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# 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

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 ≤ 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)

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

## 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.; June 2023.

## 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 |

## Keywords

**This policy was approved by the FEP® Pharmacy and Medical Policy Committee on September 8, 2023 and is effective on October 1, 2023.**