Cerner®

EHR Order Set Instructions

Creating an order group for REBLOZYL® (luspatercept-aamt) as a treatment option for anemia in adult patients with beta thalassemia or for anemia in myelodysplastic syndromes

Instructions and limitations

These instructions are for ordering product purposes only. These instructions can only be used to optimize order sets in the Cerner® electronic health record (EHR) systems and will not work for other conditions, treatments, or therapeutic areas or for other EHR systems.

Indications

REBLOZYL is indicated for the treatment of anemia in adult patients with beta thalassemia who require regular red blood cell (RBC) transfusions.

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 pages 9-10 and US Full Prescribing Information.

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

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

How to create an order group

Important tips on how to use this tool

REBLOZYL is indicated for the treatment of anemia in adult patients with beta thalassemia who require regular red blood cell (RBC) transfusions

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 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

REBLOZYL is available in two strengths as single-dose vials for reconstitution. Please be sure both the 25 mg and 75 mg vial sizes are available for order within your EHR.

You may choose to create an order set for either one or all of these approved indications:

Follow the instructions by inputting the details in the teal box to create an order set for REBLOZYL as indicated for the treatment of anemia in adult patients with beta thalassemia who require regular RBC transfusions.

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

OR

Follow the instructions by inputting the details in the pink box to create an order set for REBLOZYL as 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 **OR** the treatment of anemia failing an erythropoiesis stimulating agent and requiring 2 or more RBC units over 8 weeks in adult patients with very low- to intermediate-risk MDS-RS or MDS/MPN-RS-T.

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

Follow all steps in black text below and choose between actions reflected in the teal and/or pink boxes to customize based on your clinical preferences.

Your practice may have an existing PowerPlan available that can be used as a foundation. This PowerPlan can be modified to minimize optimization.

Step 1: Finding an existing PowerPlan to modify

1. Open **DCPtools**.
2. Select the **PowerPlan tool** in the **Order Management** section.
3. Click **Task > Open Plan** and enter one of the following search terms, depending on the indication you'd like to optimize for the order set for anemia in:

Beta thalassemia	**OR**	Myelodysplastic syndromes (MDS)

4. Double-click on the plan to display its contents.

SELECTED IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (CONT'D)

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 patients with beta thalassemia with normal baseline blood pressure, 13 (6.2%) patients developed systolic blood pressure (SBP) ≥130 mm Hg and 33 (16.6%) patients developed diastolic blood pressure (DBP) ≥80 mm Hg. In ESA-refractory or -intolerant adult patients with MDS with normal baseline blood pressure, 26 (30%) patients developed SBP ≥130 mm Hg and 23 (16%) patients developed 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.

Abbreviations: MDS/MPN-RS-T, myelodysplastic/myeloproliferative neoplasm with ring sideroblasts and thrombocytosis; MDS-RS, myelodysplastic syndromes with ring sideroblasts; RBC, red blood cell.

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How to create an order group (cont'd)

Step 2: Modifying the PowerPlan

1. The description will list all clinical subcategories and orders. Apply any changes to the laboratory orders, nursing orders, comments and other orders. Update both the **display description** and the **description** to:

REBLOZYL® (luspatercept-aamt) for the treatment of anemia in adult patients with beta thalassemia who require regular RBC transfusions.

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

OR

REBLOZYL® (luspatercept-aamt) 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 **OR** REBLOZYL® (luspatercept-aamt) for the treatment of anemia failing an erythropoiesis stimulating agent and requiring 2 or more RBC units over 8 weeks in adult patients with very low- to intermediate-risk MDS-RS or MDS/MPN-RS-T. REBLOZYL is not indicated for use as a substitute for RBC transfusions in patients who require immediate correction of anemia.

2. In the **reference text field**, enter:

Recommended Dosage in Beta Thalassemia

The recommended starting dose of REBLOZYL is 1 mg/kg once every 3 weeks by subcutaneous injection for patients with beta thalassemia. Prior to each REBLOZYL dose, review the patient's hemoglobin and transfusion record. Titrate the dose based on responses according to Table 1 [of the Package Insert (https://packageinserts.bms.com/pi/pi_reblozyl.pdf#page=2)]. Interrupt treatment for adverse reactions as described in Table 2 [of the Package Insert (https://packageinserts.bms.com/pi/pi_reblozyl.pdf#page=2)]. Discontinue REBLOZYL if a patient does not experience a decrease in transfusion burden after 9 weeks of treatment (administration of 3 doses) at the maximum dose level or if unacceptable toxicity occurs at any time.

If a planned administration of REBLOZYL is delayed or missed, administer REBLOZYL as soon as possible and continue dosing as prescribed, with at least 3 weeks between doses.

Dose Modifications for Response

Assess and review hemoglobin results prior to each administration of REBLOZYL. If an RBC transfusion occurred prior to dosing, use the pretransfusion hemoglobin for dose evaluation.

If a patient does not achieve a reduction in RBC transfusion burden after at least 2 consecutive doses (6 weeks) at the 1 mg/kg starting dose, increase the REBLOZYL dose to 1.25 mg/kg. Do not increase the dose beyond the maximum dose of 1.25 mg/kg. In the absence of transfusions, if hemoglobin increase is greater than 2 g/dL within 3 weeks or the predose hemoglobin is greater than or equal to 11.5 g/dL, reduce the dose or interrupt treatment with REBLOZYL as described in Table 1 [of the Package Insert (https://packageinserts.bms.com/pi/pi_reblozyl.pdf#page=2)].

(continued on next page)

SELECTED IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (CONT'D)

Extramedullary Hematopoietic (EMH) Masses

In adult patients with transfusion-dependent beta thalassemia, EMH masses were observed in 3.2% of REBLOZYL-treated patients, with spinal cord compression symptoms due to EMH masses occurring in 1.9% of patients (BELIEVE and REBLOZYL long-term follow-up study).

Abbreviations: MDS/MPN-RS-T, myelodysplastic/myeloproliferative neoplasm with ring sideroblasts and thrombocytosis; MDS-RS, myelodysplastic syndromes with ring sideroblasts; RBC, red blood cell.

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How to create an order group (cont'd)

Step 2: Modifying the PowerPlan (cont'd)

2. In the **reference text field**, enter: (cont'd)

Beta Thalassemia — REBLOZYL Dose Titration for Response [Adapted from Table 1 of the Package Insert (https://packageinserts.bms.com/pi/pi_reblozyl.pdf#page=2)]

- Starting dose: 1 mg/kg every 3 weeks

Dose Increases for Insufficient Response at Initiation of Treatment

- No reduction in RBC transfusion burden after at least 2 consecutive doses (6 weeks) at the 1 mg/kg starting dose: increase the dose to 1.25 mg/kg every 3 weeks
- No reduction in RBC transfusion burden after 3 consecutive doses (9 weeks) at 1.25 mg/kg: discontinue treatment

Dose Modifications for Predose Hemoglobin Levels or Rapid Hemoglobin Rise

- Predose hemoglobin is greater than or equal to 11.5 g/dL in the absence of transfusions: interrupt treatment [and] restart when the hemoglobin is no more than 11 g/dL
- Increase in hemoglobin greater than 2 g/dL within 3 weeks in the absence of transfusions and
  - Current dose is 1.25 mg/kg: reduce dose to 1 mg/kg
  - Current dose is 1 mg/kg: reduce dose to 0.8 mg/kg
  - Current dose is 0.8 mg/kg: reduce dose to 0.6 mg/kg
  - Current dose is 0.6 mg/kg: discontinue treatment

Do not increase the dose if the patient is experiencing an adverse reaction as described in Table 2 [of the Package Insert (https://packageinserts.bms.com/pi/pi_reblozyl.pdf#page=2)]

Dose Modifications for Toxicity

For patients experiencing Grade 3 or higher adverse reactions, modify treatment as described in Table 2 [of the Package Insert (https://packageinserts.bms.com/pi/pi_reblozyl.pdf#page=2)]

Beta Thalassemia — REBLOZYL Dosing Modifications for Adverse Reactions [Adapted from Table 2 of the Package Insert (https://packageinserts.bms.com/pi/pi_reblozyl.pdf#page=2)]

- Grade 3 or 4 hypersensitivity reactions: discontinue treatment
- Other Grade 3 or 4 adverse reactions: interrupt treatment [and] restart when the adverse reaction resolves to no more than Grade 1

See Section 2.1 of the PI for more information on recommended dosage modifications in beta thalassemia (https://packageinserts.bms.com/pi/pi_reblozyl.pdf#page=2)

[Adverse events: Grade 1 is mild, Grade 2 is moderate, Grade 3 is severe, and Grade 4 is life-threatening.]

SELECTED IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (CONT'D)

Extramedullary Hematopoietic (EMH) Masses (Cont'd)

In a study of adult patients with non-transfusion-dependent beta thalassemia, a higher incidence of EMH masses was observed in 6.3% of REBLOZYL-treated patients vs. 2% of placebo-treated patients in the double-blind phase of the study, with spinal cord compression due to EMH masses occurring in 1 patient with a prior history of EMH. REBLOZYL is not indicated for use in patients with non-transfusion-dependent beta thalassemia.

Abbreviation: RBC, red blood cell.

Please see Important Safety Information on pages 9-10 and US Full Prescribing Information.

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How to create an order group (cont'd)

Step 2: Modifying the PowerPlan (cont'd)

2. In the **reference text field**, enter: (cont'd)

Recommended Dosage for MDS-Associated Anemia

The recommended starting dosage of REBLOZYL is 1 mg/kg once every 3 weeks by subcutaneous injection for the treatment of anemia of MDS. Prior to each REBLOZYL dose, review the patient's hemoglobin and transfusion record. Titrate the dose based on responses according to Table 3 [of the Package Insert (https://packageinserts.bms.com/pi/pi_reblozyl.pdf#page=2)]. Interrupt treatment for adverse reactions as described in Table 4 [of the Package Insert (https://packageinserts.bms.com/pi/pi_reblozyl.pdf#page=3)]. Discontinue REBLOZYL if a patient does not experience a reduction in transfusion burden including no increase from baseline hemoglobin after 9 weeks of treatment (administration of 3 doses) at the maximum dose level (1.75 mg/kg) or if unacceptable toxicity occurs at any time.

If a planned administration of REBLOZYL is delayed or missed, administer REBLOZYL as soon as possible and continue dosing as prescribed, with at least 3 weeks between doses.

Dose Modification for Response

Assess and review hemoglobin results prior to each administration of REBLOZYL.

If an RBC transfusion occurred prior to dosing, use the pretransfusion hemoglobin for dose evaluation.

If a patient is not RBC transfusion-free after at least 2 consecutive doses (6 weeks) at the 1 mg/kg starting dose, increase the REBLOZYL dose to 1.33 mg/kg [Table 3 of the Package Insert (https://packageinserts.bms.com/pi/pi_reblozyl.pdf#page=2)].

If a patient is not RBC transfusion-free after at least 2 consecutive doses (6 weeks) at the 1.33 mg/kg dose level, increase the REBLOZYL dose to 1.75 mg/kg. Do not increase the dose more frequently than every 6 weeks (2 doses) or beyond the maximum dose of 1.75 mg/kg.

In the absence of transfusions, if hemoglobin increase is greater than 2 g/dL within 3 weeks or if the predose hemoglobin is greater than or equal to 11.5 g/dL, reduce the dose or interrupt treatment with REBLOZYL as described in Table 3 [of the Package Insert (https://packageinserts.bms.com/pi/pi_reblozyl.pdf#page=2)].

If, upon dose reduction, the patient loses response (i.e., requires a transfusion) or hemoglobin concentration drops by 1 g/dL or more in 3 weeks in the absence of transfusion, increase the dose by one dose level. Wait a minimum of 6 weeks between dose increases.

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SELECTED IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (CONT'D)

Extramedullary Hematopoietic (EMH) Masses (Cont'd)

Possible risk factors for the development of EMH masses in patients with beta thalassemia include history of EMH masses, splenectomy, splenomegaly, hepatomegaly, or low baseline hemoglobin (<8.5 g/dL). Signs and symptoms may vary depending on the anatomical location. Monitor patients with beta thalassemia at initiation and during treatment for symptoms and signs or complications resulting from the EMH masses and treat according to clinical guidelines. Discontinue treatment with REBLOZYL in case of serious complications due to EMH masses. Avoid use of REBLOZYL in patients requiring treatment to control the growth of EMH masses.

Abbreviations: MDS, myelodysplastic syndromes; RBC, red blood cell.

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How to create an order group (cont'd)

Step 2: Modifying the PowerPlan (cont'd)

2. In the **reference text field**, enter: (cont'd)

MDS-Associated Anemia — REBLOZYL Dose Titration for Response [Adapted from Table 3 of the Package Insert (https://packageinserts.bms.com/pi/pi_reblozyl.pdf#page=2)]

- Starting Dosage: 1 mg/kg every 3 weeks

Dose Increases for Insufficient Response at Initiation of Treatment

- Not RBC transfusion-free after at least 2 consecutive doses (6 weeks) at the 1 mg/kg starting dose: increase the dose to 1.33 mg/kg every 3 weeks
- Not RBC transfusion-free after at least 2 consecutive doses (6 weeks) at 1.33 mg/kg: increase the dose to 1.75 mg/kg every 3 weeks
- No reduction in RBC transfusion burden or increase in hemoglobin from baseline after at least 3 consecutive doses (9 weeks) at 1.75 mg/kg: discontinue treatment

Dose Modifications for Predose Hemoglobin Levels or Rapid Hemoglobin Rise

- Predose hemoglobin is greater than or equal to 11.5 g/dL in the absence of transfusions: interrupt treatment [and] restart when the hemoglobin is no more than 11 g/dL
- Increase in hemoglobin greater than 2 g/dL within 3 weeks in the absence of transfusions and
  - Current dose is 1.75 mg/kg: reduce dose to 1.33 mg/kg
  - Current dose is 1.33 mg/kg: reduce dose to 1 mg/kg
  - Current dose is 1 mg/kg: reduce dose to 0.8 mg/kg
  - Current dose is 0.8 mg/kg: reduce dose to 0.6 mg/kg
  - Current dose is 0.6 mg/kg: discontinue treatment

Do not increase the dose if the patient is experiencing an adverse reaction as described in Table 4 [of the Package Insert (https://packageinserts.bms.com/pi/pi_reblozyl.pdf#page=3)]

Dose Modification for Toxicity

For patients experiencing grade 3 or higher adverse reactions, modify treatment as described in Table 4 [of the Package Insert (https://packageinserts.bms.com/pi/pi_reblozyl.pdf#page=3)]

MDS-Associated Anemia — REBLOZYL Dosing Modifications for Adverse Reactions [Adapted from Table 4 of the Package Insert (https://packageinserts.bms.com/pi/pi_reblozyl.pdf#page=3)]

- Grade 3 or 4 hypersensitivity reactions: discontinue treatment
- Other Grade 3 or 4 adverse reactions: interrupt treatment [and] when the adverse reaction resolves to no more than Grade 1, restart treatment at the next lower dose level per Table 3 [of the Package Insert (https://packageinserts.bms.com/pi/pi_reblozyl.pdf#page=2)] dose reductions
- If the dose delay is >12 consecutive weeks, discontinue treatment

See Section 2.2 of the PI for more information on recommended dosage modifications in MDS (https://packageinserts.bms.com/pi/pi_reblozyl.pdf#page=2)

[Adverse events: Grade 1 is mild, Grade 2 is moderate, Grade 3 is severe, and Grade 4 is life-threatening.]

SELECTED IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (CONT'D)

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.

Abbreviations: MDS, myelodysplastic syndromes; RBC, red blood cell.

Please see Important Safety Information on pages 9-10 and US Full Prescribing Information.

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How to create an order group (cont'd)

Step 2: Modifying the PowerPlan (cont'd)

3. In the **evidence text field**, add any link to an evidence-based resource or REBLOZYL studies as desired.
4. Click the **Cycle Settings** field. Select the **number of weeks** in each cycle:
    i. **Cycle 1 and onward:** 21-day cycles (3 weeks) with REBLOZYL
5. Click on the **Treatment Regimen** section to update the **Treatment Regimen Cycles**. Select the **number of weeks in each cycle**:
    i. **Cycle 1 and onward:** 21-day cycles (3 weeks) with REBLOZYL
6. Select the **Medications Category** and complete the medication details as follows:
    i. **Cycle 1 and onward:**
        a. (Day 1:) REBLOZYL 1 mg/kg once every 3 weeks by subcutaneous injection
7. Enter **REBLOZYL** in the lower right-hand panel in the **Start Search** field.
   Click the **right arrow** to move **REBLOZYL** to the **Current List** box and click **Add**.
8. Add the **medication details** using a note to the instructions. Refer to Section 2 Dosage and Administration of the full Prescribing Information (https://packageinserts.bms.com/pi/pi_reblozyl.pdf#page=2)
9. Click on the **Labs** section to update the **Labs**.
    a. Enter **Hemoglobin (Complete Blood Count [CBC])** in the lower right-hand panel in the **Start Search** field. Click the **right arrow** to move **CBC (Complete Blood Count)** to the **Current List** box and click **Add**. Additional product details may be optimized in the upper right-hand **Attributes** folder (Include, Required,...).
    b. Add the following text in the **Note section**:
       Review hemoglobin (Hgb) results prior to each administration. If an RBC transfusion occurred prior to dosing, use the pretransfusion hemoglobin for dose evaluation. See Dosage and Administration (2.1 and 2.2) of the Prescribing Information (https://packageinserts.bms.com/pi/pi_reblozyl.pdf#page=2)
10. Click **Task > Save Plan**.
11. Validate the newly optimized order set.
12. Release to the production environment after satisfactory testing has been completed.

SELECTED IMPORTANT SAFETY INFORMATION

ADVERSE REACTIONS

Beta-Thalassemia

Serious adverse reactions occurred in 3.6% of patients on REBLOZYL. Serious adverse reactions occurring in 1% of patients included cerebrovascular accident and deep vein thrombosis. A fatal adverse reaction occurred in 1 patient treated with REBLOZYL who died due to an unconfirmed case of acute myeloid leukemia (AML).

Most common adverse reactions (at least 10% for REBLOZYL and 1% more than placebo) were headache (26% vs 24%), bone pain (20% vs 8%), arthralgia (19% vs 12%), fatigue (14% vs 13%), cough (14% vs 11%), abdominal pain (14% vs 12%), diarrhea (12% vs 10%) and dizziness (11% vs 5%).

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Notes

- The organization shall be solely responsible for implementation, testing, and monitoring of the instructions to ensure proper orientation in the organization's EHR system. The organization has sole and complete responsibility for ensuring the accuracy of the organization's EHR system at all times
- The organization is responsible for performing its own clinical review of these instructions and any other materials provided by Bristol Myers Squibb (BMS)
- Capabilities, functionality, and setup (customization) for each individual EHR system vary. BMS shall not be responsible for revising the implementation instructions it provides to any organization in the event that the HCP 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 EHRs may assist HCPs in identifying appropriate patients for consideration of assessment and treatment, the decision and action should ultimately be decided by an HCP 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 meet and are not tools and/or solutions for meeting Meaningful Use 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's FDA-approved indications. BMS makes no representation as to their applicability for use outside of REBLOZYL's approved indications
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Abbreviations: EHR, electronic health record; FDA, Food and Drug Administration; HCP, healthcare provider.

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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 patients with beta thalassemia with normal baseline blood pressure, 13 (6.2%) patients developed systolic blood pressure (SBP) ≥130 mm Hg and 33 (16.6%) patients developed diastolic blood pressure (DBP) ≥80 mm Hg. In ESA-refractory or -intolerant adult patients with MDS with normal baseline blood pressure, 26 (30%) patients developed SBP ≥130 mm Hg and 23 (16.%) patients developed 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.

Extramedullary Hematopoietic (EMH) Masses

In adult patients with transfusion-dependent beta thalassemia, EMH masses were observed in 3.2% of REBLOZYL-treated patients, with spinal cord compression symptoms due to EMH masses occurring in 1.9% of patients (BELIEVE and REBLOZYL long-term follow-up study).

In a study of adult patients with non-transfusion-dependent beta thalassemia, a higher incidence of EMH masses was observed in 6.3% of REBLOZYL-treated patients vs. 2% of placebo-treated patients in the double-blind phase of the study, with spinal cord compression due to EMH masses occurring in 1 patient with a prior history of EMH. REBLOZYL is not indicated for use in patients with non-transfusion-dependent beta thalassemia.

Possible risk factors for the development of EMH masses in patients with beta thalassemia include history of EMH masses, splenectomy, splenomegaly, hepatomegaly, or low baseline hemoglobin (<8.5 g/dL). Signs and symptoms may vary depending on the anatomical location. Monitor patients with beta thalassemia at initiation and during treatment for symptoms and signs or complications resulting from the EMH masses and treat according to clinical guidelines. Discontinue treatment with REBLOZYL in case of serious complications due to EMH masses. Avoid use of REBLOZYL in patients requiring treatment to control the growth of EMH masses.

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

Beta-Thalassemia

Serious adverse reactions occurred in 3.6% of patients on REBLOZYL. Serious adverse reactions occurring in 1% of patients included cerebrovascular accident and deep vein thrombosis. A fatal adverse reaction occurred in 1 patient treated with REBLOZYL who died due to an unconfirmed case of acute myeloid leukemia (AML).

Most common adverse reactions (at least 10% for REBLOZYL and 1% more than placebo) were headache (26% vs 24%), bone pain (20% vs 8%), arthralgia (19% vs 12%), fatigue (14% vs 13%), cough (14% vs 11%), abdominal pain (14% vs 12%), diarrhea (12% vs 10%) and dizziness (11% vs 5%).

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IMPORTANT SAFETY INFORMATION (CONT'D)

ADVERSE REACTIONS (CONT'D)

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-2300387 08/23

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