Ryplazim® (plasminogen, human-tvmh)
(Intravenous)

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I. Length of Authorization

Coverage will be provided initially for 12 weeks.

- In patients with complete response, coverage will be renewed annually thereafter.
- In patients with less than complete response, coverage will be renewed for an additional 12 weeks to optimize frequency of administration.

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

- Ryplazim 68.8 mg single-dose vial: 11 vials per 2 days

B. Max Units (per dose and over time) [HCPCS Unit]:

- 759 billable units (759 mg) every 2 days

III. Initial Approval Criteria [1,2]

Coverage is provided in the following conditions:

- Patient is at least 11 months of age; **AND**
- Patient blood pressure is controlled prior to initiation of treatment**; AND**
- Patient has healing of lesions or wounds suspected as a source of a recent bleeding event prior to initiating therapy**; AND**
- Patient has had baseline plasminogen activity measured prior to therapy and plasminogen activity level is ≤ 45% *(Note: If patient is receiving plasminogen supplementation with fresh frozen plasma, allow for a 7-day washout period before obtaining baseline plasminogen activity level)*; **AND**

Universal Criteria [1]

- Patients on concomitant therapy with anticoagulants, antiplatelet drugs, or other agents which may interfere with normal coagulation will be monitored during and for 4 hours after infusion of Ryplazim; **AND**

Plasminogen Deficiency Type 1 (Hypoplasminogenemia) † Φ [1]

- Patient has a history of visible or non-visible lesions (e.g., confirmed by computed tomography, magnetic resonance imaging, ultrasound, etc.)

Note: *All patients must initiate therapy at a frequency of every three days.*

† FDA-approved indication(s); ‡ Compendia Recommended Indication(s); Φ Orphan Drug

IV. Renewal Criteria [1]

Coverage can be renewed based on the following criteria:

- Patient continues to meet the universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in section III; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: severe bleeding, respiratory distress due to tissue sloughing, hypersensitivity reactions, including anaphylaxis, etc.; **AND**
  - Patient has demonstrated a beneficial response to therapy (i.e., resolution of lesions); **OR**
  - Patient's lesions have not resolved after an initial 12 weeks of therapy OR there are new or recurrent lesions; **AND**
    - Patient may increase dosage frequency, as outlined below, in one day increments every 4-8 weeks up to the max dosing frequency (i.e., every two days); **AND**
    - Re-assess trough plasminogen activity level if, after 12 additional weeks of dose optimization, no clinical effect has been noted; **AND**
      - If trough plasminogen activity level is <10% above baseline, repeat trough. If low plasminogen is confirmed AND no clinical effect has been demonstrated, consider treatment discontinuation

V. Dosage/Administration [1]

Indication	Dose
Type 1 Hypo-plasminogenemia	The recommended dosage of Ryplazim is 6.6 mg/kg of body weight administered intravenously every 2 to 4 days. Initiate dosing at a frequency of every three days, then adjust as below. Determination of Dosing Frequency • Obtain baseline plasminogen activity level (allow for a 7-day washout period if the patient has been receiving fresh frozen plasma); **AND** • Obtain trough plasminogen activity level 72 hours following the initial dose and prior to the second dose; **AND** – Plasminogen activity level is <10%* above baseline, increase frequency of therapy to every 2 days

	– Plasminogen activity level is ≥10 and ≤20%* above baseline, maintain therapy at frequency of every 3 days – Plasminogen activity level is >20%* above baseline, decrease frequency of therapy to every 4 days • Maintain dosing frequency above for 12 weeks while treating active lesions; **AND** – If lesions have resolved, continue therapy and re-assess in 12 weeks – If lesions have not resolved, or there are new or recurrent lesions, increase the dosing frequency in one-day increments every 4-8 weeks up to dosing every 2 days. If desired clinical effect is not seen in 12 weeks, assess trough plasminogen activity level; **AND** ○ Plasminogen activity level ≥10%* above baseline, consider other additional treatments (e.g., surgical removal) ○ Plasminogen activity level <10%* above baseline, then repeat trough to confirm. If low trough is confirmed, consider discontinuing therapy if no clinical efficacy has been demonstrated
*Plasminogen activity (%) as absolute change	

VI. Billing Code/Availability Information

HCPCS Code:

- J2998 – Injection, plasminogen, human-tvmh, 1 mg; 1 billable unit = 1 mg

NDC:

- Ryplazim 68.8 mg single-dose vial: 70573-0099-xx

VII. References

1. Ryplazim [package insert]. Laval, Quebec, CA; Prometric Bioproduction, Inc.; November 2021. Accessed April 2023.
2. Shapiro AD, Nakar C, Parker JM, et al. Plasminogen replacement therapy for the treatment of children and adults with congenital plasminogen deficiency. Blood. 2018 Mar 22;131(12):1301-1310. doi: 10.1182/blood-2017-09-806729. Epub 2018 Jan 10.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
E88.02	Plasminogen deficiency

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD), Local Coverage Determinations (LCDs), and Local Coverage Articles may exist and compliance with these policies is required where applicable. They can be found at: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/LCA): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC