DRUG DETERMINATION POLICY

Title: DDP-53 Plasminogen Deficiency: Ryplazim

Effective Date: 4/26/23

Physicians Health Plan
PHP Insurance Company
PHP Service Company

Important Information - Please Read Before Using This Policy

The following policy applies to health benefit plans administered by PHP and may not be covered by all PHP plans. Please refer to the member's benefit document for specific coverage information. If there is a difference between this general information and the member's benefit document, the member's benefit document will be used to determine coverage. For example, a member's benefit document may contain a specific exclusion related to a topic addressed in a coverage policy.

Benefit determinations for individual requests require consideration of:

1. The terms of the applicable benefit document in effect on the date of service.
2. Any applicable laws and regulations.
3. Any relevant collateral source materials including coverage policies.
4. The specific facts of the particular situation.

Contact PHP Customer Service to discuss plan benefits more specifically.

1.0 Policy:

This policy describes the determination process for coverage of specific drugs.

This policy does not guarantee or approve benefits. Coverage depends on the specific benefit plan. Drug Determination Policies are not recommendations for treatment and should not be used as treatment guidelines.

2.0 Background or Purpose:

Ryplazim is a specialty drug indicated for the treatment of Plasminogen Deficiency type I by reducing pseudo-membrane lesions in the conjunctiva of the eyes, respiratory and central nervous system. These criteria were developed and implemented to ensure appropriate use for the intended diagnosis, if possible.

3.0 Clinical Determination Guidelines:

Document the following with chart notes:

I. Ryplazim intravenous (human plasminogen IV) [must meet all listed below]

A. Age: all ages

B. Prescriber: Ophthalmologist, Hematology/Oncology

C. Diagnosis and severity

1. Clinical features [must meet at least one listed below]

a. Pseudo-membrane formation in various organ systems

b. Impaired wound healing

c. First degree relative with plasminogen deficiency

2. Laboratory and genetic testing [must meet both listed below]

   a. Plasminogen activity: activity level below 45 percent (normal range 75 to 120 percent)

   b. Genetic testing: biallelic pathogenic variants in plasminogen

D. Other therapies: Only for patients that do not have access to plasminogen concentrate (eg. plasma, estrogen, immunosuppression)

E. Dosage regimen: Ryplazim intravenous (human plasminogen IV)

Initial Dosing*		**Maintenance Dosing**			
Plasminogen activity level from baseline*	Dose (mg/Kg)	Frequency (days)	Duration (weeks)	Assessment at week 12: have lesions resolved or stabilized	
< 10% increase	6.6	2	12	Yes: Continue every 2 days	No: Continue until improvement
≥10% to ≤ 20% increase		3		Yes: Continue every 3 days	No: increase dosing frequency to every 2 days
>20% increase		4		Yes: Continue every 4 days	No: increase dosing frequency at 1-day increments every 4-8 weeks
If lesions have not resolved by 12 weeks after titrating to a dosage frequency of every 2 days, a trough plasminogen level should be drawn					
Trough plasminogen activity level from baseline		Action			
≥10% increase		Consider other treatment options (e.g. surgical removal of lesions in addition to Ryplazim)			
<10% increase		Redraw trough to confirm and consider discontinuing			

**Draw Plasminogen activity level 72 hours after initial 6.6mg/kg dose*

F. Approval

1. Initial: three months

2. Reapproval: three to six months depending on maintenance dose assessment

4.0 Coding:

CODES AFFECTED				
Code	**Brand**	**Generic**	**Billing (1u)**	**Prior Approval Required**
J2998	Ryplazim	plasminogen human-tvmh	1mg	Yes

5.0 References, Citations & Resources:

1. Lexi comp Online® Lexi-Drugs®, Hudson, Ohio: Lexi-Comp, Inc.; Ryplazim accessed March 2023.
2. UpToDate Plasminogen deficiency https://www.uptodate.com/contents/plasminogen-deficiency?search=plasminogen%20deficiency&source=search_result&selectedTitle=1~27&usage_type=default&display_rank=1 accessed February 2022

6.0 Appendices:

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7.0 Revision History:

Original Effective Date: 05/05/2023

Next Review Date: 05/01/2024

Revision Date	Reason for Revision
3/22	Annual review, clarified policy instructions and formatting changes
2/23	Annual review, updated coding table, clarified dosing table

Appendix I: Patient Safety and Monitoring

Drug	Adverse Reactions	Monitoring	REMS
Ryplazim intravenous human plasminogen IV	• Gastrointestinal: Abdominal pain, bloating, constipation, gastric dilation, nausea, xerostomia • Hematologic & oncologic: Hemorrhage • Immunologic: Antibody development • Nervous system: Dizziness, fatigue, headache • Neuromuscular & skeletal: Arthralgia, back pain, limb pain	• Labs: Plasminogen activity level at baseline, 72 hours after initial dose and as clinically indicated. • Hematology/oncology: if coagulation disorder monitor for bleeding • Respiratory: if airway disease monitor for obstruction or hemoptysis	None