NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE
Proposed Health Technology Appraisal

Eltrombopag for treating severe aplastic anaemia following insufficient response to immunosuppressive therapy

Draft scope (pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of eltrombopag within its marketing authorisation for treating severe aplastic anaemia following insufficient response to immunosuppressive therapy.

Background

Aplastic anaemia is a rare disease caused by damage to the bone marrow, which affects the production of red blood cells, white blood cells and platelets. People with aplastic anaemia develop symptoms of anaemia, thrombocytopenia and neutropenia. The cause of aplastic anaemia is unknown in approximately 70-80% of cases. In approximately 15-20% of cases, the disease is hereditary. Other causes include exposure to radiation or chemotherapy following treatment for cancer. The estimated incidence of aplastic anaemia in Europe is 2 cases per 1 million people.

Aplastic anaemia is initially diagnosed with a full blood count, reticulocyte count and blood film. It is diagnosed when at least two of the following are found; (i) haemoglobin <100 g/l (ii) platelet count <50 x 10^9/l (iii) neutrophil count <1.5 x10^9 /l. Aplastic anaemia is classified as non-severe, severe, or very severe based on blood count parameters and bone marrow findings.

Guidelines from the British Committee for Standards in Haematology on the diagnosis and management of aplastic anaemia states that the initial management for severe or very severe aplastic anaemia involves allogeneic bone marrow stem cell transplantation, if the patient is less than 40 years of age and has a human leukocyte antigen (HLA)-identical sibling donor. Immunosuppressive therapy with antithymocyte globulin and ciclosporin is recommended for patients with severe or very severe aplastic anaemia over 40 years of age or for younger people who lack a HLA-identical sibling donor. For patients whose disease is unresponsive to immunosuppressive therapy, matched unrelated donor bone marrow transplantation can be considered if they are less than 60 years of age or, second line immunosuppressive therapy can be considered.

The technology

Eltrombopag (Revolade, GlaxoSmithKline and Novartis) is a glycoprotein hormone involved in the regulation of megakaryopoiesis and platelet production through the activation of the thrombopoietin receptor. Eltrombopag is administered orally.

Eltrombopag does not currently have a marketing authorisation in the UK for aplastic anaemia. It has been studied in a small, non-comparative trial (n=44) in people with severe or very severe aplastic anaemia whose disease has not responded to immunosuppressive therapy.

Intervention(s)	Eltrombopag
Population(s)	People with severe or very severe aplastic anaemia whose disease has not responded to immunosuppressive therapy
Comparators	Best supportive care.
Outcomes	The outcome measures to be considered include: • changes in platelet count • platelet transfusion requirement • red blood cell transfusion • neutrophil count • bleeding events • 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. The availability of any patient access schemes for the intervention or comparator technologies should be taken into account.
Other considerations	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	None
Related National Policy	NHS England (2013) Haematopoietic Stem Cell Transplantation Clinical Commissioning Policy.

Questions for consultation

How many people in England are estimated to have severe or very severe aplastic anaemia that has not sufficiently responded to immunosuppressive therapy?

Which treatments are considered to be established clinical practice in the NHS for aplastic anaemia that has not sufficiently responded to immunosuppressive therapy?

Will eltrombopag be used in addition to current treatment or as a replacement for an existing treatment?

Are there specific immunosuppressive therapies that would still be used for people whose disease have not responded to immunosuppressive therapy?

How should best supportive care be defined?

Are there any subgroups of people in whom eltrombopag 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 eltrombopag 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 eltrombopag 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 eltrombopag 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.

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)