

RITUXIMAB (Truxima® ▼, Rixathon® ▼) for immune (idiopathic) thrombocytopenic purpura

The Pan Mersey Area Prescribing Committee recommends the prescribing of RITUXIMAB by specialists only for immune (idiopathic) thrombocytopenic purpura before romiplostin and eltrombopag.

RED

Immune (idiopathic) thrombocytopenic purpura (ITP) is an acquired autoimmune disorder most commonly resulting from auto-antibody mediated peripheral platelet destruction and, in many cases, impaired platelet production. In the majority of adults, treatment is indicated in those with very low platelet counts ($<30 \times 10^9/L$), or significant bleeding.

Rituximab is not licensed for the treatment of ITP and this use is off-label. Rituximab is used as an intermittent treatment course of four weeks.

NICE TA293 and TA221 discuss the use of eltrombopag and romiplostin as treatment options for ITP⁽¹⁾. Eltrombopag and romiplostin can be offered to patients who have not had a splenectomy and failed with other second line therapies including rituximab⁽¹⁾.

Haematology consultants only may decide to start patients on rituximab. However all haematology trained doctors may prescribe rituximab for this indication once a consultant decision has been made. Prescribing should be retained by the specialist team.

UK incidence of ITP in adults in the order of 1.6 to 3.9 per 100,000 per year⁽²⁾. The estimated childhood incidence of ITP in the UK is in the order of 3.0 to 4.8 per 100,000 children per year, of which 15 to 20% will go on to develop the chronic form. A conservative estimate based on the most recent surveys suggests the prevalence of chronic childhood ITP is around 4.6 per 100,000 children.

Comparing the cost of rituximab with other second-line treatments is difficult because rituximab is usually given as intermittent courses and is intended to induce long-term remission. Other second-line treatments usually need to be given continuously. Specialist opinion suggests that further treatment with rituximab may be given to people whose ITP initially responds to treatment with rituximab, but then relapses. Rescue treatment may also be needed in people whose condition relapses after receiving rituximab. Both of these factors may increase the costs associated with rituximab for ITP⁽²⁾.

The only other treatment for ITP that is a one-off treatment aimed at inducing long-term remission is splenectomy. By comparison, the cost to commissioners of an elective splenectomy is estimated to be in the range of £3252 to £4548, depending on the complexity of the procedure⁽²⁾.

Note: Patients who are not eligible for treatment under this statement may be considered on an individual basis where their GP or consultant believes exceptional circumstances exist that warrant deviation from the rule of this policy. In this situation, follow locally defined processes.

Rituximab (Rixathon® ▼, Truxima® ▼) for immune (Idiopathic) thrombocytopenic purpura

Effectiveness^(1,2)

Rituximab is a monoclonal antibody that targets the CD20 antigen expressed on the surface of B-lymphocytes. This induces cell lysis and cell death by apoptosis. It is used off label as second line treatment for ITP.

Evidence for rituximab in ITP in adults is largely from observational studies with no comparator arm. Evidence includes a systemic review and meta-analysis, 2 RCTs and a retrospective cohort study. Primary endpoints differed. From the evidence, partial response was observed in 57% of patients at various time points after treatment. Complete response rate ranged from 35% to 41.5%, again at various time points. Rituximab alone was compared with placebo saline (not statistically significant), with splenectomy (no difference in composite death from bleeding or infection). Rituximab & dexamethasone was superior to dexamethasone monotherapy.

Evidence for children is weaker from 17 case series and 1 cohort study; none were done with UK populations. From these studies response and complete response was achieved in 68% and 39% of patients respectively.

Safety⁽³⁾

Infusion related reactions can be very common. Pre-medication with an antipyretic and an antihistamine (e.g. paracetamol and diphenhydramine) should always be given before intravenous rituximab. In addition, premedication with a glucocorticoid should be given (except in people with non-Hodgkin's lymphoma or chronic lymphocytic leukaemia who are receiving rituximab in combination with glucocorticoid-containing chemotherapy).

Very rare cases of fatal progressive multifocal leukoencephalopathy have been reported with rituximab use. Patients should be monitored regularly for any new or worsening neurological signs. Severe skin reactions and infections can occur – please see the SPC for further information.

Rituximab should not be administered as an intravenous push or bolus.

Cost (excluding VAT) [MIMS April 2019]

Rituximab Adult (375mg/m² weekly for 4 weeks with a body surface area of 1.86m) - £4400.68.

Child (375mg/m² weekly for 4 weeks with a body surface area of 0.89m) - £2514.64

100mg weekly for 4 weeks (some studies) - £628.66

Eltrombopag - doses range between 25mg to 75mg OD

12 month cost £9240 - £27, 720

Romiplostim - dose based on 70kg adult (1 microgram /kg/week)

12 month cost - £11,568

Estimated 8 patients per 100,000 population may be eligible for treatment with rituximab, and assuming 50% response rate this may result in annual savings of approximately £17,000 per 100,000 population compared to eltrombopag/ romiplostim.

Rituximab, eltrombopag and romiplostim are PBR-excluded drugs.

Patient factors

N/A

Prescribing information

Rituximab when used for ITP should be dosed as 375mg/m² weekly for 4 weeks in both adults and children. Alternatively a lower weekly dose of 100mg for 4 weeks may be used.

Implementation notes

Rituximab is a hospital only medicine designated RED. All prescribing and clinical care associated with rituximab must remain with the initiating specialist in hospital setting. Lack of robust evidence in both adults and children makes it difficult to draw firm conclusions regarding rituximab and ITP.

References

1. National Institute for Health and care and Excellence (2019). [Immune \(idiopathic\) thrombocytopenic purpura: rituximab. ESUOM35](#). Last accessed [8th April 2019]
2. Northern Treatment Advisory Group [Rituximab for the treatment of Immune \(Idiopathic\) Thrombocytopenic Purpura \(ITP\)](#). February 2015.
3. Medicines Compendium. (2019). Mabthera 100mg Concentrate for Solution for Infusion. [Roche Products Limited contact details](#). Available: <https://www.medicines.org.uk/emc/> Last accessed: [9TH April 2019].