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

Adalimumab for the treatment of paediatric patients with severe refractory non-infectious intermediate, posterior and pan-uveitis. (OW04)
December 2023

ONE WALES INTERIM DECISION

Adalimumab for the treatment of paediatric patients with severe refractory non-infectious intermediate, posterior and pan-uveitis.

Date of original advice: August 2016
Date of review: November 2023

The following One Wales Medicines Assessment Group (OWMAG) recommendation has been noted by the All Wales Medicines Strategy Group (AWMSG) and ratified by Welsh Government

Using the agreed starting and stopping criteria adalimumab can continue to be made available within NHS Wales to treat paediatric patients (aged ≥ 2 to ≤ 18 years) with severe refractory non-infectious intermediate, posterior and pan-uveitis. Adalimumab 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 relevant guidelines on prescribing unlicensed medicines before any off-label medicines are prescribed.

This advice will be reviewed after 3 years or earlier if new evidence becomes available.

Clinician responsibility
Clinicians will be obliged to collect and monitor patient outcomes. Evidence of clinical outcomes will be taken into consideration when reviewing the One Wales Medicines Assessment Group decision.

Health board responsibility
Health boards will take responsibility for implementing One Wales Medicines Assessment Group decisions and ensuring that a process is in place for monitoring clinical outcomes.

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 intermediate, posterior and pan-uveitis

These criteria are taken from the NHS England Clinical Commissioning policy document[1] with further adaptation from clinical experts, University Hospitals Bristol NHS Foundation and Translation Health Science (Ophthalmology), Bristol Medical School, Faculty of Health Sciences.

Start 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, and/or vitritis and/or clinically active chorioretinal lesions and/or macular oedema, defined as a sustained grade of ≥+1 cellular infiltrate in the anterior chamber, BIO score of >/= 1 and OCT evidence of macular oedema
AND
2. Failure to control uveitis to +0.5 cells or BIO score or persistent macular oedema or less with:

- Methotrexate (minimum dose of 10 mg/m^2 with a maximum dose of 25 mg/m^2) or mycophenolate mofetil, 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 or mycophenolate mofetil.

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 – BIO score of >/+ 2
- Macular oedema causing visual impairment ≤6/18 or >/= to CMT of 350um

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 or BIO score of 0.,5 or less or resolution of macular odema) 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.

Stop 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) or BIO score or maintained macular oedema over 2 consecutive readings at least a month a part
2. Sustained non-improvement with entry grade or greater for 2 consecutive readings
3. Worsening of existing ocular co-morbidity after 3 months if deemed due to persistent inflammation and not a result of progressive structural damage due to previous inflammation
4. Sustained scores as recorded at entry grade measured over 2 consecutive readings (grades 1 to 2) still present after 6 months of therapy
5. Less than 0.5+ of cellular activity or BIO score or resolution of macular oedema 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.

This is a summary of new evidence available and patient outcome data collected, to inform the review

Background: Uveitis is a term for inflammation within the eye which, in severe cases, can lead to blindness. Uveitis is classified according to the location of inflammation: anterior, intermediate, posterior and pan- uveitis. Adalimumab was licensed in 2017 for use in children from two years of age for the treatment of chronic, non-infectious anterior uveitis who have had an inadequate response to or are intolerant to conventional therapy, or in whom conventional therapy is inappropriate. Adalimumab is recommended for use in this indication by the All Wales Medicines Strategy Group (AWMSG). Treatment of non-anterior uveitis (i.e. intermediate, posterior and pan-uveitis) remains off-label and is currently supported by One Wales interim advice. Adalimumab is available in NHS England under the commissioning medicines for children in specialised services policy in line with the National Institute for Health and Care Excellence technology appraisal guidance for adults.

Current One Wales Decision: The solution for injection (pre-filled pen, pre-filled syringe or vial) is supported for use for this indication.

Licence status: Adalimumab is not currently licensed to treat paediatric patients with severe refractory non-infectious intermediate, posterior and pan-uveitis; its use in this indication is off-label. AWTTC is not aware of any plans to pursue marketing authorisation of adalimumab for this indication at this time.

Guidelines: There are no changes to current guidelines.

Licensed alternative medicines or Health Technology Assessment advice for alternative medicines: No alternative medicines have been licensed for non anterior uveitis in paediatric patients since the last review.

Effectiveness: A repeat literature search identified one study (Vitale *et al* 2023) that investigated adalimumab for the treatment of non-anterior uveitis in paediatric patients. A multicentre, real world study analysed data from 21 patients (36 affected eyes) treated with adalimumab for intermediate uveitis/pars planitis (12 eyes), posterior uveitis (5 eyes) and panuveitis (19 eyes). The mean treatment duration was 30.47 months (range 3–125). After commencing on adalimumab, 11 patients (19 eyes) had no further ocular inflammation, the remaining 10 patients (17 eyes) saw significant clinical improvement in symptoms with a decrease in severity and/or frequency of ocular relapses. Occurrences of ocular flares, macular oedema and retinal vasculitis were all reduced, and mean daily glucocorticoid usage also dropped significantly among patients already treated with steroids during the study period.

Safety: One patient reported an adverse event during the study period, a generalised adenopathy which developed during the course of adalimumab treatment.

Cost-effectiveness: No relevant cost-effectiveness analyses identified in the repeat literature search.

Budget impact: AWTTC is aware of [CONFIDENTIAL DATA REMOVED] in Wales receiving adalimumab for the treatment of non-anterior uveitis in the last year. This figure is in line with the estimated number of patients considered to be eligible for treatment per year by clinical experts.

Impact on health and social care services: No new impact data have been provided, though we consider the impact of this medicine to be minimal.

Patient outcome data: [CONFIDENTIAL DATA REMOVED]

Evaluation of evidence
No new information on clinical/cost effectiveness or budget impact has been identified which would change the original recommendation. [CONFIDENTIAL DATA REMOVED]. AWTTC recommends that it would be appropriate to retain access to adalimumab for the treatment of paediatric patients with severe, refractory, non-infectious, non anterior uveitis.

Next review date: November 2026

References: a full reference list is available on request.

This document includes evidence published since the last review or full assessment of this medicine for the indication under consideration. It does not replace the original full evidence status report. Any previous reviews and the original full evidence status report are available on request by email to AWTTC@wales.nhs.uk.

Care has been taken to ensure the information is accurate and complete at the time of publication. However, the All Wales Therapeutics and Toxicology Centre (AWTTC) do not make any guarantees to that effect. The information in this document is subject to review and may be updated or withdrawn at any time. AWTTC accept no liability in association with the use of its content. An Equality and Health Impact Assessment (EHIA) has been completed in relation to the One Wales policy and this found there to be a positive impact. Key actions have been identified and these can be found in the One Wales Policy EHIA document.

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