

**NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE**

**Single technology appraisal (STA)**

**Ustekinumab for the treatment of moderate to severe psoriasis**

**Appraisal consultation**

**WYETH PHARMACEUTICALS**

<b>Document</b> <i>(Appraisal consultation document, or Evaluation report)</i>	<b>Page number</b>	<b>Comment</b>
ACD	3	The British Association of Dermatologists draft Guidelines for Biological Interventions for Psoriasis 2009 state that in light of limited patient exposure, ustekinumab should be reserved for use in patients with severe psoriasis who fulfil the stated disease severity criteria AND where anti-TNF therapy has failed or is contra-indicated.
ACD	10	In the manufacturers cost-effectiveness model the assessment points were at 12 weeks for etanercept. Evidence from clinical studies demonstrates that the effectiveness of etanercept increases to up to 24 weeks. <sup>1</sup> Therefore the assessment point should be at 24 weeks.
ACD	10	The utility data used in the model were based on an estimate of the relationship between PASI response rates and changes in DLQI score from the PHOENIX-1 and PHOENIX-2 trials mapped to EQ-5D scores. This mapping shows that patients with higher PASI response show better improvements in health related quality of life, e. g. a higher utility gain with a PASI 90 than with a PASI 75. Evidence from other sources are contrary to this assumption, and support the assumption, that the biggest gain in utility is achieved up to a PASI 75. <sup>2</sup>
ACD	11	The ICER for ustekinumab compared with etanercept 25 mg given intermittently (assuming 88% of the cost of continuous etanercept) was £27,105 per QALY gained. The cost of intermittent etanercept is 73.9% of the cost of continuous etanercept, not 88% (£6,878 vs. £9.295).

ACD	12 / 13	The manufacturer also varied the assumptions about the cost and efficacy of intermittent etanercept. The cost of intermittent compared with continuous etanercept was changed from the base-case estimate of 88% to 74% (the figure used in TA103) and to 98%. Using an assumption of 74%, the ICER for ustekinumab compared with intermittent etanercept 25 mg increased from £27,105 to £68,339 per QALY gained. The figure of 74% should be used, based on the difference between £6,878 for intermittent etanercept and £9.295 for continuous etanercept, which is 73.9%. Therefore the ICER for ustekinumab compared with the NICE recommended dose for etanercept is more likely to be £68,339 per QALY gained.
ACD	13	The ERG noted that in the mixed treatment comparison, data from the weight-based dosing analysis of ustekinumab were taken from a subgroup of the trial data, whereas for the comparator trials data for all patients were used. This leads probably to an underestimation of the effectiveness of the comparators used.
ACD	15	The Appraisal Committee reviewed the data available on the clinical and cost effectiveness of ustekinumab, having considered evidence on the nature of the condition and the value placed on the benefits of ustekinumab by people with psoriasis, those who represent them, and clinical specialists. It was also mindful of the need to take account of the effective use of NHS resources. The British Association of Dermatologists draft Guidelines for Biological Interventions for Psoriasis 2009 state that in light of limited patient exposure, ustekinumab should be reserved for use in patients with severe psoriasis who fulfil the stated disease severity criteria AND where anti-TNF therapy has failed or is contra-indicated. Therefore, and given the wealth of data on safety and efficacy available for anti-TNF therapies, the Appraisal Committee should follow the BAD and restrict the use of ustekinumab only to those patients who fulfil the stated disease severity criteria AND where anti-TNF therapy has failed or is contra-indicated.
ACD	15	The Appraisal Committee heard from the clinical specialists that there are currently no treatments that they considered to be effective for people whose psoriasis does not respond adequately to the tumour necrosis factor (TNF) inhibitors (that is, adalimumab, infliximab and etanercept). In addition, with the withdrawal of efalizumab there are no treatment options for people in whom TNF inhibitors are contraindicated, such as people with heart failure or demyelinating disease. The Appraisal Committee should follow the BAD and restrict the use of ustekinumab only to those patients who fulfil the stated disease severity

		criteria AND where anti-TNF therapy has failed or is contra-indicated.
ACD	16	The Committee heard from the clinical specialists that ustekinumab is a new drug that has been given to far fewer people than the other biological therapies, and therefore its long-term safety profile is less certain. Therefore, and given the wealth of data on safety and efficacy available for anti-TNF therapies, the Appraisal Committee should follow the BAD and restrict the use of ustekinumab only to those patients who fulfil the stated disease severity criteria AND where anti-TNF therapy has failed or is contra-indicated.
ACD	17	The Committee heard from the clinical specialists that biological therapies for psoriasis, including etanercept, are usually used on a continuous basis in clinical practice. Even as Wyeth has submitted to obtain a license, including intermittent and continuous treatment options, treatment will still be initiated with intermittent treatment, and only patients in whom it will be necessary will receive continuous treatment with etanercept. Current market research suggests that approximately 74% of patients receive etanercept intermittently. <sup>3</sup> Therefore, intermittent etanercept is the right comparator.
ACD	18	The Committee also heard from the clinical specialists that the cost of £288 per day for an inpatient stay, as assumed in the model, may be too low. The cost for a rheumatological infusion is £407. <sup>4</sup> Therefore the true cost of ustekinumab may have been underestimated in the current appraisal.
ACD	21	The Committee was aware that the clinical specialists had indicated that ustekinumab may be used after a person's psoriasis has failed to respond to TNF inhibitors. The Committee noted that the manufacturer had provided no detailed evidence of clinical effectiveness and no cost-effectiveness evidence for this subgroup. Approximately 40–50% of people in the PHOENIX trials had previously tried a biological therapy such as a TNF inhibitor and therefore agreed that the estimates of clinical effectiveness were based on a population that included a reasonable proportion of people who had tried biological therapies before. Therefore, and given the wealth of data on safety and efficacy available for anti-TNF therapies, the Appraisal Committee should follow the BAD and restrict the use of ustekinumab only to those patients who fulfil the stated disease severity criteria AND where anti-TNF therapy has failed or is contra-indicated. <sup>5 6</sup>
ACD	23 / 24	It is proposed that the guidance on this technology is considered for review together with the review of other drugs for the treatment of psoriasis 'Etanercept and efalizumab for the

		treatment of adults with psoriasis (NICE technology appraisal guidance 103), 'Infliximab for the treatment of adults with psoriasis (NICE technology appraisal guidance 134) and 'Adalimumab for the treatment of adults with psoriasis' (NICE technology appraisal guidance 146). The Institute would particularly welcome comments on this proposal.  Wyeth supports this proposal.
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## REFERENCES

<sup>1</sup> van de Kerkhof PCM, et al. Once weekly administration of etanercept 50 mg is efficacious and well tolerated in patients with moderate-to-severe plaque psoriasis: a randomized controlled trial with open-label extension. *Brit J Derm.* 2008; 159: 1177-1185

<sup>2</sup> CHE/CRD Technology Assessment Group. Technology Assessment Report commissioned by the HTA Programme on behalf of The National Institute for Clinical Excellence. Efalizumab and Etanercept for the Treatment of Psoriasis. February 2005.

<sup>3</sup> Wyeth data on file.

<sup>4</sup> HRG4

<sup>5</sup> Leonardi CL, et al. Efficacy and safety of ustekinumab, a human interleukin-12/23 monoclonal antibody, in patients with psoriasis: 76-week results from a randomised, double-blind, placebo-controlled trial (PHOENIX 1). *Lancet* 2008; 371: 1665–74

<sup>6</sup> Papp KA, et al. Efficacy and safety of ustekinumab, a human interleukin-12/23 monoclonal antibody, in patients with psoriasis: 52-week results from a randomised, double-blind, placebo-controlled trial (PHOENIX 2). *Lancet* 2008; 371: 1675–84