RYTELO™
(imetelstat) for Injection 47 mg 188 mg

Reconstitution and Administration Guide

Instructions for healthcare professionals

INDICATION

RYTELO™ (imetelstat) is indicated for the treatment of adult patients with low- to intermediate-1 risk myelodysplastic syndromes (MDS) with transfusion-dependent anemia requiring 4 or more red blood cell units over 8 weeks who have not responded to or have lost response to or are ineligible for erythropoiesis-stimulating agents (ESA).

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Thrombocytopenia

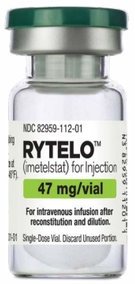
RYTELO can cause thrombocytopenia based on laboratory values. In the clinical trial, new or worsening Grade 3 or 4 decreased platelets occurred in 65% of patients with MDS treated with RYTELO.

Monitor patients with thrombocytopenia for bleeding. Monitor complete blood cell counts prior to initiation of RYTELO, weekly for the first two cycles, prior to each cycle thereafter, and as clinically indicated. Administer platelet transfusions as appropriate. Delay the next cycle and resume at the same or reduced dose, or discontinue as recommended.

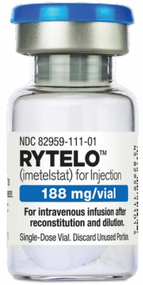
Please see additional Important Safety Information on pages 10-11 and full Prescribing Information and Medication Guide.

RYTELO is supplied in 2 strengths in single-dose vials for reconstitution[1]

RYTELO for injection is a white to off-white or slightly yellow lyophilized powder supplied in a single-dose vial for reconstitution.



47 mg
NDC 82959-112-01



188 mg
NDC 82959-111-01

Instructions for storing RYTELO[1]

Store vials refrigerated
at 2°C to 8°C (36°F-46°F)
in original carton

DO NOT freeze

RYTELO **does not contain** a preservative

Please see Important Safety Information on pages 10-11 and full Prescribing Information and Medication Guide.

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Important considerations for administering RYTELO[1]

Premedications

To prevent or reduce potential infusion-related reactions, patients should receive both of the following medications, or equivalents, either intravenously or orally, at least 30 minutes prior to dosing with RYTELO.

diphenhydramine or equivalent (25 to 50 mg) + **hydrocortisone** or equivalent (100 to 200 mg)

Administer RYTELO

- **Administer the diluted** RYTELO solution by IV infusion only, **over a period of 2 hours, every 4 weeks**

⚠ **DO NOT** administer RYTELO as an IV push or bolus injection

RYTELO is administered as an intravenous (IV) infusion over 2 hours every 4 weeks[1]

Monitor patients

- **Monitor patients** for adverse reactions for **at least 1 hour** after the infusion has been completed
- **Monitor complete blood cell counts prior to administration of RYTELO**, weekly for the first 2 cycles, prior to each cycle thereafter, and as clinically indicated
- **Monitor liver function tests prior to administration of RYTELO**, weekly for the first cycle, prior to each cycle thereafter, and as clinically indicated

For complete dosing information, please see the RYTELO Prescribing Information.

Reconstitution volumes[1,*]

Strength	Volume of 0.9% Sodium Chloride Injection for reconstitution per vial	Final concentration of reconstituted solution per vial	Deliverable volume per vial
47 mg	1.8 mL	31.4 mg/mL[†]	1.5 mL
188 mg	6.3 mL	31.4 mg/mL[†]	6.0 mL

- **Use aseptic technique** to prepare RYTELO

*Recommended to use the appropriate combination of vial strengths to most closely match the intended dose based on the patient's weight.
[†]Each vial contains an overfill to account for loss of liquid during preparation and extraction of the reconstituted solution, resulting in the final concentration.

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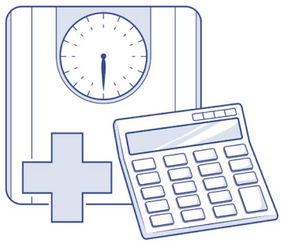
Instructions for reconstituting RYTELO[1]



Step 1

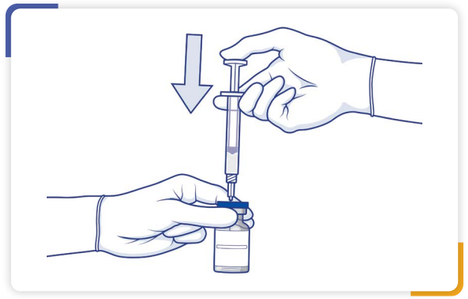
Calculate the dose of RYTELO needed based on the patient's body weight (kg).

Step 2

Determine the number of RYTELO vials needed to achieve the required dose (total mg). More than one vial may be needed to achieve a full dose.

Step 3

Remove the RYTELO vials from the refrigerator and allow the vials to sit for 10 to 15 minutes (not to exceed 30 minutes) to adjust to room temperature, 20°C to 25°C (68°F-77°F) before use.



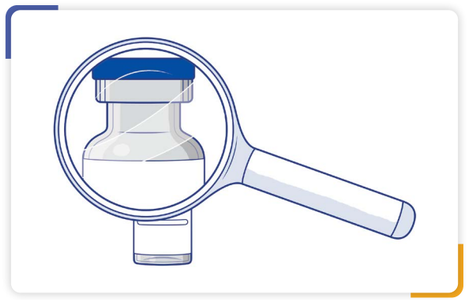
Step 4

Reconstitute each vial of RYTELO **with the volume of 0.9% Sodium Chloride Injection** required for the given vial size *(see calculator on page 5)* directly onto the lyophilized powder to obtain a concentration of 31.4 mg/mL of imetelstat.

Step 5

Swirl each vial gently to avoid foaming until the powder is fully reconstituted (not to exceed 15 minutes).

⚠ **DO NOT shake.**



Step 6

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. The reconstituted solution in each vial should appear as a clear to slightly hazy solution and be essentially free of visible contaminants, particles, and/or particulates.

⚠ **DO NOT** use if discoloration or particulate matter is present.

Use the reconstituted solution immediately.

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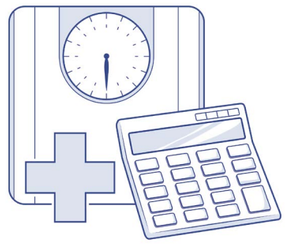
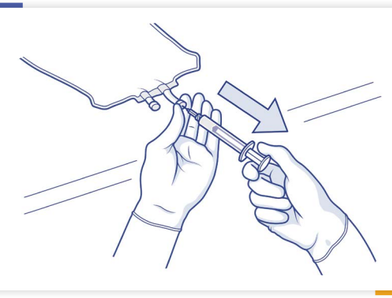
Instructions for diluting RYTELO[1]



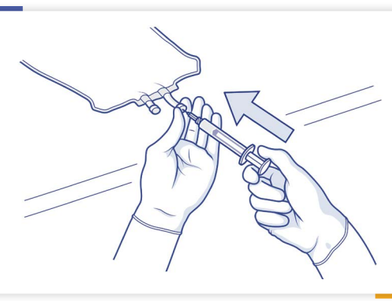
Step 1

Calculate the required volume of the reconstituted RYTELO solution needed to obtain the appropriate dose according to the patient's body weight.



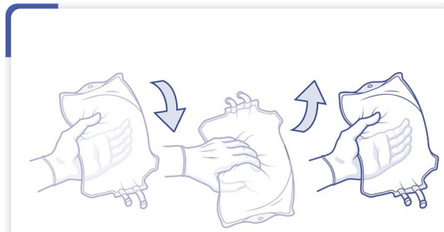
Step 2

Withdraw a volume equal to the required reconstituted RYTELO solution from a 500 mL infusion bag of **0.9% Sodium Chloride Injection** and discard it.



Step 3

Add the required volume of reconstituted RYTELO solution into the infusion bag so that the total final volume of RYTELO solution in the bag is approximately 500 mL. Discard any unused portion of the reconstituted solution remaining in each vial.



Step 4

Gently invert the infusion bag at least 5 times to ensure that the reconstituted RYTELO is well mixed. Do not shake the infusion bag prior to administration.

Storing diluted solution[1]

- If not used immediately, ensure that the diluted solution for infusion is used within the total time frames specified below, according to storage temperature:

When stored at room temperature, 20°C to 25°C (68°F-77°F):

- The **total time** from the reconstitution of RYTELO to completion of IV infusion **should not exceed 18 hours** from the time of reconstitution

When stored in refrigerator, 2°C to 8°C (36°F-46°F):

- The **total time** from the reconstitution of RYTELO to completion of IV infusion **should not exceed 48 hours** from the time of reconstitution

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Important Safety Information

WARNINGS AND PRECAUTIONS

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Monitor patients with thrombocytopenia for bleeding. Monitor complete blood cell counts prior to initiation of RYTELO, weekly for the first two cycles, prior to each cycle thereafter, and as clinically indicated. Administer platelet transfusions as appropriate. Delay the next cycle and resume at the same or reduced dose, or discontinue as recommended.

Neutropenia

RYTELO can cause neutropenia based on laboratory values. In the clinical trial, new or worsening Grade 3 or 4 decreased neutrophils occurred in 72% of patients with MDS treated with RYTELO.

Monitor patients with Grade 3 or 4 neutropenia for infections, including sepsis. Monitor complete blood cell counts prior to initiation of RYTELO, weekly for the first two cycles, prior to each cycle thereafter, and as clinically indicated. Administer growth factors and anti-infective therapies for treatment or prophylaxis as appropriate. Delay the next cycle and resume at the same or reduced dose, or discontinue as recommended.

Infusion-Related Reactions

RYTELO can cause infusion-related reactions. In the clinical trial, infusion-related reactions occurred in 8% of patients with MDS treated with RYTELO; Grade 3 or 4 infusion-related reactions occurred in 1.7%, including hypertensive crisis (0.8%). The most common infusion-related reaction was headache (4.2%). Infusion-related reactions usually occur during or shortly after the end of the infusion.

Premedicate patients at least 30 minutes prior to infusion with diphenhydramine and hydrocortisone as recommended and monitor patients for one hour following the infusion as recommended. Manage symptoms of infusion-related reactions with supportive care and infusion interruptions, decrease infusion rate, or permanently discontinue as recommended.

Embryo-Fetal Toxicity

RYTELO can cause embryo-fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with RYTELO and for 1 week after the last dose.

IMPORTANT SAFETY INFORMATION (cont'd)

ADVERSE REACTIONS

Serious adverse reactions occurred in 32% of patients who received RYTELO. Serious adverse reactions in >2% of patients included sepsis (4.2%), fracture (3.4%), cardiac failure (2.5%), and hemorrhage (2.5%). Fatal adverse reactions occurred in 0.8% of patients who received RYTELO, including sepsis (0.8%).

Most common adverse reactions (≥10% with a difference between arms of >5% compared to placebo), including laboratory abnormalities, were decreased platelets, decreased white blood cells, decreased neutrophils, increased AST, increased alkaline phosphatase, increased ALT, fatigue, prolonged partial thromboplastin time, arthralgia/myalgia, COVID-19 infections, and headache.

Please see full Prescribing Information and Medication Guide.

A patient support program providing access information for RYTELO

REACH4 RYTELO™

Learn more at RYTELOHCP.com

For patient support resources, click, call, or email
1-844-4RYTELO | support@reach4rytelo.com

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Reference: 1. RYTELO. Prescribing information. Geron Corp.; 2024.

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