Clinical Policy: ADAMTS13, Recombinant-krhn (Adzynma)

Reference Number: CP.PHAR.635
Effective Date: 11.09.23
Last Review Date: 02.24
Line of Business: Commercial, HIM, Medicaid

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

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 health plans affiliated with Centene Corporation® 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 (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

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

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B)*;
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. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

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 – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents;

B. Acquired/immune thrombotic thrombocytopenic purpura.

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	P&T Approval Date
Policy created pre-emptively	07.11.23	08.23
Drug is now FDA-approved – criteria updated per FDA labeling: added age ≥ 2 years per Prescribing Information, added criterion for defining an acute TTP event for on demand therapy requests, added documentation of member's body weight in kg for dose calculation, updated FDA-labeled maximum dosing, updated 6 month initial and 12 month continued approval durations are specific to prophylaxis dosing while on-demand dosing duration is for 2 weeks, and added continued acute therapy criterion for provider justification of continued acute dosing exceeding 2 weeks; references reviewed and updated.	12.04.23	02.24

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members

and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.