Electronic Health Record (EHR) Instructions:

Create a Clinical Decision Support alert for patients taking REBLOZYL® (luspatercept-aamt) who may benefit from a physician assessment to evaluate response/treatment in an agnostic EHR system

INSTRUCTIONS FOR CREATING A CLINICAL DECISION ALERT

The below instructions are designed to create an alert to help identify patients who may be appropriate for REBLOZYL dose escalation.

Instructions and Limitations

These instructions are created specifically to generate a Clinical Decision Alert in an agnostic 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:

Patients who may be appropriate candidates for a physician assessment of response/treatment (includes any patient currently taking REBLOZYL 1 mg/kg or 1.33 mg/kg dosing for 2 cycles or had a dose reduction to <1 mg/kg).

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

The patient is documented with a medication from the list below:

- **REBLOZYL 1 mg/kg**
- **REBLOZYL 1.33 mg/kg**

Once the patient is identified, a further assessment can be scheduled.

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:

All EHRs have functionality to create clinical decision support alerts. The alerts create awareness for the appropriate clinical stakeholders and may include a solution to cover the patient's care gap or opportunity.

To create a clinical decision support alert, different components must be created and connected:

- A unique name for the alert
- Criteria to trigger the alert
- Logic between the criteria to set up the alert
- A message to inform the stakeholder why the alert appears
- A solution to address the care gap/opportunity

Some EHRs offer functionality beyond the basic elements. This additional functionality may include restrictions (identifying stakeholders, role types, locations, departments, etc), limiting how often the alert needs to be sent, reports specific to alert utilization and compliance, and other factors.

A suggested, unique name for the alert:
Potential candidate for REBLOZYL dose escalation

The suggested criteria to trigger the alert are:
The patient is documented with a diagnosis ICD-10 code from the list below:

- **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

The patient is documented with a medication from the list below with a lookback of 3 weeks:

- **REBLOZYL 1 mg/kg**
- **REBLOZYL 1.33 mg/kg**

Age: greater than or equal to (≥)18 years

Suggested logic between the criteria to set up the alert:
Diagnosis codes
AND
Medications
AND
Age

The suggested message to inform the stakeholder why the alert appears:
Evaluate patient response to current treatment by considering TRANSFUSION FREQUENCY and/or Hb LEVELS to confirm TREATMENT CHOICE and APPROPRIATE DOSE

A solution to address the care gap/opportunity:
A link to the REBLOZYL order in the EHR and/or other assessment functionality.

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.

-

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

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™

2007-US-2300305 11/23

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