

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Avatrombopag in combination for treating chronic immune thrombocytopenia

Draft scope

**Draft 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.<sup>1</sup> 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  $450 \times 10^9$  per litre.<sup>1,2</sup> Bleeding does not usually occur until the platelet count is below  $30 \times 10^9$  per litre.<sup>2</sup> ITP is defined as persistent 3 to 12 months after diagnosis, and chronic when it lasts longer than 12 months.<sup>1</sup>

The UK incidence of adult ITP is estimated to be between 1.6 to 3.9 per 100,000 adults per year.<sup>3</sup> 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.<sup>4</sup>

Treatment for ITP is usually required when the platelet count is below  $30 \times 10^9$  per litre.<sup>4</sup> 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.<sup>4</sup>

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 does not currently have a marketing authorisation in the UK for chronic immune thrombocytopenia. It has been studied in a clinical trial in combination with standard of care compared with placebo in combination with standard of care in people with chronic immune thrombocytopenia that is refractory to other treatments.

<b>Intervention(s)</b>	Avatrombopag in combination with standard of care (i.e., corticosteroids, azathioprine, mycophenolate mofetil, danazol or cyclosporine A)
<b>Population(s)</b>	Adults with chronic immune thrombocytopenia that is refractory to other treatments
<b>Comparators</b>	<p>Established clinical management without avatrombopag, which may include:</p> <ul style="list-style-type: none"> <li>• Thrombopoietin receptor agonists (romiplostim and eltrombopag)</li> <li>• Immunosuppressive agents (rituximab, mycophenolate mofetil, azathioprine, dapsone, danazol and cyclosporin A [currently none have a marketing authorisation in the UK for this indication])</li> <li>• fostamatinib (subject to ongoing NICE appraisal)</li> <li>• watch and rescue</li> <li>• splenectomy</li> </ul>
<b>Outcomes</b>	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> <li>• platelet count</li> <li>• response rate and duration</li> <li>• use of concurrent treatments and rescue treatments</li> <li>• reduction in symptoms</li> <li>• mortality</li> <li>• adverse effects of treatment</li> <li>• health-related quality of life.</li> </ul>
<b>Economic analysis</b>	<p>The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.</p> <p>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.</p> <p>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.</p> <p>Costs will be considered from an NHS and Personal Social Services perspective.</p> <p>The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account.</p>

<p><b>Other considerations</b></p>	<p>If the evidence allows the following subgroups will be considered:</p> <ul style="list-style-type: none"> <li>• prior splenectomy</li> <li>• prior rituximab</li> </ul> <p>The availability and cost of biosimilar and generic products should be taken into account.</p> <p>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.</p>
<p><b>Related NICE recommendations and NICE Pathways</b></p>	<p><b>Related Technology Appraisals</b></p> <p><a href="#">Eltrombopag for treating chronic immune (idiopathic) thrombocytopenic purpura</a> (2013) NICE technology appraisal 293. Updated November 2018.</p> <p><a href="#">Romiplostim for the treatment of chronic immune (idiopathic) thrombocytopenic purpura</a> (2011) NICE technology appraisal 221. Updated November 2018.</p> <p><a href="#">Avatrombopag for treating thrombocytopenia in people with chronic liver disease needing a planned invasive procedure</a> (2020) NICE technology appraisal 626.</p> <p><a href="#">Lusutrombopag for treating thrombocytopenia in people with chronic liver disease needing a planned invasive procedure</a> (2020) NICE technology appraisal 617.</p> <p><b>Appraisals in development</b></p> <p><a href="#">Fostamatinib for treating persistent or chronic immune thrombocytopenia</a>. NICE technology appraisals guidance [ID1087] Publication date to be confirmed.</p> <p><b>Proposed technology appraisals</b></p> <p><a href="#">Avatrombopag for treating chemotherapy-induced thrombocytopenia in non-haematological cancers</a>. Proposed NICE technology appraisal [ID3837]. Publication date to be confirmed.</p> <p><b>NICE advice</b></p> <p><a href="#">Immune (idiopathic) thrombocytopenic purpura: rituximab</a> (2014) NICE evidence summary of unlicensed or off-label medicines 35.</p> <p><b>Related Guidelines</b></p> <p><a href="#">Blood transfusion</a> (2015) NICE guideline NG24.</p> <p><b>Related NICE Pathways</b></p> <p><a href="#">Blood conditions</a> (2016) NICE Pathway.</p>

<p><b>Related National Policy</b></p>	<p>The NHS Long Term Plan, 2019. <a href="#">NHS Long Term Plan</a>.  NHS England (2018/2019) <a href="#">NHS manual for prescribed specialist services (2018/2019)</a> 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.  <a href="https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017">https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017</a>.</p>
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**Questions for consultation**

Which treatments are considered to be established clinical practice in the NHS for chronic immune thrombocytopenia?

Are all comparators included in the scope relevant to NHS practice?

Are any relevant comparators missing from the scope?

Are the outcomes listed appropriate?

Are there any subgroups of people in whom avatrombopag is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Are the subgroups suggested in ‘other considerations appropriate? Are there any other subgroups of people in whom avatrombopag is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Where do you consider avatrombopag will fit into the existing NICE pathway, [Blood conditions](#)?

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which avatrombopag will be licensed;
- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;
- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts.

Do you consider avatrombopag to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of avatrombopag can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits.

To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at <http://www.nice.org.uk/article/pmg19/chapter/1-Introduction>).

NICE has published an addendum to its guide to the methods of technology appraisal (available at <https://www.nice.org.uk/Media/Default/About/what-we-do/NICE-guidance/NICE-technology-appraisals/methods-guide-addendum-cost-comparison.pdf>), which states the methods to be used where a cost comparison case is made.

- Would it be appropriate to use the cost comparison methodology for this topic?
- Is the new technology likely to be similar in its clinical efficacy and resource use to any of the comparators?
- Is the primary outcome that was measured in the trial or used to drive the model for the comparator(s) still clinically relevant?
- Is there any substantial new evidence for the comparator technology that has not been considered? Are there any important ongoing trials reporting in the next year?

### 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.