Medical Policy Bulletin

Title:
ADAMTS13, recombinant-krhn (Adzynma)
Policy #:
MA08.171

The Company makes decisions on coverage based on the Centers for Medicare and Medicaid Services (CMS) regulations and guidance, benefit plan documents and contracts, and the member's medical history and condition. If CMS does not have a position addressing a service, the Company makes decisions based on Company Policy Bulletins. Benefits may vary based on contract, and individual member benefits must be verified. The Company determines medical necessity only if the benefit exists and no contract exclusions are applicable. Although the Medicare Advantage Policy Bulletin is consistent with Medicare's regulations and guidance, the Company's payment methodology may differ from Medicare.

When services can be administered in various settings, the Company reserves the right to reimburse only those services that are furnished in the most appropriate and cost-effective setting that is appropriate to the member's medical needs and condition. This decision is based on the member's current medical condition and any required monitoring or additional services that may coincide with the delivery of this service.

This Policy Bulletin document describes the status of CMS coverage, medical terminology, and/or benefit plan documents and contracts at the time the document was developed. This Policy Bulletin will be reviewed regularly and be updated as Medicare changes their regulations and guidance, scientific and medical literature becomes available, and/or the benefit plan documents and/or contracts are changed.

Policy

Coverage is subject to the terms, conditions, and limitations of the member's Evidence of Coverage.

In the absence of coverage criteria from applicable Medicare statutes, regulations, NCDs, LCDs, CMS manuals, or other Medicare coverage documents, this policy uses internal coverage criteria developed by the Company in consideration of peer-reviewed medical literature, clinical practice guidelines, and/or regulatory status.

The Company reserves the right to reimburse only those services that are furnished in the most appropriate and cost-effective setting that is appropriate to the member's medical needs and condition.

MEDICALLY NECESSARY
PROPHYLACTIC TREATMENT

ADAMTS13, recombinant-krhn (Adzynma) is considered medically necessary and, therefore, covered for the **prophylactic** treatment of congenital thrombotic thrombocytopenic purpura (cTTP) in adult and pediatric individuals, when all of the following criteria are met, including dosing and frequency:

Initial Criteria

- Diagnosis of cTTP
  - ADAMTS13 mutation is confirmed by molecular genetic testing with biallelic mutations in the ADAMTS13 gene.
  - The individual has an ADAMTS13 activity level of less than 10% at the time of diagnosis.
- ADAMTS13, recombinant-krhn (Adzynma) is being prescribed for routine prophylactic treatment to prevent thrombotic thrombocytopenic purpura (TTP) events
- Prescribed by or in consultation with a hematologist
- Dosing and frequency for ADAMTS13, recombinant-krhn (Adzynma)
  - 40 IU/kg body weight once every other week intravenously
  - The prophylaxis dosing frequency may be adjusted to 40 IU/kg body weight once weekly based on prior prophylactic dosing regimen or clinical response.

Continuation Criteria

- The individual has previously received routine prophylactic treatment with ADAMTS13, recombinant-krhn (Adzynma)
- Documentation of positive clinical response to ADAMTS13, recombinant-krhn (Adzynma) therapy (e.g., reduction or maintenance of number of TTP events, increase in platelet count, decrease in lactate dehydrogenase [LDH] level).
- Prescribed by or in consultation with a hematologist

TREATMENT

ADAMTS13, recombinant-krhn (Adzynma) is considered medically necessary and, therefore, covered for **on demand treatment** of an acute TTP event in adult and pediatric individuals, when all of the following criteria are met, including dosing and frequency:

- Diagnosis of cTTP
    - ADAMTS13 mutation is confirmed by molecular genetic testing with biallelic mutations in the ADAMTS13 gene
    - The individual has an ADAMTS13 activity level of less than 10% at the time of diagnosis
- Adzynma is being prescribed for on-demand treatment of an acute TTP event
- Prescribed by or in consultation with a hematologist
- Dosing and frequency for Adzynma (ADAMTS13, recombinant-krhn)
    - 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 2 days after the acute event is resolved.

EXPERIMENTAL/INVESTIGATIONAL

All other uses for ADAMTS13, recombinant-krhn (Adzynma) are considered experimental/investigational and, therefore, not covered unless the indication is supported as an accepted off-label use, as defined in the Company medical policy on off-label coverage for prescription drugs and biologics.

DOSING AND FREQUENCY REQUIREMENTS

The Company reserves the right to modify the Dosing and Frequency Requirements listed in this policy to ensure consistency with the most recently published recommendations for the use of ADAMTS13, recombinant-krhn (Adzynma). Changes to these guidelines are based on a consensus of information obtained from resources such as, but not limited to: the US Food and Drug Administration (FDA); Company-recognized authoritative pharmacology compendia; or published peer-reviewed clinical research. The professional provider must supply supporting documentation (i.e., published peer-reviewed literature) in order to request coverage for an amount of ADAMTS13, recombinant-krhn (Adzynma) outside of the Dosing and Frequency Requirements listed in this policy. For a list of Company-recognized pharmacology compendia, view our policy on off-label coverage for prescription drugs and biologics.

Accurate member information is necessary for the Company to approve the requested dose and frequency of this drug. If the member’s dose, frequency, or regimen changes (based on factors such as changes in member weight or incomplete therapeutic response), the provider must submit those changes to the Company for a new approval based on those changes as part of the utilization management activities. The Company reserves the right to conduct postpayment review and audit procedures for any claims submitted for ADAMTS13, recombinant-krhn (Adzynma).

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include, but are not limited to: records from the professional provider's office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the service.

When coverage of ADAMTS13, recombinant-krhn (Adzynma) is requested outside of the Dosing and Frequency

Requirements listed in this policy, the prescribing professional provider must supply documentation (i.e., published peer-reviewed literature) to the Company that supports this request.

Guidelines

BENEFIT APPLICATION

Subject to the terms and conditions of the applicable Evidence of Coverage, ADAMTS13, recombinant-krhn (Adzynma) is covered under the medical benefits of the Company's Medicare Advantage products when the medical necessity criteria listed in this medical policy are met.

US FOOD AND DRUG ADMINISTRATION (FDA) STATUS

ADAMTS13, recombinant-krhn (Adzynma) was approved by the FDA on November 9, 2023, for the prophylactic and on-demand treatment of adult and pediatric patients with congenital thrombotic thrombocytopenic purpura (cTTP).

PEDIATRIC USE

The safety and effectiveness have been established in the pediatric population for ADAMTS13, recombinant-krhn (Adzynma).

Description

DRUG INFORMATION

ADAMTS13, recombinant-krhn (Adzynma), is a human recombinant "A disintegrin and metalloproteinase with thrombospondin motifs 13" (rADAMTS13) indicated for prophylactic or on-demand enzyme replacement therapy (ERT) in adult and pediatric individuals with congenital thrombotic thrombocytopenic purpura (cTTP).

CONGENITAL ADAMTS13 DEFICIENCY

cTTP is an autosomal recessive disorder caused by biallelic mutations on the ADAMTS13 gene. It is characterized by less than 10% ADAMTS13 enzyme activity and the accumulation of ultra-large von Willebrand factor (VWF). The buildup of ultra-large VWF multimers leads to uncontrolled platelet aggregation, platelet adhesion, and abnormal clotting in the small blood vessels. cTTP often causes seemingly mild and nonspecific symptoms such as lethargy, headache, loss of concentration, and abdominal discomfort.

ADAMTS13 deficiency is most commonly acquired due to anti-ADAMTS13 autoantibodies. It can also be inherited in the congenital form as a result of biallelic mutations in the ADAMTS13 gene.

cTTP is a rare blood disorder characterized by blood clotting due to a deficiency in the enzyme ADAMTS13, affecting fewer than 1000 people in the United States. Most common presentation of cTTP are thrombocytopenia, microangiopathic hemolytic anemia, headaches, and abdominal pain. Mortality of acute TTP events can reach 90% or higher if the disease is left untreated. Treatment has normally included prophylactic plasma-based therapy.

The 2020 International Society on Thrombosis and Haemostasis (ISTH) good practice statements for the clinical care of individuals with thrombotic thrombocytopenic purpura (TPP) state TTP should be considered in individuals presenting with thrombocytopenia and microangiopathic hemolytic anemia. cTTP should be suspected in individuals with any of the following presentations: severe neonatal hyperbilirubinemia, recurrent thrombocytopenia in a child or young adult, transient neurologic symptoms of stroke in a child or young adult, embolic stroke of undetermined source, or new onset TTP and absence of an ADAMTS13 inhibitor. Once suspected, individuals should be tested for decreased ADAMTS13 enzyme activity, and if the enzymatic activity is less than 10% of normal without ADAMTS13 antibodies, genetic testing showing biallelic mutations in the ADAMTS13 gene will be confirmatory of cTPP.

PEER-REVIEWED LITERATURE

SUMMARY

The safety and effectiveness of ADAMTS13, recombinant-krhn (Adzynma), were demonstrated in a global study evaluating prophylactic and on-demand ERT with ADAMTS13, recombinant-krhn (Adzynma) compared to plasma-based therapies in individuals with cTTP. The efficacy of ADAMTS13, recombinant-krhn (Adzynma) in the prophylactic treatment of individuals with cTTP was evaluated in 46 individuals who were randomly assigned to receive 6 months of treatment with either ADAMTS13, recombinant-krhn (Adzynma) or plasma-based therapies (Period 1), then crossed over to the other treatment for 6 months (Period 2). The efficacy was demonstrated based on the incidence of TTP events, and TTP manifestations, as well as the incidence of the need for supplemental doses.

The efficacy of on-demand ERT was evaluated based on the proportion of acute TTP events responding to ADAMTS13, recombinant-krhn (Adzynma) in both the prophylactic and the on-demand cohorts throughout the duration of the study. All acute and subacute TTP events resolved after treatment with either ADAMTS13, recombinant-krhn (Adzynma) or plasma-based therapies.

The most common side effects associated with ADAMTS13, recombinant-krhn (Adzynma), include headache, diarrhea, migraine, abdominal pain, nausea, upper respiratory tract infection, dizziness and vomiting. During the clinical studies, no adverse events, including allergic reactions, were observed during the administration of ADAMTS13, recombinant-krhn (Adzynma). Thirteen (one individual in Study 1 and 12 individuals in a long-term extension study) of 67 individuals treated prophylactically with ADAMTS13, recombinant-krhn (Adzynma) with confirmed cTTP tested positive for low-titer binding antibodies against ADAMTS13 with no observable clinical impact on the safety or efficacy of ADAMTS13, recombinant-krhn (Adzynma), and no increase in antibody titers over time. No individuals with cTTP tested positive for neutralizing antibodies against ADAMTS13.

The application was awarded a Rare Pediatric Disease Priority Review Voucher, and granted Priority Review, Fast Track, and Orphan designations.

OFF-LABEL INDICATIONS

There may be additional indications contained in the policy section of this document due to evaluation of criteria highlighted in the company's off-label policy, and/or review of clinical guidelines issued by leading professional organizations and government entities.

References

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Coding

Inclusion of a code in this table does not imply reimbursement. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.

The codes listed below are updated on a regular basis, in accordance with nationally accepted coding guidelines. Therefore, this policy applies to any and all future applicable coding changes, revisions, or updates.

In order to ensure optimal reimbursement, all health care services, devices, and pharmaceuticals should be reported using the billing codes and modifiers that most accurately represent the services rendered, unless otherwise directed by the Company.

The Coding Table lists any CPT, ICD-10, and HCPCS billing codes related only to the specific policy in which they appear.

CPT Procedure Code Number(s)
N/A

ICD - 10 Procedure Code Number(s)
N/A

ICD - 10 Diagnosis Code Number(s)
D69.42 Congenital and hereditary thrombocytopenia purpura

HCPCS Level II Code Number(s)
J7171 Injection, adamts13, recombinant-krhn, 10 iu

Revenue Code Number(s)
N/A

Policy History

MA08.171

12/15/2025	This policy has been reissued in accordance with the Company's annual review process.
12/16/2024	This version of the policy will become effective 12/16/2024. This new policy has been issued to communicate the Company's coverage position and criteria for ADAMTS13, recombinant-krhn (Adzynma).

Version Effective Date:
12/15/2025
Version Issued Date:
12/15/2025
Version Reissued Date:
N/A