a Markov state transition structure

3.12 A Markov state transition model was used to assess the cost effectiveness of certolizumab pegol. It included the assumption that treatments improved quality of life but did not extend length of life. The model contained 4 health states: induction treatment, maintenance treatment, best supportive care and death. All patients entered the model in the induction state and had the first treatment in a given sequence. They moved from the induction state to the maintenance state if there was at least a PASI 75 response measured at the end of induction. From there, some patients could stop treatment for any reason and move to the next treatment in the sequence. Patients in whom there was not a PASI 75 response moved to the induction phase of the next treatment in the sequence. Patients moved to the best supportive care state if their psoriasis did not respond to the last active treatment in a sequence. All patients could move to the death state at any time.

The company compared 9 treatment sequences in the model when comparing certolizumab pegol with other biological treatments

3.13 The company's decision problem compared a sequence of treatments including certolizumab pegol with 8 treatment sequences excluding certolizumab pegol. Because of the structure of the model (that is, 5 treatments had to be set in each sequence), if shorter sequences were explored, the 'extra' treatments were set to best supportive care. The treatment sequences chosen by the company were:

- The first treatment was either certolizumab pegol or another biological treatment (adalimumab, brodalumab, etanercept, guselkumab, ixekizumab, secukinumab or ustekinumab [40 mg or 90 mg dose]).
- The second treatment was ustekinumab (90 mg), except in the sequences in which ustekinumab was used as the first treatment; in these sequences, adalimumab was used as the second treatment.
- The third treatment was infliximab.
- After that, treatments in all sequences were best supportive care.

The company chose these sequences based on expert advice. The committee was aware that, over time, a sequence of biologicals will be used to treat severe psoriasis in current NHS practice as people switch from 1 option to another. It was also aware that additional factors should be considered when comparing treatment sequences, such as the best ordering of treatments and the effect of including treatments that may not be cost effective. The committee agreed that, in principle, it was appropriate to compare treatment sequences in this appraisal.

Assumptions in the economic model

Key assumptions in the economic model were acceptable for decision making

3.14 The company made several assumptions in the economic model that were consistent with the approach taken in previous appraisals for psoriasis, including:

- a common stopping rate of 20% for all treatments during maintenance treatment
- an equal treatment effect regardless of the position of a treatment in a sequence
- a treatment effect that is sustained throughout the entire treatment period.

The committee was aware that there was limited evidence to support or

dispute these assumptions, but concluded that they were consistent with previous appraisals so were acceptable for decision making.

The company incorporated several of the ERG's preferred assumptions into its base case

3.15 In response to clarification, the company updated its network meta-analysis to better reflect the clinical evidence available for guselkumab. At this time, the company updated it base-case analysis to incorporate several of the ERG's preferred base-case assumptions, including:

- basing utility values only on patients with a DLQI score of greater than 10 to reflect patients who would have biological treatment in the NHS
- assuming that utility values for patients who had treatment with biologicals and best supportive care were equal
- using the drug acquisition costs of the biosimilars of etanercept and infliximab in place of costs for the reference product.

The committee concluded that including these assumptions was appropriate.

Costs in the economic model

The cost of best supportive care for moderate to severe psoriasis is uncertain

3.16 The company calculated the cost of best supportive care based on:

- drug acquisition costs from the British National Formulary, with proportions of patients on each treatment based on clinical expert opinion and mean treatment duration from Fonia et al. (2010)
- secondary care costs from Fonia et al. inflated to 2017 values.

The committee was aware that previous appraisals used drug acquisition costs from either NICE's guideline on psoriasis (based on Fonia et al.) or Fonia et al. itself. This company's alternative approach

resulted in a lower cost for best supportive care because of a fall in the price of ciclosporin and because fumaric acid esters were excluded from best supportive care. The committee was also aware that secondary care costs from Fonia et al. did not reflect clinical practice and were likely to have overestimated the costs of secondary care. It concluded that the cost of best supportive care for moderate to severe psoriasis was uncertain. The committee further concluded that defining costs associated with psoriasis that reflect current clinical practice was an important area for research.

The ERG's analysis using alternative best supportive care costs is useful for decision making

3.17 The lower cost of best supportive care used in the company's base case (see section 3.16) had important implications for the cost-effectiveness results from the economic model. Firstly, compared with best supportive care, no treatment in the company's model had an incremental cost-effectiveness ratio (ICER) lower than £30,000 per quality-adjusted life year (QALY) gained. Secondly, biological treatments with a lower efficacy could appear to be more cost effective than biologicals with a higher efficacy and a similar cost. This was because treatments with lower response rates led to patients in the model advancing to best supportive care more quickly, which was the most cost-effective state. The committee also noted that, in clinical practice, there are several biologicals available so, at the point of stopping a biological, most people will have other biological options available. Treatment sequences in the company's model reached best supportive care after 3 biologicals, which may be less reflective of clinical practice in the NHS. The ERG also did an alternative analysis in which best supportive care costs for all treatments were derived from assumptions in NICE's technology appraisal guidance on brodalumab. This analysis also used the utility values and a 40-year time horizon from the brodalumab appraisal. The ERG noted that these assumptions were not necessarily superior to those in the company's

base case but were presented for illustrative purposes. In this analysis, several biologicals were cost effective compared with best supportive care. The committee concluded that it was appropriate to consider the ERG's analysis using alternative best supportive care costs in its decision making.

Cost-effectiveness estimates

Treatment sequences may result in misleading cost-effectiveness estimates

3.18 The committee was aware that treatment sequences, although more likely to reflect the treatment switching seen in clinical practice, may have provided misleading cost-effectiveness estimates for certolizumab pegol. It noted that some of the treatments were not cost effective in the model. Therefore, the cost effectiveness of any new treatment included early in these sequences would likely be driven by avoiding potentially cost-ineffective subsequent treatments, or by choosing treatments with lower response rates, resulting in an earlier transition to best supportive care (see section 3.17). The committee was also aware that the company's model compared a limited number of all potential treatment sequences. The ERG set subsequent options in all sequences to best supportive care, so that the only difference between sequences was the first treatment used. The committee concluded that it would consider these comparisons of individual treatments with best supportive care in its decision making to account for potential bias caused by analysing treatment sequences.

Considering incremental net monetary benefit in addition to ICERs is appropriate for decision making

3.19 In both the company's and ERG's analyses none of the biological treatments had an ICER that was lower than £30,000 per QALY gained compared with best supportive care (see section 3.17). The committee noted that certolizumab pegol is unlikely to displace best supportive care. Therefore, the relative cost effectiveness of alternative biologicals was considered. The company did this by doing a fully incremental analysis of

treatment sequences using the cheapest biological (etanercept) as a baseline. The committee noted that several treatments had only small differences in total costs and QALY gains, and that these similar results could be difficult to see using ICERs from fully incremental or pairwise analyses. The ERG therefore presented the cost-effectiveness results in a net monetary benefit framework. The incremental net monetary benefit of each comparator was compared with best supportive care at opportunity costs of £20,000 and £30,000 per QALY gained. The committee concluded that incremental net monetary benefit was useful in determining the relative cost effectiveness of the interventions with similar costs and QALYs, and that it should be considered alongside the company's and the ERG's ICERs.

Certolizumab pegol is cost effective compared with other biological treatments for severe psoriasis

3.20 The committee considered whether certolizumab pegol would be a cost-effective use of NHS resources for people with severe psoriasis in whom non-biological treatment has failed or is contraindicated or not tolerated. To do this, it took into account the patient access schemes associated with brodalumab, guselkumab, ixekizumab and secukinumab. The committee noted that certolizumab pegol was similarly or more cost effective compared with alternative biological treatments in both the company's and ERG's base cases but recalled that these analyses may have disadvantaged treatments with higher response rates (see section 3.17). It therefore considered the ERG's alternative base case and noted that, in this analysis, compared with best supportive care, certolizumab pegol had a similar pairwise ICER (range about £20,000 to £29,000 per QALY gained) to the interleukin inhibitors (brodalumab, ixekizumab, guselkumab, secukinumab and ustekinumab), which are currently recommended for use in the NHS. The committee agreed that people with psoriasis, particularly those whose psoriasis does not respond to adalimumab, would value the option of an alternative TNF-alpha inhibitor that was more effective than etanercept and could be used during

pregnancy (see sections 3.6 and 3.11). The committee therefore concluded that it could recommend certolizumab pegol as an option for treating severe chronic plaque psoriasis that has not responded to other systemic treatments, including ciclosporin, methotrexate and PUVA (psoralen and long-wave ultraviolet A radiation), or if these options are contraindicated or not tolerated.

Increasing the dose of certolizumab pegol from 200 mg to 400 mg in people whose psoriasis has not responded to certolizumab pegol is not cost effective

3.21 The committee recalled its previous conclusion that the cost effectiveness of the strategy of increasing the dose of certolizumab pegol in people with a partial response (defined as PASI 50 to a PASI 75) should be considered (see section 3.10). It noted that the company compared the following 2 sequences:

- certolizumab pegol 200 mg escalated to certolizumab pegol 400 mg, followed by ustekinumab, infliximab and best supportive care
- adalimumab 40 mg escalated to adalimumab 80 mg, followed by ustekinumab, infliximab and best supportive care.

This comparison showed that certolizumab pegol was cheaper and more effective than adalimumab. The ERG considered the company's approach to be inappropriate. It suggested that, in addition to being compared with a different dose escalation strategy, the dose escalation sequence should also be compared with switching to the next biological treatment in the treatment pathway. The ERG compared the following 2 sequences:

- certolizumab pegol 200 mg escalated to certolizumab pegol 400 mg, followed by ustekinumab, infliximab and best supportive care
- certolizumab pegol 200 mg, followed by ustekinumab, infliximab and best supportive care.

This comparison resulted in an ICER over £500,000 per QALY gained.

The committee recalled that modelling a few selective sequences may bias cost-effectiveness results (see section 3.18). It also recalled that there was no clinical evidence comparing the dose escalation strategy with placebo or active therapy (see section 3.10). The committee agreed that it was appropriate to consider sequences involving switching to an alternative biological (as in the ERG's analysis), and concluded that the dose escalation strategy was not cost-effective.

Certolizumab pegol should be stopped if there is an inadequate response at 16 weeks

3.22 Previous NICE technology appraisals for treating psoriasis have recommended stopping treatment if there is an inadequate response; an adequate response is defined as either a 75% reduction in the PASI score from when treatment started, or a 50% reduction in the PASI score and a 5-point reduction in DLQI from when treatment started. The committee agreed that, if there is an inadequate response to certolizumab pegol, treatment should be stopped. It noted that PASI 75, assessed 16 weeks after starting treatment, was recommended as appropriate to assess response in the summary of product characteristics. It also recalled its previous conclusion that increasing the dose of certolizumab pegol when psoriasis has responded inadequately was not a cost-effective strategy (see section 3.21). The committee therefore concluded that certolizumab pegol should be stopped if there is an inadequate response at 16 weeks using the same definition of an adequate response as in previous NICE technology appraisals.

Certolizumab pegol is not cost effective earlier in the treatment pathway compared with non-biological treatments for severe psoriasis

3.23 The committee considered whether certolizumab pegol would be a cost-effective use of NHS resources for people with severe psoriasis who have not had systemic treatment, that is, when the disease has not responded to topical treatments and phototherapy, or they are

contraindicated or not tolerated (earlier than the current position for biological treatments in NHS practice). It recalled that there was no clinical evidence directly comparing certolizumab pegol with standard of care in this population; evidence for the clinical efficacy of certolizumab pegol relative to methotrexate, ciclosporin and acitretin was based on the company's network meta-analysis (see section 3.9).

- The company's base-case cost-effectiveness analysis used efficacy data from the placebo arms of the CIMPASI and CIMPACT trials as a proxy for standard of care. The committee agreed that this was inappropriate because standard of care (systemic non-biological treatment) is an active comparator (including methotrexate, ciclosporin and acitretin). The committee considered an alternative analysis presented by the company, which used efficacy data for methotrexate from the subgroup of patients who had not had systemic treatment in the company's network meta-analysis. The committee was aware that these data were based on a small number of patients, so the indirect comparison was subject to a high degree of uncertainty. It noted that, in the company's scenario analysis, certolizumab pegol had an ICER of £18,145 per QALY gained compared with methotrexate.
- The committee noted that the company's scenario analysis compared the following 2 sequences:

  – methotrexate, followed by adalimumab, ustekinumab, infliximab and best supportive care
  – certolizumab pegol 200 mg, followed by ustekinumab, infliximab and best supportive care.

  The committee agreed that the treatment sequences compared by the company were selective. It would have preferred to have seen standard of care (methotrexate) sequences that included alternative biologicals as the second treatment in the sequence, including

certolizumab pegol. The ERG presented a scenario analysis comparing the following 2 sequences:

- methotrexate, followed by certolizumab pegol 200 mg, ustekinumab, infliximab and best supportive care
- certolizumab pegol 200 mg, followed by ustekinumab, infliximab and best supportive care.

This comparison resulted in an ICER of over £400,000 per QALY gained. The committee also noted that certolizumab pegol had a similar QALY gain to methotrexate at a higher cost when the treatments following certolizumab pegol in the above sequences were set to best supportive care. It agreed that the sequences presented by the ERG should be considered in decision making. The committee therefore concluded that it could not recommend certolizumab pegol as an option for treating severe chronic plaque psoriasis that has not been treated with non-biological systemic treatments.

Other factors

Equality issues

Stakeholders consider certolizumab pegol to be safe for anyone who is planning to become pregnant

3.24 Statements from patient and professional groups noted that certolizumab pegol is a safe option for anyone who wants to become pregnant (see section 3.11). The committee understood that people would welcome an additional treatment option that can be used during pregnancy and the pre-conception period.

The PASI and DLQI may not be appropriate for all people with psoriasis

3.25 The committee noted, as in previous NICE technology appraisals on psoriasis, potential equality issues:

- the PASI might underestimate disease severity in people with darker skin
- the DLQI has limited validity in some people, and may miss anxiety and depression.

The committee concluded that, when using the PASI, healthcare professionals should take into account skin colour and how this could affect the PASI score, and make the clinical adjustments they consider appropriate. Also, it concluded that, when using the DLQI, healthcare professionals should take into account any physical, psychological, sensory or learning disabilities, or communication difficulties, that could affect the responses to the DLQI and make any adjustments they consider appropriate.

4 Implementation

4.1 Section 7(6) of the National Institute for Health and Care Excellence (Constitution and Functions) and the Health and Social Care Information Centre (Functions) Regulations 2013 requires clinical commissioning groups, NHS England and, with respect to their public health functions, local authorities to comply with the recommendations in this appraisal within 3 months of its date of publication.

4.2 The Welsh ministers have issued directions to the NHS in Wales on implementing NICE technology appraisal guidance. When a NICE technology appraisal 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 appraisal document.

4.3 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 certolizumab pegol and the doctor responsible

for their care thinks that certolizumab pegol is the right treatment, it should be available for use, in line with NICE's recommendations.

5 Proposed date for review of guidance

5.1 NICE proposes that the guidance on this technology is considered for review by the guidance executive 3 years after publication of the guidance. NICE welcomes comment on this proposed date. The guidance executive will decide whether the technology should be reviewed based on information gathered by NICE, and in consultation with consultees and commentators.

Dr Sanjeev Patel
Chair, Appraisal Committee

6 Appraisal committee members and NICE project team

Appraisal committee members

The 4 technology appraisal committees are standing advisory committees of NICE. This topic was considered by committee B.

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.

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.

Alan Lamb
Technical Lead(s)

Jamie Elvidge
Technical Adviser

Jeremy Powell
Project Manager

ISBN: [to be added at publication]