



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 where third- or fourth-line treatments, including steroids and steroid-sparing treatments have failed

July 2017

ONE WALES INTERIM COMMISSIONING DECISION

Rituximab for the treatment of pemphigus and pemphigoid disease in adults and children where third- or fourth-line treatments, including steroids and steroid-sparing treatments have failed

Date of advice: July 2017

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 third-line treatment of pemphigus 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.

One Wales advice promotes consistency of access across NHS Wales.

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

Report background

Pemphigus vulgaris is a rare autoimmune condition in which painful, fragile blisters occur on the skin and mucous membranes, most commonly inside the mouth nose, throat and genitals. Bullous pemphigoid is a similar blistering skin disease that tends to affect older people. A small number of people have pemphigus or pemphigoid that does not respond to treatment with systemic steroids or immunosuppressants.

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. This use of rituximab is currently off-label, although a submission for marketing authorisation for rituximab (MabThera®) to treat pemphigus vulgaris is expected. A phase III clinical study of rituximab to treat pemphigus vulgaris is scheduled to complete in 2019.

Clinicians in Wales consider there is an unmet need and have identified a cohort of patients who could benefit from rituximab treatment. This medicine was therefore considered suitable for assessment via the One Wales process.

Efficacy/Effectiveness

The evidence of clinical effectiveness of rituximab to treat pemphigus or pemphigoid comes from systematic reviews, retrospective case studies and case reports. Three systematic reviews of different treatment regimens of rituximab to treat pemphigus showed that, despite differences in outcome assessment, generally high (76% to 95%) rates of complete remission were achieved. The relapse rate ranged from 40% to 50%. Two systematic reviews and a case series of rituximab to treat pemphigoid also showed high rates of complete remission with most patients responding to treatment.

Safety

The most common adverse events reported were serious infections, sepsis, septicaemia and neutropenia. No new safety signals were identified for rituximab in treating pemphigus and pemphigoid. The rates of severe adverse events and mortality reported in the case series and case reports were similar for the different rituximab treatment regimens.

Patient factors

Rituximab is administered by intravenous infusion. Different doses and regimens have been used to treat pemphigus and pemphigoid. NHS England's commissioning policy recommends an adult dose of 1,000 mg on days 1 and 15, a second cycle may be considered following relapse.

Cost effectiveness

No cost-effectiveness analyses were identified in the literature and no UK-based studies were identified. A Canadian cost analysis comparing the costs of treating pemphigus and pemphigoid with rituximab and intravenous immunoglobulin indicated that rituximab was cost-saving when compared to treatment with immunoglobulin, reducing costs by around one-third.

Budget impact

Based on an estimated 6–9 patients with pemphigus vulgaris or pemphigoid disease eligible for treatment the acquisition cost of rituximab is between £18,858 and £31,433 in year one. Some patients are already receiving this regimen through Individual Patient Funding Requests and local applications, though accurate figures were not available from the health boards. Administration and treatment of adverse reactions may incur additional costs. Some alternative treatments (for example, intravenous immunoglobulin) are more expensive and also have associated administration costs.

Welsh commercial access agreement

This medicine is currently not licensed for the indication under consideration (i.e. is off-label) and therefore the Pharmaceutical Industry's code of practice prevents a company from promoting an off-label use of a medicine. For that reason, a commercial agreement cannot be offered by the company.

Impact on health and social care services

The impact is expected to be minimal considering the small numbers of patients needing treatment.

Innovation and/or advantages

Rituximab is an additional/alternative treatment for these often severe and debilitating skin diseases.