

5.20.013

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Subsection:	Biologicals	Original Policy Date:	January 14, 2022
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Last Review Date: June 11, 2026

Ryplazim

Description

Ryplazim (plasminogen, human-tvmh)

Background

Plasminogen is the zymogenic (enzymatically inactive) form of the plasma protein plasmin. Plasminogen is produced and released into systemic circulation by the liver. The circulating protein can bind to fibrin-rich clots and is converted into its active form, plasmin. Once activated, plasmin acts to dissolve the fibrin-rich clots (1).

In patients with plasminogen deficiency type 1 (hypoplasminogenemia), low plasminogen levels lead to the accumulation of fibrin-rich, ligneous pseudomembranous lesions on mucous membranes. These lesions can impair normal tissue function. Replacement therapy with plasminogen, human-tvmh increases plasma levels of plasminogen allowing for temporary correction of the deficiency and a reduction or resolution of the fibrinous lesions (1-2).

Regulatory Status

FDA-approved indication: Ryplazim (plasminogen, human-tvmh) is plasma-derived human plasminogen indicated for the treatment of patients with plasminogen deficiency type 1 (hypoplasminogenemia) (2).

Patients treated with Ryplazim can experience bleeding. Bleeding has occurred from active mucosal disease-related lesions. Depending on lesion location, this can manifest as gastrointestinal bleeding, hemoptysis, epistaxis, vaginal bleeding, or hematuria. Ryplazim can also exacerbate active bleeding not related to plasminogen deficiency type 1. Prior to initiation of Ryplazim, clinicians should confirm healing of lesions or wounds associated with a bleeding

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event. Patients using agents that interfere with blood clotting (anticoagulants or antiplatelet drugs) or are prone to bruising or bleed easily should be monitored during infusion and for 4 hours after infusion with Ryplazim (2).

Ryplazim can also precipitate tissue sloughing, particularly of lesions associated with plasminogen deficiency. Patients with confirmed lesions in the respiratory tract should be closely monitored, as treatment can result in airway obstruction and hemoptysis. At risk patients should be monitored for a minimum of 4 hours after infusion (2).

The safety and effectiveness of Ryplazim in pediatric patients has been established (2).

Related policies

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Ryplazim may be considered **medically necessary** if the conditions indicated below are met.

Ryplazim may be considered **investigational** for all other indications.

Prior-Approval Requirements

Diagnosis

Patient must have the following:

Plasminogen deficiency type 1 (hypoplasminogenemia)

AND ALL of the following:

1. Patient has a baseline plasminogen activity level $\leq 45\%$ of normal
2. Patient has a documented history of lesions and symptoms consistent with a diagnosis of plasminogen deficiency type 1 (e.g., ligneous conjunctivitis, ligneous gingivitis or gingival overgrowth, vision abnormalities, respiratory distress and/or obstruction, abnormal wound healing)

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3. Prescriber agrees to administer Ryplazim at the FDA labeled dose of 6.6 mg/kg body weight every 2 to 4 days
4. Prescriber agrees to monitor patient for tissue sloughing and serious bleeding

Prior-Approval *Renewal* Requirements

Diagnosis

Patient must have the following:

Plasminogen deficiency type 1 (hypoplasminogenemia)

AND ALL of the following:

1. Disease has improved or stabilized (e.g., improvement in lesion number and/or size, absence of new lesion development, improvement in respiratory function, etc.)
2. Prescriber agrees to administer Ryplazim at the FDA labeled dose of 6.6 mg/kg body weight every 2 to 4 days
3. Prescriber agrees to monitor patient for tissue sloughing and serious bleeding

Policy Guidelines

Pre-PA Allowance

None

Prior-Approval Limits

Duration 12 months

Prior-Approval *Renewal* Limits

Same as above

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Rationale

Summary

Ryplazim (plasminogen, human-tvmh) is indicated for the treatment of plasminogen deficiency type 1 (hypoplasminogenemia). This condition leads to the absence or inadequate production of plasminogen, which is activated to plasmin, an important enzyme in dissolving clots. Lack of functional plasminogen/plasmin can lead to the accumulation of fibrinous lesions that impair organ and tissue function. Supplementation with Ryplazim restores plasminogen levels temporarily and can lead to reduction or reversal of these fibrinous lesions. Ryplazim can cause bleeding and tissue sloughing. Patients should be monitored for serious bleeding events and airway obstruction due to tissue sloughing. The safety and effectiveness of Ryplazim in pediatric patients has been established (1-2).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of Ryplazim while maintaining optimal therapeutic outcomes.

References

1. Mutch, N. J. (2013). The role of platelets in fibrinolysis. *Platelets*, 469–485.
<https://doi.org/10.1016/b978-0-12-387837-3.00023-7>
2. Ryplazim [package insert]. Laval, Quebec, Canada: Prometic Bioproduction Inc.; January 2024.

Policy History

Date	Action
January 2022	Addition to PA
March 2022	Annual review
June 2022	Annual review
September 2023	Annual review and reference update. Changed policy number to 5.20.013
June 2024	Annual review
June 2025	Annual review and reference update
June 2026	Annual review

Keywords

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