NICE National Institute for Health and Care Excellence

NICE guidance

Certolizumab pegol for treating moderate to severe plaque psoriasis

Technology appraisal guidance
Published: 17 April 2019

www.nice.org.uk/guidance/ta574

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 Certolizumab pegol 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 phototherapy, or these options are contraindicated or not tolerated and
- the lowest maintenance dosage of certolizumab pegol is used (200 mg every 2 weeks) after the loading dosage and
- the company provides the drug according to the commercial arrangement.

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 If patients and their clinicians consider certolizumab pegol to be one of a range of suitable treatments, the least expensive should be chosen (taking into account administration costs, dosage, price per dose and commercial arrangements).

1.4 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.

1.5 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.

1.6 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 biological treatments for the condition, and also appears to be more effective than non-biological treatments.

Cost-effectiveness estimates for certolizumab pegol show that:

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

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

2 Information about certolizumab pegol

Information about certolizumab pegol

Marketing authorisation indication	Certolizumab pegol (Cimzia; UCB Pharma) 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 February 2019). The company has a commercial arrangement. It is the company's responsibility to let relevant NHS organisations know details of the arrangement.

3 Committee discussion

The appraisal committee (section 6) considered evidence submitted by UCB Pharma 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 biological treatments are also available. The drugs are used for as long as they continue to work. If the disease no longer responds to 1 biological treatment, people will be offered another

biological treatment. 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 biological treatments, 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, in previous appraisals, biological treatments were only recommended for psoriasis that has not responded to previous systemic non-biological treatments or when these treatments are contraindicated or not tolerated. The clinical experts explained that biological treatments 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 a biological treatment 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 biological treatments, but recognised there was some interest in using it earlier. It concluded that it would consider the clinical and cost effectiveness of certolizumab pegol in both positions.

The most relevant comparators to certolizumab pegol for people who have not had systemic treatments are non-biological systemic treatments

3.4 The company identified systemic non-biological treatments, such as methotrexate, ciclosporin and acitretin, as relevant comparators for people with psoriasis who had not had previous systemic treatment. The committee was aware that some other biological treatments had similar marketing authorisations to certolizumab pegol but had not been recommended for use in this population. It recalled that biological treatments are not used in this population because of their higher cost (see section 3.3). It therefore concluded that systemic non-biological treatments were the most relevant comparators to certolizumab pegol for people who have not had systemic treatments.

The most relevant comparators to certolizumab pegol for psoriasis that has not responded to systemic non-biological treatments are other biologicals

3.5 The company suggested that the systemic non-biological treatments apremilast and dimethyl fumarate, used in NHS clinical practice at the same position as systemic biological treatments, were not relevant comparators for psoriasis that has not responded to previous systemic non-biological treatments, or when these treatments are contraindicated or not tolerated. The clinical expert explained that these options were rarely used in practice because they are perceived to be less effective than biological treatments. They would only be considered for use for people for whom a biological treatment was unsuitable or who were unwilling to have a biological treatment. The committee concluded that although apremilast and dimethyl fumarate are used in the NHS for some people with psoriasis, the most relevant comparators to certolizumab pegol were other biological treatments.

Clinical evidence

The CIMPASI and CIMPACT trials provide the key clinical

evidence for certolizumab pegol

3.6 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).

Patients in the certolizumab pegol clinical trials are sufficiently generalisable to those who would have certolizumab pegol in the NHS for decision making

3.7 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 specified. 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 29% 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) and may overestimate the clinical effectiveness of certolizumab pegol. 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.

- People who had not had previous systemic therapy: 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 biological treatments in the NHS. The exception was that none of the patients in this subgroup in the clinical trials had previously had phototherapy.

  The committee concluded that, while patients in the trials did not fully reflect those who would have certolizumab pegol in NHS practice, they were sufficiently generalisable for decision making.

Certolizumab pegol is more clinically effective than placebo and etanercept

3.8 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.

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

3.9 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 concluded 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

3.10 The company's base-case network meta-analysis compared certolizumab pegol with non-biological treatments (methotrexate, acitretin and ciclosporin). The results showed that treatment with a 200 mg maintenance dose of certolizumab pegol resulted in statistically significantly improved PASI 75 response rates compared with all the non-biological treatments. The committee noted that these results were based on a small number of patients so were highly uncertain. It concluded that a PASI 75 response was more likely with certolizumab pegol than with non-biological treatments, but the extent of this benefit was unclear.

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

3.11 The company's base-case network meta-analysis also compared certolizumab pegol with other biological treatments (adalimumab, brodalumab, etanercept, guselkumab, infliximab, ixekizumab,

secukinumab and ustekinumab) using data from 65 trials. It showed that a 200 mg maintenance dose of certolizumab pegol resulted in PASI 75 response rates that were:

- statistically significantly higher than the TNF-alpha inhibitor etanercept
- higher (but not statistically significantly so) than the TNF-alpha inhibitor adalimumab
- similar to the interleukin inhibitors (brodalumab, guselkumab, ixekizumab, secukinumab and ustekinumab).

When there is a partial response to the 200 mg certolizumab pegol dose, there may be an improved response to an increased dose

3.12 The committee noted that increasing the maintenance dose from 200 mg every 2 weeks to 400 mg every 2 weeks is within certolizumab pegol's marketing authorisation. The company stated that people whose disease had a partial response (defined as a PASI 50 to PASI 74) after 16 weeks of treatment with certolizumab pegol at a maintenance dose of 200 mg were the most likely group for whom this would be considered. It presented evidence from CIMPACT showing that most patients in this group had a PASI 75 response after a further 16 weeks of treatment with certolizumab pegol at the increased maintenance dose of 400 mg. The company stated that there were no prognostic factors identified in the trial that indicated whether a person whose disease had a partial response would be likely to have a PASI 75 response after increasing the dose. 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. Also, the results for patients whose disease had a partial response were based on a small number of patients. It noted that the company's definition of partial response may have included people with a PASI 50 response and a 5-point reduction in the DLQI, which is recommended by NICE as an alternative to the PASI 75 to assess response to treatment. The committee would have preferred to see efficacy results that excluded this group, although it recognised that this exclusion would have further reduced the number of patients whose

disease was defined as having a partial response and increased the uncertainty of the clinical effectiveness of increasing the dose. The committee noted that people whose disease had a partial response to certolizumab pegol and no, or manageable, adverse events may prefer to continue on a higher dose of certolizumab pegol than to switch to an alternative treatment, which could be less well tolerated. It also noted that psoriasis is a lifelong condition and that people with psoriasis would be likely to try several treatments over their lifetime, so may wish to continue with their current treatment at a higher dose and reserve other biological treatments for future use. The committee concluded that it was appropriate to consider the cost effectiveness of increasing the dosage to 400 mg every 2 weeks in people whose disease had a partial response to certolizumab pegol 200 mg every 2 weeks.

Company's economic model

The model has a Markov state transition structure

3.13 A Markov state transition model was used to assess the cost effectiveness of certolizumab pegol. The company assumed 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. If there was not a PASI 75 response, patients 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.

There are 9 treatment sequences in the company's model when comparing certolizumab pegol with other biological treatments

3.14 The company's decision problem compared a sequence of treatments

including certolizumab pegol with 8 treatment sequences excluding certolizumab pegol. 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 [45 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, treatment in all sequences was best supportive care.

The company chose these sequences based on expert advice. The committee was aware that, over time, a sequence of biological treatments 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 are acceptable for decision making

3.15 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.

Several of the ERG's preferred assumptions are incorporated into the company's base case

3.16 In response to clarification, the company updated its 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 biological treatments 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

3.17 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

3.18 The lower cost of best supportive care used in the company's base case (see section 3.17) 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, treatments with a lower efficacy could appear to be more cost effective than treatments 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, and therefore incurring lower costs. The ERG also did an exploratory analysis incorporating assumptions from NICE's technology appraisal guidance on brodalumab, which included higher costs for best supportive care than in the company's analysis. 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 biological treatments 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

3.19 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 3.18). 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.

Certolizumab pegol is not cost effective earlier in the treatment pathway compared with non-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 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 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 3.10):

- 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 care. The committee agreed that this was inappropriate because standard care (systemic non-biological treatment) is an active comparator. 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 care (methotrexate) sequences that included alternative biological treatments 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 recalled its previous conclusion that it was appropriate to consider sequences in which subsequent biological therapies in the treatment sequence were replaced by best supportive care (see section 3.19). Modifying the ERG's scenario analysis in this way resulted in 2 sequences:
  - methotrexate, followed by certolizumab pegol 200 mg and best supportive care

— certolizumab pegol 200 mg, followed by best supportive care.

The committee noted that, in this analysis, certolizumab pegol had a similar QALY gain to methotrexate at a much higher cost. The committee considered the ERG's analysis to be more appropriate than the company's. It therefore concluded that certolizumab pegol was not a cost-effective use of NHS resources, and 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.

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

3.21 The committee considered whether certolizumab pegol would be a cost-effective use of NHS resources for people with severe psoriasis for whom non-biological treatment has failed or is contraindicated or not tolerated. To do this, it took into account the patient access schemes for brodalumab, guselkumab, ixekizumab and secukinumab. The committee noted that several treatments had only small differences in total costs and QALY gains, and that these small differences 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 committee agreed that this analysis was useful to support decision making. It noted that certolizumab pegol was similarly or more cost effective than 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 3.18). It therefore considered the ERG's alternative base case (using best supportive care costs from previous guidance) and noted that, in this analysis, compared with best supportive care, certolizumab pegol had:

- a lower pairwise ICER than the interleukin inhibitor ustekinumab and the TNF-alpha inhibitor etanercept
- a similar pairwise ICER (range about £19,500 to £21,500 per QALY gained) to the interleukin inhibitors brodalumab, ixekizumab, guselkumab and secukinumab

- a higher pairwise ICER than the TNF-alpha inhibitor adalimumab.

The committee agreed that people with psoriasis would value the option of an alternative TNF-alpha inhibitor that was more effective than etanercept and could be used during pregnancy (see section 3.25). It 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 phototherapy, or if these options are contraindicated or not tolerated.

The cost effectiveness of increasing the maintenance dose of certolizumab pegol should be assessed by comparing it with switching to another biological

3.22 The committee recalled its previous conclusion that the cost effectiveness of increasing the maintenance dose of certolizumab pegol in people whose disease partially responded should be considered (see section 3.12). It noted that the company's base case compared 2 sequences:

- certolizumab pegol 200 mg increased to certolizumab pegol 400 mg (when there is a partial response, defined as a PASI 50 to 74) or ustekinumab (when there is no response, defined as a PASI less than 50), followed by ustekinumab, infliximab and best supportive care

- adalimumab 40 mg increased to adalimumab 80 mg (for partial and no response), followed by ustekinumab, infliximab and best supportive care.

The company and the ERG also presented several scenario analyses in which increasing the dose of certolizumab pegol was compared with switching to ixekizumab, secukinumab and ustekinumab. The committee recalled that, in the CIMPACT trial, there were no prognostic factors identifying people who were likely to benefit from increasing the dose of certolizumab pegol (see section 3.12). It also noted that clinicians would be unlikely to make treatment decisions based on people needing a future dose increase because it would not be known whose disease would have a partial response and need an increased dose. Therefore, it concluded that a comparison between increasing the maintenance dose of certolizumab pegol from 200 mg to 400 mg and increasing the maintenance dose of adalimumab from 40 mg to 80 mg was not clinically relevant. It also concluded that the most relevant comparison would be between increasing the maintenance dose of certolizumab pegol from 200 mg to 400 mg and switching from certolizumab pegol to another biological treatment.

It is not cost effective to increase the dose of certolizumab pegol to 400 mg if response to the 200 mg dose is inadequate

3.23 The company noted in its response to the appraisal consultation document that the ERG scenarios switching to alternative biological treatments (see section 3.22) used efficacy data from the CIMPACT trial for certolizumab pegol (see section 3.12) and the network meta-analysis (see section 3.11) for comparators. It was concerned that this may bias results against certolizumab pegol because this approach assumed that the comparator (used second line in the sequence) is as clinically effective as if it had been used first line. The company therefore provided additional scenario analyses which used the network meta-analysis results for both certolizumab pegol and the comparator, or (in the absence of clinical trial data for the comparator) assumed that the comparator had equivalent efficacy to certolizumab pegol in CIMPACT. The committee concluded that although this was a source of uncertainty, the scenario analyses exploring alternative assumptions had only a small effect on the cost-effectiveness results and did not affect decision making. The company also explained that the cost of increasing the

maintenance dose of certolizumab pegol may have been overestimated by a small amount because, in the model, patients who stopped certolizumab pegol 200 mg because of adverse events then had certolizumab pegol 400 mg, which would not occur in clinical practice. The committee concluded that, although this was a limitation in the model structure, the resulting overestimation in costs was likely to have a minimal effect on the cost-effectiveness results because it only applied to a small number of patients. After taking into account all confidential commercial arrangements for comparator treatments, the ICERs for certolizumab pegol were considerably above the range usually considered cost effective by NICE. The committee therefore concluded that increasing the maintenance dose was not cost effective.

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

3.24 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 was 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 3.23). 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.

Equality issues

Certolizumab pegol can be used before and during pregnancy if clinically needed and while breastfeeding

3.25 The summary of product characteristics for certolizumab pegol states that it can be used during pregnancy if clinically needed and while breastfeeding. The clinical experts considered this to be reasonable. 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 (if clinically needed), or while breastfeeding. The committee concluded that these patients would value an additional treatment option.

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

3.26 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 psoriasis 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 Recommendations for research

5.1 The committee noted that the costs of best supportive care are derived from a study published in 2010 and that clinical practice has changed substantially since then. It therefore considered that it would be valuable to have studies investigating:

- the costs associated with best supportive care
- resource use, including frequency and length of hospitalisation, and associated costs.

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

Jamie Elvidge, Ross Dent
Technical advisers

Jeremy Powell
Project manager

ISBN: 978-1-4731-3364-8

Accreditation