NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Apadamtase alfa for treating congenital thrombotic thrombocytopenic purpura caused by ADAMTS-13 deficiency ID6192

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of apadamtase alfa within its marketing authorisation for treating congenital thrombotic thrombocytopenic purpura.

Background

Thrombotic thrombocytopenic purpura (TTP) is a rare blood disorder that causes blood clots in small blood vessels throughout the body. These blood clots cause damage to internal organs and red blood cells, by blocking small blood vessels. TTP can result in a very low platelet count (thrombocytopenia) and organ failure of varying severity. TTP can present as an acute life-threatening disorder requiring prompt diagnosis, early referral, and effective management. There are two main types of TTP – congenital (inherited) and acquired (autoimmune). Congenital TTP (cTTP) accounts for around 6 in every 100 cases of TTP.[1]

cTTP is caused by inheriting non-working copies of the ADAMTS-13 gene. It is an autosomal recessive condition resulting in a severe deficiency of the ADAMTS-13 enzyme. At normal levels, the enzyme breaks down a large protein called von Willebrand factor, which works with platelets to prevent bleeding. When the enzyme is not working, platelets become sticky and form blood clots in small vessels that can affect any organ. Molecular testing and analysis of the ADAMTS-13 gene and enzyme is needed to confirm a diagnosis of cTTP.

cTTP may have childhood or adult onset. Presentation of cTTP in babies or young children is commonly associated with severe neonatal jaundice, low platelet levels (thrombocytopenia) and red blood cell abnormalities. Around 62% of people are diagnosed as adults because cTTP can be asymptomatic until a precipitating event such as pregnancy or infection leads to an episode of TTP. Symptoms of TTP are wide ranging and include fever, fatigue, headache, confusion and bruises or dots on the skin.[1]

The prevalence and estimated annual incidence of cTTP are less than 1 in 1,000,000.[2] Fewer than 60 people in England are likely to have cTTP (based on the year to mid-2024 population estimate[3]).

Management of cTTP is covered by a British Society for Haematology Guideline[4] and an NHS England Commissioning service specification[5]. The aim of treatment is to replace the deficient ADAMTS-13 enzyme. This is done in clinical practice by giving blood products as a source of the enzyme, either:

- plasma (typically solvent/detergent fresh-frozen plasma [SD-FFP] or octaplas), given by infusion every 1 to 2 weeks, or
- intermediate purity factor VIII concentrate (such as 8Y), given by injection usually as a weekly dose.

The volume and frequency of plasma infusion or factor VIII is based on bodyweight, symptoms and whether there is any risk factor such as pregnancy. Prophylactic treatment with SD-FPP or intermediate purity FVIII may be considered, particularly in severe childhood cTTP and in chronic relapsing disease.[5] Acute episodes of TTP can be treated until remission.

The technology

Apadamtase alfa (ADZYNMA, Takeda UK Ltd) is an enzyme replacement therapy that has a marketing authorisation in the UK for 'the treatment of ADAMTS-13 deficiency in children and adult patients with cTTP. Apadamtase alfa can be used for all age groups.' It is licensed for prophylactic and as-needed use.

Intervention(s)	Apadamtase alfa
Population(s)	People with cTTP
Comparators	For prophylactic use of apadamtase alfa Established clinical management of cTTP without apadamtase alfa including: • plasma (SD-FFP or octaplas), or • intermediate purity factor VIII, or • no additional prophylactic treatment. For as-needed use of apadamtase alfa Established clinical management of cTTP without apadamtase alfa including: • plasma (SD-FFP or octaplas), or • intermediate purity factor VIII (such as 8Y).

Outcomes	The outcome measures to be considered include: • acute TTP events (including number and frequency) during prophylactic treatment • response to treatment for acute TTP events • time to resolution of acute events • occurrence of thrombocytopenia during prophylactic treatment • occurrence of microangiopathic haemolytic anaemia during prophylactic treatment • proportion of people with complications of TTP (for example neurological symptoms, renal dysfunction, abdominal pain and organ failure) • 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 and cost of biosimilar and generic products should be taken into account. The use of apadamtase alfa is conditional on the confirmation of ADAMTS-13 deficiency, including by ADAMTS-13 activity assay and molecular genetic testing. The economic modelling should include the costs associated with diagnostic testing for ADAMTS-13 deficiency in people with congenital thrombotic thrombocytopenic purpura who would not otherwise have been tested. A sensitivity analysis should be provided without the cost of the diagnostic testing. See section 4.8 of the guidance development manual (available here: https://www.nice.org.uk/process/pmg36/chapter/introduction-to-health-technology-evaluation).
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	**Related technology appraisals:** Caplacizumab with plasma exchange and immunosuppression for treating acute acquired thrombotic thrombocytopenic purpura (2020) NICE technology appraisal guidance 667 **Related NICE guidelines:** Blood transfusion (2015) NICE guideline NG24.

Questions for consultation

Are the comparators defined appropriately? Which treatments are considered to be established clinical practice in the NHS for prophylactic use or for treating acute episodes of congenital thrombotic thrombocytopenic purpura (cTTP)?

Could apadamtase alfa be used as a prophylactic treatment in a broader population of people with cTTP than currently have prophylactic treatments. For example, could a person having prophylactic treatment with apadamtase alfa be given additional doses as-needed during an acute episode of cTTP?

What proportion of people with cTTP have plasma infusions compared with intermediate purity factor VIII concentrate in current clinical practice? What factors would influence which of these products is used?

Where do you consider apadamtase alfa will fit into the existing care pathway for congenital thrombotic thrombocytopenic purpura (cTTP)?

Would apadamtase alfa be expected to be used as an alternative to giving plasma infusions or intermediate purity factor VIII concentrate, or in combination with these blood products in clinical practice?

Are there any relevant subgroups to consider?

Would apadamtase alfa be expected to be used independently of when cTTP was identified, such as whether it presented in babies or childhood, or later in adulthood? Would it be used as an acute treatment as-needed, as a prophylactic treatment option, or both? What factors would influence this decision?

How is cTTP diagnosed in current clinical practice? Have people who receive current treatments had diagnostic testing that includes molecular genetic testing to confirm the diagnosis of cTTP?

Please select from the following, will apadamtase alfa be:
A. Prescribed in primary care with routine follow-up in primary care
B. Prescribed in secondary care with routine follow-up in primary care
C. Prescribed in secondary care with routine follow-up in secondary care
D. Other (please give details):
For comparators and subsequent treatments, please detail if the setting for prescribing and routine follow-up differs from the intervention.

Would apadamtase alfa be a candidate for managed access?

Do you consider that the use of apadamtase alfa can result in any potential 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 committee to take account of these benefits.

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 apadamtase alfa is 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.

NICE intends to evaluate this technology through its Single Technology Appraisal process. (Information on NICE's health technology evaluation processes is available at https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance/changes-to-health-technology-evaluation).

References

1. ttpnetwork (2024) About TTP. Accessed November 2025.

2. Orpha.net (2020). Rare diseases – Congenital ADAMTS-13 deficiency. Accessed November 2025.

3. ONS (2025) England population mid-year estimate. Accessed November 2025.

4. Scully M, Rayment R, Clark A et al. (2023) A British Society for Haematology Guideline: Diagnosis and management of thrombotic thrombocytopenic purpura and thrombotic microangiopathies. Br J Haematol 203: 546–563.

5. NHS England. Thrombotic thrombocytopenic purpura (TTP). Section 2.5 Congenital pathway. NHS commissioning of specialised services for specialist blood disorders (2022): Service specification 1668. Accessed November 2025.