0NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Avatrombopag in combination for treating chronic immune thrombocytopenia

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of avatrombopag within its marketing authorisation for treating chronic immune thrombocytopenia.

Background

Immune thrombocytopenia (ITP, also called immune thrombocytopenic purpura) is an autoimmune condition characterised by increased platelet destruction and, in some cases, inadequate platelet production.[1] Platelets are made in the bone marrow and they travel through blood vessels and stick together to stop any bleeding that may happen if a blood vessel is damaged. ITP can result in low platelet counts and bleeding. In a blood test, a normal platelet count (concentration) is between 150 and 450 × 10^9 per litre.[1,2] Bleeding does not usually occur until the platelet count is below 30 × 10^9 per litre.[2] ITP is defined as persistent 3 to 12 months after diagnosis, and chronic when it lasts longer than 12 months.[1]

The UK incidence of adult ITP is estimated to be between 1.6 to 3.9 per 100,000 adults per year.[3] People with ITP may be asymptomatic or have symptoms including fatigue, anxiety, spontaneous bruising, mucosal bleeding and, in severe cases, gastrointestinal or intracranial bleeding. Diagnosis is based on excluding other possible causes of the symptoms.[4]

Treatment for ITP is usually required when the platelet count is below 30 × 10^9 per litre.[4] Treatment is typically initiated with rescue therapies such as low-dose corticosteroids and intravenous immunoglobulins. People who are intolerant or refractory to these treatments can use active therapies such as mycophenolate and rituximab, and thrombopoietin receptor agonists (TPO-RAs). Splenectomy is an option, but is rarely used in the UK.[4]

NICE technology appraisals TA221 and TA293 recommend TPO-RAs (romiplostim and eltrombopag) for adults with chronic ITP whose condition is refractory to standard active and rescue therapies or those who are at high risk of bleeding and require frequent courses of rescue therapies.

The technology

Avatrombopag (Doptelet, Swedish Orphan Biovitrum) is a small-molecule thrombopoietin receptor agonist which targets the c-Mpl thrombopoietin cell surface receptor on megakaryocytes to stimulate platelet production. It is administered orally.

Avatrombopag has a marketing authorisation in the UK for treating primary chronic immune thrombocytopenia in adults who are refractory to other treatments (for example, corticosteroids and immunoglobulins).

Intervention(s)	Avatrombopag
Population(s)	Adults with chronic immune thrombocytopenia that is refractory to other treatments
Comparators	Established clinical management without avatrombopag, which may include: • Thrombopoietin receptor agonists (romiplostim and eltrombopag) • Immunosuppressive agents (rituximab, mycophenolate mofetil, azathioprine, dapsone, danazol and cyclosporin A [currently none have a marketing authorisation in the UK for this indication]) • watch and rescue • splenectomy
Outcomes	The outcome measures to be considered include: • platelet count • response rate and duration • use of concurrent treatments and rescue treatments • reduction in symptoms • mortality • adverse effects of treatment • health-related quality of life.
Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. If the technology is likely to provide similar or greater health benefits at similar or lower cost than technologies recommended in published NICE technology appraisal guidance for the same indication, a cost-comparison may be carried out. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective. The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account.

Other considerations	If the evidence allows the following subgroups will be considered: • prior rituximab The availability and cost of biosimilar and generic products should be taken into account. Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.
Related NICE recommendations and NICE Pathways	**Related Technology Appraisals** Eltrombopag for treating chronic immune (idiopathic) thrombocytopenic purpura (2013) NICE technology appraisal 293. Updated November 2018. Romiplostim for the treatment of chronic immune (idiopathic) thrombocytopenic purpura (2011) NICE technology appraisal 221. Updated November 2018. Avatrombopag for treating thrombocytopenia in people with chronic liver disease needing a planned invasive procedure (2020) NICE technology appraisal 626. Lusutrombopag for treating thrombocytopenia in people with chronic liver disease needing a planned invasive procedure (2020) NICE technology appraisal 617. **Appraisals in development** Fostamatinib for treating persistent or chronic immune thrombocytopenia. NICE technology appraisals guidance [ID1087] Publication date to be confirmed. **Proposed technology appraisals** Avatrombopag for treating chemotherapy-induced thrombocytopenia in non-haematological cancers. Proposed NICE technology appraisal [ID3837]. Publication date to be confirmed. **NICE advice** Immune (idiopathic) thrombocytopenic purpura: rituximab (2014) NICE evidence summary of unlicensed or off-label medicines 35. **Related Guidelines** Blood transfusion (2015) NICE guideline NG24. **Related NICE Pathways** Blood conditions (2016) NICE Pathway.
Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan.

	NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019) Section 132. Specialist services for haemophilia and other related bleeding disorders (adults and children). Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domain 2. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017.

References

1. Rodeghiero F, Stasi R, Gernsheimer T, Michel M, Provan D, Arnold DM et al. Standardization of terminology, definitions and outcome criteria in immune thrombocytopenic purpura of adults and children: report from an international working group. *Blood* 2009; 113(11):2386-2393.

2. Lymphoma Action (2019) Thrombocytopenia (low platelets). Accessed December 2020.

3. DR Terrell, LA Beebe, SK Vesely, BR Neas. 2010. The incidence of immune thrombocytopenic purpura in children and adults: A critical review of published reports. *Am. J. Hematol*. 85:174– 180

4. BMJ Best Practice (2019) Immune thrombocytopenia. Accessed December 2020.