Electronic Health Record (EHR) Instructions for the Epic® EHR System:

Create a Clinical Decision Alert to identify patients with very low- to intermediate-risk MDS and a recent hemoglobin result and who are not previously treated with ESA agents or REBLOZYL (luspatercept-aamt) in the **Epic EHR system**

INSTRUCTIONS FOR CREATING A CLINICAL DECISION ALERT

The below instructions are designed to create an alert to help identify patients with very low- to intermediate-risk MDS and a recent hemoglobin result and who are not previously treated with ESA agents or REBLOZYL.

Instructions and Limitations

These instructions are created specifically to generate a Clinical Decision Alert in the Epic EHR system and will not work for other conditions, treatments, or therapeutic areas.

The process outlined here is variable, and not all steps will apply to every health system. Any steps or settings that are not part of a health system's standard process should be excluded or modified accordingly. Any questions should be directed to the appropriate service provider. The practice is solely responsible for implementing, testing, monitoring, and ongoing operation of any EHR tools.

The criteria for the alert are listed below:

- The patient is documented with a diagnosis ICD-10 code from the list below:
  - **D46** Myelodysplastic syndromes
    - **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
    - **D46.4** Refractory anemia, unspecified
    - **D46.Z** Other myelodysplastic syndromes
    - **D46.9** Myelodysplastic syndrome, unspecified
- Lab result for hemoglobin (Hgb): <10 g/dL
- Medications:
  - **Not** previously treated with ESA (erythropoiesis-stimulating agent, ie, epoetin alfa and darbepoetin alfa) medications
  - **Not** previously treated with REBLOZYL (luspatercept-aamt)

INDICATIONS

REBLOZYL is indicated for the treatment of anemia without previous erythropoiesis stimulating agent use (ESA-naïve) in adult patients with very low- to intermediate-risk myelodysplastic syndromes (MDS) who may require regular red blood cell (RBC) transfusions.

REBLOZYL is indicated for the treatment of anemia failing an erythropoiesis stimulating agent and requiring 2 or more red blood cell (RBC) units over 8 weeks in adult patients with very low- to intermediate-risk myelodysplastic syndromes with ring sideroblasts (MDS-RS) or with myelodysplastic/myeloproliferative neoplasm with ring sideroblasts and thrombocytosis (MDS/MPN-RS-T).

REBLOZYL is not indicated for use as a substitute for RBC transfusions in patients who require immediate correction of anemia.

SELECTED IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Thrombosis/Thromboembolism

In adult patients with beta thalassemia, thromboembolic events (TEE) were reported in 8/223 (3.6%) of REBLOZYL-treated patients. TEEs included deep vein thrombosis, pulmonary embolus, portal vein thrombosis, and ischemic stroke. Patients with known risk factors for thromboembolism (splenectomy or concomitant use of hormone replacement therapy) may be at further increased risk of thromboembolic conditions. Consider thromboprophylaxis in patients at increased risk of TEE. Monitor patients for signs and symptoms of thromboembolic events and institute treatment promptly.

Please see Important Safety Information on last page and US Full Prescribing Information.

GLOBAL: https://packageinserts.bms.com/pi/pi_reblozyl.pdf

Reblozyl®
(luspatercept-aamt)
for injection 25mg • 75mg

Instructions:

Epic's Clinical Decision Support solution, a BestPractice Advisory (BPA), may be created or customized to align with the health system's clinical preferences and workflow. A BPA creates a reminder for the clinical staff and displays a suggested follow-up recommendation to the end user.

Step 1: Create the diagnosis and medication grouper records (this step may be optional, depending on the availability of existing grouper records)

Diagnosis Grouper for MDS (a separate Diagnosis Grouper needs to be created for each of the queries):
1. Access the **Grouper Record Editor** in **Tools>Management Console**
2. Select the **Diagnoses (EDG) master file** and set the type to **ICD**
3. Add the **ICD codes** listed in the **Instructions and Limitations** to the diagnosis grouper
4. Click **Save**

Medications Grouper for ESA medications:
1. Access the **Grouper Record Editor** in **Tools>Management Console**
2. Select the **Medications (ERX) master file**
3. Add the **desired ESA** (erythropoiesis-stimulating agent, ie, epoetin alfa and darbepoetin alfa) medications to the medication grouper
4. Click **Save**

> **Note:** Creating grouper records may require administrative rights. Consult your organization if administrative user rights are required to access the reporting solutions.

Step 2: : Create the BestPractice Advisory

BPA Criteria Records:

Criteria Record 1: Diagnosis Grouper:
1. Access the **BestPractice Advisory Editor** by searching for **BestPractice** or following the path **Tools>Management Console>Decision Support**
2. Start with creating the **Criteria record** (select the **Criteria Record type**), start editing the record and click **+ Add Criteria Type**
3. Select the **Diagnoses by grouper** criteria type. In the **Diagnosis Grouper** field, enter the **ICD-10 Diagnoses** grouper record created in Step 1
4. When the Criteria record is completed, select **Released**

Criteria Record 2: Last Hemoglobin Result:
1. Access the **BestPractice Advisory Editor** by searching for **BestPractice** or following the path **Tools>Management Console>Decision Support**
2. Start with creating the **Criteria record** (select the **Criteria Record type**), start editing the record and click **+ Add Criteria Type**
3. Select the **Lab Component** criteria type. In the **Common Name** field, enter and search for **hemoglobin and set the desired range (<10 g/dL)**
4. When the Criteria record is completed, select **Released**

Reblozyl®
(luspatercept-aamt)
for injection 25mg • 75mg

Criteria Record 3: Medications: Grouper for ESA (erythropoiesis-stimulating agent, ie, epoetin alfa and darbepoetin alfa):

1. Access the **BestPractice Advisory Editor** by searching for **BestPractice** or following the path **Tools>Management Console>Decision Support**
2. Start with creating the **Criteria record** (select the **Criteria Record type**), start editing the record and click **+ Add Criteria Type**
3. Select the **Medications (Exclude)** criteria type. In the **Medication grouper** field, enter the **Medication grouper** created in Step 1
4. When the Criteria record is completed, select **Released**

Criteria Record 4: Medication: REBLOZYL (luspatercept-aamt):

1. Access the **BestPractice Advisory Editor** by searching for **BestPractice** or following the path **Tools>Management Console>Decision Support**
2. Start with creating the **Criteria record** (select the **Criteria Record type**), start editing the record and click **+ Add Criteria Type**
3. Select the **Medications (Exclude)** criteria type. In the **Medications** field, enter **REBLOZYL (luspatercept-aamt)**
4. When the Criteria record is completed, select **Released**

BPA Base Record:

1. Access the **BestPractice Advisory Editor** by searching for **BestPractice** or following the path **Tools>Management Console>Decision Support**
2. Create the **Base record** (select the **Base Record type**), start editing the record and click **+ Add Criteria Type**
3. In the **Display** section:
   a. Select **Yes** for **Display to User**
   b. Enter a **Summary Text** to describe the Advisory (for example *First-line [1L] MDS patient with REBLOZYL treatment opportunity*)
   c. For the **Unformatted Display Text**, enter: *"Consider evaluating treatment options and transfusion data for this 1L patient with MDS. Treatment options include REBLOZYL (review the patient's hemoglobin [Hgb] value before each administration)"*
4. In the **Criteria** section:
   a. Add the **Criteria records** created in step 1 in the **Linked Criteria**
   b. In the **Logic** section, set the **logic** to **(Criteria 1 AND Criteria 2)** AND NOT **(Criteria 3 AND Criteria 4)**
      i. Use the **Logic Tester** to confirm the BPA works as expected
5. In the **Restrictions**, set any desired restrictions. In *Encounter Limitation Inclusion*, select the **desired Location, Specialty or Department** to reflect the **ambulatory care setting** (the selection of the filter may vary depending on how the Epic EHR system was set up). Select the **Department Specialty and/or Provider Type** and set the role to **hematology**
6. Set the desired **Triggers** for the **BPA** per institution's conventions
7. Set the desired **Actions**:
   a. Actions: **Order**
      - Set the order to **direct to REBLOZYL**
8. Preview the BPA to **confirm the expected display result**
9. Select the **Test activity** and complete any **Testing (Troubleshooting)** if needed and consider additional end user testing before **Releasing** the BPA

Please see Important Safety Information on last page and US Full [Prescribing Information](#).

Reblozyl®
(luspatercept-aamt)
for injection 25mg • 75mg

Notes:

- The Customers (ie, physician, medical group, IDN) shall be solely responsible for implementation, testing, and monitoring of the instructions to ensure proper orientation in each Customer's EHR system.

- Capabilities, functionality, and set-up (customization) for each individual EHR system vary. BMS shall not be responsible for revising the implementation instructions it provides to any Customer in the event that Customer modifies or changes its software, or the configuration of its EHR system, after such time as the implementation instructions have been initially provided by BMS.

- While BMS tests its implementation instructions on multiple EHR systems, the instructions are not guaranteed to work for all available EHR systems, and BMS shall have no liability thereto.

- While EHRs may assist providers in identifying appropriate patients for consideration of assessment and treatment, the decision and action should ultimately be decided by a provider in consultation with the patient, after a review of the patient's records to determine eligibility, and BMS shall have no liability thereto.

- The instructions have not been designed to and are not tools and/or solutions for meeting Advancing Care Information and/or any other quality/accreditation requirement.

- BMS will make every effort to update materials provided by BMS in a timely manner, but the customer is ultimately responsible for ensuring the accuracy of the EHR system.

- Any clinical decision to prescribe REBLOZYL is based upon the best interests of the patient and is unrelated to the services provided by BMS.

- The instructions and materials provided by BMS are based on REBLOZYL FDA-approved indications. BMS makes no representation as to their applicability for use outside of REBLOZYL approved indications.

- All products are trademarks of their respective holders, all rights reserved. Reference to these products is not intended to imply affiliation with or sponsorship of BMS and/or its affiliates.

Reblozyl®
(luspatercept-aamt)
for injection 25mg • 75mg

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Thrombosis/Thromboembolism

In adult patients with beta thalassemia, thromboembolic events (TEE) were reported in 8/223 (3.6%) of REBLOZYL-treated patients. TEEs included deep vein thrombosis, pulmonary embolus, portal vein thrombosis, and ischemic stroke. Patients with known risk factors for thromboembolism (splenectomy or concomitant use of hormone replacement therapy) may be at further increased risk of thromboembolic conditions. Consider thromboprophylaxis in patients at increased risk of TEE. Monitor patients for signs and symptoms of thromboembolic events and institute treatment promptly.

Hypertension

Hypertension was reported in 11.4% (63/554) of REBLOZYL-treated patients. Across clinical studies, the incidence of Grade 3 to 4 hypertension ranged from 2% to 9.6%. In ESA-refractory or -intolerant adult patients with MDS with normal baseline blood pressure, 26 (30%) patients developed systolic blood pressure (SBP)≥130 mm Hg and 23 (16%) patients developed diastolic blood pressure (DBP) ≥80 mm Hg. In ESA-naïve adult patients with MDS with normal baseline blood pressure, 23 (36%) patients developed SBP ≥140 mm Hg and 11(6%) patients developed DBP ≥80 mm Hg. Monitor blood pressure prior to each administration. Manage new or exacerbations of preexisting hypertension using anti-hypertensive agents.

Embryo-Fetal Toxicity

REBLOZYL may cause fetal harm when administered to a pregnant woman. REBLOZYL caused increased post-implantation loss, decreased litter size, and an increased incidence of skeletal variations in pregnant rat and rabbit studies. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment and for at least 3 months after the final dose.

ADVERSE REACTIONS

ESA-naïve adult patients with Myelodysplastic Syndromes

Grade ≥3 (≥2%) adverse reactions included hypertension and dyspnea.

The most common (≥10%) all-grade adverse reactions included diarrhea, fatigue, hypertension, peripheral edema, nausea, and dyspnea.

ESA-refractory or -intolerant adult patients with Myelodysplastic Syndromes

Grade ≥3 (≥2%) adverse reactions included fatigue, hypertension, syncope and musculoskeletal pain. A fatal adverse reaction occurred in 5 (2.1%) patients.

The most common (≥10%) adverse reactions included fatigue, musculoskeletal pain, dizziness, diarrhea, nausea, hypersensitivity reactions, hypertension, headache, upper respiratory tract infection, bronchitis, and urinary tract infection.

LACTATION

It is not known whether REBLOZYL is excreted into human milk or absorbed systemically after ingestion by a nursing infant. REBLOZYL was detected in milk of lactating rats. When a drug is present in animal milk, it is likely that the drug will be present in human milk. Because many drugs are excreted in human milk, and because of the unknown effects of REBLOZYL in infants, a decision should be made whether to discontinue nursing or to discontinue treatment. Because of the potential for serious adverse reactions in the breastfed child, breastfeeding is not recommended during treatment and for 3 months after the last dose.

DRUG ABUSE POTENTIAL

Abuse: Abuse of REBLOZYL may be seen in athletes for the effects on erythropoiesis. Misuse of drugs that increase erythropoiesis, such as REBLOZYL, by healthy persons may lead to polycythemia, which may be associated with life-threatening cardiovascular complications.

Please see US Full [Prescribing Information](#) for REBLOZYL.

Bristol Myers Squibb™

Reblozyl®
(luspatercept-aamt)
for injection 25mg • 75mg