NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Avatrombopag for treating chemotherapy-induced thrombocytopenia in non-haematological cancers

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of avatrombopag within its marketing authorisation for treating chemotherapy-induced thrombocytopenia in non-haematological cancers.

Background

Thrombocytopenia happens when there are lower than normal platelet levels in the blood. 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. In a blood test, a normal platelet count (concentration) is between 150 and 450 × 10^9 per litre. Thrombocytopenia is usually defined as a platelet count of less than 150 x 10^9 per litre of blood. Chemotherapy induced thrombocytopenia is defined as a platelet count less than 100×10^9/L, with or without bleeding in cancer patients receiving myelosuppressive chemotherapy.[1]

The most common cause of thrombocytopenia in people with cancer is bone marrow suppression related to chemotherapy. Chemotherapy destroys rapidly dividing cells, such as those in the bone marrow which become platelets. In 2018-19 there were around 6,047 admissions for thrombocytopenia in England.[2] The most common signs and symptoms include easy or excessive bruising (purpura), small red or purple spots on the skin (petechiae), prolonged bleeding from cuts, bleeding from gums or nose, blood in urine or stools, unusually heavy menstrual flows, fatigue and enlarged spleen. Chemotherapy induced thrombocytopenia can also lead to changes and delays to cancer treatment.[4]

For chemotherapy induced thrombocytopenia, the suspected chemotherapy is stopped. Platelet counts usually recover within 2 weeks. Platelet transfusions may be required to treat severe thrombocytopenia. Other supportive measures include high-dose intravenous immunoglobulin or a brief course of corticosteroids[4]

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 treating chemotherapy-induced thrombocytopenia in non-haematological cancers. It is currently being studied in a clinical trial compared with placebo in adults with ovarian, lung (small cell or non-small cell) or bladder cancer with severe thrombocytopenia (platelet count <50 x 10^9/L) during chemotherapy.

Intervention	Avatrombopag
Population	Adults with non-haematological cancers and chemotherapy-induced thrombocytopenia
Comparators	Established clinical management without avatrombopag (including but not limited to blood or platelet transfusion)
Outcomes	The outcome measures to be considered include: • platelet count • response rate and duration • number of platelet transfusions • number of blood transfusions • use of concurrent treatments and rescue treatments • bleeding score • 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. 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.
Other considerations	If the evidence allows, subgroups by cancer type will be considered. 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**: Avatrombopag for treating thrombocytopenia in people with chronic liver disease needing a planned invasive procedure (2020). NICE Technology Appraisal 626. Review date Jan 2023. Lusutrombopag for treating thrombocytopenia in people with chronic liver disease needing a planned invasive procedure (2020). NICE Technology Appraisal 617. Review date Jan

	2023. **Related NICE Pathways**: Blood conditions (2017) NICE Pathway Liver conditions (2017) 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). Chapter 105. Specialist cancer services (adults). Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 1, 2, 3. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017

Questions for consultation

What treatments are used in clinical practice in the NHS for chemotherapy induced thrombocytopenia?

- Have all relevant comparators for avatrombopag been included in the scope?
- At what platelet level would treatment usually be started?
- Is avatrombopag likely to be used for severe thrombocytopenia only?
- Would chemotherapy be stopped during treatment for thrombocytopenia in all patients?

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?

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).

References

1 Zhang X, et al (2017) Thrombopoietin receptor agonists for prevention and treatment of chemotherapy-induced thrombocytopenia in patients with solid tumours. Cochrane Database of Systematic Reviews Issue 11. Accessed December 2020.

2 NHS Digital. Hospital Admitted Patient Care Activity, 2018-19. Available from: https://digital.nhs.uk/data-and-information/publications/statistical/hospital-admitted-patient-care-activity/2018-19 [Accessed December 2020].

3 Cancer Research UK (2020) About side effects of chemotherapy. Accessed December 2020.

4 Izak M, and Bussel JB. (2014) Management of thrombocytopenia. F1000Prime Rep. 6 (45). Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4047949/