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: 08/08/2024

Ryplazim® (plasminogen)

HCPCS: J2998

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. Plasminogen activity level ≤ 45%
   d. 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 Limits: Align with FDA recommended dosing
   b. 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:

- Ryplazim is a plasma-derived human plasminogen indicated for the treatment of patients with plasminogen deficiency type 1 (hypoplasminogenemia).

- Plasminogen is a naturally occurring protein that is synthesized by the liver and circulates in the blood. Activated plasminogen, known as plasmin, is an enzymatic component of the fibrinolytic system and the main enzyme involved in the lysis of clots and clearance of extravasated fibrin. Activated plasminogen is also involved in wound healing, cell migration, tissue remodeling, angiogenesis, and embryogenesis.

- Plasminogen deficiency type 1 is a disorder that results in inflamed growths on the mucous membranes, which are the moist tissues that line body openings such as the eyelids and the inside of the mouth. The most common and visible lesion associated with plasminogen deficiency is ligneous conjunctivitis, which is characterized by thick, woody (ligneous) growths on the conjunctiva of the eye, and if left untreated, can lead to corneal damage and blindness. While ligneous conjunctivitis is the best characterized and visible lesion, plasminogen deficiency type 1 is a multi-systemic disease that can also affect the ears, sinuses, tracheobronchial tree, genitourinary tract, and gingiva.

- A diagnosis of plasminogen deficiency type 1 is based upon identification of characteristic symptoms, a family account of their medical history (anamnesis), a detailed patient history, and a thorough clinical evaluation. Specific laboratory tests can confirm a diagnosis, specifically tests that measure the activity of plasminogen, which will be severely deficient in individuals with plasminogen deficiency. The prevalence of plasminogen deficiency type 1 has been estimated at 1.6 per one million people.

- Congenital plasminogen deficiency type II, also called dysplasminogenemia, is not believed to be associated with any symptoms.

- 15 patients were enrolled in Ryplazim Trial 2, a single-arm, open-label, Phase II/III study. All study participants had a baseline plasminogen activity level <45% (normal plasminogen activity range is between 70% and 130%). All study participants showed an increase in baseline trough plasminogen activity levels during an initial 12-week treatment period (success defined as at least and absolute 10% above baseline for at least 3 measurements). Additionally, all patients with any lesion at baseline had at least 50% improvement in the number/size of their lesions.

References:

1. Ryplazim [prescribing information]. Fort Lee, NJ; Prometic Bioproduction Inc. November 2021
2. Plasminogen deficiency. Liminal BioSciences. https://liminalbiosciences.com/pipeline/plasminogen/plasminogen-deficiency-clinical-trials/ accessed July 2021
3. Tefs K, Gueorguieva M, Klammt J, et al. Molecular and clinical spectrum of type I plasminogen deficiency: a series of 50 patients. Blood. 2006;108(9):3021-3026.
4. IPD Analytics. Ryplazim (plasminogen, human-tvmh). New drug review. June 2021. Accessed July 15, 2021. https://www.ipdanalytics.com
5. National organization for rare disease NORD. Rare disease database, congenital plasminogen deficiency. https://rarediseases.org/rare-diseases/congenital-plasminogen-deficiency/ accessed July 2021

<table>
<tr><th colspan="3">Policy History</th></tr>
<tr><th>#</th><th>Date</th><th>Change Description</th></tr>
<tr><td>1.5</td><td>Effective Date: 08/08/2024</td><td>Annual review of medical policy. No changes to the criteria were made as this time.</td></tr>
<tr><td>1.4</td><td>Effective Date: 08/10/2023</td><td>Annual review of medical policy. No changes to the criteria were made as this time.</td></tr>
<tr><td>1.3</td><td>Effective Date: 08/04/2022</td><td>Annual review of medical policy. No changes to the criteria were made as this time.</td></tr>
<tr><td>1.2</td><td>Effective Date: 01/17/2022</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: 09/17/2021</td><td>UM medical management system update BCBSM 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>
<tr><td>1.0</td><td>Effective Date: 08/12/2021</td><td>New policy</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.*