From: Williams Hywel [Hywel.Williams@nottingham.ac.uk]
Sent: 04 September 2007 13:10
To: Natalie Bemrose
Subject: STA Infliximab for the treatment of adults with psoriasis

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Dear Ms Bemrose
Thank you for asking me to comment on the appraisal consultation document for Infliximab for the treatment of adults with psoriasis.

In my view, the committee's requests for further clarification from the manufacturer of Infliximab are entirely reasonable. My main concerns with many of these single technology appraisals is interpretation at the other end by clinicians. We seem to be treading a familiar path - that of launching a new and very expensive, potentially very effective and also potentially very toxic product in the NHS. Such products are typically tested in 4 or 5 placebo controlled randomised controlled trials, and not surprisingly, the relative risks compared with placebo for efficacy measures are huge, ie. the drug works! Often these trials are short-term (10 weeks) which would not be the typical way they might be used in clinical practice in combination with other medicines. The absence of active comparator studies then leaves us struggling with less satisfactory methods such as indirect comparisons. We are told in section 3.4 that the pooled relative risk using a random effects model was 20.49 - how as a clinician do I use this information in practice?
Do I tell my patients that Infliximib used for 10 weeks is 20 times better than giving them sugar sweets? What I really need to know is the comparative efficacy over a long time window with alternative medication such as Etanercept or Methotrexate or photochemotherapy, as well as more emphasis on serious adverse events. If possible, these estimates should be given as absolute event rates according to a range of plausible baseline event rates of the sort of patients that we see in secondary care in the UK. Number needed to treat and number needed to harm are also very helpful summary measures for interpretation in clinical practice. I do appreciate that you have to work with relative risks for the mathematical modellings, but the clinical interpretability of the evidence suffers as a result unless they are supplemented by NNT and absolute rates.

I have no objection to placebo controlled trials in principle (as long as only a few are done rather than scores), but I would like to see more realistic scenarios tested, ie. longer term administration with maintenance treatment or other combinations of treatment modelled over a one year period. Psoriasis is not a condition that goes after a few weeks when stopping a powerful treatment - it tends to come back and plague the patient on a continuous basis for many years. Time windows for comparisons are therefore crucial and I would suggest that one year is a reasonable time period to aim for.

Your choice of Etanercept as a principle comparator seems entirely reasonable, but I would love to see data on Methotrexate and photochemotherapy as well to put things in clinical context, if at all possible.

I hope these comments are helpful

Best wishes

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