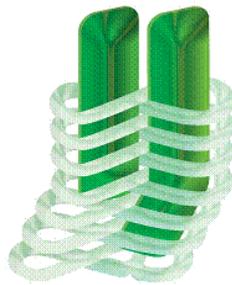




UCB

**Certolizumab pegol (CIMZIA®) for the
treatment of Rheumatoid Arthritis**



**Manufacturers response to the West
Midlands report to the NICE MTA**

January 12th 2010



Dr Carole Longson
Director, Centre for Health Technology Evaluation
NICE

Dear Dr Longson,

Thank you for the report from the West Midlands HTAC on the appraisal of adalimumab, etanercept, infliximab, rituximab and abatacept for the treatment of rheumatoid arthritis after the failure of a TNF inhibitor.

The opportunity for UCB Pharma to comment is rather limited, in view of our position as a comparator rather than a consultee. However the conclusions of the Committee could have a significant impact on the use of certolizumab pegol and the potential for this innovative treatment to be used as widely as possible to benefit patients.

The response from UCB pharma to the West Midlands HTAC report is structure into four key areas:

1. Process and the completeness of the final guidance
2. The comparative benefit and costs of conventional DMARD treatment
3. Consideration of the UCB certolizumab patient access scheme
4. Sensitivity analysis for administration costs

Each of these areas is expanded and we look forward to your thoughts on each area.

Yours sincerely,


UCB Pharma Ltd

Section 1: Process and the completeness of the final guidance

Key point: The final guidance when published will not include several new biologic agents that will be available in the NHS and likely to be in routine use at this time. In addition the evidence exists to assess these agents from their STA NICE submissions. This may lead to restriction of these agents in sequential treatments.

Detail:

The NICE appraisal process for the sequential use of TNF inhibitors was referred in June 2004 (NICE website). It is likely that guidance will not be issued until June 2010 at the earliest. This guidance will therefore reflect the availability of licensed products from several years ago and not truly reflect the treatment options available to clinicians mid way through 2010. The NICE base case should represent the most appropriate comparators and this is clearly not the case with the current MTA.

Since 2004, two additional TNF inhibitors (certolizumab pegol and golimumab) and a biologic in a new treatment class (tocilizumab, an IL6) have been licensed. Both tocilizumab and certolizumab pegol have been appraised by NICE and are awaiting final guidance from the committee over the next few weeks.

PCTs and policy makers will soon be faced with the challenge of interpreting single technology guidance within the context of the new multiple technology appraisal. The most likely response of PCTs will be to restrict the use of products not directly referred to by the guidance.

The West Midlands HTAC report (page 38, section 4.1) states that the third decision that should be made by this technology appraisal is:

- Whether the interventions are clinically effective and cost-effective compared to other biologic agents (including tocilizumab, golimumab, and certolizumab pegol).

Without inclusion of these newer agents (and their assessment in the Birmingham Rheumatoid Arthritis Model [BRAM] as a direct comparator) it will not be possible to draw any reasonable conclusion. We ask that certolizumab pegol is evaluated within the BRAM for comparative costs and clinical response so that an evaluation can reasonably be made by clinicians and policy makers, even if the final guidance cannot refer to certolizumab pegol directly

In addition in section 4.4, relevant comparators on page 40, the appraisal group recognized the likely availability of other biologic agents and that they are subject to NICE appraisals, making the following comment:

- It was proposed that tocilizumab, golimumab and/or certolizumab pegol could have been reviewed in the assessment report as a comparator if marketing authorisation of the technology was obtained before the submission of the protocol for this assessment report. This condition was not met.

In summary the guidance that will be produced will necessarily be incomplete because the scoping did not extend to the treatments that would be available and routinely used at the time the guidance will be confirmed. In addition the process could have considered evidence submitted by manufacturers to the appraisal committee however a decision was taken to limit comparator evidence to those products that had a marketing authorization at the time the report evidence was submitted. UCB would like to understand the justification for this decision.

Section 2: Assessment of the benefits of non biological DMARD treatment as base case compararor

Key point: The evidence base for the cost and clinical effectiveness of conventional DMARDs after the failure of a first TNF inhibitor is overstated and lacks evidential support.

Detail:

As outline in section 5.4, page 142 of the report, the RCT evidence does not support the effectiveness of the technologies compared to newly initiated conventional DMARDs:

- “No study addressing the comparison was found.”

This compares with a comparatively strong evidence base for the TNF inhibitors.

In addition, on page 209 in section 6.3.1.2. referring to the data used within the BRAM it states that the only evidence for the effectiveness of conventional DMARDs (cDMARDs) was taken from trials in early RA – at a much earlier and less severe stage of the disease and after the failure of the first biologic – so potentially five years later in a disease areas that is progressive.

In order to address this, the effectiveness of cDMARDs in late RA was simply halved compared to their effectiveness in early RA.

There is no demonstrable evidence base to suggest that cDMARDs will be effective in this group, indeed as all patients have failed on at least two cDMARDs prior to the initiation of a TNF inhibitor, there is significant evidence that they will be ineffective.

The view shared with UCB from clinical and patient experts is that the effect of conventional DMARDs has been greatly overstated and that new agents will have much less effectiveness, with give shorter term relief that assumed in the report.

The effect of this approach is to greatly overstate the health gain from conventional treatments and make the consequent ICER for biologic therapies higher. In addition if the health gain assumption for cDMARDs is lower in true clinical practice, the costs of these therapies will be higher due to the need for more supportive interventions and a greater long term deterioration in the HAQ score.

UCB would therefore like to better understand the evidence supporting the underlying assumption of the effectiveness of cDMARDs in late, severe RA.

Section 3: Sequencing of TNF inhibitors where a patient access scheme exists

Key point : The Department of Health has agreed a UCB sponsored patient access scheme that allows certolizumab pegol to be given without cost until the clinical response is measured. The cost effectiveness of the TNF inhibitors in the report should reflect this significant reduction in the cost of using sequential TNF inhibitors where this kind of patient access scheme exists. Not including this feature, greatly and unfairly disadvantages certolizumab pegol.

Detail:

The submission for certolizumab pegol to NICE on the 22nd of June included a proposed patient access scheme. Following significant discussion with prescribers and payers UCB decided to offer the first 10 vials (12 weeks) of treatment for no charge to the NHS. This will take the patient to the first reasonable measure of clinical effectiveness. From our clinical trials and as reflected in our statement of product characteristics, “Available data suggest that clinical response is usually achieved within 12 weeks of treatment”. In order to respond to the continuing pressure from payers and organizations like NICE to ensure new therapies are cost effective and affordable for the NHS, UCB decided that no payer will be charged for certolizumab pegol until the response can be assessed, usually at the 12 to 14 week clinic review.

Approximately 25% of patients who are TNF inhibitor naive will fail to show an adequate initial response to their first biologic. In the secondary failure patient group (patients who have responded to a TNF inhibitor but who then go on to experience an adverse event or loss of effective response) this lack of adequate response then rises as high as 50% for treatment with a second TNF inhibitor.

The incremental cost effectiveness ratio (ICER) for sequenced failure of TNF inhibitors (a patient failing to show an adequate response to two agents) is increasingly unaffordable for the NHS in a cost constrained environment. The addition of a patient access scheme that removes the costs of initial failure - or allows the patient to be moved without cost to another therapy that may prove effective and therefore deliver the health gain associated with the increased cost of biologic therapy – has not been considered within the Birmingham model. If the second choice TNF inhibitor is free of cost until an effective response could be judged then the ICER will have been significantly reduced.

UCB requests that one of the treatment options – either the initial therapy or the second TNF treatment reflects the availability of a patient access scheme and that the final sequential ICER reflects this. It is not unreasonable to assume that in a cost constrained environment that either the first TNF inhibitor or the follow up TNF inhibitor would be certolizumab and so the treatment cost of this sequence will have been significantly reduced.

Section 4: Cost sensitivity analysis

Key point: The administration costs for the infusion products represent the internal hospital cost rather than the effective price that could be paid by a primary care trust for the management of the patient.

The cost of administration of biologic therapies that require infusion (rituximab, tocilizumab, infliximab) has always been a significant point of debate when compared to treatments that have a more mundane route of administration such as sub-cutaneous self administration (etanercept, certolizumab, adalimumab). In the West Midlands HTAC report the cost of infusion has been placed at £141.83.

This cost is seen as representing the cash cost to the NHS trust treating the patient. In reality the cost of this treatment will be recharged to the PTC that is managing the patient and this recharge will happen at a level higher than the simple “true” NHS cost due to the operation of the internal market.

Given that the whole NHS economy will need to use this cost base to then make cost effectiveness decisions, the numbers chosen should reflect the level actually paid by primary care trusts rather than the cash cost to the NHS hospital trust providing the service. Even if the base case assumption remains the same it is reasonable to ask for a sensitivity analysis that will reflect the amount paid by PCTs. In this way PCTs will be able to assess whether the assumptions in the appraisal reflect their true cost base.

In the recent submission for certolizumab pegol in response to challenges that our estimates of infusion costs were too high we varied the cost downwards to £267, taking the administration cost from the ERG estimate for rituximab in RA in 2004. When a reasonable inflation estimate is applied the 2009 figure is £305.

Table 1 below shows the simple drug acquisition and administration costs for each of the infusion products in the first year of treatment. The variation of the administration costs has a significant impact in the first year which may justify a sensitivity analysis.

Table 1: Comparison of impact on the drug acquisition and administration costs for infusion biologic treatments looking at three administration charges in year one.

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