



AWTTC

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

Rituximab for the treatment of pemphigus and pemphigoid disease in adults and children

December 2019

ONE WALES INTERIM COMMISSIONING DECISION

Rituximab for the treatment of adults and children with pemphigus (excluding pemphigus vulgaris) after failure of first-line treatments including steroids and steroid-sparing treatments and after failure of third-line treatments for pemphigoid disease including steroids and steroid-sparing treatments

Date of original advice: July 2017

Date of review: December 2019

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

Rituximab can be made available within NHS Wales for the second-line treatment of pemphigus (excluding pemphigus vulgaris) and fourth-line treatment of pemphigoid disease in adults and children whose disease has not responded to previous treatments including steroids and steroid-sparing agents.

Rituximab 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 rituximab 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.

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 Interim Commissioning decision.

Health board responsibility

Health boards will take responsibility for implementing One Wales Interim Commissioning decisions and ensuring that a process is in place for monitoring clinical outcomes.

One Wales advice promotes consistency of access across NHS Wales.

Background

Pemphigus is a group of rare autoimmune conditions in which painful, fragile blisters occur on the skin and mucous membranes, most commonly inside the mouth, nose, throat and genitals. Pemphigus variants include pemphigus vulgaris, pemphigus foliaceus and paraneoplastic pemphigus. Bullous pemphigoid is a similar blistering skin disease that tends to affect older people. The NHS England Clinical Commissioning Policy recommends rituximab as an option for people with pemphigus or pemphigoid whose disease has not responded to steroids and steroid-sparing agents. Based on unmet need to treat this cohort of patients this medicine was considered suitable for assessment via the One Wales process.

Current One Wales Interim Commissioning Decision

Rituximab can be made available within NHS Wales for the second-line treatment of pemphigus (excluding pemphigus vulgaris) and fourth-line treatment of pemphigoid disease in adults and children whose disease has not responded to previous treatments including steroids and steroid-sparing agents. August 2019.

Licence status

Rituximab (MabThera®) was granted a licence extension by the European Medicines Agency (EMA) on 11 March 2019 to include the treatment of patients with moderate to severe pemphigus vulgaris¹. The company has not submitted for appraisal by the All Wales Medicines Strategy Group (AWMSG) and therefore a statement of advice has been issued by AWMSG for MabThera® for this indication². Accordingly the use of MabThera® for pemphigus vulgaris can no longer be endorsed by One Wales and this review applies only to other variants of pemphigus and all variants of pemphigoid approved in 2018. The One Wales Interim Commissioning Decision was updated accordingly in August 2019.

Rituximab for the treatment of adults and children with pemphigus (excluding pemphigus vulgaris) and for pemphigoid disease remains off-label.

Guidelines

There have been no new guidelines or updates to existing guidelines identified.

Licensed alternative medicines/Health Technology Appraisal advice for alternative medicines

There remain no alternative licensed medicines or health technology appraisal advice for this indication.

Efficacy/Effectiveness

A systematic review published in 2018 investigated the efficacy of rituximab (off-label use; n = 62) and omalizumab (off-label use; n = 22) for the treatment of bullous pemphigoid³. The rituximab and omalizumab dosing regimens and the baseline characteristics of patients, including prior treatments, varied between the studies. Data for specific outcome measures were not available for all patients. Complete response rates were similar for rituximab (85%; n = 52) and omalizumab (84%; n = 16). Of the 52 patients who had a complete response following treatment with rituximab, relapse occurred in 15 (29%) patients within a mean range of 10.2 ± 7 months following the last rituximab treatment. Relapse occurred in 8 (80%) patients receiving omalizumab within a mean range of 3.4 ± 1.9 months. There were no non-responders in the rituximab group and one non-responder for omalizumab³.

Safety

The systematic review reported that 24% of patients (n = 13) receiving rituximab experienced adverse effects possibly related to treatment³. These included infections, anaemia, neutropenia, syndrome of inappropriate antidiuretic hormone secretion, drug fever, acute pruritus, peripheral arterial occlusive disease and tachycardia. Two patients died and these were considered possibly related to rituximab treatment as death occurred near the time of administration, however for both patients their deaths were most likely due to significant co-morbidities³. The EMA's updated Summary of Product Characteristics for rituximab (MabThera®) for the treatment of patients with moderate to severe pemphigus vulgaris reported no new safety information⁴.

Cost effectiveness

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

Budget impact

Clinicians from three health boards have provided information on patient numbers. None of these clinicians have used rituximab in the last year. The original evidence status report, which included pemphigus vulgaris, estimated that between six and nine patients would be eligible for rituximab treatment annually.

Impact on health and social care services

The impact on the service remains minimal.

Patient outcome data

No patient outcome data have been provided.

References

1. European Medicines Agency. MabThera[®]. Procedural steps taken and scientific information after the authorisation. Jul 2019. Available at: https://www.ema.europa.eu/en/documents/procedural-steps-after/mabthera-epar-procedural-steps-taken-scientific-information-after-authorisation_en.pdf. Accessed Jul 2019.
2. All Wales Medicines Strategy Group. Rituximab (MabThera[®]) 100 mg and 500 mg concentrate for solution for infusion. Reference number: 3192. Appraisal information. Jun 2019. Available at: <http://www.awmsg.org/awmsgonline/app/appraisalinfo/3192>. Accessed Aug 2019.
3. Kremer N, Snast I, Cohen ES et al. Rituximab and Omalizumab for the Treatment of Bullous Pemphigoid: A Systematic Review of the Literature. *American Journal of Clinical Dermatology*. 2019;20:209-216.
4. European Medicines Agency. Assessment Report: MabThera[®]. Procedure No.: EMEA/H/C000165 - II/0150. Jul 2019. Available at: https://www.ema.europa.eu/en/documents/product-information/mabthera-epar-product-information_en.pdf. Accessed Jul 2019.