

HOPE IS IN SIGHT FOR PLASMINOGEN DEFICIENCY TYPE 1

 **Ryplazim**[®]
plasminogen, human-tvmh



Discover the
FIRST AND ONLY
FDA-approved
treatment for
plasminogen
deficiency type 1
(PLGD-1).

APPROVED USE

RYPLAZIM[®] (plasminogen, human-tvmh) is used for the treatment of patients with plasminogen deficiency type 1 (hypoplasminogenemia).

IMPORTANT SAFETY INFORMATION

Do not use RYPLAZIM if you are a patient with known hypersensitivity to plasminogen or other components of RYPLAZIM.

Please see complete Important Safety Information on page 11 and accompanying full Prescribing Information.

PLGD-1: a rare diagnosis with a clear path forward



What gives me hope is knowing that there's ongoing research and a growing focus on finding answers. I always believed that the solution was out there, and with RYPLAZIM®, it's finally here.

—Amy Steele

Caregiver for Regan,
her daughter with PLGD-1



1

Getting the correct diagnosis for PLGD-1 can be a long and difficult journey. But with RYPLAZIM, the **first and only FDA-approved treatment for PLGD-1**, hope is in sight.



PLGD-1 is genetic and can be inherited; if you have been diagnosed, your close relatives should be tested too.

IMPORTANT SAFETY INFORMATION, cont.

- Bleeding: Use of RYPLAZIM may lead to bleeding at disease-related lesion sites or worsen active bleeding not related to disease lesions. Discontinue RYPLAZIM if serious bleeding occurs. If you are treated at a healthcare provider's office or center, your healthcare provider will need to monitor you during the infusion and for 4 hours afterward, especially if you have

PLGD-1 essentials

Why plasminogen is important

- Plasminogen is a protein that breaks down blood clots and helps wounds heal. In PLGD-1, plasminogen levels are **too low** and the plasminogen that's present **doesn't work properly**.
- Without enough functioning plasminogen, **hard lesions** can form on the mucous membranes of the body (in the nose, mouth, lungs, and more).
- PLGD-1 most commonly appears with **lesions in the eye (ligneous conjunctivitis)**. It may initially look like pink eye, but won't improve with typical treatment and can develop into hard, thick lesions.
- PLGD-1 impacts **organs throughout the body**, both internal and external.

60% of RYPLAZIM clinical trial participants had lesions on multiple organs

Lesions due to PLGD-1



Symptoms to watch for:

- Chronic pink eye
- Chronic ear infections
- Hearing loss
- Lesions on the gums
- Hoarseness
- Loss of voice
- Chronic respiratory infections
- Impaired kidney function
- Kidney stones
- Ulcers
- Painful menstruation

IMPORTANT SAFETY INFORMATION, cont.

a predisposition to bleeding or are taking anticoagulants, antiplatelet drugs, or other medications that may interfere with normal coagulation. If you infuse RYPLAZIM at home, you or your caregiver must also monitor you during and for 4 hours after the infusion under the same circumstances.

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How does RYPLAZIM® work?



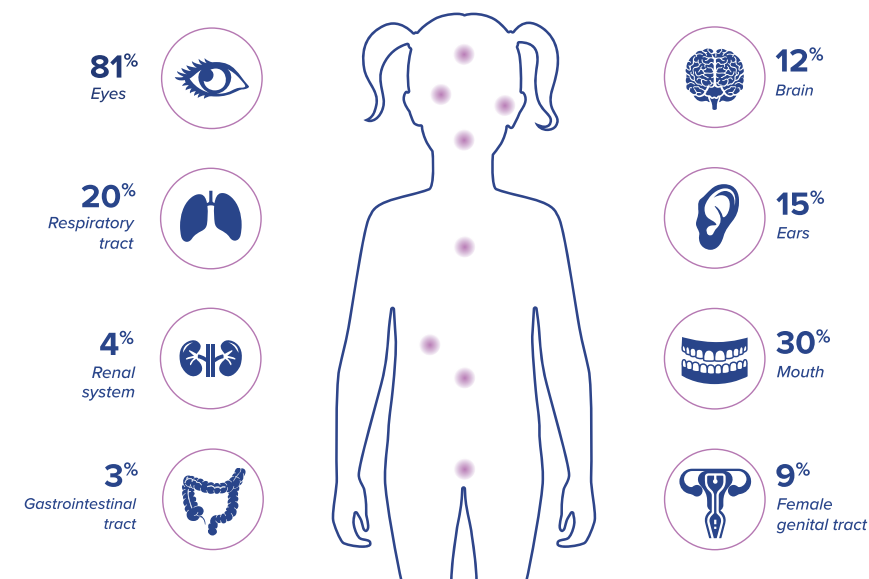
Boosts
plasminogen
levels



Reduces
or resolves
lesions

Systemic treatment is needed because PLGD-1 can affect multiple organs throughout the body

Frequency of lesions on parts of the body:



IMPORTANT SAFETY INFORMATION, cont.

- **Tissue Sloughing:** If you have mucosal lesions in your respiratory tract, especially the tracheobronchial tree, and are treated with RYPLAZIM, respiratory distress may occur due to tissue sloughing. Please monitor appropriately.
- **Transmission of Infectious Agents:** RYPLAZIM is made from human plasma and therefore carries a risk of transmitting infectious agents, e.g., viruses, the variant Creutzfeldt-Jakob disease (vCJD) agent, and theoretically, the Creutzfeldt-Jakob Disease (CJD) agent. You should consult with your healthcare provider if you have any questions or concerns.

Get to know RYPLAZIM



The only FDA-approved treatment for PLGD-1



RYPLAZIM is the only prescription medicine that can temporarily replace your missing plasminogen



Contains a highly concentrated form of human plasminogen, a vital protein that helps break down blood clots and heal wounds



Maintaining proper dosing helps control lesions.

Because RYPLAZIM only restores plasminogen for a short time, levels can drop between infusions. This means **regular infusions are key** to keeping lesions under control.

Treatment with RYPLAZIM

BEFORE



DURING



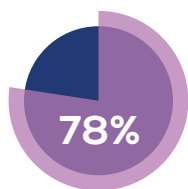
IMPORTANT SAFETY INFORMATION, cont.

- **Hypersensitivity Reactions:** Hypersensitivity reactions, including anaphylaxis, may occur with RYPLAZIM. Immediately report any of the following signs or symptoms of an allergic reaction to your healthcare provider: swelling of the throat, tightness of the chest, low blood pressure, rash, nausea, vomiting, a tingling or pricking sensation, restlessness, wheezing or shortness of breath.

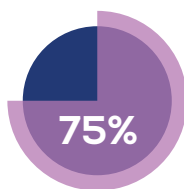
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RYPLAZIM® clinical success*

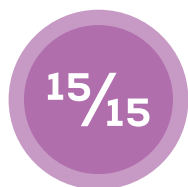
15 people with PLGD-1 received RYPLAZIM over the course of 48 weeks



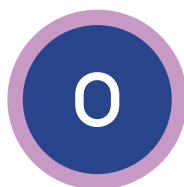
of **external lesions** resolved completely



of **internal lesions** resolved completely



ALL patients saw improvement in visible or other measurable lesions*



NO new or recurrent lesions in any patient through week 48

*Clinical success defined as a decrease in lesion number or size by at least half.

RYPLAZIM controls lesions as long as you stay on treatment

In a separate long-term study...

- 12 individuals treated with RYPLAZIM were observed for **~5 years**.
- No new or recurrent lesions developed in those with **uninterrupted treatment**.
- Upon reduced or missed doses, 4 of 12 people had lesions come back that rapidly improved after resuming recommended treatment.



Dive deeper into RYPLAZIM safety and efficacy

IMPORTANT SAFETY INFORMATION, cont.

Neutralizing Antibodies: Antibodies neutralizing plasminogen (also known as inhibitors) which can make the product less effective or ineffective, may form with the use of RYPLAZIM, although they were not observed in clinical trials. If clinical efficacy is not maintained (e.g., development of new or recurrent lesions), your healthcare provider will determine low levels of plasminogen in your plasma.



Riley's PLGD-1 journey

Stories help us make sense
of the world, and can help
us understand PLGD-1.

Early symptoms

Riley first noticed problems with her eyes. She had lesions on the inside of her eyelids that made her eyes red, sore, and swollen. She was repeatedly treated for pink eye, but her symptoms kept coming back. After many unsuccessful lesion removals and a ligneous conjunctivitis diagnosis, her ophthalmologist referred her to a geneticist where Riley was ultimately diagnosed with PLGD-1—a condition that impacts multiple parts of the body.

Finding lesions on other parts of the body

In addition to the eye lesions, Riley experienced multiple UTIs, acute kidney disease, and suffered from an episode of dangerously high blood pressure—symptoms that could be linked to a deeper issue. Since PLGD-1 impacts internal and external organs, not all lesions are visible and symptoms are often mistaken for those of more common conditions.

Treatment with RYPLAZIM

Before 2021, there were no FDA-approved treatments for PLGD-1. Now, thanks to RYPLAZIM, Riley infuses at home on her own terms. Because vein access was a challenge, a port was placed to make treatment easier. Riley described getting her port as “no big deal.” With twice-weekly infusions, RYPLAZIM controls lesions inside and outside her body—giving her the freedom to do what she loves. For Riley, that means swimming, playing softball, and traveling.



Scan to explore patient video stories.

**Please see complete Important Safety Information on page 11
and accompanying full Prescribing Information.**

Possible side effects

Common side effects of RYPLAZIM®

Abdominal pain	3 (16%)	Constipation	2 (11%)
Gastric dilation (bloating/feeling bloated)	3 (16%)	Dry mouth	2 (11%)
Nausea	3 (16%)	Headache	2 (11%)
Fatigue	3 (16%)	Dizziness	2 (11%)
Pain in extremity	3 (16%)	Arthralgia	2 (11%)
Hemorrhage	3 (16%)	Back pain	2 (11%)

(reported as number of people out of 19 in clinical studies)

Tell your healthcare provider if you:

- Have had other medical problems, particularly bleeding problems.
- Use any medicine, including prescription and over-the-counter drugs, supplements, or herbal remedies.
- Have had reactions to any medications.
- Are pregnant or planning to become pregnant. It is not known whether RYPLAZIM may affect your pregnancy or unborn baby.
- Are breastfeeding or are planning to breastfeed. It is not known whether RYPLAZIM affects milk production, passes into breast milk, or may have an effect on your baby.

IMPORTANT SAFETY INFORMATION, cont.

Laboratory Abnormalities: Due to the activity of RYPLAZIM, you may have elevated blood levels of D-dimer that may interfere with screening for venous thromboembolism (VTE) using D-dimer levels.

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RYPLAZIM is given by intravenous (IV) infusion



You have options for where you can receive your treatment.*



By yourself
if you have been
taught how to
infuse RYPLAZIM



By a caregiver
at home



By a nurse
at a healthcare
facility, like a
hospital or a clinic



Specialty pharmacy support helps manage product and infusion supply shipments for people who have been approved for at-home infusions. Your healthcare provider or specialty pharmacy will help set up the best care plan for your needs.

*If you have mucosal lesions in your respiratory tract, especially the tracheobronchial tree, and are treated with RYPLAZIM, respiratory distress may occur due to tissue sloughing. Tissue sloughing is an expected response to RYPLAZIM. For this reason, it is recommended that your first infusion occur in a clinical setting to monitor for respiratory distress.

RYPLAZIM support through Kedrion Biopharma



Dedicated Treatment Support

is provided by a Kedrion Nurse Educator, who will work with you at every point along your treatment journey.

Connect with a nurse educator.



The RYPLAZIM Co-Pay Assistance Program

may offer financial support to help with your deductible, co-pay, and/or coinsurance for RYPLAZIM. This is coordinated with Kedrion through your specialty pharmacy. Explore savings at ryplazim.com/support

Community support

Get to know others impacted
by PLGD-1

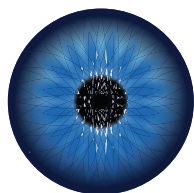
PLASMINOGEN DEFICIENCY

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FOUNDATION



Connect with the Plasminogen Deficiency Foundation

- To learn more about PLGD-1, connect with other patients and caregivers, locate a disease specialist, find a medical home, or access resources, visit **plasminogendeficiency.org**



PLGD
Insight
Forum



Join the patient and caregiver PLGD-1 Insight Forum

- Learn more about an in-person seminar where families can engage in discussion regarding their PLGD-1 journey, stories, and insights at **ryplazim.com/community**

IMPORTANT SAFETY INFORMATION, cont.

- Adverse Reactions: The most frequent (incidence $\geq 10\%$) adverse reactions in clinical trials were abdominal pain, bloating, nausea, fatigue, extremity pain, hemorrhage, constipation, dry mouth, headache, dizziness, arthralgia, and back pain.

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**You may report side effects to +1(855)-353-7466 and
US_Medicalinfo@kedrion.com or FDA at 1-800-FDA-1088
or www.fda.gov/medwatch.**

Please see accompanying full Prescribing Information.



**EMPOWERED
TO FACE
THE FUTURE**

Learn more at
RYPLAZIM.com



Not actual patient.



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