NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Avatrombopag and lusutrombopag for treating thrombocytopenia in people with chronic liver disease needing an elective procedure

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of avatrombopag and lusutrombopag within their marketing authorisations for treating thrombocytopenia in people with chronic liver disease needing an elective procedure.

Background

Thrombocytopenia is characterised as a reduction in the number of circulating platelets within the blood. Platelets come from megakaryocytes in the bone marrow. They play a critical role in haemostasis, a process which causes bleeding to stop. Thrombocytopenia can generally be classified on the basis of the platelet count in the blood. It is usually defined as a platelet count of less than 150 x 10^9 per litre of blood.

Thrombocytopenia is a common complication in people with chronic liver disease either as a direct result of the liver pathology or a consequence of interferon-based antiviral therapy. While mild to moderate thrombocytopenia rarely causes bleeding during procedures including liver biopsy or liver transplantation, severe thrombocytopenia increases the risk of excessive bleeding during and after surgery and can have a significant impact on the clinical management of chronic liver disease. It can delay or prevent the start of appropriate therapy leading to increased morbidity and mortality and a reduced quality of care.

The prevalence of thrombocytopenia in people with chronic liver disease varies from 15% to 70% depending on the stage of liver disease and differences in platelet count cut-off used to define thrombocytopenia. Between 2016 and 2017, Hospital Episode Statistics showed 27,927 admissions[1] with liver disease in England.

There are currently no licensed treatment options in the UK for treating thrombocytopenia in people with chronic liver disease requiring surgery. Therapies include stimulation of megakaryocyte maturation and platelet production. Treatment for severe thrombocytopenia can include platelet transfusion, splenic artery embolisation and surgical splenectomy.

The technology

Avatrombopag (brand name unknown, Dova Pharmaceuticals) is a small molecule thrombopoietin receptor agonist which targets the c-Mpl

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thrombopoietin cell surface receptor on megakaryocytes to stimulate platelet production. Avatrombopag is administered orally. It does not currently have a marketing authorisation in the UK. It is currently being studied in clinical trials compared with placebo in people with thrombocytopenia associated with chronic liver disease requiring an elective procedure.

Lusutrombopag (Mulpeta, Shionogi Inc) is a small molecule thrombopoietin receptor agonist which targets the c-Mpl thrombopoietin cell surface receptor on megakaryocytes to stimulate platelet production. Lusutrombopag is administered orally. It does not currently have a marketing authorisation in the UK. It is currently being studied in clinical trials compared with placebo in adults with thrombocytopenia with a platelet count of $<50 \times 10^9$ per blood litre associated with chronic liver disease requiring elective invasive surgery.

Intervention(s)	• Avatrombopag • Lusutrombopag
Population(s)	People with thrombocytopenia associated with chronic liver disease needing an elective procedure
Comparators	The interventions listed above compared with each other where appropriate, and with: • Established clinical management without avatrombopag and lusutrombopag (including, but not limited to platelet transfusion)
Outcomes	The outcome measures to be considered include: • platelet count • response rate • number of platelet transfusions • number of blood transfusions • return to operating theatre • need for rescue treatments • use of concurrent treatments • bleeding score • mortality • adverse effects of treatment • health-related quality of life.

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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	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	Blood conditions (2017) NICE Pathway Liver conditions (2017) NICE Pathway
Related National Policy	NHS England (2016) Manual for prescribed specialised services 2016/17 Chapter 69 Liver transplant services (adults and children) 131 Specialist services for complex liver, biliary and pancreatic diseases in adults NHS England (June 2015) Treatment of chronic hepatitis C in patients with cirrhosis Interim Clinical Commissioning Policy Statement Ref: B07/P/a NHS England (2015) Operational delivery networks for Hepatitis C care in adults Service Specifications NHS England (2013) 2013/14 Standard Contract for Hepatobiliary and Pancreas (adult) Particulars, schedule 2 The Services, Service Specifications Ref: A02/S/a NHS England (2013) 2013/14 NHS Standard Contract for Live Liver Transplantation Service Particulars, Schedule 2 the services, A service specifications Ref: A02/S(HSS)/a **National Service Frameworks** Long Term Conditions (including neurological) – archived Department of Health and Social Care (2016) NHS

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	outcomes framework 2016 to 2017

References

1. Hospital Episode Statistics Admitted Patient Care England 2016-17 (2017). Accessed 19/03/2018

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