RYTELO®
(imetelstat) for Injection 47 mg 188 mg

Instructions for creating a list of patients who may be appropriate for RYTELO® in the Oracle Health® EHR system

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 Important Safety Information throughout and click for full Prescribing Information including Medication Guide.

Instruction Set Overview and Limitations

This instruction set was developed to help identify patients who may be appropriate for RYTELO®. These instructions are specific to the Oracle Health® electronic health record (EHR) system and are not appropriate for other EHR systems. The content given does not include all details in the RYTELO Prescribing Information, and the clinical data included are only examples. This information will not work for other conditions, treatments, or therapeutic areas. **This document is not intended to provide any clinical advice or recommendations, which are solely the responsibility of the organization.**

The process outlined in this document is variable, and not all steps will apply to every organization. Any steps or settings that are not part of an organization's standard process should be excluded or modified accordingly and independently reviewed by the organization for clinical appropriateness. Any questions should be directed to the appropriate EHR service provider. **The organization is solely responsible for implementing, testing, monitoring, and the ongoing operation of any EHR tools.**

Notes

- Capabilities, functionality, and setup (customization) for each EHR system may vary. Geron shall not be responsible for revising the information it provides to any organization if the customer modifies or changes its software, or the configuration of its EHR system, after such time as the information has been initially provided by Geron. While Geron tests its implementation instructions on multiple EHR systems, the instructions are not guaranteed to work for all available EHR systems, and Geron shall have no liability thereto.
- While EHRs may assist providers in identifying appropriate patients for consideration of assessment, treatment, and referral, the decision and action should ultimately be decided by each provider in consultation with the patient, after a review of the patient's records to determine eligibility, and Geron shall have no liability thereto.
- These instructions have not been designed for, and are not a tool and/or solution for, meeting Meaningful Use, Advancing Care Information, and/or any other quality/accreditation requirement. Any clinical decision to prescribe RYTELO is based upon the best interests of the patient and is unrelated to the instructions provided by Geron.
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- The instructions and materials provided by Geron are based on the RYTELO FDA-approved indication. Geron makes no representation as to their applicability for any use outside of the RYTELO approved indication.

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.

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Considerations and Suggested Criteria

Below you will find suggested criteria for creating the patient query utilizing the EHR instruction set described herein. The organization and its providers are solely responsible for the criteria used and implemented.

The suggested criteria for the instruction set are:

International Classification of Diseases, Tenth Revision (ICD-10) Codes

There are no specific ICD-10 codes for lower-risk myelodysplastic syndromes (LR-MDS); however, these general MDS codes are frequently used to identify lower-risk subtypes:

- D46.0 Refractory anemia without ring sideroblasts, so stated
- D46.1 Refractory anemia with ring sideroblasts
- D46.A Refractory cytopenia with multilineage dysplasia
- D46.B Refractory cytopenia with multilineage dysplasia and ring sideroblasts
- D46.Z Other myelodysplastic syndromes
- D46.4 Refractory anemia, unspecified
- D46.9 Myelodysplastic syndrome, unspecified

Medications

- Current or prior treatment with erythropoiesis-stimulating agents (ESA) (e.g., epoetin alfa or darbepoetin alfa)

Labs

- Erythropoietin (EPO) serum level greater than 500 mU/mL
- Consider adding additional lab criteria that may be relevant to patient assessment, such as hemoglobin, neutrophils, platelets, and liver function tests (LFTs).

Red Blood Cell (RBC) Transfusion History

RBC transfusion history will not be found in the EHR chart but may be included in individual patient notes.

Note: Consider running the report on a regular basis. Once the initial report has been created, it can be saved for future use and subsequent reports can be rerun. Running reports over time helps identify new patients who meet the criteria.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Neutropenia (cont'd)

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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Instruction Set for Identifying Patients Who May Be Appropriate for RYTELO

Oracle Health's Discern Analytics 2.0 is a reporting tool capable of creating patient queries. Consult your organization if additional user rights are required to access this functionality.

1. Launch Discern Analytics 2.0. It may be found as DA2.exe in the applications folder.
2. Click the **Domains** tab to access available domains.
3. Select **File** > **New** > **Query** or select the desired domain by double-clicking it.
4. The query wizard will display available categories.
5. In the Qualifications window, select the **Diagnosis Code Filter** and click **Modify Filter List**.
6. In the search field, enter the ICD-10 codes listed in the Suggested Criteria section on page 3 and select all ICD codes. Since there is no specific code for LR-MDS, use the standard MDS problem and review the chart manually to confirm LR-MDS status. Click **Include**.
7. In the Qualifications window, select the **Order Synonym ID Filter** and click **Modify Filter List**.
8. In the search field, enter and select the ESA pharmaceutical class. Click **Include**.
9. To add lab results or findings, consider adding the **Clinical Events** criterion.
10. In the Qualifications window, select the **Clinical Events Results** and click **Modify Filter List**.
11. In the search field, enter and select Erythropoietin (EPO) serum level and specify the value range to greater than 500 mU/mL. Click **Include**.
12. Set the criterion logic:
    - **a.** For the patient report of ICD-10 code and ESA medications:

      MDS diagnoses

      AND

      ESA
    - **b.** For the patient report of ICD-10 code and EPO results > 500 mU/mL:

      MDS diagnoses

      AND

      EPO > 500 mU/mL

continued on the next page

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.

Instruction Set for Identifying Patients Who May Be Appropriate for RYTELO (cont'd)

13. For the display columns, enter and select current and past medications and click the right arrow or drag it to the Columns window. Repeat this for any other desired display columns. Add a display column for Order Date and Time to confirm the length of treatment for the ESA medications exceeds 6 months.
14. Set the general criteria for the report and enter a unique name (e.g., "Potential RYTELO Patients").
15. Click **Query** > **Query Review** or **Run Query in Viewer** in the Query tab to run the query. The results will display. The results may be further evaluated if desired or exported to Excel. Note: A manual chart review will be needed to assess each patient's RBC transfusion history. Transfusion history may be found in the patient chart notes. In addition, a manual chart review is recommended to confirm the medication profile.
16. Save the query for future use.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Infusion-Related Reactions (cont'd)

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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Important Safety Information

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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%).

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 RYTELO full Prescribing Information, including Medication Guide.

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