

28th January 2008



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Ustekinumab for treatment of moderate to severe psoriasis

The Evidence Review Group, Southampton Health Technology Assessments Centre (SHTAC), and the technical team at NICE have now had an opportunity to take a look at submission by Janssen-Cilag. In general terms they felt that it is well presented and clear. However the ERG and the NICE technical team would like further clarification relating to the clinical and cost effectiveness data.

Both SHTAC and the technical team at NICE will be addressing these points in their reports. As there will not be any consultation on the evidence report prior to the Appraisal Committee meeting, you may want to address these issues and provide further discussion from your perspective at this stage.

We request you to provide a written response to this letter to the Institute by **11th February 2009**. Two versions of this written response should be submitted; one with academic/commercial in confidence information clearly marked and one from which this information is removed.

Please underline all confidential information, and separately highlight information that is submitted under 'commercial in confidence' in red and all information submitted under 'academic in confidence' in yellow.

If you present data that is not already referenced in the main body of your submission and that data is seen to be academic/commercial in confidence information, please complete the attached checklist for in confidence information.

If you have any further queries on the technical issues raised in this letter then please contact Raphael Yugi (raphael.yugi@nice.org.uk). Procedural questions should be addressed to Bijal Chandarana (bijal.chandarana@nice.org.uk) in the first instance.

Yours sincerely

Dr Elisabeth George
Associate Director – Appraisals
Centre for Health Technology Evaluation

Encl. checklist for in confidence information

Section A: Clarification on effectiveness data

- A1. In the Phoenix 1 and 2 trials, the placebo treatment arms divide at 12 weeks. Please clarify if this was a randomised split or if the population was split by some other means.
- A2. Table 6.3.1, page 30, does not include the proportion of people in each ustekinumab trial arm who were above and below 100kg. Please provide this information.
- A3. In section 6.4.1, page 47, the text states that 742 participants were included in the efficacy analysis. However, the corresponding figure suggests all 766 were included. The same issue appears on page 50 for the Phoenix 2 trial. Please clarify which figures were used for the efficacy analyses.
- A4. In Table 6.6.2, page 74, the ustekinumab weight-based results across the three trials show the same number of participants for the 45mg and 90mg groups. Please clarify if this is an error, and if so, please correct the table accordingly.
- A5. Please provide a network diagram for the mixed treatment comparison (MTC).
- A6. We note that a subgroup will be recommended in the SPC. Please provide details of the analysis for this subgroup, the results of which are used in the MTC and the economic model. In particular, please provide a description of the method used which justifies the cut-off weight of 100kg for the use of a higher dose of ustekinumab.
- A7. On page 109, the submission indicates that it has been demonstrated that the response rate for ustekinumab continues to rise after 12 weeks and therefore the assumption that the response at 16 weeks is the same as 12 weeks is justified. This statement is not referenced back to another section of text in the submission. Please clarify which section of the submission you are referring back to.

Section B: Clarification on cost-effectiveness data

- B1. Please clarify the number of references/studies deemed appropriate for critical appraisal in the cost effectiveness literature search. The numbers in 7.1.1 (overview of literature review results, page 93) do not appear to add up.
- B2. Please provide the source for the range of the efficacy variable for intermittent etanercept used in the sensitivity analysis in Table 7.2.13, page 125.

- B3. Please provide an additional economic analysis that does not incorporate the patient access scheme.
- B4. Please provide an economic analysis that uses a 28 week stopping rule for the trial period, as per the guidance given in the SPC.
- B5. Please clarify the length of time over which the patient access scheme will remain in place ***CIC removed***.
- B6. Please clarify the assumption that all patients will be able to self-inject. If there is a proportion of patients that are unable to self-inject, please provide an estimate of this proportion.
- B7. Appendix 11 does not appear to contain any methodological details. Given the role that the outcomes of this meeting played in deriving assumptions used in the model, please provide further information on the nature of the advisory board and the way the information was obtained.

Section C: Textual clarifications and additional points

- C1. Please provide a copy of the draft or final CHMP EPAR.
- C2. Please provide a list of abbreviations (for example it is unclear what eCRF, CNTO stand for).
- C3. In section 6.9.1, the text is obliterated by the table 6.9. Please replicate the paragraph that cannot be seen on page 89.