How to Dose REBLOZYL to Achieve Or Regain a Response

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Hello, my name is Octavia, and I am an executive therapeutic area specialist at Bristol Myers Squibb. Prior to joining the BMS team, I practiced for 11 years as an oncology nurse. I am a certified nurse practitioner with a Doctor of Nursing practice degree.

As you know, REBLOZYL® (luspatercept-aamt) is FDA approved for the first-line treatment of adults with myelodysplastic syndromes–associated anemia. What I'd like to talk about today is how to dose REBLOZYL to achieve initial and subsequent responses.

REBLOZYL (luspatercept-aamt) 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 not indicated for use as a substitute for RBC transfusions in patients who require immediate correction of anemia.

So you've decided to prescribe REBLOZYL to one of your patients to help treat their anemia. It's important to note that 80% of all first-line patients receiving REBLOZYL required a dose increase at least once. Because it's not if, but when—most REBLOZYL patients will need dose increases.

It's helpful to know that dose increases are key to achieving initial and subsequent responses. Here is a 3-step approach you can use with every REBLOZYL patient.

1) Expect Response 2) Evaluate Response 3) Escalating the dose to achieve an initial or subsequent response Let's start with expected response.

Setting expectations and treatment goals with your patients is often one of our first steps after choosing a treatment option. To do this, we need to know the expected response from the COMMANDS clinical study.

The results of the COMMANDS clinical trial can help us understand the link between efficacy and dose increases with REBLOZYL.

With REBLOZYL, you should target both increased hemoglobin and transfusion independence.

Based on the Phase 3 head-to-head COMMANDS study comparing REBLOZYL versus epoetin alfa. Patients treated with REBLOZYL were 2x more likely to respond compared to patients treated with epoetin alfa. 58.5% of patients treated with REBLOZYL met the composite primary endpoint of hemoglobin increase of at least 1.5 g/dL and concurrent transfusion independence for at least 12 weeks, versus 31.2% of patients treated with epoetin alfa. In order to achieve this endpoint, 80% of patients required at least 1 dose increase.

Now that you know what response looks like, evaluating your patient's response before each dose is Step 2. You'll want to monitor their hemoglobin levels, transfusion needs, and how well patients are tolerating REBLOZYL to be ready to increase, pause, or reduce the dose. Based on what you have monitored, you can assess the need to increase, pause, or reduce their dose based on the answers to the following questions and considerations.

First, how much has your patient's hemoglobin increased since their last dose? Next, has your patient required a transfusion? And finally, has your patient experienced an adverse reaction?

A majority of adverse reactions in the clinical trial were Grade 1 or 2, mild or moderate. Here you can see the most common all-grade adverse events occurring in greater than 10% of patients.

Adverse events of Grade 3 or higher were also seen in the trial, with the following occurring in greater than 2% of patients. The laboratory abnormalities seen in at least 10% of patients were glomerular filtration rate and total bilirubin increased. And finally, injection site reactions made up a small number of clinically relevant adverse events that were reported in fewer than 5% of patients.

Evaluating response before each dose will help you to be ready to increase, pause, or reduce the dose. It's key to remember that after 2 consecutive doses at the same level, you can consider a dose increase.

Remember, it's not if, but when–most patients will need dose increases. Once you have all the information gathered, Step 3 is to escalate to a therapeutic dose to achieve an initial or subsequent response. You may also need to pause or dose reduce to manage adverse reactions or rapid hemoglobin rise.

Now, let's take a look at how to safely and effectively help patients achieve initial and subsequent responses. 80% of all first-line patients receiving REBLOZYL required a dose

increase at least once. For all patients, the starting dose is 1 mg/kg, administered once every 3 weeks by subcutaneous injection.

If, after 2 consecutive doses at the same level, a transfusion was required, increase the dose to 1.33 mg/kg. Again, if after 2 doses, a transfusion was required, increase the dose. Continue at 1.75 mg/kg as long as there is a reduction in transfusion burden or increase in hemoglobin.

In the COMMANDS trial, 65% of all first-line patients receiving REBLOZYL were eventually increased to 1.75 mg/kg. Once you have escalated to 1.75 mg/kg, continue as long as there is either a reduction in transfusion burden or an increase in hemoglobin. As you consider your patient's response, it is important to know that per the USPI, in the absence of transfusions, pre-dose hemoglobin should not exceed 11.5 g/dL.

Additionally, the National Comprehensive Cancer Network (NCCN) recommends treating to a hemoglobin range of 10 to 12 g/dL and not to exceed 12 g/dL. In some circumstances, a treatment pause, or dose reduction may also be necessary. If hemoglobin is 11.5 g/dL or higher pause treatment until hemoglobin is 11 g/dL.

Then you can resume treatment at the same dose level. If hemoglobin increases over 2 g/dL within 3 weeks of the last dose in the absence of transfusions, reduce dose and continue treatment. If a Grade 3 to 4 adverse reaction occurs, pause treatment until it resolves to Grade 1 or lower, then reduce the dose and resume treatment.

Please see accompanying Full Prescribing Information for discontinuation criteria, including for Grade 3 or 4 hypersensitivity and dose delays for greater than 12 weeks, missed dose criteria and loss of response following a dose reduction or at the maximum dose. If you evaluate your patient's response and they are meeting their treatment goals and are transfusion independent, continue treatment at the current dose level.

In conclusion, to help your patients achieve initial and subsequent responses with REBLOZYL,

1) Expect 2) Evaluate and 3) Escalate because it's not if, but when—most patients will need dose increases.

If you have questions about this topic or any other, you can contact your local representative or visit REBLOZYLpro.com for more information. On our website you can watch a video called “Real-Life Patient Cases Showcasing Clinical Best Practices for Dosing REBLOZYL.” In it, Dr. Benton presents his experience dosing REBLOZYL with his own patients.

INDICATIONS

REBLOZYL (luspatercept-aamt) 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.

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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 ESA-naïve adult patients with MDS with normal baseline blood pressure 23 (36%) patients developed systolic blood pressure greater than or equal to 140mm of mercury and 11 (6%) patients developed diastolic blood pressure greater than or equal to 80mm of mercury. 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

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.

LACTACTION

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 accompanying US Full Prescribing Information for REBLOZYL.