Resources to Support the Reimbursement Process

The information provided in this reimbursement guide is valid as of November 2019 and is subject to change.
Important Safety Information

WARNINGS AND PRECAUTIONS

Thrombosis/Thromboembolism

Thromboembolic events (TEE) were reported in 8/223 (3.6%) 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 10.7% (61/571) of REBLOZYL-treated patients. Across clinical studies, the incidence of Grade 3 to 4 hypertension ranged from 1.8% to 8.6%. In patients with beta thalassemia with normal baseline blood pressure, 13 (6.2%) patients developed systolic blood pressure (SBP) >150 mm Hg and 33 (16.6%) patients developed diastolic blood pressure (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 last dose.

ADVERSE REACTIONS

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%).

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.

Please see full Prescribing Information for REBLOZYL.
Product Information for REBLOZYL

Indication
REBLOZYL is indicated for the treatment of anemia in adult patients with beta thalassemia who 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.

Dosage and Administration
- The recommended starting dose of REBLOZYL is 1 mg/kg once every 3 weeks by subcutaneous injection.
- 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.
- Assess and review hemoglobin (Hgb) results prior to each administration. If an RBC transfusion occurred prior to dosing, the pretransfusion Hgb must be considered for dosing purposes.
- If the pre-dose Hgb is ≥11.5 g/dL and the Hgb level is not influenced by recent transfusion, delay dosing until the Hgb is ≤11 g/dL.
- 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.
- If a patient experienced a response followed by a lack of or lost response to REBLOZYL, initiate a search for causative factors (e.g., a bleeding event). If typical causes for a lack or loss of hematologic response are excluded, follow dosing recommendations for management of patients with an insufficient response to REBLOZYL therapy.
- 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.

NDC and Packaging Information

<table>
<thead>
<tr>
<th>Product/Strength</th>
<th>Package/Description</th>
<th>National Drug Code (NDC)</th>
</tr>
</thead>
<tbody>
<tr>
<td>REBLOZYL injection 25 mg</td>
<td>25 mg lyophilized powder for solution for injection in a single-dose vial for reconstitution</td>
<td>11-digit NDC: 59572-0711-01</td>
</tr>
<tr>
<td>REBLOZYL injection 75 mg</td>
<td>75 mg lyophilized powder for solution for injection in a single-dose vial for reconstitution</td>
<td>11-digit NDC: 59572-0775-01</td>
</tr>
</tbody>
</table>

SELECTED IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Thrombosis/Thromboembolism
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Billing Codes for REBLOZYL

Overview of Billing Codes
There are 4 main codes required to accurately submit a claim. Each is discussed in more detail within this resource.

<table>
<thead>
<tr>
<th>Code</th>
<th>Purpose</th>
</tr>
</thead>
<tbody>
<tr>
<td>NDC</td>
<td>Allows payers to identify the drug administered when a miscellaneous J code is used (NDC is required for billing)</td>
</tr>
<tr>
<td>HCPCS (Healthcare Common Procedure Coding System)</td>
<td>States which drugs were given and/or which supplies were used during the patient visit</td>
</tr>
<tr>
<td>CPT® (Current Procedural Terminology)</td>
<td>Describes the medical services and procedures performed and/or the drug or medical supply administered</td>
</tr>
<tr>
<td>ICD-10-CM (International Classification of Diseases, Tenth Revision, Clinical Modification)</td>
<td>Indicates the patient’s diagnosis (or the purpose of the procedure)</td>
</tr>
</tbody>
</table>

The codes provided in this resource are for reference. It is recommended that each payer’s specific billing requirements be confirmed when submitting a claim for REBLOZYL, as they may vary by insurer.

It is important to note that costs associated with administration are separate from the cost of the product.

All claims for the administration of Medicare Part B anti-anemia drugs (other than ESAs) used in the treatment of cancer that are not self-administered require reporting of the most recent hemoglobin or hematocrit reading. Therefore, reporting of hemoglobin or hematocrit values may be required.

For institutional claims, the hemoglobin reading is reported with value code 48 and a hematocrit reading is reported with value code 49. For paper claims, test results are reported on the CMS-1500 claim form under item 19. For electronic claims (837P), hemoglobin or hematocrit readings are reported in Loop 2400 MEA segment MEA01=TR (for test results), MEA02=R1 (for hemoglobin) or R2 (for hematocrit), and MEA03=the test results.

Abbreviation: ESA, erythropoiesis-stimulating agent.
Billing Codes for REBLOZYL (cont’d)

HCPCS codes
HCPCS codes are used for billing drugs and services to Medicare, Medicaid, and the commercial payer. Until a permanent HCPCS code is issued, REBLOZYL should be billed with a miscellaneous, not otherwise classified (NOC) code. Below is a list of miscellaneous codes that could apply for REBLOZYL.

<table>
<thead>
<tr>
<th>HCPCS Code</th>
<th>Descriptor</th>
</tr>
</thead>
<tbody>
<tr>
<td>J3490</td>
<td>Not otherwise classified drugs</td>
</tr>
<tr>
<td>J3590</td>
<td>Not otherwise classified biologics</td>
</tr>
<tr>
<td>J9999</td>
<td>Not otherwise classified antineoplastic drugs</td>
</tr>
<tr>
<td>C9999</td>
<td>Unclassified or biologicals (hospital outpatient use only)</td>
</tr>
</tbody>
</table>

- Depending on payer preferences for billing and coding, the required miscellaneous J code for claim submission may vary. Therefore, the provider should confirm preference with the payer prior to submitting.
- Note the use of a miscellaneous C code (C9999) for when REBLOZYL is used in a hospital infusion center.

Billing Unit Conversion

<table>
<thead>
<tr>
<th>Billing Unit Conversion</th>
<th>1 mg</th>
<th>1 unit</th>
<th>25-mg vial</th>
<th>25 units</th>
<th>75-mg vial</th>
<th>75 units</th>
</tr>
</thead>
</table>

It is important to note that for accurate reimbursement, any quantity of REBLOZYL that is discarded after treatment should be coded with a JW modifier. A JW modifier indicates unused drug or biological from a single-use vial in the event that the entire dose/quantity is not administered and the remainder is discarded. This does not apply to Part B drugs or biologicals obtained under the Competitive Acquisition Program (CAP).

Revenue Codes (Hospital Use)
Revenue codes categorize services in the hospital by revenue center. Medicare and most Medicaid and private payer claims must include revenue codes in field 42 of form UB-04 (CMS-1450).

<table>
<thead>
<tr>
<th>Revenue codes that may be used for administration of REBLOZYL</th>
<th>Code</th>
<th>Revenue Center</th>
</tr>
</thead>
<tbody>
<tr>
<td>o636</td>
<td></td>
<td>Drugs requiring detailed coding</td>
</tr>
<tr>
<td>o250</td>
<td></td>
<td>Pharmacy</td>
</tr>
</tbody>
</table>

CPT® Code for Administration
CPT codes are used to indicate which medical services and procedures were performed on a patient and/or how a drug or medical supply was administered.

<table>
<thead>
<tr>
<th>CPT code that can be used for administration of REBLOZYL</th>
<th>CPT Code</th>
<th>Descriptor</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>96372</td>
<td>Therapeutic, prophylactic, or diagnostic injection (specify substance or drug); subcutaneous or intramuscular</td>
</tr>
</tbody>
</table>

Note that only a single unit of service may be billed for 96372, even if the volume of an injected dose requires that it be split into 2 or more syringes.

ICD-10-CM Diagnosis Codes for Beta Thalassemia

<table>
<thead>
<tr>
<th>ICD-10-CM Code</th>
<th>Descriptor</th>
</tr>
</thead>
<tbody>
<tr>
<td>D56.1</td>
<td>Beta thalassemia major and intermediate</td>
</tr>
<tr>
<td>D56.2</td>
<td>Beta thalassemia major</td>
</tr>
<tr>
<td>D56.3</td>
<td>Cooley’s anemia</td>
</tr>
<tr>
<td>D56.4</td>
<td>Homozygous beta thalassemia</td>
</tr>
<tr>
<td>D56.5</td>
<td>Severe beta thalassemia</td>
</tr>
<tr>
<td>D56.6</td>
<td>Thalassemia intermedia</td>
</tr>
<tr>
<td>D56.7</td>
<td>Thalassemia major</td>
</tr>
</tbody>
</table>

The 2019 version of ICD-10-CM took effect on October 1, 2018.

SELECTED IMPORTANT SAFETY INFORMATION
WARNINGS AND PRECAUTIONS
Hypertension
Hypertension was reported in 10.7% (61/571) of REBLOZYL-treated patients. Across clinical studies, the incidence of Grade 3 to 4 hypertension ranged from 1.8% to 8.6%. 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. Monitor blood pressure prior to each administration. Manage new or exacerbations of preexisting hypertension using anti-hypertensive agents.

Please see Important Safety Information on page 2 and full Prescribing Information.

**Sample Claim Forms**

**Physician Office Sample Claim Form: CMS-1500**

Coding specifics for the CMS-1500 claim form:

- For reimbursement of REBLOZYL administered in an infusion center or a physician’s office, providers must submit a CMS-1500 claim form for the drug and associated services.
- As of November 8, 2019, REBLOZYL has not been assigned a product-specific permanent J code. Until CMS issues a permanent code, the appropriate NOC code (based on payer specifications) should be used.

A claim for REBLOZYL should include the following:

- A proper HCPCS code to define the drug and billing unit.
- The quantity of billing units provided to the patient.
- A CPT code that indicates how the physician administered the drug.

In addition to coding specifics, some payers may require additional information, such as a drug purchase invoice or documentation of medical necessity.

**Hospital Outpatient Department Sample Claim Form: UB-04 (CMS-1450)**

- UB-04 is used for reimbursement of REBLOZYL administered in an institutional setting, such as a hospital, a clinic, or an ambulatory surgical center. Providers must submit a UB-04 claim form documenting the drug administered and associated services.
- Coding specifics for the UB-04 claim form:
  - As of November 8, 2019, REBLOZYL has not been assigned a product-specific permanent J code. Until CMS issues a permanent code, the appropriate NOC code (based on payer specifications) should be used.

Medicare and most Medicaid and private payer claims must include revenue codes in field 42, a description or NDC must be indicated.

Enter the HCPCS code for the outpatient service (and modifier[s], if applicable).

Enter the number of units discarded (if applicable) on a separate line and include the JW modifier from field 44.

Enter the number of units used.

Please see Important Safety Information on page 2 and full Prescribing Information.

*Any outpatient red blood cell transfusions given to address hemoglobin levels in patients with beta thalassemia entail their own set of HCPCS and CPT codes.


*Any outpatient red blood cell transfusions given to address hemoglobin levels in patients with beta thalassemia entail their own set of HCPCS and CPT codes. Certain level II HCPCS codes and CPT codes require the use of modifiers to improve coding accuracy.

†When HCPCS codes are required, the units equal the number of times the reported procedure or service was performed.
Prior Authorization Checklist

Some insurers may require prior authorization. It is essential to confirm which form should be used and ensure it is filled out completely. It is also important to become familiar with the insurer’s requirements.

The following checklist can help with the process:

- Prior authorization request form
- Patient information (e.g., name, date of birth, insurance policy numbers)
- Diagnosis and clinical notes/patient history
- Physician or facility information
- Date of service
- Relevant procedure and HCPCS codes for services or products to be performed/provided
- Product NDC
- Letter of medical necessity
- Patient chart/notes in support of the treatment decision, including:
  - Previous treatments
  - Patient clinical notes detailing the relevant diagnosis
  - Relevant laboratory results
  - Product prescribing information

Letter of Medical Necessity

A letter of medical necessity may be required by some insurers.

This Letter of Medical Necessity Template is made available as a convenience to you. The medical and health information disclosed through the use of this Template is subject to applicable confidentiality and security obligations under state and federal law, including the Health Insurance Portability and Accountability Act. The responsibility for meeting these requirements rests with the entities transmitting the medical and health information. In providing this Template, Celgene assumes no responsibility for complying with these obligations.

SELECTED IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

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 last dose.

Please see Important Safety Information on page 2 and full Prescribing Information.
Commercial and Private Payer Coverage (cont’d)

Appeals Checklist
If a claim is denied, there may be an appeal process for requesting review of coverage. The required documentation and appeal process will vary by insurer, so it is important to review the insurer’s guidelines. The following checklist may help in the navigation of the appeal process:

It is important to check that:

☑ The patient’s information was correctly entered
  (eg, name, date of birth, insurance information)

☑ The patient’s insurer covers the medication for the specific diagnosis

☑ Prior authorization was obtained
  (if required by the insurer)

☑ The correct product coding was used

Some claims may be denied for submission errors. It is critical to ensure that the claim was submitted with the correct information.

Ideally, the components of the appeal process—including necessary forms and guidelines as outlined by the insurer—should be confirmed. It is also essential to note any deadlines for submission and timelines for review. Understanding the reason for the denial (often outlined in the explanation of benefits [EOB]) helps determine what documentation needs to be provided for review.

Your local Field Reimbursement Specialist can help identify what documentation would support your appeal to the insurance provider. Documents such as:

- Letter of medical necessity
- Letter of appeal
- The EOB containing the specifics of the denial
- Documentation supporting treatment decisions related to the claim:
  - Charts/notes with patient history and diagnosis
  - Prior therapies and outcomes
  - Relevant laboratory results
  - Product prescribing information

Letter of Appeal
Prescribers may submit a letter of appeal as part of the appeal process when a request for PA or coverage is denied. In this way, they are able to request reconsideration of coverage by addressing the reason(s) for denial and by reiterating the documentation that supports a particular treatment for their patient.

This Letter of Appeal Template is made available as a convenience to you. The medical and health information disclosed through the use of this Template is subject to applicable confidentiality and security obligations under state and federal law, including the Health Insurance Portability and Accountability Act. The responsibility for meeting these requirements rests with the entities transmitting the medical and health information. In providing this Template, Celgene assumes no responsibility for complying with these obligations.

### Selected Important Safety Information

**Adverse Reactions**

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). Please see Important Safety Information on page 2 and full Prescribing Information.

Abbreviations: FDA, Food and Drug Administration; PA, prior authorization.

**Reblozyl (luspatercept-aamt)**

*for injection 25mg • 75mg*
Medicare Coverage

Coverage of REBLOZYL by Medicare is expected to follow guidance within chapter 15 of the Medicare Benefit Policy Manual, which states that “the program covers drugs that are furnished ‘incident to’ a physician’s service provided that the drugs are not usually self-administered by the patients who take them.” An injectable drug or biologic is typically eligible for inclusion under the “incident to” benefit when it is FDA approved, in a form not usually self-administered, furnished by a physician, and administered by the physician or by auxiliary personnel employed by the physician and under the physician’s personal supervision. It also can be furnished by other healthcare professionals. In addition, the drug must also be reasonable and necessary for an individual patient, as well as safe and effective.

Medicaid Coverage

Medicaid is a joint federal-state program that pays for medical assistance for individuals and families with low incomes and relatively few assets. Medicaid programs are established and administered by each individual state. Although pharmacy coverage is an optional benefit under federal Medicaid law, all states currently provide coverage for outpatient prescription drugs to all categorically eligible individuals and most other enrollees within their state Medicaid programs. Benefits for Medicaid patients should be verified to identify additional needs, such as prior authorizations.

 celgene patient support®

Celgene Patient Support® provides

- A single Specialist assigned to help patients in each geographic area
- A Field Reimbursement Specialist in each region with information on payer policies, billing, and coding for REBLOZYL
- Assistance with understanding patient insurance coverage for REBLOZYL
- Information about financial assistance for REBLOZYL

Financial assistance

There are programs and organizations that may help pay for REBLOZYL, depending on a patient’s insurance situation:

- Celgene Commercial Co-pay Program
  - Co-pay responsibility for REBLOZYL is reduced to $0 (subject to annual benefit limit) for eligible patients with commercial or private insurance (including healthcare exchanges).*
- Celgene Patient Assistance Program (PAP)
  - REBLOZYL may be available at no cost for qualified patients who are uninsured or underinsured.

Independent third-party organizations

Patients who are unable to afford their medication (including patients with Medicare, Medicaid, or other government-sponsored insurance) may be able to receive help from independent third-party organizations.†

Insurance-related assistance

Our Specialists are available to assist with each of the following steps in the insurance approval process for REBLOZYL:§

- Benefits investigation
- Prior authorization/precertification assistance¶
- Appeals assistance¶
- Educating patients about insurance coverage or other programs for which they may qualify

Enrolling in Celgene Patient Support®

Visit us at www.celgenepatientsupport.com

Email us at patientsupport@celgene.com or fax to 1-800-822-2496

For more information on Celgene Patient Support®

Call us at 1-800-931-8691,
Monday–Friday, 8 AM–8 PM ET
(translation services available)

*Other eligibility requirements and restrictions apply. Please see full Terms and Conditions on the Celgene Patient Support® website.
†Patients must meet specified financial and insurance eligibility requirements to qualify for assistance. Please see Eligibility Requirements on the Celgene Patient Support® website.
‡Financial and medical eligibility requirements vary by organization.
§Celgene cannot provide insurance advice or make insurance decisions.
¶Celgene provides a facilitation service and will not provide any medical input into a prior authorization or an appeal.

Please see Important Safety Information on page 2 and full Prescribing Information.
References


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