Ryplazim® (Plasminogen, Human-Tvmh)

Policy Number: CS2024D0070H
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Application

This Medical Benefit Drug Policy does not apply to the states listed below; refer to the state-specific policy/guideline, if noted:

State	Policy/Guideline
Indiana	Ryplazim® (Plasminogen, Human-Tvmh) (for Indiana Only)
Kansas	None
Louisiana	Ryplazim® (Plasminogen, Human-Tvmh) (for Louisiana Only)
Mississippi	Ryplazim® (Plasminogen, Human-Tvmh) (for Mississippi Only)
North Carolina	None
Ohio	Ryplazim® (Plasminogen, Human-Tvmh) (for Ohio Only)
Texas	Refer to drug specific criteria found within the Texas Medicaid Provider Procedures Manual

Coverage Rationale

Ryplazim® (plasminogen, human-tvmh) is proven and medically necessary for the treatment of plasminogen deficiency type 1 (hypoplasminogenemia) when the following criteria are met:[1-2]

- For **initial therapy**, **all** of the following:
  - Diagnosis of hypoplasminogenemia as measured by plasminogen activity level ≤ 45% of laboratory standard; **and**
  - Presence of clinical signs and symptoms of the disease (e.g., ligneous conjunctivitis, gingivitis, tonsillitis, abnormal wound healing, etc.); **and**
  - Prescribed by or in consultation with a hematologist; **and**
  - Dosing is in accordance with the U.S. Food and Drug Administration (FDA) approved labeling; **and**
  - Initial authorization will be for no more than 12 months
- For **continuation of therapy**, **all** of the following:
  - Patient has previously received treatment with Ryplazim® therapy; **and**

- Patient has experienced a positive clinical response to Ryplazim® therapy (e.g., improved (reduction) in lesion number/size, improvement in wound-healing, plasminogen activity trough level has increased by at least 10 percentage points from baseline, etc.); **and**
- Prescribed by or in consultation with a hematologist; **and**
- Dosing is in accordance with the U.S Food and Drug Administration (FDA) approved labeling; **and**
- Reauthorization will be for no more than 12 months

Ryplazim® is unproven and not medically necessary for the treatment of idiopathic pulmonary fibrosis.

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by federal, state, or contractual requirements and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

HCPCS Code	Description
J2998	Injection, plasminogen, human-tvmh, 1 mg

Diagnosis Code	Description
E88.02	Plasminogen deficiency

Background

Plasminogen is a naturally occurring protein synthesized by the liver. Plasminogen is converted to plasmin, which then leads to lysis of fibrin clots in the blood and/or on cell surfaces (wound healing, angiogenesis, tissue remodeling, etc.).

Plasminogen deficiency type 1, or hypoplasminogenemia, is a rare autosomal-recessive disorder of the fibrinolytic system. Deficiency of plasminogen levels cause abnormal extravascular accumulation or growth of fibrin-rich ligneous pseudomembranous lesions on mucous membranes throughout the body. Consequently, the most common clinical manifestation of plasminogen deficiency type 1 is ligneous conjunctivitis (LC), characterized by inflamed, woody growth on the conjunctival membranes which, if left untreated, may result in visual impairment or blindness. Replacement therapy may increase the plasma level of plasminogen, thereby allowing a temporary correction of the deficiency and reduction of extravascular fibrinous lesions.[2-4]

Clinical Evidence

The efficacy of plasminogen, human-tvmh in pediatric and adult patients with plasminogen deficiency type 1 was evaluated in RYPLAZIM trial 2, a single-arm, open-label clinical trial (n = 15). Enrolled patients, aged 4 to 42 years, had a baseline plasminogen activity level between < 5% and 45% of normal, and biallelic mutations in the *plasminogen (PLG)* gene. All patients received plasminogen, human-tvmh at a dose of 6.6 mg/kg administered every 2 to 4 days for 48 weeks, with a primary endpoint of achieving at least an increase of individual trough plasminogen activity by an absolute 10% above baseline. Secondary endpoint was establishment of overall rate of clinical success at 48 weeks, defined by patients with visible (sites mainly located in the eyes, nose, gums, hands, and feet) or measurable non-visible lesions (cervix, bronchus, colon, vagina, and uterus) achieving ≥ 50% improvement in lesion number/size, or functionality impact from baseline. Authors found that 78% of external lesions and 75% of internal lesions were resolved by week 48, with no recurrent or new external or internal lesions in any patient through week 48 (NCT02690714). [1-2]

U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

Ryplazim® (plasminogen, human-tvmh) is plasma-derived human plasminogen indicated for the treatment of patients with plasminogen deficiency type 1 (hypoplasminogenemia).[1]

References

1. Ryplazim® [package insert]. Rockville, MD: ProMetic BioTherapeutics, Inc.; November 2021.
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 Jan 10.
3. Tefs K, Gueorguieva M, Klammt J, et al. Molecular and clinical spectrum of type I plasminogen deficiency: A series of 50 patients. Blood. 2006 Nov 1;108(9):3021-6.
4. Schuster V, Hügle B, Tefs K. Plasminogen deficiency. J Thromb Haemost. 2007 Dec;5(12):2315-22.

Policy History/Revision Information

Date	Summary of Changes
04/01/2024	**Coverage Rationale** • Changed duration for initial authorization from "no more than ***6*** months" to "no more than ***12*** months" **Supporting Information** • Archived previous policy version CS2023D0070G

Instructions for Use

This Medical Benefit Drug Policy provides assistance in interpreting UnitedHealthcare standard benefit plans. When deciding coverage, the federal, state, or contractual requirements for benefit plan coverage must be referenced as the terms of the federal, state, or contractual requirements for benefit plan coverage may differ from the standard benefit plan. In the event of a conflict, the federal, state, or contractual requirements for benefit plan coverage govern. Before using this policy, please check the federal, state, or contractual requirements for benefit plan coverage. UnitedHealthcare reserves the right to modify its Policies and Guidelines as necessary. This Medical Benefit Drug Policy is provided for informational purposes. It does not constitute medical advice.

UnitedHealthcare may also use tools developed by third parties, such as the InterQual® criteria, to assist us in administering health benefits. The UnitedHealthcare Medical Benefit Drug Policies are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.