RYTELO™ (imetelstat) for Injection 47 mg 188 mg

NAVIGATING PAYER RESTRICTIONS

This resource describes relevant considerations for navigating coverage and is for informational purposes only. It is always the provider's responsibility to determine details specific to individual patients' insurance plans and to submit true and correct claims for the products and services rendered. Providers should contact third-party payers for specific information on their coding, coverage, payment policies, and fee schedules. Geron and its agents make no guarantee regarding reimbursement for any service or item. **This resource is not intended as reimbursement advice, legal advice, medical advice, or a substitute for a provider's independent professional judgment.**

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 throughout and full Prescribing Information, including Medication Guide.

Navigating Coverage and Reimbursement for RYTELO to Support Patient Access

Overview

Commercial and government payers all have different coverage and payment policies for medications and services. Your office or facility should check directly with the patient's payer(s) to verify specific coding and billing requirements. Coverage and reimbursement for RYTELO may vary based on the type of payer coverage your patients have, as well as the site at which the medication is administered.

RYTELO is administered as an intravenous (IV) infusion. IV medications are usually managed under the patient's medical benefit. A payer may create a medical policy to provide guidelines outlining specific coverage requirements that must be met before it will pay for a medication. An example of this would be defining appropriate use or appropriate patient-selection criteria in accordance with a medication's Prescribing Information.

Each insurance plan's medical policy may vary. Be sure to check the patient's individual insurance plan for its medical policy coverage for RYTELO.

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IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

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.

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Different Types of Insurance Coverage for RYTELO

Benefits Investigation

Understanding a patient's coverage for RYTELO begins with a thorough benefits investigation to determine key clinical and coverage criteria applicable to each individual patient. A benefits investigation verifies a patient's insurance plan coverage and identifies any restrictions and patient cost-sharing responsibilities. If RYTELO is included in a payer pathway, a PA may not be necessary.

For more information about conducting a benefits investigation, review the **Benefits Investigation Guide**.

REACH4RYTELO can provide benefits investigation support.
Call REACH4RYTELO at **1-844-4RYTELO (1-844-479-8356),**
Monday through Friday, from 8:00 AM to 8:00 PM ET.[a]

Original Medicare

Original Medicare, also known as Medicare fee-for-service, includes Parts A and B. Infused medications are covered under Part B, which reimburses outpatient physician services, including medication administration, based on the Medicare physician-fee schedule.[1] Physician-administered medications are typically covered under Part B and are based on the drug's calculated ASP, plus six percent (this payment is sometimes reduced through a process called sequestration).[1,2] Medicare pays for 80% of the allowed charges for a medication and its administration, with the patient responsible for some or all of the remaining 20% coinsurance.[3] Patients with Medical Supplemental Insurance may be able to use that to cover their coinsurance and any other OOP costs. See below for more information on Medicare Supplemental Insurance.

In the absence of an NCD from CMS, local MACs determine coverage for a medication. MACs may implement specific billing and utilization guidelines and/or coverage criteria through LCDs.

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[a]All programs provided through REACH4RYTELO are subject to eligibility requirements. Geron reserves the right to modify or discontinue REACH4RYTELO at any time without notice.

ASP=average sales price; CMS=Centers for Medicare and Medicaid Services; LCD=local coverage determination; MAC=Medicare Administrative Contractor; NCD=national coverage determination; OOP=out of pocket; PA=prior authorization.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

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.

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Different Types of Insurance Coverage for RYTELO (cont'd)

Commercial and Medicare Advantage (Part C)

For patients with commercial insurance, including Medicare Advantage, each payer will have its own policy benefit dictating coverage and reimbursement for RYTELO and its associated costs. Before treating a patient with RYTELO, it is advisable to conduct a benefits investigation.

Commercial insurance plans, including Medicare Advantage, may not have a medical coverage policy in place for RYTELO. In this case, if your request is denied, you will need to thoroughly read the information or response provided by the insurance plan and submit a PA, medical exception request, or appeal with your rationale for the medication to be covered for this patient. Providing supporting information as a part of a medical exception request or appeal can help streamline the process. This may include published, peer-reviewed journal articles, CMS-recognized compendia if available, and the FDA approval letter.

Medicare Supplemental Insurance

Medicare Supplemental Insurance, also known as Medigap, helps pay some of the patient OOP costs that Original Medicare does not (eg, copays, coinsurance, and deductibles). Medigap policies are sold by private insurance companies.[1] A benefits investigation can help determine if your patient has a Medigap policy that may cover costs not covered by Original Medicare.

Medicaid

Medicaid coverage and reimbursement information varies by state, is updated quarterly, and can be found on the **Medicaid.gov** website.[4]

Consult with your local MAC regarding LCD guidelines for infusion drugs with a Not Otherwise Classified code. A letter of medical necessity may be required.

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FDA=US Food and Drug Administration.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

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.

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%).

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Different Types of Insurance Coverage for RYTELO (cont'd)

Dual-eligible (Medicare and Medicaid)

You may have patients who are dual-eligible beneficiaries, meaning they are enrolled in both Medicare and Medicaid; specifically, they are enrolled in Medicare Part A and/or Part B and receive full benefits and/or assistance with Medicare premiums or cost-sharing through the Medicare Savings Program. For dual-eligible patients, Medicaid may cover medical costs in the absence of Medicare coverage.[5] Conducting a comprehensive benefits investigation for both Medicare and Medicaid coverage will assist in determining your patient's coverage.

Coordination of Benefits

In the case of multiple payers, your benefits investigation must establish which payer is primary, which is secondary, and, if applicable, which is tertiary.

Continuing RYTELO When Insurance Changes

It is important to track and understand changes in your patient's health insurance, including primary and secondary payers.

- Patients may transition to Medicare from Medicaid, making Medicare the primary payer and Medicaid the secondary payer.
- Patients may change health insurance during treatment, which may require a PA from a different insurance plan.
- Insurance claims submitted to the wrong primary payer will likely be rejected and will need to be resubmitted to the correct payer.

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ALT=aminotransferase.

IMPORTANT SAFETY INFORMATION (cont'd)

ADVERSE REACTIONS (cont'd)

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.

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Prior Authorization (PA) for RYTELO

After completing the benefits investigation, your practice or facility may need to obtain prior approval from an insurance plan before RYTELO is covered for your patient. This request for approval is known as a PA, precertification, or coverage determination. If a benefits investigation determines a plan has a restriction in place for RYTELO, you may proactively include the necessary documentation to request an exception upon submission of the PA request.

PAs are common for medications such as RYTELO, because they enable insurance plans to ensure medications are being used by appropriate patients only. After 6 to 12 months, some insurance plans may require a PA reauthorization, also known as a recertification, for your patient to continue taking RYTELO.

When requesting a PA, it is important to understand that each payer has different requirements with which your practice or facility must become familiar. With a PA, the payer requires approval of the coverage of a medication or treatment before it is administered.

Commercial plans, including Medicare Advantage, may not have a medical coverage policy in place for RYTELO. In this case, if your request is denied, you will need to thoroughly read the information or response provided by the insurance plan and submit a medical exception request or an appeal with your rationale for the medication to be covered for this patient. Providing supporting information as a part of the medical exception request or appeal can help streamline the process. This may include published, peer-reviewed journal articles, CMS-recognized compendia if available, and the FDA approval letter.

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IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

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PA for RYTELO (cont'd)

Step 1: Complete the PA Request

Completing the following steps may help prevent your patient's PA request from being denied due to a preventable error.

- ☐ Ensure the proper form is being utilized and submitted. Forms may vary based on insurance plan.
- ☐ Include a letter of medical necessity, if needed, to strengthen the request.
- ☐ Refer to pages 13-14 for more information on letters of medical necessity.
- ☐ Prepare supplemental documentation to support the PA request. Each insurance plan may require different information, so it is essential to identify the plan-specific documents required, which may include
  - peer-reviewed journal articles on the clinical trials supporting the use of RYTELO
  - CMS-recognized compendia
  - letter of approval for RYTELO from the FDA
  - medication history and relevant medical history, such as evidence of RBC transfusion dependence and other prior treatments
  - RYTELO Prescribing Information

The PA process timeline may vary based on each patient's insurance plan. If you have questions about how long the insurance approval process is taking, contact your patient's insurance plan directly.

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RBC=red blood cell.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Neutropenia

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Sample Prior Authorization Form

The below is provided only as an example. Each provider is responsible for submission of complete and accurate information to payers. Example information provided does not provide a guarantee of reimbursement.

Filling out a PA form

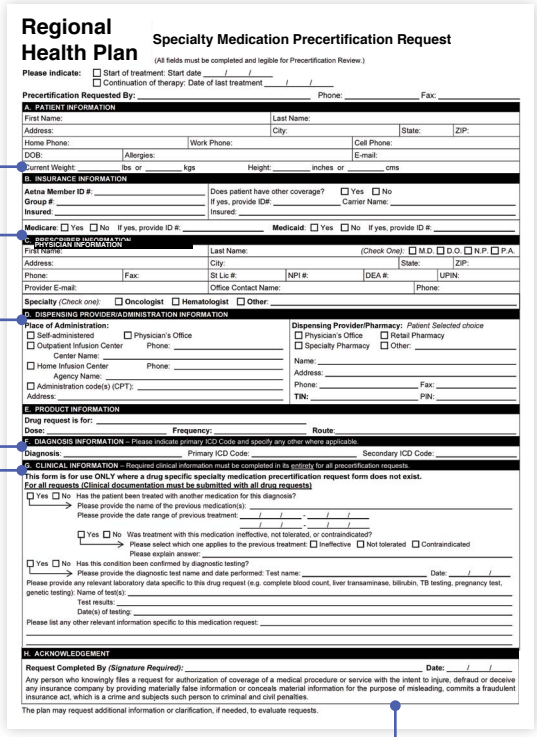
Patient and insurance information: List the patient's name exactly as it appears on the insurance card, and provide all relevant information.

Physician information: Fill in the prescribing information, diagnosis, prior medications used, and RBC transfusion history.

Dispensing provider/administration information: For place of administration, select the facility type. For the dispensing provider/pharmacy section, indicate how RYTELO will be obtained (eg, specialty distributor, specialty pharmacy, etc).

Diagnosis and medication information: Use a detailed diagnosis (as well as *ICD-10-CM* code). Enter the medication name, dosage, and NDC number. Note HCPCS code if required. See the **Billing and Coding Guide** for more information.

Clinical information and patient treatment history: Provide a detailed explanation describing why RYTELO is medically necessary. List relevant medications and RBC transfusion history. Review the patient's benefits investigation. If the treatment is outside of a health plan's policy, you may need to prepare additional documentation and a letter of medical necessity.



Regional Health Plan

Specialty Medication Precertification Request

(All fields must be completed and legible for Precertification Review.)

Please indicate: ☐ Start of treatment: Start date ___/___/___
☐ Continuation of therapy: Date of last treatment ___/___/___

Precertification Requested By: _____ Phone: _____ Fax: _____

A. PATIENT INFORMATION

First Name: | Last Name:
Address: | City: | State: | ZIP:
Home Phone: | Work Phone: | Cell Phone:
DOB: | Allergies: | E-mail:
Current Weight: _____ lbs or _____ kgs Height: _____ inches or _____ cms

B. INSURANCE INFORMATION

Aetna Member ID #: _____ Does patient have other coverage? ☐ Yes ☐ No
Group #: _____ If yes, provide ID#: _____ Carrier Name: _____
Insured: _____

Medicare: ☐ Yes ☐ No If yes, provide ID #: _____ Medicaid: ☐ Yes ☐ No If yes, provide ID #: _____

C. PRESCRIBER INFORMATION / PHYSICIAN INFORMATION

First Name: | Last Name: (Check One): ☐ M.D. ☐ D.O. ☐ N.P. ☐ P.A.
Address: | City: | State: | ZIP:
Phone: | Fax: | St Lic #: | NPI #: | DEA #: | UPIN:
Provider E-mail: | Office Contact Name: | Phone:
Specialty (Check one): ☐ Oncologist ☐ Hematologist ☐ Other: _____

D. DISPENSING PROVIDER/ADMINISTRATION INFORMATION

Place of Administration:
☐ Self-administered ☐ Physician's Office
☐ Outpatient Infusion Center Phone: _____
Center Name: _____
☐ Home Infusion Center Phone: _____
Agency Name: _____
☐ Administration code(s) (CPT): _____
Address: _____

Dispensing Provider/Pharmacy: *Patient Selected choice*
☐ Physician's Office ☐ Retail Pharmacy
☐ Specialty Pharmacy ☐ Other: _____
Name: _____
Address: _____
Phone: _____ Fax: _____
TIN: _____ PIN: _____

E. PRODUCT INFORMATION

Drug request is for: _____
Dose: _____ Frequency: _____ Route: _____

F. DIAGNOSIS INFORMATION – Please indicate primary ICD Code and specify any other where applicable.

Diagnosis _____ Primary ICD Code: _____ Secondary ICD Code: _____

G. CLINICAL INFORMATION – Required clinical information must be completed in its entirety for all precertification requests.

This form is for use ONLY where a drug specific specialty medication precertification request form does not exist.
For all requests (Clinical documentation must be submitted with all drug requests)

☐ Yes ☐ No Has the patient been treated with another medication for this diagnosis?
→ Please provide the name of the previous medication(s): _____
Please provide the date range of previous treatment: ___/___/___ - ___/___/___
___/___/___ - ___/___/___
☐ Yes ☐ No Was treatment with this medication ineffective, not tolerated, or contraindicated?
→ Please select which one applies to the previous treatment: ☐ Ineffective ☐ Not tolerated ☐ Contraindicated
Please explain answer: _____
☐ Yes ☐ No Has this condition been confirmed by diagnostic testing?
→ Please provide the diagnostic test name and date performed: Test name: _____ Date: ___/___/___
Please provide any relevant laboratory data specific to this drug request (e.g. complete blood count, liver transaminase, bilirubin, TB testing, pregnancy test, genetic testing): Name of test(s): _____
Test results: _____
Date(s) of testing: _____
Please list any other relevant information specific to this medication request: _____

H. ACKNOWLEDGEMENT

Request Completed By ***(Signature Required):*** _____ **Date:** ___/___/___

Any person who knowingly files a request for authorization of coverage of a medical procedure or service with the intent to injure, defraud or deceive any insurance company by providing materially false information or conceals material information for the purpose of misleading, commits a fraudulent insurance act, which is a crime and subjects such person to criminal and civil penalties.

The plan may request additional information or clarification, if needed, to evaluate requests.

Physician signature: Ensure that the prescribing physician signs all documentation where required.

Mistakes or omissions in a claim form may result in a denial and a delay in patient treatment. Make sure to check over the form before submission.

HCPCS=Healthcare Common Procedure Coding System; *ICD-10-CM=International Classification of Diseases, Tenth Revision, Clinical Modification*; NDC=National Drug Code.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Infusion-Related Reactions

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PA for RYTELO (cont'd)

Step 2: Submit the PA Request

- ☐ Determine the appropriate submission method for the PA form (eg, fax, email, insurance plan's website). This information is often listed on the form itself.
- ☐ It may be necessary to speak to an insurance plan representative on the phone before submitting a PA.
- ☐ Document how you submitted the PA request and any associated phone or fax numbers.
- ☐ Keep a copy of everything your practice or facility submits with the request. You may need to reference these documents in the future for many reasons, including if your patient needs financial support because they are unable to afford their OOP costs.

Step 3: Track the Status of the Request and Follow Up as Needed

- ☐ Keep track of dates and methods of correspondence with the payer.
- ☐ Record the names of contacts and reviewers with whom you speak and summarize your conversations. Obtain and record reference numbers for all calls, if possible.
- ☐ If the insurance plan requests additional documentation, respond to their request with the information as soon as possible to help your patient have a timely start to their RYTELO treatment.

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IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

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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.

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%).

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Common Reasons for PA Denials

There may be several reasons that an authorization is denied. One of the main reasons PA requests are denied is incomplete or inaccurate information on the PA form. Check to ensure all information is complete and accurate. Resubmit the form if necessary. If the denial was for clinical reasons, determine what additional information may be required to demonstrate the medical necessity of RYTELO for the patient and contact the payer to obtain its appeals process.

One of the main reasons PA requests are denied is incomplete or inaccurate information on the PA form. Check to ensure all information is complete and accurate.

See pages 16-19 in this guide for more information about how to address an appeal if the PA request is denied.

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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.

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Requesting a Medical Exception for RYTELO

You may encounter a situation where a benefits investigation determines that RYTELO is not covered by an insurance plan or coverage is denied for a certain patient. Under these circumstances, it may be necessary to request a medical exception. Additionally, in the post-launch time frame before medical policies are established, RYTELO may need to be accessed with a medical exception. A medical exception communicates a physician's request to use a medication that is non-preferred or not covered by the patient's insurance plan, citing the patient's individual circumstances.

Commercial plans, including Medicare Advantage, may not have a medical coverage policy in place for RYTELO. In this case, if your request is denied, you will need to thoroughly read the information or response provided by the insurance plan and submit a medical exception request or appeal with your rationale for the medication to be covered for this patient. Providing supporting information as a part of the medical exception request or appeal can help streamline the process. This may include published, peer-reviewed journal articles, CMS-recognized compendia if available, and the FDA approval letter.

Step 1: Complete the Request for Medical Exception and Include a Letter of Medical Necessity as Needed

- ☐ Check with your patient's insurance provider to determine if a plan-specific form or a separate letter from your office is needed.
- ☐ Provide additional information and documentation where applicable.

Carefully and accurately complete the medical exception request to avoid a possible denial due to missing or incorrect information.

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Requesting a Medical Exception for RYTELO (cont'd)

Step 2: Submit the Medical Exception Request and Check in on its Status Regularly

To properly submit the medical exception request, determine the following:

- ☐ The appropriate medical exception submission method (eg, fax, email, online portal)
- ☐ The individual contact person at the patient's insurance plan regarding the medical exception request for check-ins

Regularly check the medical exception request until a decision is made by the insurance plan. Some states have legislation that requires insurance plans to respond to medical exception requests within a certain period of time.

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Letter of Medical Necessity

Letter of Medical Necessity Scenarios

To demonstrate that your patient is an appropriate candidate for RYTELO, it may be important to submit a letter of medical necessity. The following are situations in which your practice or facility may need to demonstrate medical necessity for RYTELO:

- **The required PA is received but denied due to lack of medical necessity.**
- **The patient does not meet the policy requirements for treatment and administration of RYTELO, but the prescribing physician feels the treatment is medically necessary (medical exception based on policy).**
- **Reauthorization is required for patients who previously have been treated with RYTELO but have since been denied.**
- **Change of coverage policy impacts the coverage of RYTELO.**
- **When making a request for RYTELO from a secondary insurance plan when attempts for primary insurance coverage have been exhausted.**

Please refer to pages 13-14 for more information about writing a letter of medical necessity and review an example of a Sample Letter of Medical Necessity.

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Tailor the Letter of Medical Necessity to Your Patient's Needs

When writing a letter of medical necessity, clearly communicate your patient's individual circumstances and consider the following:

Consider providing background on your patient's diagnosis based on clinical diagnostic tests

- ☐ Summarize their clinical status and provide evidence of any diagnostic tests.

Consider providing clinical justification supporting the choice of RYTELO, and a medical evaluation of potential disease progression if the patient does not receive treatment

- ☐ Clinical justification supporting RYTELO treatment for your patient, and cite any relevant literature
- ☐ Patient-specific reasons for treatment choice
- ☐ Review the specific insurance plan's medical policy criteria and point out the criteria that your patient meets.
  - Clinical rationale on why your patient should be excluded from any criteria they do not meet

Consider providing additional documentation that supports your request

- ☐ Medication history and medical history, such as evidence of RBC transfusion dependence or other prior treatment
- ☐ Prescribing Information and Medication Guide for RYTELO
- ☐ RYTELO clinical publications
- ☐ Letter of approval from the FDA

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IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

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.

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%).

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Common Reasons for Medical Exception Denial and Suggested Actions

The following considerations will help you determine a course of action in the event that your patient's medical exception is denied.

Denied due to inaccurate or incomplete information

- ☐ Consider resubmitting the request with the additional required information, if necessary.

Denied due to clinical reasons

- ☐ Consider arranging for the prescribing provider to contact the patient's insurance plan directly to speak with a clinical representative or medical director for a peer-to-peer discussion. **Always request a physician in the same field for a peer-to-peer.**
  - Before your meeting, confirm the meeting date and time, gather all required documentation, and be prepared to explain why you have determined that RYTELO is the most appropriate treatment. Note that the peer reviewer may be in a specialty other than hematology or oncology.
  - The peer-to-peer discussion should include detailed information about the patient's medical and medication history, as well as the reason for requesting RYTELO.
  - Discussion may help the insurance plan understand the concerns you have for your patient and why there is a medical exception request for your choice of treatment with RYTELO.

If the peer-to-peer discussion does not facilitate an approval, the next step is to consider an appeal. **Peer-to-peers can override an appeal, so be sure to read all documentation carefully so that any rights to appeals or determination changes are not forfeited.**

See pages 16-19 in this guide for more information about how to address an appeal if the PA request is denied.

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IMPORTANT SAFETY INFORMATION (cont'd)

ADVERSE REACTIONS (cont'd)

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.

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Appealing an Insurance Plan's Denial of RYTELO

Even if treatment with RYTELO is medically necessary, coverage may be denied by the patient's insurance company. If an insurance plan denies a PA, medical exception, or request for reauthorization, your patient has the right to appeal the decision, and you may be asked to submit the appeal to the patient's insurance plan on their behalf.

Step 1: Understand the Reason for the Denial

The PA or medical exception could be denied for several reasons; therefore, it is important to read the denial letter carefully to understand why. You may also call and speak with the patient's insurance plan to ask any questions about the reason for the denial and find a way to quickly resolve the matter.

Timing is critical for submitting an appeal. Refer to the denial letter to find the time frame for submitting your appeal.

Step 2: Request an Appeal

It's important to follow the insurance plan's guidelines and time frames when requesting an appeal. Be sure to contact your patient's insurance plan with any questions and to obtain a written description of its appeals process. On appeal, physicians may want to submit specific patient documentation, a letter of medical necessity, and any additional information about a patient's medical history to support the request to reverse the initial denial of coverage.

The appeals process may vary depending on the insurance plan, and being sensitive to minor nuances in the process can make a difference.

- Some insurance plans have their own appeal request forms. Call the insurance plan or check their website, as forms may be available.
- Prepare a letter of appeal.
- Review the appeal request in detail to ensure all the information provided is complete and accurate.

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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.

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Appealing an Insurance Plan's Denial of RYTELO (cont'd)

Step 2: Request an Appeal (cont'd)

A Letter of Appeal Is Generally a Critical Component

An effective appeal letter may include the following elements

- ☐ patient information, including name, policy number, and the case or claim number provided by the insurance plan in the denial letter
- ☐ the reason for the denial as listed in the denial letter
- ☐ the patient's medical history and current diagnosed health condition(s), including evidence of transfusion-dependent anemia
- ☐ the reason(s) you disagree with the denial
- ☐ an explanation of medical necessity for RYTELO
- ☐ patient-specific reasons for choosing RYTELO, such as the expected effect of treatment
- ☐ the clinical consequences of not receiving RYTELO
- ☐ indication and Prescribing Information for RYTELO
- ☐ any additional evidence to support your treatment decision

Additional Information in the Letter of Appeal May Help Justify the Use of RYTELO

Content that may help strengthen your patient's appeal include

- ☐ peer-reviewed, published scientific literature of the clinical trials for RYTELO
- ☐ RYTELO's letter of approval from the FDA
- ☐ examples of other insurance-plan policies in which the patient would be approved for RYTELO, if applicable

Consider calling the insurance plan directly to have a peer-to-peer discussion regarding the patient, clinical issues, and the reasons for prescribing RYTELO. This may help your patient's insurance plan understand the letter of appeal and rationale for treatment with RYTELO. See page 15 for more information on peer-to-peer discussions.

Review the appeal before submission to avoid processing errors.

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IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

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.

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If the Appeal Is Denied, Your Patient May Request an Independent External Review

If coverage is still denied, the next step is for your patient to request an independent external review.

REQUESTING AN EXTERNAL REVIEW

Your patient must file a written request with their insurance plan within a certain period of time of an insurance plan's final determination on the appeal.[a] Directions on requesting the external review should be provided with the denial letter.[6]

An independent medical professional will review your patient's case within 60 days of receipt of the request, with decisions generally made as soon as possible.

CONCURRENT REVIEWS

In urgent cases, your patient may request an external review at the same time the internal review is conducted to speed up the process. Requests can be made verbally, and an insurance plan is required to make a decision within 4 business days of receiving the request.[6]

An expedited appeal may be granted under the following circumstances[6]:

- Your patient is currently prescribed RYTELO and a reauthorization is needed or the patient's insurance changed.
- A delay in treatment would result in any of the following:
  - puts their life or overall health at risk
  - affects their ability to maintain transfusion independence
  - subjects them to severe pain

SECONDARY INSURANCE PLAN SUBMISSION

If your patient has secondary health insurance coverage, you should submit to the secondary insurance plan for coverage after attempts with the primary insurance plan have been exhausted.

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[a]Some plans may allow more time to file the request. Check with the individual plan for more information.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

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If the Appeal Is Denied, Your Patient May Request an Independent External Review (cont'd)

Different Types of Reviews

Specialist Review	Medical Director Review	Resource Utilization
Request a specialist familiar with infused therapies, such as RYTELO, to review the claim for medical necessity.	Direct physician-to-medical director communication is recommended.	State insurance department resources may be used as a final means of arbitration.

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Reauthorization for RYTELO

Commercial, Medicaid, and Medicare Advantage payers will likely require an authorization renewal for RYTELO after a certain time period. It is important to:

- **Know the intervals for reauthorization.**

  Become familiar with the medical policy for RYTELO on the patient's insurance plan, and be mindful of the duration of coverage and the patient's start date.

- **Meet the requirements of reauthorization.**

  These typically include payer-specific reauthorization criteria and documentation of efficacy and safety. Providing documentation of efficacy to insurance plans in a timely fashion may help enable the patient to continue treatment uninterrupted.

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Important Safety Information

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Notes

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