RECONSTITUTION & ADMINISTRATION

Ryplazim®
plasminogen, human-tvmh

DOSING

CALCULATE THE DOSE

Infusion volume (mL) = Body weight (kg) x 1.2

CALCULATE THE NUMBER OF VIALS

Number of vials = Infusion volume (mL) x 0.08

See Section 2.1 of the Prescribing Information for more details.

Always use a clean surface and wash hands before beginning.

Do not mix or administer with other medications.

INDICATIONS AND USAGE

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

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS:

RYPLAZIM is contraindicated in patients with known hypersensitivity to plasminogen or other components of RYPLAZIM.

Please see additional Important Safety Information on back and accompanying full Prescribing Information.

RECONSTITUTION OF RYPLAZIM®

EQUIPMENT NEEDED

NOT TO SCALE

One 20-mL syringe per vial of RYPLAZIM
&
One (or more) administration syringe(s)

See step 9 for more details

Alcohol wipes

Antiseptic surface wipes

Sterile water for injection (SWFI)

18- to 22-gauge needles for reconstitution and administration

INSTRUCTIONS

Check the expiration date of each vial of RYPLAZIM. Be sure to read all instructions completely before beginning.

1. Allow the vial to remain at room temperature for at least 15 minutes before reconstitution.
2. Remove the caps from the RYPLAZIM and SWFI vials to expose the central portion of the rubber stoppers.
3. Clean the surface of the rubber stoppers with alcohol wipes and allow to dry. **Do not blow on it.**
4. Using a 20-mL sterile syringe with a sterile 18- to 22-gauge needle, withdraw 12.5 mL of SWFI for each vial of RYPLAZIM. Ensure air bubbles have been removed.
5. Using the same needle and syringe, gently and slowly add the 12.5 mL of SWFI to the RYPLAZIM vial, directing the syringe down toward the side of the RYPLAZIM vial to prevent foaming. This should resemble a stream along the side of the vial. Discard the used syringe and needle properly in a sharps container.
6. Gently swirl the vial by rotating it slowly to ensure that the lyophilized powder dissolves fully. Do not shake the vial. RYPLAZIM should fully dissolve within 10 minutes. Discard the vial if RYPLAZIM is not fully dissolved after 10 minutes.
7. Observe the reconstituted vials; the solution should be colorless and clear to slightly opalescent. Discard the vial if discoloration or particulate matter is observed.
8. Repeat steps 1-7 to reconstitute each additional vial of RYPLAZIM.
9. Using a new syringe and new 22g sterile needle*, slowly draw up the full 12.5-mL volume of the RYPLAZIM vial. The same syringe and needle can be used to draw up RYPLAZIM from multiple vials.

**Note: A 30-mL syringe can hold up to 2 vials of reconstituted RYPLAZIM and a 60-mL syringe can hold up to 4 vials.*

Use immediately or within 3 hours after reconstitution.

Please see Important Safety Information on back and accompanying full Prescribing Information.

ADMINISTRATION OF RYPLAZIM®

Ryplazim® plasminogen, human-tvmh

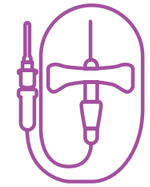
ADDITIONAL EQUIPMENT NEEDED

NOT TO SCALE

One 20-mL syringe

One syringe disc filter per infusion (Baxter Supor® 5 micron Syringe Filter or equivalent)

10 mL normal saline



Butterfly needle of sterile infusion set

22-gauge needle

Medical tape

Sterile gauze pad

Band-aid

INSTRUCTIONS

For intravenous use only through a syringe disc filter. Administer RYPLAZIM through a separate infusion line—it should not be administered with other medications.

1. One filter is needed per infusion.
2. Inspect the solution of RYPLAZIM in the syringe. Do not use if discoloration or particulate matter is observed.
3. Draw 10 mL of normal saline into a different syringe. Push the plunger down to remove any air bubbles.
4. Attach a syringe disc filter to the syringe of normal saline. Attach the infusion tubing with the butterfly needle to the other side of the filter.
5. Inject the normal saline through the syringe disc filter and butterfly needle tubing to remove any air bubbles.
6. Remove the normal saline syringe. **The syringe disc filter must remain attached to the tubing,** as it is required for administration of RYPLAZIM. Discard the normal saline syringe in a sharps container.
7. Attach the administration syringe containing RYPLAZIM to the syringe disc filter that is connected to the butterfly needle tubing.
8. Choose a peripheral vein (e.g., antecubital or dorsum of hand). Clean the injection site with a sterile alcohol wipe and allow to dry. **Do not blow on it.**
9. Insert the butterfly infusion set needle in the peripheral vein, and tape in place.
10. Infuse the total dose of RYPLAZIM **slowly over 10-30 minutes** (approximately 5 mL/min). Using a timer (e.g., watch or clock), push the plunger of the syringe approximately 1 mL every 12 seconds.
11. Discard any open vials, unused solution, and administration equipment in a sharps container following administration.

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INDICATIONS AND USAGE

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IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS:

- Bleeding: RYPLAZIM administration may lead to bleeding at active mucosal disease-related lesion sites or worsen active bleeding not related to disease lesions. Discontinue RYPLAZIM if serious bleeding occurs. Monitor patients during and for 4 hours after infusion when administering RYPLAZIM to patients with bleeding diatheses and patients taking anticoagulants, antiplatelet drugs, or other agents which may interfere with normal coagulation.
- Tissue Sloughing: Respiratory distress due to tissue sloughing may occur in patients with mucosal lesions in the tracheobronchial tree following RYPLAZIM administration. 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.
- Hypersensitivity Reactions: Hypersensitivity reactions, including anaphylaxis, may occur with RYPLAZIM. If symptoms occur, discontinue RYPLAZIM and administer appropriate treatment.
- Neutralizing Antibodies: Neutralizing antibodies (inhibitors) may develop, although they were not observed in clinical trials. If clinical efficacy is not maintained (e.g., development of new or recurrent lesions), determine plasminogen activity trough levels in plasma.
- Laboratory Abnormalities: Patients receiving RYPLAZIM may have elevated blood levels of D-dimer. D-dimer levels will lack interpretability in patients being screened for venous thromboembolism (VTE).

ADVERSE REACTIONS:

The most frequent (incidence ≥ 10%) adverse reactions in clinical trials were abdominal pain, bloating, nausea, fatigue, extremity pain, hemorrhage, constipation, dry mouth, headache, dizziness, arthralgia, and back pain.

To report SUSPECTED ADVERSE REACTIONS, contact KEDRION at 1-855-427-6378 or the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch

Reference: 1. RYPLAZIM [prescribing information]. Fort Lee, NJ. Kedrion Biopharma Inc. 2021.

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