AWTTC
All Wales Therapeutics & Toxicology Centre
Canolfan Therapiwteg a Thocsicoleg Cymru Gyfan

Adalimumab (Humira®) for the treatment of paediatric patients with severe refractory non-infectious uveitis

October 2016

ONE WALES INTERIM COMMISSIONING DECISION

Adalimumab (Humira®) for the treatment of paediatric patients with severe refractory non-infectious uveitis

Date of advice: October 2016

The following Interim Pathways Commissioning Group (IPCG) recommendation has been endorsed by health board Chief Executives.

Using the agreed starting and stopping criteria adalimumab (Humira®) can be made available within NHS Wales to treat paediatric patients (aged ≥ 2 to ≤ 18 years) with severe refractory non-infectious uveitis.

Adalimumab (Humira®) should be initiated in specialist centres for this indication.

Adalimumab is not licensed to treat this indication and is therefore 'off-label'. Each provider organisation must ensure all internal governance arrangements are completed before this medicine is prescribed.

The risks and benefits of the off-label use of adalimumab for this indication should be clearly stated and discussed with the patient to allow informed consent.

Providers should consult the General Medical Council Guidelines on prescribing unlicensed medicines before any off-label medicines are prescribed.

This advice will be reviewed after 12 months or earlier if new evidence becomes available.

One Wales advice promotes consistency of access across NHS Wales.

Starting and stopping criteria for adalimumab for the treatment of paediatric patients with severe refractory non-infectious uveitis

These criteria are taken from the NHS England Clinical Commissioning policy document[1].

Starting and stopping criteria

Starting criteria:

Children eligible for the use of adalimumab for the treatment of uveitis would meet the following criteria:

1. The presence of active anterior uveitis, defined as a sustained grade of ≥+1 cellular infiltrate in the anterior chamber
AND
2. Failure to control uveitis to +0.5 cells or less with:
   - Methotrexate (minimum dose of 10 mg/m^2 with a maximum dose of 25 mg/m^2), usually in combination with
   - 0.1mg/kg/day of oral prednisolone
     and
   - 2 drops of topical steroid eye drops per day.

Treatment effect should be assessed after at least 12 weeks.
When the patient is methotrexate intolerant an adequate trial (3-6 months) of an alternative conventional immunosuppressant should be given).
Exceptionally a child, presenting with very severe sight-threatening disease, will be considered for adalimumab before the end of a 12-week trial of prednisolone and methotrexate.

Very severe sight -threatening features at presentation include:
- Severe inflammatory activity (≥3+ cells)
- Cataract
- Glaucoma (Intraocular pressure >21mmHg with evidence of optic neuropathy)
- Hypotony (Intraocular pressure ≤5mmHg)
- Dense vitreous opacity
- Macular oedema causing visual impairment ≤6/18

As this is an unlicensed treatment clinicians must follow their employers' requirements regarding patient/carer consent for treatment.

Adalimumab should always be initiated in a specialised ophthalmology centre.

The dose of adalimumab administered in clinical trials was 20 mg for patients weighing < 30 kg and 40 mg in patients weighing ≥ 30 kg every 2 weeks.

Dose frequency may be escalated to 40 mg once every week if safe to do so in patients with partial response and sight-threatening disease within three months of treatment. If no response is achieved in three months then treatment is considered a failure and treatment should be stopped.

In treatment
Response to therapy should be assessed after 3 months of therapy and re-assessed every 3 months whilst treatment continues. The following data points must be collected by for each patient every 3 months:

- Standardisation of the Uveitis Nomenclature (SUN) cell activity score
- Total oral corticosteroid use
- Frequency of topical steroid eye drops
- Visual acuity measured by age-appropriate Logarithm of Minimum Angle of Resolution (LogMAR) assessment
- Presence of optic neuropathy,
- Presence of cataract
- Presence of hypotony
- Presence of macular oedema

Children who respond to treatment with adalimumab (as defined by reduction of inflammation to 0.5+ cellular activity or less) will continue treatment for 18 months at which time a trial of treatment withdrawal will be undertaken. If relapse occurs, restarting adalimumab will be considered using the same start criteria in the policy.
Serious adverse events must be reported to the MHRA using the yellow card system.

Stopping criteria:

Adalimumab for the treatment of uveitis is stopped using the following criteria:
1. 2-step increase from baseline in SUN cell activity score (anterior chamber [AC] cells) over 2 consecutive readings
2. Sustained non-improvement with entry grade or greater for 2 consecutive readings
3. Only partial improvement (1 grade) or no improvement with the development of other ocular co-morbidity which is sustained
4. Worsening of existing ocular co-morbidity after 3 months
5. Sustained scores as recorded at entry grade measured over 2 consecutive readings (grades 1 to 2) still present after 6 months of therapy
6. Less than 0.5+ cellular activity at 18 months of treatment

Refer also to the dosing section above under “starting criteria”.

Reference

1 NHS England. Interim Clinical Commissioning Policy: Adalimumab for children with severe refractory uveitis. Ref. D12X02. 2015. Available at: https://www.england.nhs.uk/commissioning/wp-content/uploads/sites/12/2015/11/d12x02-paediatric-uveitis-anti-tnf.pdf Accessed Jun 2016.

KEY FINDINGS: This is an abbreviated summary of the evidence provided to IPCG

Report background

Uveitis is a term for inflammation within the eye which, in severe cases, can lead to blindness. Corticosteroids and immunosuppressants are the mainstay treatment for uveitis, but are not always effective and can be associated with undesirable adverse effects. Adalimumab may offer an additional treatment option in paediatric patients with severe non-infectious uveitis refractory to corticosteroid and methotrexate treatments. Although it received a licence in June 2016 for the treatment of refractory non-infectious uveitis in adults, it is not licensed for this indication in children and therefore its use is off-label. Adalimumab is available for the off-label indication for paediatric patients in NHS England through clinical commissioning. A cohort of patients has been identified based on the data from individual patient funding request (IPFR) panels in NHS Wales and, based on unmet need within the service, this medicine was considered to be suitable for assessment via the One Wales process. The treatment of adults with severe refractory non-infectious uveitis is considered in a separate Evidence Status Report (ESR).

Efficacy/Effectiveness

Results from a randomised controlled trial demonstrated significant improvements in the time to treatment failure in the adalimumab group versus placebo in patients with juvenile idiopathic arthritis-associated uveitis. Single-arm studies further support the efficacy of adalimumab for the treatment of uveitis.

Safety

No new safety signals have been observed for adalimumab for the treatment of paediatric patients with severe refractory non-infectious uveitis.

Patient factors

Adalimumab is administered every two weeks by subcutaneous injection. It may be self-administered or administered by a caregiver.

Cost effectiveness

There are no published studies on the cost effectiveness of adalimumab for the treatment of severe refractory non-infectious uveitis. Limited cost effectiveness estimates have been reported in the NHS England commissioning Policy but they are subject to uncertainty due to the assumptions made in their calculation. Comparing use of a biologic (risk of blindness 1%) to conventional immunosuppressant therapy (risk of blindness 8%) resulted in an Incremental Cost Effectiveness Ratio (ICER) of £6,400. Increasing the risk of blindness on biologic therapy from 1% to 5% increased the ICER to £40,200.

Budget impact

There are estimated to be 10–15 new patients per year in Wales requiring two year treatment with adalimumab for this indication. This would result in a budget impact of between £99,760 and £149,640 in year one and between £199,520 and £299,280 in year two using the list price of adalimumab together with monitoring costs. The patient population includes patients for whom treatment has been funded via the IPFR route and therefore the budget impact is most likely to lie at the lower end of this estimate.

Impact on health and social care services

Minimal increased use of existing services.

Innovation and/or advantages

Adalimumab offers a new treatment choice for patients with refractory uveitis.