Blue Cross Blue Shield Blue Care Network of Michigan

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Medical benefit drug policies are a source for BCBSM and BCN medical policy information only. These documents are not to be used to determine benefits or reimbursement. Please reference the appropriate certificate or contract for benefit information. This policy may be updated and therefore subject to change.

Effective Date: 12/12/2024

Adzynma (ADAMTS13, recombinant-krhn)

HCPCS: J7171

Policy:

Requests must be supported by submission of chart notes and patient specific documentation.

A. Coverage of the requested drug is provided when all the following are met:
   a. FDA approved indication
   b. FDA approved age
   c. Confirmation of diagnosis by serum assay showing less than 10% of normal ADAMTS13 enzyme activity and genetic testing showing a mutation in the ADAMTS13 gene
   d. Must not be used in combination with any other therapy for the treatment of congenital thrombotic thrombocytopenic purpura (cTTP)
   e. Trial and failure, contraindication, OR intolerance to the preferred drugs as listed in BCBSM/BCN's utilization management medical drug list.

B. Quantity Limitations, Authorization Period and Renewal Criteria
   a. Quantity Limit: Align with FDA recommended dosing
   b. Initial Authorization Period: One year at a time
   c. Renewal Criteria: Clinical documentation must be provided to confirm that current criteria are met and that the medication is providing clinical benefit

***Note: Coverage and approval duration may differ for Medicare Part B members based on any applicable criteria outlined in Local Coverage Determinations (LCD) or National Coverage Determinations (NCD) as determined by Center for Medicare and Medicaid Services (CMS). See the CMS website at http://www.cms.hhs.gov/. Determination of coverage of Part B drugs is based on medically accepted indications which have supported citations included or approved for inclusion determined by CMS approved compendia.

Background Information:

- Congenital thrombotic thrombocytopenic purpura (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. In many patients, symptoms are ongoing without a clear time of onset or resolution. Thrombocytopenia and microangiopathic hemolytic anemia can occur, but neurologic symptoms can occur without thrombocytopenia or anemia, and thrombocytopenia may occur without apparent hemolysis. Acute, severe exacerbations are uncommon but may be life-threatening without appropriate treatment. Exacerbations of the disease can be triggered during the neonatal period, pregnancy, infections, or surgeries although none of these has to occur for an acute attack to happen.

- The 2020 International Society on Thrombosis and Haemostasis (ISTH) good practice statements for the clinical care of patients 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, patients 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.

- The standard of care for cTTP up until now has been plasma transfusions. Plasma transfusions allow for rapid replacement of ADAMTS13 during an acute attack and can be used prophylactically to minimize the risk of future attacks. The main complications of plasma infusion are allergic reactions. These may be treated or prevented using antihistamines. If allergic reactions are severe, other therapies, such as, a plasma-derived factor VIII concentrate that contains ADAMTS13 may be used.

- Adzynma provides an additional treatment option for cTTP. It is a human recombinant ADAMTS13 indicated for prophylactic or on demand enzyme replacement therapy (ERT) in adult and pediatric patients with cTTP.

- Safety and efficacy of Adzynma were evaluated in a Phase III, randomized, controlled, open-label, crossover, trial of 46 patients with cTTP. Patients were randomized to receive 6 months of treatment with either 40 IU/kg Adzynma or plasma-based therapies during the first period of the trial and then crossed over to receive the other treatment for 6 months during the second period. The mean annualized event rate of thrombocytopenia manifestations was 2.0 for patients receiving Adzynma (9 of 37 patients) compared to 4.44 in patients receiving plasma-based therapies (19 of 38 patients). Pharmacokinetic results showed patients (n = 23) receiving 40 IU/kg Adzynma IV achieved a four- to five-fold increase in ADAMTS13 enzyme activity after a single infusion compared to plasma-based therapies.

- Adzynma has not been studied and there is no data to support use in combination with other medications or treatment modalities used to treat cTTP.

References:

1. Adzynma [prescribing information]. Lexington, MA: Takeda Pharmaceuticals U.S.A., Inc.; June 2024.
2. Kremer Hovinga JA & George JN. Hereditary thrombotic thrombocytopenic purpura. NEJM. 2019 Oct 24; 381 (17): 1653 – 62.
3. Alwan F, Vendramin C, Liesner R, et al. Characterization and treatment of congenital thrombotic thrombocytopenic purpura. Blood. 2019 Apr 11; 133 (15): 1644 - 51.
4. Borogovac A & George JN. Stroke and myocardial infarction in hereditary thrombotic thrombocytopenic purpura: similarities to sickle cell anemia. Blood Adv. 2019; 3 (23): 3973 - 6.
5. Hamroun A, Prouteau C, & Provôt F. Hereditary thrombotic thrombocytopenic purpura. NEJM. 2020 Jan 23; 382 (4): 392 - 3.
6. Page EE, Kremer Hovinga JA, Terrell DR, et al. Thrombotic thrombocytopenic purpura: diagnostic criteria, clinical features, and long-term outcomes from 1995 through 2015. Blood Adv. 2017 Apr 6; 1 (10): 590 - 600.
7. Zheng XL, Vesely SK, Cataland SR, et al. ISTH guidelines for treatment of thrombotic thrombocytopenic purpura. J Thromb Haemost. 2020 Oct; 18: 2496 – 502.
8. Clinicaltrials.gov. A study of BAX 930 in children, teenagers, and adults born with thrombotic thrombocytopenic purpura (TTP) (NCT03393975). Available at: https://classic.clinicaltrials.gov/ct2/show/NCT03393975. Accessed on November 13, 2023.
9. Clinicaltrials.gov. A study of TAK-755 in participants with congenital thrombotic thrombocytopenic purpura (NCT04683003). Available at: https://classic.clinicaltrials.gov/ct2/show/study/NCT04683003. Accessed on November 13, 2023.

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<tr><th colspan="3">Policy History</th></tr>
<tr><th>#</th><th>Date</th><th>Change Description</th></tr>
<tr><td>1.3</td><td>Effective Date: 12/12/2024</td><td>Annual review of criteria was performed, no changes were made</td></tr>
<tr><td>1.2</td><td>Effective Date: 03/01/2024</td><td>UM medical management system update for MAPPO and BCNA
<table><tr><th>Line of Business</th><th>PA Required in Medical Management System (Yes/No)</th></tr><tr><td>BCBS</td><td>Yes</td></tr><tr><td>BCN</td><td>Yes</td></tr><tr><td>MAPPO</td><td>Yes</td></tr><tr><td>BCNA</td><td>Yes</td></tr></table></td></tr>
<tr><td>1.1</td><td>Effective Date: 12/14/2023</td><td>New policy</td></tr>
<tr><td>1.0</td><td>Effective Date: 11/30/2023</td><td>UM medical management system update for BCBS and BCN
<table><tr><th>Line of Business</th><th>PA Required in Medical Management System (Yes/No)</th></tr><tr><td>BCBS</td><td>Yes</td></tr><tr><td>BCN</td><td>Yes</td></tr><tr><td>MAPPO</td><td>No</td></tr><tr><td>BCNA</td><td>No</td></tr></table></td></tr>
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** The prescribing information for a drug is subject to change. To ensure you are reading the most current information it is advised that you reference the most updated prescribing information by visiting the drug or manufacturer website or http://dailymed.nlm.nih.gov/dailymed/index.cfm.*