POLICY: Hematology – Adzynma Utilization Management Medical Policy

- Adzynma™ (ADAMTS13 recombinant-krhn intravenous infusion – Takeda)

EFFECTIVE DATE: 3/15/2024
LAST REVISION DATE: 09/16/2024

COVERAGE CRITERIA FOR: All UCare Plans

Overview

Adzynma, a human recombinant "A disintegrin and metalloproteinase with thrombospondin motifs 13" (ADAMTS13) product, is indicated for prophylactic or on demand enzyme replacement therapy for the management of congenital thrombotic thrombocytopenia purpura in adult and pediatric patients.[1]

Disease Overview

Congenital thrombotic thrombocytopenic purpura is a very rare, inherited blood clotting disorder.[2,3] It is due to a mutation in the ADAMTS13 gene that makes a key enzyme, also named ADAMTS13, that regulates blood clotting. A deficiency in this enzyme causes blood clots to form in the small blood vessels throughout the body. The disease impacts fewer than 1,000 people in the US. Symptoms typically start in infancy or early childhood, but in some cases may develop in adulthood and can initially manifest during pregnancy. Patients with congenital thrombotic thrombocytopenic purpura may experience severe bleeding episodes, strokes, and damage to vital organs. The condition can be fatal if not managed. Treatment for congenital thrombotic thrombocytopenic purpura currently involves prophylactic plasma-based therapy to reduce the risk of clotting/bleeding by replenishing the absent/low ADAMTS13 enzyme; on-demand therapy can also be given.

Guidelines

Adzynma has not been specifically addressed in guidelines post FDA-approval.[4] The International Society on Thrombosis and Haemostasis (ISTH) has guidelines for the treatment of thrombotic thrombocytopenic purpura (2020). For patients with congenital thrombotic thrombocytopenic purpura who are in remission, the panel suggests either plasma infusion or a watch and wait strategy. For patients with congenital thrombotic thrombocytopenic purpura who are pregnant, the panel recommends prophylactic treatment over no prophylactic treatment. In this clinical scenario, plasma infusion is recommended over Factor VIII products.

The British Society of Haemtology published guidelines for the diagnosis and management of thrombotic thrombocytopenic purpura and thrombotic microangiopathies.[5] The diagnosis of congenital thrombotic thrombocytopenic purpura is defined by ADAMTS13 activity < 10 IU/dL, no anti-ADAMTS13 antibodies, and confirmation of homozygous or compound heterozygous variants in the ADAMTS13 gene. For an acute episode, solvent detergent plasma infusion is

recommended. ADAMTS13 prophylaxis should be considered for all patients with an individualized approach to dose and frequency according to symptoms, whether overt or non-overt. For pregnant women with congenital thrombotic thrombocytopenic purpura, regular solvent/detergent fresh frozen plasma replacement therapy should be given prophylactically to prevent clinical relapse.

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of Adzynma. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indication. Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). Because of the specialized skills required for evaluation and diagnosis of patients treated with Adzynma as well as the monitoring required for adverse events and long-term efficacy, approval requires Adzynma to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Documentation: Documentation is required for use of Adzynma as noted in the criteria as **[documentation required]**. Documentation may include, but is not limited to, chart notes, laboratory data, genetic test results, and/or other information.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Adzynma is recommended in those who meet the following criteria:

FDA-Approved Indication

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1. **Congenital Thrombotic Thrombocytopenic Purpura.** Approve for 1 year if the patient meets the following (A, B, C, and D):
   - **A)** At baseline (prior to therapy) ADAMTS13 activity is < 10% (< 10 IU/dL) **[documentation required]**; AND
     Note: Baseline refers to before any treatment was received, such as Adzynma or plasma-based therapies.
   - **B)** Patient does not have anti-ADAMTS13 autoantibodies as determined by a diagnostic test **[documentation required]**; AND
   - **C)** Patient has a pathogenic variant or a mutation in the ADAMTS13 gene **[documentation required]**; AND
     Note: Pathogenic variants or gene mutations are usually homozygous or compound heterozygous.
   - **D)** Medication is prescribed by or in consultation with a hematologist.

   Dosing. Approve the following dosing regimens (A and/or B):

A) Routine prophylaxis: approve up to 40 IU/kg by intravenous infusion once weekly; AND/OR

B) On demand therapy: approve up to 135 IU/kg by intravenous infusion per week as needed for the treatment of acute event(s).
Note: On demand therapy is given as a daily dose until 2 days after the acute event resolves; however, the total weekly dose should not exceed 135 IU/kg.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Adzynma is not recommended in the following situations.

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Adzynma™ intravenous infusion [prescribing information]. Lexington, MA: Takeda; November 2023.
2. Food and Drug Administration News Release. FDA approves first treatment for patients with rare inherited blood clotting disorder. November 9, 2023. Available at: https://www.fda.gov/news-events/press-announcements/fda-approves-first-treatment-patients-rare-inherited-blood-clotting-disorder. Accessed on November 26, 2023.
3. Kremer Hovingo JA, George JN. Hereditary thrombotic thrombocytopenic purpura. *N Engl J Med*. 2019;381:1653-1662.
4. Zheng XL, Vesely SK, Cataland SR, et al. International Society on Thrombosis and Haemostasis (ISTH) guidelines for the treatment of thrombotic thrombocytopenic purpura. *J Thromb Haemost*. 2020;18:2496-2502.
5. Scully M, Rayment R, Clark A, et al, on behalf of the BSH Committee. A British Society of Haematology Guideline: diagnosis and management of thrombotic thrombocytopenia purpura and thrombotic microangiopathies. *Br J Haematol*. 2023;203:546-563.

HISTORY

Type of Revision	Summary of Changes	Review Date
New Policy	--	12/06/2023
UCare P&T Review	Policy reviewed and approved by UCare P&T committee. Annual review process	09/16/2024