

## Clinical Policy: ADAMTS13, Recombinant-krhn (Adzynma)

Reference Number: PA.CP.PHAR.635

Effective Date: 02/2024

Last Review Date: 01/2025

### Description

ADAMTS13, recombinant-krhn (Adzynma<sup>®</sup>) is a human recombinant “A disintegrin and metalloproteinase with thrombospondin motifs 13” (rADAMTS13).

### FDA Approved Indication(s)

Adzynma is indicated for prophylactic or on demand enzyme replacement therapy in adult and pediatric patients with congenital thrombotic thrombocytopenic purpura (cTTP).

### Policy/Criteria

*Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.*

It is the policy of PA Health & Wellness<sup>®</sup> that Adzynma is **medically necessary** when the following criteria are met:

### I. Initial Approval Criteria

#### A. Congenital Thrombotic Thrombocytopenic Purpura (must meet all):

1. Diagnosis of severe cTTP confirmed by all of the following (a, b, and c):
  - a. Genetic test confirming biallelic ADAMTS13 mutation;
  - b. ADAMTS13 activity < 10 % of normal, unless member is currently receiving prophylactic plasma therapy;
  - c. One of the following (i or ii):
    - i. Absence of ADAMTS13 functional inhibitor;
    - ii. Absence of anti-ADAMTS13 antibodies;
2. Prescribed by or in consultation with a hematologist;
3. Age ≥ 2 years;
4. Failure of plasma therapy (i.e., plasma infusion, therapeutic plasma exchange), unless contraindicated or clinically significant adverse effects are experienced (*see Appendix D*);
5. For prophylaxis requests, member has TTP signs or symptoms that are persistent or recurrent (*see Appendix D*);
6. For acute (on demand) treatment requests, member has an acute TTP event defined by both the following (a and b):
  - a. Platelet count < 100,000/ $\mu$ L or a drop in platelet count ≥ 50% of the baseline platelet count;
  - b. Microangiopathic hemolytic anemia with a lactate dehydrogenase (LDH) elevation greater than two times the baseline or two times the upper limit of normal;
7. Documentation of member’s current body weight (in kg);
8. Dose does not exceed the following (a or b):
  - a. For prophylactic therapy: 40 IU/kg once weekly;

- b. For acute treatment: 40 IU/kg on day 1, followed by 20 IU/kg on day 2, and 15 IU/kg/day until two days after the acute event is resolved.

**Approval duration:**

**Prophylaxis: 6 months**

**Acute treatment: Up to 2 weeks per acute episode**

**B. Other diagnoses/indications**

1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

**II. Continued Therapy**

**A. Congenital Thrombotic Thrombocytopenic Purpura (must meet all):**

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies;
2. Member is responding positively to therapy as evidenced by, including but not limited to, improvement in any of the following parameters (a-c):
  - a. Thrombocytopenia;
  - b. Microangiopathic hemolytic anemia;
  - c. Symptom improvement (e.g., less headaches, lethargy, and/or abdominal pain);
3. Documentation of member's current body weight (in kg);
4. If request is for a dose increase, new dose does not exceed the following (a or b):
  - a. For prophylactic therapy: 40 IU/kg once weekly;
  - b. For acute treatment, both (i and ii):
    - i. 40 IU/kg on day 1, followed by 20 IU/kg on day 2, and 15 IU/kg/day until two days after the acute event is resolved;
    - ii. If request exceeds 2 weeks of treatment: provider justification for continued acute dosing.

**Approval duration:**

**Prophylaxis: 12 months**

**Acute treatment: Up to 2 weeks per acute episode**

**B. Other diagnoses/indications (must meet 1 or 2):**

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies.

**Approval duration: Duration of request or 12 months (whichever is less); or**

2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

**III. Diagnoses/Indications for which coverage is NOT authorized:**

- A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – PA.CP.PMN.53

**IV. Appendices/General Information**

*Appendix A: Abbreviation/Acronym Key*

cTTP: congenital thrombotic thrombocytopenic purpura	rADAMTS13: a disintegrin and metalloproteinase with thrombospondin motifs 13
FDA: Food and Drug Administration	
LDH: lactate dehydrogenase	

*Appendix B: Therapeutic Alternatives*

*This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.*

<b>Drug Name</b>	<b>Dosing Regimen</b>	<b>Dose Limit/ Maximum Dose</b>
Plasma infusion <ul style="list-style-type: none"> <li>• Fresh frozen plasma</li> <li>• Solvent/detergent plasma</li> <li>• Thawed plasma</li> <li>• Plasma frozen within 24 hours of collection</li> </ul>	10-15 mL/kg at a frequency of every 1-3 weeks for maintenance therapy or daily for a symptomatic patient until the symptoms resolve and normalization of platelet counts	Varies

*Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.*

*Appendix C: Contraindications/Boxed Warnings*

- Contraindication(s): life threatening hypersensitivity reactions to Adzynma or its components
- Boxed warning(s): none

*Appendix D: General Information*

- Examples of failure with plasma therapy in cTTP include, but are not limited to, previous stroke, kidney failure, persistent thrombocytopenia, recurrent microangiopathic hemolytic anemia, and persistent neonatal hyperbilirubinemia.
  - Microangiopathic hemolytic anemia is a descriptive term for non-immune hemolytic anemia from intravascular red blood cell fragmentation.
- Examples of TTP signs and symptoms include, but are not limited to, persistent thrombocytopenia, recurrent microangiopathic hemolytic anemia, proteinuria, stroke, transient ischemic attack, lethargy, headaches, loss of concentration, and abdominal discomfort.
- Treatment for an acute TTP episode depends on the duration of an episode. Per the International Hereditary Thrombotic Thrombocytopenic Purpura Registry (van Dorland et al, 2019), the median duration of an acute episode was seven days. Per the Adzynma pivotal trial, the duration of an acute episode for Adzynma treatment ranged from 2-4 days.

**V. Dosage and Administration**

Indication	Dosing Regimen	Maximum Dose
cTTP	<p><i>Prophylactic therapy</i>                      40 IU/kg IV every 2 weeks. Dosing frequency may be adjusted to 40 IU/kg body weight once weekly based on prior prophylactic dosing regimen or clinical response.</p> <p><i>On-demand therapy</i>                      40 IU/kg IV on day 1, followed by 20 IU/kg IV on day 2, and then 15 IU/kg/day on day 3 and beyond until two days after the acute event is resolved. Dose is based on body weight.</p>	<p>Prophylactic therapy: 40 IU/kg/week</p> <p>On-demand therapy: 40 IU/kg/day</p>

**VI. Product Availability**

Lyophilized powder in single-dose vials: 500 IU, 1,500 IU

**VII. References**

1. Adzynma Prescribing Information. Lexington, MA: Takeda Pharmaceuticals USA, Inc.; June 2024. Available at: <https://www.adzynma.com/>. Accessed November 20, 2024.
2. Scully M, Antun A, Cataland SR, et al. Recombinant ADAMTS13 in congenital thrombotic thrombocytopenic purpura. *N Engl J Med.* 2024;390(17):1584-1596.
3. Alwan F, Vendramin C, Liesner R, et al. Characterization and treatment of congenital thrombotic thrombocytopenic purpura. *Blood.* 2019;133(15):1644-1651.
4. Scully M, Cataland S, Coppo P, et al. Consensus on the standardization of terminology in thrombotic thrombocytopenic purpura and related thrombotic microangiopathies. *J Thromb Haemost.* 2017;15(2):312-322.
5. van Dorland HA, Taleghani MM, Sakai K, et al. The International Hereditary Thrombotic Thrombocytopenic Purpura Registry: Key findings at enrollment until 2017. *Haematologica.* 2019;104(10):2107-2115.
6. Kremer Hovinga JA, George JN. Hereditary thrombotic thrombocytopenic purpura. *N Engl J Med.* 2019;381(17):1653-1662.
7. Scully M, Rayment R, Clark A, et al. A British Society for Haematology Guideline: Diagnosis and management of thrombotic thrombocytopenic purpura and thrombotic microangiopathies. *Br J Haematol.* 2023;203(4):546-563.

**Coding Implications**

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J7171	Injection, adamts13, recombinant-krhn, 10 iu

<b>Reviews, Revisions, and Approvals</b>	<b>Date</b>
Policy created	01/2024
1Q 2025 annual review: no significant changes; added HCPCS code [J7171] and removed HCPCS codes [J3590, C9399]; references reviewed and updated.	01/2025