UKCPA
CLINICAL PHARMACY ASSOCIATION

Multiple Technology Appraisal (MTA)
Appraisal Consultation Document
Infliximab, adalimumab and golimumab for treating moderately to severely active ulcerative colitis after the failure of conventional therapy (including a review of TA140 and TA262)

Appraisal Consultation Document, October 2014

Response UK Clinical Pharmacy Association (UKCPA)

Response to the specific questions that you ask:

- Has all of the relevant evidence been taken into account?
- Are the summaries of clinical and cost effectiveness reasonable interpretations of the evidence?
- Are the provisional recommendations sound and a suitable basis for guidance to the NHS?

Has all of the relevant evidence been taken into account?

- It has been felt that patients view has not been taken into account at an adequate and proportional level. It is acknowledged that there is not sound clinical evidence of the long-term impact of uncontrolled disease and/or surgery on patient quality of live, but ignoring patients views clearly voiced through Crohn's and Colitis UK and other patient representatives groups is in our view not acceptable.
- In view of the impact that uncontrolled disease and/or surgery has on the patient reviewing short term outcomes based on current trials only does not represent patients reality.
- Surgery as an event rather than comparator seems to be acceptable as acknowledged during the scoping workshop, data on the long-term effect of surgery is scant and it seems that the major impact of surgery on this young patient group at the beginning of their lives is ignored.

- Pouch surgery, as reported by the pouch registry, had major impact on the quality of patients' lives in view of reduced female fertility by 40-50%, unacceptable high number of daily defaecation rates, high occurrence of pouchitis (50%) and recurrent need for surgery.
- It is unclear why for the modelling it was chosen to enter the patient at age of 40 as the main manifestation of UC is between the ages of 15 and 25. Trials do not represent normal population but are trying to prove that they work at any age. So basing the model on an artificially aged patient group is not acceptable.
- Crohn's and Colitis showed in 2011 that uncontrolled disease has an 50-70% productivity loss for the most sever affected patients. Educational attainment is curtailed, carrier options restricted and starting work life curtailed. This comes at a considerable cost to society which is difficult to quantify but of considerable size. Just to ignore this hidden cost due to difficulties of modelling is not acceptable.
- It is debatable if conventional therapy is appropriate as a comparator. As UK patients would have failed conventional therapy prior to starting biologics it can safely be assumed that they would need continuous or repeated tretemtns with steroids incurring considerably long-term adverse effects of this therapy option. Alternatively it would mean surgery with the long-term impact outlined above. Surgery is not a cure but a therapy option with considerable detrimental impact on patients' lives and negative long-term outcomes. The current modelling does not take this into account as it assumes that patients would continue with conventional therapy and behave in the same way as the initial patients group. The right comparator would be patients failed on conventional therapy not treated with biologics.
- Stopping rules may not have evidence from RCTs but there is enough evidence to show that stopping biologics once patient is in deep remission is an effective treatment strategy. (Molander, IBD 2014, Steenholdt Scand J GE 2012, Farkas Scand J GE 2013, Villafranca JCC 2014). STORI data has been shown to stratify patients successfully in Crohn's disease and similar studies show that stopping rules can be developed for UC.

Are the summaries of clinical and cost effectiveness reasonable interpretations of the evidence?

It is felt that extrapolating trial data from international trials to the reality of UK practice is not useful. In the UK only patients having failed conventional therapy would be offered biologics. Trials include treatment naïve and patients failed on conventional therapies. It is very likely that treatment failure patients behave differently to patients who would have responded to conventional therapy but were offered biologics straight away. We are not yet in the situation where we can predict which patients respond to certain therapies but it is evident that there are distinct patient subgroups that behave differently and have a different disease progression and response to treatment.

Are the provisional recommendations sound and a suitable basis for guidance to the NHS?

It is felt that too many maybe difficult to assess factors have been neglected or omitted in the final modelling that the model as it stands is neither representing the reality of the patient population nor the current UK practice and assumptions based on inappropriate data sources have been used to populate the model.

Recommendation 1.3 is ambiguous as it is not clear which patient group is meant with current.

It could be interpreted as patients started on infliximab under TAG 163 then could continue with the treatment as they were started within the NHS.

In addition by adopting these MTA the UK would be at odds with the international IBD community ignoring consensus statements and guidelines such as ECCO 2102 and American College of Gastroenterology UC guidelines 2010.

We would like to ask the committee to take the concerns about the appraisal process into consideration when finalising the guidance.

[redacted] Interest Group Gastroenterology