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

Create a Clinical Decision Support 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 **Cerner 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 Cerner EHR systems 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.

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

Instructions:

Cerner's Discern Alerts can create awareness for clinical staff about events requiring attention. The steps to create a Discern Alert module are described below. Analyst administrative rights are typically required to access this functionality.

1. To start creating an alert, open the **Expert Knowledge Module** by selecting **DiscernDev.exe or DiscernLaunch.exe**
2. Complete the desired **name** (for example, *First-line [1L] MDS patient with REBLOZYL treatment opportunity)* and other parameters. Set the status to **testing**.
3. Create the **Evoke section** parameters:
   E1:
   i. Select **OPENCHART**
   ii. Select **EKS_APPLICATION_E** and for **Application** select **HNA: Powerchart**
   E2:
   i. Select **OPENCHART**
   ii. Select **EKS_USER_POSITION_E** and for **POSITION** select the desired **Provider Type** and set the desired **role types**, limiting the role to hematology
   An encounter location/setting may be added to restrict the alert to the ambulatory care setting. Select the appropriate template to limit the alert (local builds may differ; consider PATIENT_EVENT and selecting the Encounter Type to ambulatory clinics)
4. Set the **Logic section** parameters:
   L1:
   i. Select **EKS_DIAGNOSIS_FIND_L**
   ii. Set the **OPT_DIAGNOSIS to the ICD-10 codes listed** (D46.0, D46.1, D46.A, D46.B, D46.4, D46.Z, D46.9)
   iii. Select **Ok** to complete setting the parameter
   L2:
   i. Select **EKS_CE_RESULT_MOST_RECENT_L**
   ii. Set the **most recent result for hemoglobin** (Hgb)
   iii. Set the **EVALUATION** to the desired range (<10 g/dL)
   iv. Select **Ok** to complete setting the parameter
   L3:
   i. Select **EKS_ORDER_FIND_L**
   ii. Set the **ORD_METHOD** to whose primary mnemonic is
   iii. Set the **OPT_ORDERS** to **ESA** (erythropoiesis-stimulating agent, ie, epoetin alfa and darbepoetin alfa) medications
   iv. Set the **OPT_ORDERS_STATUS** to **COMPLETED**
   v. Select **Ok** to complete setting the parameter
   L4:
   i. Select **EKS_ORDER_FIND_L**
   ii. Set the **ORD_METHOD** to whose primary mnemonic is
   iii. Set the **OPT_ORDERS** to **REBLOZYL** (luspatercept-aamt)
   iv. Set the **OPT_ORDERS_STATUS** to **COMPLETED**
   v. Select **Ok** to complete setting the parameter
5. Finally set the **Action section** parameters:
   a. Set the **operator logic** to **(L1 AND L2)** AND NOT (L3 AND L4)
   b. To set up a **text alert**, select **EKS_BUILD_MESSAGE_A. Enter the following message:** *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)*.
   c. Complete the text alert by inserting a link to the **REBLOZYL (OPT_FORM)**
6. **Test** the new alert and **activate and release** once satisfactory testing has been completed.

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.
-

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™

2007-US-2300599 01/24

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