

**Clinical Expert Summary**  
**Adalimumab (Humira®) 40 mg solution for injection (pre-filled pen,  
pre-filled syringe and vial)**

Adalimumab (Humira®) for the treatment of moderately active Crohn's disease in paediatric patients (from 6 years of age) who have had an inadequate response to conventional therapy including primary nutrition therapy, and a corticosteroid and/or an immunomodulator, or who are intolerant to or have contraindications for such therapies

**1. Existing guidelines**

Reference was made to the NICE guidance approving adalimumab in adult patients for the same indication. It was also noted that adalimumab is already used for moderately active Crohn's disease in children in the UK.

**2. Disease prevalence/incidence**

The incidence of moderately active Crohn's disease in children was estimated to be 2–3 patients per year in south-west Wales.

**3. Current treatment options**

Clinical expert opinion was that infliximab (off-label) is the most relevant current treatment option for the indication under consideration. There was also some off-label use of adalimumab in this indication prior to extension of the licence.

**4. Knowledge of product in given indication**

It was envisaged that adalimumab would be used as primary biological therapy within the indication for patients where there are issues with venous access (phobia of needles or difficult venous access), hospital attendance, or reduced/loss of response to infliximab following development of anti-infliximab antibodies.

**Appendix: Previous AWMSG clinical expert summary (published July 2013)**

This document was published as part of a previous AWMSG appraisal of adalimumab (Humira<sup>®</sup>) (Advice number 2013). The advice from this appraisal has been superseded by advice number 3916. The original appraisal documentation is included here for completeness.

## **Enc 5 Appx 3**

### **Clinical Expert Summary Adalimumab (Humira®) 40 mg/0.8 ml solution for injection (pre-filled pen, pre-filled syringe and vial)**

Adalimumab (Humira®) for the treatment of severe active Crohn's disease in paediatric patients (6 to 17 years of age) who have had an inadequate response to conventional therapy including primary nutrition therapy, a corticosteroid, and an immunomodulator, or who are intolerant to or have contraindications for such therapies.

#### **1. Existing guidelines**

Experts noted the following guidance:

- British Society of Paediatric Gastroenterology Hepatology and Nutrition (BSPGHAN). Guidelines for the Management of Inflammatory Bowel Disease (IBD) in Children in the United Kingdom. 2008.<sup>1</sup>
- National Institute of Health and Care Excellence (NICE) Clinical Guideline 152 Crohn's disease: Management in adults, children and young people. 2012.<sup>2</sup>
- NICE Technology Appraisal 187. Infliximab (review) and adalimumab for the treatment of Crohn's disease. 2010.<sup>3</sup>

Experts highlighted a Paediatric Gastroenterology Clinical Network in South Wales that meets regularly to produce guidelines and discuss difficult patients. There are also European Crohn's and Colitis Organisation (ECCO) guidelines for paediatric Crohn's patients in progress, which will be published this year<sup>4</sup>.

#### **2. Disease prevalence/incidence**

One expert that has collected and published data from South Wales for over 20 years stated a Crohn's disease prevalence of 2–3 per 100,000 children/young people aged 16 years and below. They stated that in Wales, approx 50 children and young people currently receive a biologic agent for Crohn's disease. This expert further stated that in their tertiary paediatric gastroenterology centre, they have treated 60–70 patients with biologics over the last 12 years and, although infliximab is the most common (first-line) agent, they have 5–8 patients now receiving adalimumab, predominantly because of infliximab failure/loss of response. They estimated that, of the 60–100 paediatric Crohn's patients currently followed-up by their "network", 20% will need a biological agent (e.g. adalimumab); therefore a maximum of 10–20 children over the next few years.

Another expert stated that there are around 300 patients under 16 in Wales with IBD. They estimated that currently 5–15% of paediatric patients need infliximab. Adalimumab is used for patients who have no response or lose response to infliximab, so are likely to comprise around 2–5% of the total paediatric Crohn's population in Wales.

Another expert stated that, of their 20–30 IBD patients on biologics, around 2–3 per year require second-line treatments such as adalimumab.

An expert in Cambridge, with a catchment area of around four million people, estimated that of about 200 children with IBD, about 10% receive infliximab and less than five patients receive adalimumab Humira.

#### **3. Current treatment options**

Experts stated that, for disease not responding to induction treatment (enteral nutrition or steroids) and background immunosuppression (thiopurines or methotrexate), the current treatment options are biologic agents (i.e. infliximab and adalimumab) or extensive surgery. Adalimumab is currently regarded as the second-line biologic option.

Experts stated that infliximab is used as first-line biologic treatment for most children with Crohn's disease due to the rapid onset of action and available paediatric data. There is currently limited evidence for adalimumab in children, and the slower onset of action makes it less preferable.

#### **4. Unmet needs**

Experts noted that there is a definite need for a therapeutic approach for children who lose responsiveness or have had an adverse reaction to infliximab. It was noted that children and young people with refractory Crohn's disease have a high burden of disease that does not always respond to currently available medical treatments, meaning extensive surgery, usually with the need for a permanent stoma.

#### **5. Knowledge of product in given indication**

One expert noted that in their area (London), adalimumab is available to treat adolescents with moderate to severe Crohn's disease, including fistulating disease, who have not responded to steroids or an immunomodulator. Other experts considered adalimumab an important therapy for use in children and young people with Crohn's disease that have lost responsiveness or experienced an adverse reaction to infliximab.

One expert stated that adalimumab has been used successfully in children and young people in Wales over the last few years. Data regarding its use are increasing, and a UK Paediatric Gastroenterology 'Biologics' database audit has been set up in the last few years. It was noted that evidence for the use of adalimumab has been published by the British Society of Paediatric Gastroenterology, Hepatology and Nutrition<sup>5</sup>. In addition, it was highlighted that infliximab is less painful to administer than adalimumab, but requires hospital admission for infusion (day case), unlike adalimumab which is a subcutaneous injection that can be administered at home more easily by children and families. One expert noted that at present there are more data available for the long-term use of infliximab, and hence will remain first-line choice of biologic agent, if one is required.

It should be noted that one expert declared a personal specific interest and one expert declared a personal non-specific interest in relation to adalimumab for the indication under consideration.

#### **References**

- 1 Sandhu BK, Fell JME, Beattie RM et al. Guidelines for the Management of Inflammatory Bowel Disease in Children in the United Kingdom. *Journal of Pediatric Gastroenterology and Nutrition* 2010; 50.
- 2 National Institute for Health and Care Excellence. Clinical Guideline 152. Crohn's disease: Management in adults, children and young people. 2012. Available at: <http://guidance.nice.org.uk/CG152>. Accessed May 2013.
- 3 National Institute for Health and Care Excellence. Technology Appraisal 187. Infliximab (review) and adalimumab for the treatment of Crohn's disease. 2010. Available at: <http://publications.nice.org.uk/infliximab-review-and-adalimumab-for-the-treatment-of-crohns-disease-ta187>. Accessed Apr 2013.
- 4 European Crohn's and Colitis Organisation. ECCO Guidelines: Current overview. 2013. Available at: <https://www.ecco-ibd.eu/publications/ecco-guidelines-science.html>. Accessed May 2013.
- 5 Russell RK, Wilson ML, Loganathan S et al. A British Society of Paediatric Gastroenterology, Hepatology and Nutrition survey of the effectiveness and safety of adalimumab in children with inflammatory bowel disease. *Alimentary Pharmacology & Therapeutics* 2011; 33 (8): 946-53.