AWMSG Secretariat Assessment Report – Limited submission Adalimumab (Humira®) 40 mg solution for injection (pre-filled pen, pre-filled syringe and vial)

Company: AbbVie Ltd.

Licensed indication under consideration:
Treatment of paediatric chronic non-infectious anterior uveitis in patients from two years of age who have had an inadequate response to or are intolerant to conventional therapy, or in whom conventional therapy is inappropriate.

Date of licence extension: 5 September 2017.

Comparator(s)

- No comparator was included in the company submission. There are currently no other licensed biologic treatment options in the UK for the treatment of children with chronic non-infectious anterior uveitis.

Limited submission details

The limited submission criteria were met based on:
- a minor licence extension
- anticipated usage in NHS Wales is considered to be of minimal budgetary impact.

Clinical effectiveness

- Adalimumab (Humira®) was licensed in 2016 for use in adults with refractory non-infectious intermediate uveitis, posterior uveitis and panuveitis, and is recommended for use in this indication (with some restrictions) by the National Institute for Health and Care Excellence.
- In October 2016, the One Wales Interim Pathways Commissioning Group recommended off-label adalimumab in Wales for the treatment of children with severe refractory non-infectious uveitis, using agreed starting and stopping criteria. All Wales Medicines Strategy Group advice will supersede One Wales advice on the use of adalimumab to treat children with chronic non-infectious anterior uveitis, which is now covered by the licensed indication. Treatment of uveitis in patients not covered by the licensed indication will continue to be guided by One Wales advice.
- As of September 2017, adalimumab is the only licensed treatment option in children with uveitis refractory to corticosteroid and immunosuppressant treatments. Corticosteroid and immunosuppressant treatments are not always effective and can be associated with undesirable adverse effects.
- The company submission included evidence from SYCAMORE, a multicentre, double-blind, randomised, placebo-controlled study. The study involved 90 eligible patients (all from the UK) aged 2–18 years with active juvenile idiopathic arthritis (JIA)-associated uveitis that was refractory to at least 12 weeks of methotrexate treatment. Patients received either 20 mg or 40 mg of adalimumab (according to body weight) or placebo. Treatment was administered subcutaneously every two

weeks, in combination with the baseline dose of methotrexate, and continued for 18 months or until treatment failure.

- Median time to treatment failure was significantly longer in the adalimumab group compared to the placebo group (24.1 weeks for the placebo arm; not estimable for the adalimumab arm as less than half the subjects reported treatment failure). Adalimumab reduced the risk of treatment failure by 75% compared to placebo (hazard ratio 0.25; 95% confidence interval 0.12 to 0.49; $p < 0.0001$).
- Serious adverse events occurred in 22% of patients treated with adalimumab and 7% of patients treated with placebo. Infections and infestations were the most commonly reported serious adverse events in the adalimumab group. Adverse events observed in children were similar in frequency and type to those seen in adult patients, and no new safety issues were identified for the treatment of refractory non-infectious uveitis.
- The SYCAMORE study investigated JIA-associated uveitis. Uveitis in childhood is frequently associated with various inflammatory arthropathies, predominantly JIA, which is associated with 20–25% of all uveitis cases. Evidence has not been presented for the efficacy of adalimumab in people with idiopathic uveitis.

Budget impact

- The company estimated that 16 children in Wales are eligible for adalimumab based on a 0.03% prevalence figure and 0.004% incidence figure for childhood uveitis applied to the Welsh population aged 2–18 years. It is assumed that 65% of patients will receive ongoing therapy and of these, 20% would have an inadequate response to methotrexate.
- The annual acquisition cost of adalimumab for this group of patients is £9,187, based on a dose of 20–40 mg injected subcutaneously every other week, in combination with methotrexate. Although patients require different doses according to body weight, it is assumed that all patients would require a single 40 mg vial per injection.
- In addition to adalimumab acquisition costs, budget impact estimates also include methotrexate costs, 12 blood tests per year (for the 25% of patients for whom the medicine is not administered by a hospital nurse), and tuberculosis screening prior to treatment initiation. The company's anticipated uptake of adalimumab and net budget impact forecasts of adalimumab are commercial in confidence.
- Some children eligible for treatment will already be receiving adalimumab, either in line with the One Wales interim commissioning decision, or as part of the treatment of other conditions for which adalimumab is indicated, predominantly JIA (10–30% of children with JIA are estimated to have anterior uveitis). Therefore, the true budget impact is likely to be lower than this estimate.

Additional information

- AWTTC is of the opinion that, if recommended, adalimumab (Humira®) is appropriate for specialist only prescribing within NHS Wales for the indication under consideration.
- The company anticipate that adalimumab (Humira®) may be supplied by a home healthcare provider.

Evidence search

Date of evidence search: 12 September 2017.
Date of range of evidence search: No date limits were applied to database searches.

Further information

This assessment report will be considered for review every three years.

References are available on request. Please email AWTTC at awttc@wales.nhs.uk for further information.

This report should be cited as: All Wales Therapeutics and Toxicology Centre. AWMSG Secretariat Assessment Report. Adalimumab (Humira®) 40 mg solution for injection (pre-filled pen, pre-filled syringe and vial). Reference number: 3035. November 2017.