PHARMACY POLICY STATEMENT
TRICARE

DRUG NAME	Ryplazim (plasminogen, human-tvmh)
BENEFIT TYPE	Medical
STATUS	Prior Authorization Required

Ryplazim is a plasma-derived human plasminogen indicated for the treatment of patients with plasminogen deficiency type 1 (hypoplasminogenemia). It was approved by the FDA on June 4, 2021 and is the first approved treatment for plasminogen deficiency type 1.
Individuals with this disease lack a protein called plasminogen, which is responsible for the ability of the body to break down fibrin clots. Plasminogen deficiency leads to an accumulation of fibrin, causing the development of growths (lesions) that can impair normal tissue and organ function and may lead to blindness when these lesions affect the eyes. Ligneous conjunctivitis (LC) appears to be the most common clinical manifestation and is characterized by inflamed, woody growths on the conjunctival membranes that, if left untreated, can result in visual impairment or blindness.
Treatment with Ryplazim temporarily increases plasminogen levels in blood. The effectiveness and safety of Ryplazim (plasminogen) is primarily based on one single-arm, open-label (unblinded) clinical trial enrolling 15 adult and pediatric patients with plasminogen deficiency type 1. All patients received Ryplazim administered every two to four days for 48 weeks. The effectiveness of Ryplazim was demonstrated by at least 50% improvement of their lesions in all 11 patients who had lesions at baseline, and absence of recurrent or new lesions in any of the 15 patients through the 48 weeks of treatment.

Ryplazim (plasminogen, human-tvmh) will be considered for coverage when the following criteria are met:

Hypoplasminogenemia

For **initial** authorization:
1. Member must be at least 11 months old; AND
2. Medication must be prescribed by or in consultation with a hematologist; AND
3. Member has a documented history of disease-related lesions and symptoms consistent with a diagnosis of hypoplasminogenemia; AND
4. Documentation of baseline plasminogen activity level ≤ 45%.
5. **Dosage allowed/Quantity limit:** 6.6 mg/kg body weight given intravenously every 2 to 4 days

If all the above requirements are met, the medication will be approved for 12 weeks.

For **reauthorization**:
Ryplazim will be reauthorized when chart notes show at least **ONE** of the following:

a) Absence of recurrent or new lesions;
b) Decrease in the lesion number and/or size;
c) Increase in trough plasminogen activity level by at least 10% from baseline.

If all the above requirements are met, the medication will be approved for an additional 12 months.

TRICARE Prime® Demo by CareSource Military & Veterans™ considers Ryplazim (plasminogen, human-tvmh) not medically necessary for the treatment of conditions that are not listed in this document. For any other indication, please refer to the Off-Label policy.

DATE	ACTION/DESCRIPTION
10/06/2021	Ryplazim policy creation
05/17/2024	Added reference (Shapiro, et al 2023); removed geneticist as prescriber option; added in consultation with for prescriber.

References:

1. Ryplazim [package insert]. Laval, Quebec, CA; Prometric Bioproduction, Inc.; 2021.
2. Shapiro, Amy D. et al. 'Plasminogen replacement therapy for the treatment of children and adults with congenital plasminogen deficiency. *Blood*. 2018 Mar 22;131(12):1301-1310
3. Shapiro AD, Nakar C, Parker JM, Thibaudeau K, Crea R, Sandset PM. Plasminogen, human-tvmh for the treatment of children and adults with plasminogen deficiency type 1. *Haemophilia*. 2023;29(6):1556-1564. doi:10.1111/hae.14849
4. Shapiro AD, et al. An international registry of patients with plasminogen deficiency (HISTORY). *Haematologica*. 2020;105(3):554-561

Effective date: 01/01/2026
Revised date: 05/17/2024