AWMSG Secretariat Assessment Report – Limited submission

Belimumab (Benlysta®▼) 120 mg and 400 mg powder for solution for infusion

Company: GlaxoSmithKline

Licensed indication under consideration: as an add-on treatment for therapy in patients aged ≥ 5 years to < 18 years with active, autoantibody-positive systemic lupus erythematosus (SLE) with a high degree of disease activity (e.g., positive anti-dsDNA and low complement) despite standard therapy

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions.

In line with the National Institute for Health and Care Excellence (NICE) advice for use in adults the company's submission focusses on a subpopulation of the licensed indication: in children aged ≥ 5 years to < 18 years with serological disease activity (defined as positive anti-double-stranded DNA AND low complement) and a Safety of Estrogen in Lupus National Assessment – Systemic Lupus Erythematosus Disease Activity Index (SELENA-SLEDAI) score of greater than or equal to 10 despite standard treatment.

Date of licence extension: 21 October 2019

Comparator(s)

- The comparator included in the company's submission is off-label rituximab.

Limited submission details

- The limited submission criteria were met based on a minor licence extension.

Clinical effectiveness

- Belimumab is recommended by the National Institute for Health and Care Excellence (NICE) for the treatment of active, autoantibody-positive SLE in adults (June 2016, [TA397]), only if there is evidence of serological disease activity and SELENA-SLEDAI score is greater than or equal to 10 despite standard treatment. Belimumab is available in NHS Wales for adults under a Department of Health Patient Access Scheme (PAS).
- This submission covers the licence extension for belimumab to include paediatric patients aged ≥ 5 years to < 18 years, and the company has restricted their submission to patients who have serological disease activity and SELENA-SLEDAI score greater than or equal to 10 despite standard treatment, in line with the recommendation by NICE for use in adults.

- Belimumab is the first licensed biological treatment for patients with active, autoantibody-positive systemic lupus erythematosus (SLE) disease, who are already receiving standard therapy.
- The current standard of care includes the use of non-steroidal anti-inflammatory medicines, corticosteroids, antimalarials or immunosuppressants. AWTTC sought clinical expert opinion confirmed that off-label rituximab is a suitable comparator.
- The Summary of Product Characteristics for belimumab requires patients to be reviewed at six months; treatment should be only continued if the SELENA-SLEDAI score has improved by 4 points or more in line with NICE TA397 recommendation.
- The company submission includes results from a one year, phase II, multicentre, randomised, double-blind placebo-controlled study (BEL114055) that evaluated the clinical efficacy, safety and pharmacokinetics of belimumab plus standard of care (n=53) versus placebo plus standard of care (n=40) in paediatric patients aged ≥ 5 years to < 18 years with clinically active SLE (SELENA-SLEDAI disease activity score of ≥ 6 at screening).
- The primary efficacy endpoint was response at week 52, assessed using the SLE Responder Index that measured improvement in SLE disease activity (≥ 4 point reduction from baseline in SELENA-SLEDAI score), without worsening in any organ system, or in the patient's overall condition. The proportion of children achieving an improvement in disease activity, was numerically higher in patients receiving belimumab plus standard therapy (52.8%) compared with placebo plus standard therapy (43.6%). The difference was not statistically significant, but numerically the response rate was similar to the response rate in the phase 3 studies in adults.
- BEL114055 was not powered for any formal comparisons between belimumab and placebo. The Committee for Medicinal Products for Human Use (CHMP) acknowledged the rarity of the disease and considered it was acceptable to extrapolate efficacy to paediatric patients based on pharmacokinetic data and a numerical comparison of the clinical results between the paediatric and adult studies. The CHMP concluded the differences observed are largely comparable to the differences observed in adults, supporting belimumab for use in patients aged ≥ 5 years to < 18 years.
- The reported overall safety profile of belimumab in BEL114055 was similar to that seen in adults. The most frequently reported treatment-emergent adverse event were infections and infestations. The CHMP noted long-term safety data is limited, especially those aged 5 to 11 years old. An open-label, belimumab safety extension study in the paediatric population is ongoing. The applicant company also aim to collect further safety data within established registries, with particular focus on infections from paediatric patients being followed up long-term.

Budget impact

- The company estimates that in Year 1 there are 9 paediatric patients aged ≥ 5 years to < 18 years in Wales eligible for treatment with belimumab increasing to 14 paediatric patients in Year 5. This is based on population data for Wales, published prevalence and incidence data for SLE in the UK and internal company data. It is likely the number of eligible patients is an overestimate as it includes patients with lupus nephritis and CNS lupus and these indications are outside the licensed indication.
- The cost of treatment differs according to the patient's weight. The annual cost per patient for belimumab was calculated based on the average weight (53kg) for paediatric patients aged ≥ 5 years to < 18. The company has not provided sensitivity analyses to assess variation in costs due to a patient's body weight.
- Based on the company's market share projections, belimumab is assumed to partly displace off-label ritixumab. Assuming 50% displacement of rituximab by belimumab, the company estimate that six children aged between ≥ 5 years to < 18 years will receive belimumab and continue treatment in Year 1, increasing to 10 children in Year 5. The net medicine acquisition cost of introducing belimumab is estimated to be [commercial in confidence figure removed] in Year 1 increasing to [commercial in confidence figure removed] in Year 5, based on the approved PAS discount price for belimumab and list price for the comparator.
- The net resource implications (administration costs) were estimated to total £15,015 in Year 1 increasing to £27,310 in Year 5.
- Whilst there are limitations to the company's budget impact calculations; overall these are likely to result in an overestimate of the company's budget impact analysis.

Additional information

- AWTTC is of the opinion that, if recommended, belimumab (Benlysta▼) is appropriate for specialist only prescribing within NHS Wales for the indication under consideration.

Evidence search

Date of evidence search: 13 January 2020
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. Belimumab (Benlysta▼) 120mg and 400mg powder for solution for infusion. Reference number: 3778. April 2020