Original Effective Date: 03/28/2024
Current Effective Date: 03/28/2024
Last P&T Approval/Version: 01/31/2024
Next Review Due By: 07/2024
Policy Number: C27325-A

Adzynma (ADAMTS13, recombinant-krhn)

PRODUCTS AFFECTED

Adzynma (ADAMTS13, recombinant-krhn)

COVERAGE POLICY

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any. This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DIAGNOSIS:
Congenital thrombotic thrombocytopenic purpura

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by-case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review. When the requested drug product for coverage is dosed by weight, body surface area or other member specific measurement, this data element is required as part of the medical necessity review. The Pharmacy and Therapeutics Committee has determined that the drug benefit shall be a mandatory generic and that generic drugs will be dispensed whenever available.

A. CONGENITAL THROMBOTIC THROMBOCYTOPENIC PURPURA:
   1. Documented diagnosis of congenital thrombotic thrombocytopenic purpura
      AND

2. Documentation diagnosis confirmed by molecular genetic testing AND ADAMTS13 activity <10%, as measured by the fluorescent resonance energy transfer-von Willebrand factor 73 (FRETS-VWF73) assay [DOCUMENTATION REQUIRED]
   AND
3. Documentation of members prophylactic (if applicable) and on-demand treatment plan [DOCUMENTATION REQUIRED]
   AND
4. Documentation of prescriber baseline disease activity evaluation and goals for treatment to be used to evaluate efficacy of therapy at renewal
   AND
5. Prescriber attests to (or the clinical reviewer has found that) the member not having any FDA labeled contraindications that haven't been addressed by the prescriber within the documentation submitted for review [Contraindications to Adzynma (ADAMTS13, recombinant-krhn) include: patients who have manifested life threatening hypersensitivity reactions to ADZYNMA or its components.]

CONTINUATION OF THERAPY:

A. CONGENITAL THROMBOTIC THROMBOCYTOPENIC PURPURA:
   1. Prescriber attests to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity
      AND
   2. Documentation of positive clinical response as demonstrated by low disease activity and/or improvements in the condition's signs and symptoms [DOCUMENTATION REQUIRED]

DURATION OF APPROVAL:
Initial authorization: 6 months, Continuation of Therapy: 12 months

PRESCRIBER REQUIREMENTS:
Prescribed by or in consultation with a board-certified hematologist, oncologist, intensive care specialist, or specialist in rare genetic hematologic diseases [If prescribed in consultation, consultation notes must be submitted with initial request and reauthorization requests]

AGE RESTRICTIONS:
None

QUANTITY: per FDA label
Prophylactic therapy- 40 IU/body weight once every other week (may provide higher dosing based on clinical response with medical record documentation support)- ONE MONTH per dispense.
On-demand therapy- 40 IU/kg body weight on day 1, 20 IU/kg body weight on day 2, 15 IU/kg body weight on day 3 and beyond until two days after the acute event is resolved. 3 on-demand doses per dispense.

PLACE OF ADMINISTRATION:
The recommendation is that infused medications in this policy will be for pharmacy or medical benefit coverage administered in a place of service that is a non-inpatient hospital facility-based location.

DRUG INFORMATION

ROUTE OF ADMINISTRATION:
Intravenous

DRUG CLASS:
Agents for Congenital Thrombotic Thrombocytopenic Purpura

FDA-APPROVED USES:
Indicated for prophylactic or on demand enzyme replacement therapy (ERT) in adult and pediatric patients with congenital thrombotic thrombocytopenic purpura (cTTP)

COMPENDIAL APPROVED OFF-LABELED USES:
None

APPENDIX

APPENDIX:
None

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:
Thrombotic thrombocytopenic purpura (TTP) is a thrombotic microangiopathy (TMA) caused by severely reduced activity of the von Willebrand factor-cleaving protease ADAMTS13. It is characterized by arteriolar platelet-rich thrombi that cause organ ischemia and produce neurologic abnormalities, kidney dysfunction, thrombocytopenia, and microangiopathic hemolytic anemia (MAHA).

Congenital TTP (cTTP) – Refers to severe deficiency of the ADAMTS13 protease due to biallelic germline pathogenic variants in the ADAMTS13 gene. ADAMTS13 activity is typically undetectable. This condition is also called hereditary TTP (hTTP), inherited TTP, familial TTP, and Upshaw-Schulman syndrome. cTTP is autosomal recessive. Pathogenic variants affecting both alleles of the ADAMTS13 gene are required to cause deficiency severe enough to lead to the clinical syndrome.
Genetic testing of the ADAMTS13 gene is the definitive means of documenting the diagnosis of hTTP and is appropriate in any individual with suspected hTTP based on undetectable or severely deficient ADAMTS13 activity without an inhibitor. Identification of biallelic pathogenic variants in ADAMTS13 confirms the diagnosis of hTTP. Individuals who are heterozygous for a pathogenic variant in ADAMTS13 are considered unaffected, but they may have an increased risk of stroke or cardiovascular disease.

Adzynma is a purified recombinant form of the ADAMTS13 enzyme that works by providing a replacement for the low levels of the deficient enzyme in patients with cTTP. Adzynma is administered intravenously (IV) once every other week for prophylactic enzyme replacement therapy (ERT), and once daily for on-demand ERT.

The safety and effectiveness of Adzynma were demonstrated in a randomized, crossover phase 3 study evaluating prophylactic and on-demand ERT with Adzynma compared to plasma-based therapies in patients with cTTP.
Study participants in the prophylaxis cohort (N=46) were randomly assigned to receive 6 months of treatment with either Adzynma or plasma based therapy in the first part of the trial (Period 1), and then crossed over to the other treatment for 6 months in the second part of the trial (Period 2). Thirty-five patients entered the 6-month single arm continuation period (Period 3).

There were no acute TTP events throughout the study among patients who received Adzynma. One acute TTP event occurred in a patient who received plasma-based therapy. Additionally, no subacute TTP events were reported among those who received Adzynma during Periods 1 and 2. Two patients receiving Adzynma had 2 subacute events of which one was treated with 4 supplemental doses. Four patients

receiving plasma-based therapy had 5 subacute TTP events in Periods 1 and 2. A total of 7 supplemental doses were given to 3 of these patients.

The study also investigated the efficacy of on-demand ERT based on the proportion of acute TTP events that responded to Adzynma throughout the duration of the study. Patients were randomly assigned to receive on-demand treatment with Adzynma (n=2) or plasma-based therapy (n=3). Findings showed that all 6 acute TTP events resolved after treatment with either Adzynma or plasma based therapy.

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:
All other uses of Adzynma (ADAMTS13, recombinant-krhn) are considered experimental/investigational and therefore, will follow Molina's Off- Label policy. Contraindications to Adzynma (ADAMTS13, recombinant-krhn) include: patients who have manifested life threatening hypersensitivity reactions to ADZYNMA or its components.

OTHER SPECIAL CONSIDERATIONS:
Patients may develop antibodies to rADAMTS13 which could potentially result in a decreased or lack of response to rADAMTS13. Patients may develop antibodies to host cell proteins which could potentially result in adverse reactions. There are no data on risk in previously untreated patients (subjects naïve to plasma based products).

CODING/BILLING INFORMATION

Note: 1) This list of codes may not be all-inclusive. 2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement

HCPCS CODE	DESCRIPTION
J3590	Unclassified biologic (Adzynma)

AVAILABLE DOSAGE FORMS:
Adzynma KIT 500UNIT single-dose vial, 1 each 10 mL Syringe, 1 each 25 gauge Infusion Set, 2 each Alcohol Pad or Swab, 1 each Diluent, 1 each Transfer Device
Adzynma KIT 1500UNIT single-dose vial, 1 each 20mL Syringe, 1 each 25 gauge Infusion Set, 2 each Alcohol Pad or Swab, 1 each Diluent, 1 each Transfer Device

REFERENCES

1. Adzynma (ADAMTS13, recombinant-krhn) lyophilized powder for Injection, for intravenous use [prescribing information]. Lexington, MA: Takeda Pharmaceuticals U.S.A., Inc.; November 2023.
2. Asmis, LM, et al. Recombinant ADAMTS13 for hereditary thrombotic thrombocytopenic purpura. N Engl J Med. 2022;387(25):2356-2361. doi:10.1056/NEJMoa2211113
3. Scully M, et al. S305: Phase 2 randomized, placebo-controlled, double-blind, multicenter study of recombinant ADAMTS13 in patients with immune-mediated thrombotic thrombocytopenic purpura. Hemasphere. 2023;7(Suppl):e8651306. Published August 8, 2023. doi:10.1097/01.HS9.0000968132.86513.06
4. Kremer Hovinga JA, George JN. Hereditary Thrombotic Thrombocytopenic Purpura. N Engl J Med 2019; 381:1653.
5. Alwan F, Vendramin C, Liesner R, et al. Characterization and treatment of congenital thrombotic thrombocytopenic purpura. Blood 2019; 133:1644.
6. Scully M, et al. Recombinant ADAMTS-13: first-in-human pharmacokinetics and safety in congenital

thrombotic thrombocytopenic purpura. Blood. 2017;130(19):2055-2063. doi:10.1182/blood-2017-06-788026
7. Zheng XL, et al. Good practice statements (GPS) for the clinical care of patients with thrombotic thrombocytopenic purpura. J Thromb Haemost. 2020;18(10):2503-2512. doi:10.1111/jth.15009

SUMMARY OF REVIEW/REVISIONS	DATE
NEW CRITERIA CREATION	Q1 2024