Abbott's response to the Appraisal Consultation Document 2 of adalimumab and infliximab for the treatment of Crohn's disease

Abbott welcomes the opportunity to comment on the Appraisal Consultation Document (ACD2) prepared by the Committee for the appraisal of adalimumab and infliximab for the treatment of Crohn's disease. Abbott's comments are set out under section headings containing the questions NICE asks consultees to comment on for the ACD.

1. Do you consider that all of the relevant evidence has been taken into account?

Abbott welcomes the decision of the Appraisal Committee that adalimumab should be recommended for the induction and maintenance therapy of adult Crohn's patients as outlined in section 1 of the ACD2.

Based on comments on the first Appraisal Consultation Document there has been extensive discussion on the expected cost of infliximab based on patient weight and costs of infusion. Section 1.1 and 1.2 set out further evidence on these points which may be of interest to the Appraisal Committee.

1.1 Average weight of Crohn's Disease (CD) patients in the UK

Available data from pivotal multinational clinical trials for adalimumab indicate that the average weight of patients with Crohn's disease is 70 kg or more[1],[2],[3]. Data on the recorded weight of adult patients with Crohn's disease from the UK General Practice Research Database gives a mean weight of 70kg[4]. Table 1.1 gives the weight distribution of CD patients in the UK from the GPRD database categorised by weight according to how many vials of infliximab they would require per dose.

Table 1.1. Weight distribution of CD patients from the UK General Practice Research Database (GPRD) linked to the number of infliximab vials that would be required to treat these patients

Weight range from adult Crohn's Disease patients from GPRD database	% of population	No. of vials*	Maintenance drug cost only (£) (Every 8 weeks dosing schedule)*
<40kg	0.6%	2	5,455
40kg-60kg	26.7%	3	8,183
61kg-80kg	47.9%	4	10,910
81kg-100kg	19.3%	5	13,638
101kg-120kg	4.6%	6	16,365
>121kg	0.9%	7	19,093
Weighted average cost (£)			£11,004

*****Costs have been calculated including drug wastage for the unused portion of opened vials. This cost is based on 6.5 infusions per year which excludes the loading dose cost in year 1.

Furthermore, the subgroup of severe patients from the CHARM trial with a CDAI score of ≥300 had a mean weight of 69kg at baseline. It could be hypothesised that the mean weight of patients from multinational clinical trials may not accurately reflect severe UK Crohn's patients. In order to assess this, the mean weight of UK patients from the CHARM (M02-404) and CARE (M06-829) studies was calculated. Table 1.2 presents these data for UK patients included in these studies.

Table 1.2. Weight distribution in kilograms of CD patients in the UK from the CHARM and CARE studies

Clinical Study	N	Mean	Median	Std Dev	Minimum	Maximum
M02-404 (CHARM)	25	70.1	66.0	16.2	47.0	108.0
M06-829 (CARE)	73	68.7	64.0	19.1	45.0	124.0
All UK patients	98	69.1	64.0	18.3	45.0	124.0
Severe patients only (CDAI ≥ 300)*						
M02-404 (CHARM) CDAI>300	15	70.8	64.0	17.8	47.0	108.0

*CDAI score was collected only in a subsample of subjects in the CARE study therefore classification of severe patients by CDAI has not been performed in this study.

These data indicate that using an average weight of 70kg is appropriate for estimating the cost of treating severe patients with Crohn's disease with infliximab in the UK. Abbott considers it is unlikely that treatment of CD patients using infliximab would be less costly than treating patients with adalimumab, and on average infliximab is likely to be significantly more costly.

1.2 Cost of intravenous infusion

Abbott considers that a cost of £99.25 per infusion is an unrealistic cost for preparing and administering an intravenous injection with infliximab. NICE appraisals of infliximab for rheumatoid arthritis, psoriatic arthritis and ankylosing spondylitis have applied a higher administration cost. The cost of £99.25 is significantly lower than the NHS national tariff for a planned day case admission for inflammatory bowel disease, and therefore the costs applied in the economic modelling do not overestimate the total cost of infliximab to the NHS.

2. Do you consider that the summaries of clinical and cost effectiveness are reasonable interpretations of the evidence and that the preliminary views on the resource impact and implications for the NHS are appropriate?

2.1 Factual accuracy of clinical and cost effectiveness summaries

Abbott has checked the ACD for factual accuracy and suggests the following point should be amended:

- **Page 13 of 36, paragraph 4.1.9.** This paragraph states that "*the primary outcome was the proportion of patients in remission (at week 56 for CHARM and at weeks 26 and 56 in CLASSIC II"*. However, this statement is incorrect as it was the CHARM study that had co-primary endpoints of remission at week 26 and 56 not CLASSIC II. The primary endpoint in CLASSIC II was measured at week 56 only.

3. Do you consider that the provisional recommendations of the Appraisal Committee are sound and constitute a suitable basis for the preparation of guidance to the NHS?

Abbott welcomes the decision of the Appraisal Committee that adalimumab should be recommended for the induction and maintenance therapy of adult Crohn's patients as outlined in section 1 of the ACD2.

Given the extensive and lengthy discussion of evidence in this appraisal, Abbott considers it would be premature to consider this topic for review in September 2011. Abbott considers that it would be appropriate for the Institute's Guidance Executive to consider the need for review 3 years after publication of final guidance, in line with the standard timelines for NICE MTA reviews.

4. Are there any equality related issues that may need special consideration?

None that Abbott is aware of.

References

[1] Colombel JF, Sandborn WJ, Rutgeerts P, et al. Adalimumab for Maintenance of Clinical Response and Remission in Patients with Crohn's Disease: The CHARM Trial. Gastroenterology 2007; 132: 52–65.
[2] Hanauer SB, Sandborn WJ, Rutgeerts P, et al. Human anti-tumor necrosis factor monoclonal antibody (adalimumab) in Crohn's disease: the CLASSIC-I trial. Gastroenterology 2006; 130: 323–333.
[3] Sandborn WJ, Rutgeerts P, Enns R, et al. Adalimumab Induction Therapy for Crohn Disease Previously Treated with Infliximab: A Randomized Study. Ann Intern Med. 2007; 146: 829–838.
[4] Abbott data on file taken from General Practice Research Database.