Clinical Policy: ADAMTS13, Recombinant-krhn (Adzynma)

Reference Number: PA.CP.PHAR.635
Effective Date: 02/2024
Last Review Date: 01/2024

Description
ADAMTS13, recombinant-krhn (Adzynma®) 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® 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/µL 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.LTSS.PHAR.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.LTSS.PHAR.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
FDA: Food and Drug Administration
LDH: lactate dehydrogenase
rADAMTS13: a disintegrin and metalloproteinase with thrombospondin motifs 13

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 for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Plasma infusion • Fresh frozen plasma • Solvent/detergent plasma • Thawed plasma • Plasma frozen within 24 hours of collection	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	*Prophylactic therapy* 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. *On-demand therapy* 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.	Prophylactic therapy: 40 IU/kg/week On-demand therapy: 40 IU/kg/day

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.; November 2023. Available at: https://content.takeda.com/?contenttype=PI&product=ADZ&language=ENG&country=USA&documentnumber=1. Accessed December 1, 2023.
2. ClinicalTrials.gov. A study of BAX 930 in children, teenagers, and adults born with thrombotic thrombocytopenic purpura (TTP). Last updated February 28, 2023. Available at: https://clinicaltrials.gov/ct2/show/NCT03393975. Accessed December 1, 2023.
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.

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
J3590	Unclassified biologics
C9399	Unclassified drugs or biologicals

Reviews, Revisions, and Approvals	Date
Policy created	01/2024