Policy Title:	**Ryplazim (plasminogen, human-tvmh)** (Intravenous)		
		Department:	PHA
Effective Date:	04/01/2022		
Review Date:	03/10/2022, 03/02/2023		

Purpose: To support safe, effective and appropriate use of Ryplazim (plasminogen, human-tvmh).

Scope: Medicaid, Commercial, Medicare-Medicaid Plan (MMP)

Policy Statement:

Ryplazim (plasminogen, human-tvmh) is covered under the Medical Benefit when used within the following guidelines. Use outside of these guidelines may result in non-payment unless approved under an exception process.

Procedure:

Coverage of will be reviewed prospectively via the prior authorization process based on criteria below.

Documentation:

Submission of the following information is necessary to initiate the prior authorization review:

A. Initial requests: documentation of baseline plasminogen activity level and chart notes documenting number and severity of lesions
B. Continuation of therapy requests: documentation of plasminogen activity level 72 hours after first dose and chart notes documenting clinical response, and additional plasminogen activity level, if applicable

Initial Criteria:

1. Patient has documented diagnosis of plasminogen deficiency (PLGD) type I;
    a. Diagnosis is evidenced by the following:
        i. Plasminogen activity level ≤45%
        ii. Documented history of lesions (external and/or internal) and symptoms consistent with a diagnosis of congenital PLGD (the severity of disease will be highly individualized and may even vary between members of the same family);
        AND
2. Documented vaccination history to Hepatitis A virus (HAV) and Hepatitis B virus (HBV), or patient has received their first vaccine dose and is scheduled to receive the second vaccine dose; AND
3. Prescribed by or in consultation with a hematologist; AND
4. Patient is ≥2 years of age; AND

5. Ryplazim is dosed according to the US Food and Drug Administration labeled dosing for PLGD type 1 (see Dosage/Administration table below); AND
6. MMP members who have previously received this medication within the past 365 days are not subject to Step Therapy Requirements

Continuation of Therapy Criteria:

- Patient continues to meet all initial criteria and is tolerating therapy with Ryplazim; AND
- Documentation of a positive clinical response to therapy as evidenced by resolution of lesions and no new or reoccurring lesions have occurred; AND
- Ryplazim is dosed according to the US Food and Drug Administration labeled dosing for PLGD type 1 (see Dosage/Administration table below)

Coverage durations:

- Initial coverage: 12 weeks
- Continuation of therapy coverage: 6 months

*** Requests will also be reviewed to National Coverage Determination (NCD) and Local Coverage Determinations (LCDs) if applicable.***

Dosage/Administration:

Indication	Dose	Maximum dose
PLGD type 1	6.6mg/kg every 2-4 days Ryplazim is dosed based on trough levels and clinical response: a. Baseline plasminogen trough level obtained and Ryplazim is initially dosed at 6.6mg/kg every 3 days b. Trough level is ordered at 72 hours after 1st dose (prior to second dose): i. If trough plasminogen activity level increases from baseline at 72 hours <10%, increase frequency to every 2 days, ii. If trough plasminogen activity level increases from baseline at 72 hours ≥10% but ≤20%, maintain frequency of every 3 days, iii. If trough plasminogen activity level increases from baseline at 72 hours >20%, decrease frequency to every 4 days; c. At 12 weeks: i. If lesions still present or new/reoccurrence, increase dosing frequency in 1 day increments every 4-8 weeks up to every 2 days until lesions resolve or stabilize ii. If lesions resolve, continue same dosing frequency.	6.6mg/kg every 2-4 days

	iii. If desired clinical response does not occur in 12 weeks, check trough plasminogen activity level a. If trough plasminogen level <10% above the baseline trough level at 12 weeks, confirm plasminogen trough level and if confirmed, consider discontinuation. b. If trough plasminogen level ≥10% above the baseline trough level at 12 weeks, consider surgical removal of lesions.	

Investigational use: All therapies are considered investigational when used at a dose or for a condition other than those that are recognized as medically accepted indications as defined in any one of the following standard reference compendia: American Hospital Formulary Service Drug information (AHFS-DI), Thomson Micromedex DrugDex, Clinical Pharmacology, Wolters Kluwer Lexi-Drugs, or Peer-reviewed published medical literature indicating that sufficient evidence exists to support use. Neighborhood does not provide coverage for drugs when used for investigational purposes.

Applicable Codes:
Below is a list of billing codes applicable for covered treatment options. The below tables are provided for reference purposes and may not be all-inclusive. Requests received with codes from tables below do not guarantee coverage. Requests must meet all criteria provided in the procedure section.

The following HCPCS/CPT codes are:

HCPCS/CPT Code	Description
C9090	Injection, plasminogen, human-tvmh, 1mg

References:
1. Ryplazim (plasminogen, human-tvmh) [prescribing information]. Prometric Biotherapeutics Inc. Laval, Quebec, Canada; 2021.