NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Caplacizumab for treating an episode of acquired thrombotic thrombocytopenic purpura

Updated final scope

Final remit/appraisal objective

To appraise the clinical and cost effectiveness of caplacizumab within its marketing authorisation for treating acquired thrombotic thrombocytopenic purpura.

Background

Thrombotic thrombocytopenic purpura (TTP) is a rare blood disorder that causes blood clots in small blood vessels. These blood clots cause damage to internal organs and red blood cells, by blocking small blood vessels and can result in a very low blood platelet count, breakdown of red blood cells, and organ failure of varying severity. TTP can present as an acute life-threatening disorder requiring prompt diagnosis, early referral and effective immediate management.

TTP is caused by the inactivation of an enzyme called ADAMTS13 which breaks down large von Willebrand factor multimers. When ADAMTS13 levels are very low, the ultra-large von Willebrand factor multimers can cause a thrombotic microangiopathy that is, damage to small blood vessels in vital organs (typically the brain, the heart, and kidneys). If left untreated, acquired TTP can lead to lack of oxygen to tissue in vital organs, loss of function of organs and can be fatal. People who recover from an acquired TTP episode can have cognitive deficits, depression, arterial hypertension, autoimmune diseases, and a shortened life expectancy. ADAMTS13 deficiency can be inherited (because of an inherited genetic mutation) or acquired through 'antibody mediated destruction'. Acquired TTP can be associated with pregnancy, HIV, other autoimmune conditions. Symptoms can include neurological changes, pyrexia, renal dysfunction, thrombocytopenia, and cardiac impairment.

TTP has an annual incidence of between 1.2 to 11 cases per million in the UK[1] and is more common in females than males. There are between 100 and 150 cases of TTP per year. Relapses have been reported in 30% to 40% of patients[2].

Guidelines on the diagnosis and management of thrombotic thrombocytopenic purpura and other thrombotic microangiopathies from the British Committee for Standards in Haematology recommend daily plasma exchange therapy (PEX), preferably with spun apheresis. If there is a delay in PEX, large volume

plasma infusions are recommended. Additionally, PEX in combination with steroids and rituximab (unlicensed for this indication) may also be offered as treatment options for TTP.

The technology

Caplacizumab (Cablivi, Sanofi) is a bivalent anti-von Willebrand factor humanised nanobody. It stops von Willebrand factor interacting with collagen and platelets to prevent clots forming in blood vessels. It is intended to treat episodes of acquired TTP by stopping blood clots forming when administered in addition to standard of care treatment. Caplacizumab is administered subcutaneously (other than the first initial loading dose, which is intravenous).

Caplacizumab has a marketing authorisation in the UK for treating adults experiencing an episode of acquired thrombocytopenic purpura, in conjunction with plasma exchange and immunosuppression. On 30 April 2020, the European Medicines Agency's Committee for Medicinal Products for Human Use adopted a positive opinion recommending that a marketing authorisation extension is granted for caplacizumab for 'adolescents of 12 years of age and older weighing at least 40 kg'.

Intervention(s)	Caplacizumab in addition to plasma exchange and immunosuppression
Population(s)	People experiencing an episode of acquired thrombotic thrombocytopenic purpura
Comparators	• Plasma exchange therapy (with or without spun apheresis, steroids or rituximab), without caplacizumab. For people with severe refractory acquired TTP, a combination of one or more of: • Plasma exchange therapy (with or without spun apheresis, steroids, rituximab, splenectomy, vincristine or immunosuppression e.g. cyclophosphamide) without caplacizumab.

Outcomes	The outcome measures to be considered include: • change in cognitive function • mortality • major thromboembolic events • recurrence of disease • reduction of time-to-recovery • time to platelet count response • TTP-related events • neuro-psychological impact (including depressive symptoms, anxiety and PTSD) following an episode • length of hospital stay • volume and frequency of plasma exchange • 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 evidence allows, subgroup analysis of people with severe refractory acquired TTP will be considered. 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	None

Related National Policy	Department of Health, NHS Outcomes Framework 2016-2017 (published 2016): Domains 1, 2 and 4 https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017 The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019) NHS England (2017) Commissioning medicines for children in specialised services policy

References

1. TTP network. About TTP. www.ttpnetwork.org.uk/about-ttp/ Accessed August 2019
2. Orpha.net. Acquired thrombotic thrombocytopenic purpura. www.orpha.net/ Accessed July 2019