DISCOVER THE FIRST AND ONLY ERYTHROID MATURATION AGENT* INDICATED FOR ADULTS WITH **RBC TRANSFUSION-DEPENDENT ANEMIA ASSOCIATED WITH β-THALASSEMIA**

REBLOZYL® (luspatercept for injection) is indicated for the treatment of adult patients with red blood cell (RBC) transfusion-dependent anemia associated with beta(β)-thalassemia.[1]

REBLOZYL is an erythroid maturation agent. It is not indicated for use as a substitute for RBC transfusions in patients who require immediate correction of anemia.[1]

No clinically meaningful change in liver iron concentration was observed in β-thalassemia patients treated with REBLOZYL plus best supportive care (BSC) compared to patients treated with placebo plus BSC at 48 weeks.[1]

* Comparative clinical significance has not been established.

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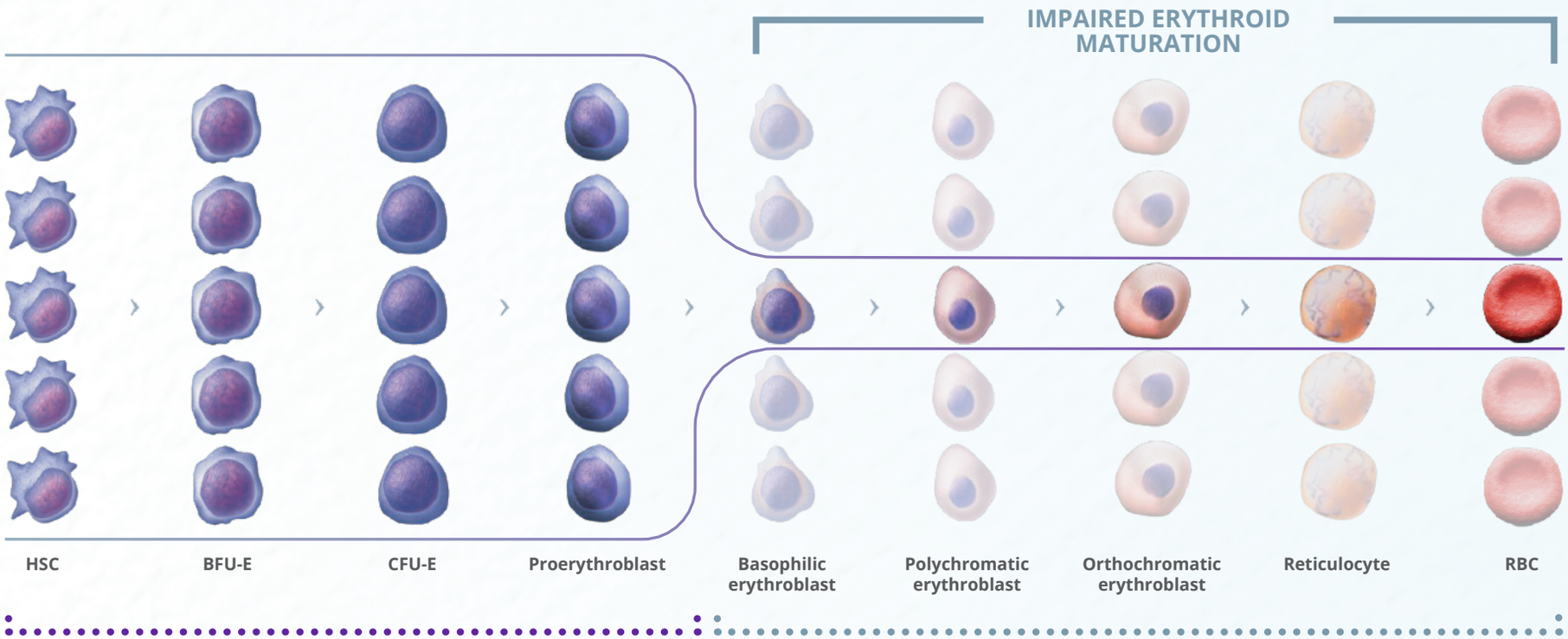
Bristol Myers Squibb™

Pr Reblozyl®
luspatercept for injection

Pr Reblozyl® luspatercept for injection

IMPAIRED ERYTHROID MATURATION CONTRIBUTES TO **INEFFECTIVE ERYTHROPOIESIS, RESULTING IN LOW PRODUCTION OF RBCs AND ANEMIA**[2]



Early-stage erythropoiesis[3]

Endogenous erythropoietin regulates proliferation

Late-stage erythropoiesis[4,5]

Select TGF-β superfamily ligands help regulate maturation

TGF-β superfamily signalling through SMAD2/3 is abnormally high in diseases characterized by ineffective erythropoiesis, which leads to impaired erythroid maturation of RBCs

Adapted from Lodish *et al*, 2010; Fortunel *et al*, 2000; Suragani *et al*, 2014.
HSC: Hematopoietic stem cell; BFU-E: Burst-forming unit erythroid; CFU-E: Colony-forming unit erythroid; RBC: Red blood cell; TGF-β: Transforming growth factor beta.

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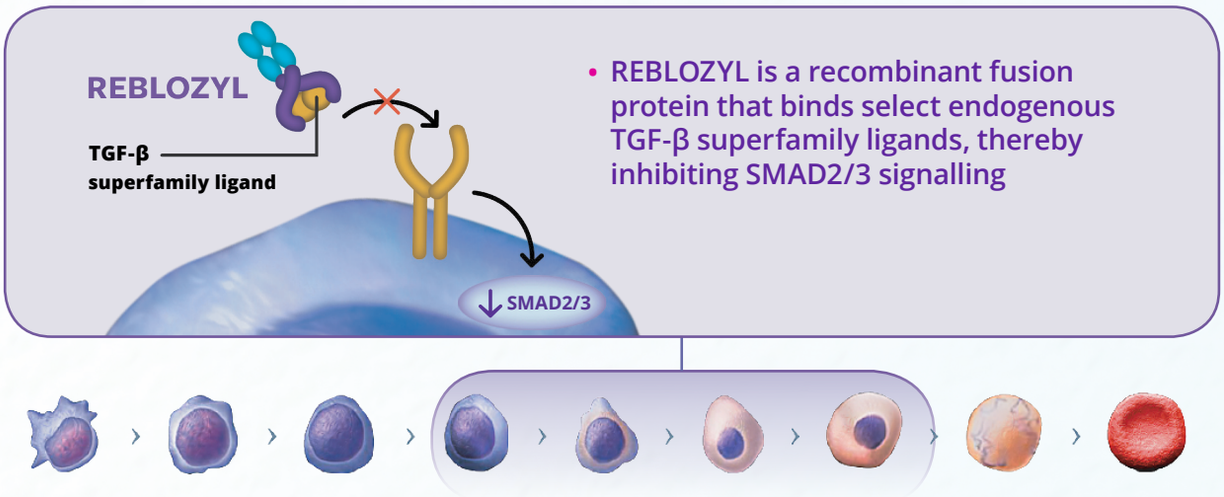
REBLOZYL IS THE **FIRST AND ONLY ERYTHROID MATURATION AGENT*** INDICATED FOR ADULTS WITH RBC TRANSFUSION-DEPENDENT ANEMIA ASSOCIATED WITH β-THALASSEMIA

THE REBLOZYL MOA IS BASED ON PRECLINICAL STUDIES WITH MICE[1†]



- REBLOZYL is a recombinant fusion protein that binds select endogenous TGF-β superfamily ligands, thereby inhibiting SMAD2/3 signalling

REBLOZYL PROMOTED ERYTHROID MATURATION
through differentiation of late-stage erythroid precursors (normoblasts)

In a model of β-thalassemia, REBLOZYL:

- Decreased abnormally elevated SMAD2/3 signalling
- Improved hematology parameters associated with ineffective erythropoiesis in mice

Adapted from the REBLOZYL Product Monograph.

RBC: Red blood cell; TGF-β: Transforming growth factor beta.
* Comparative clinical significance has not been established.
† Clinical significance is unknown.

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REBLOZYL WAS STUDIED IN THE **PHASE III, MULTICENTRE, DOUBLE-BLIND, RANDOMIZED, PLACEBO-CONTROLLED BELIEVE TRIAL**[1]

PATIENT POPULATION (N = 336)

Key inclusion criteria:

- Adults ≥ 18 years of age with β-thalassemia
- Transfusion requirements:
  - Regular transfusions: 6–20 RBC units per 24 weeks
  - No transfusion-free period > 35 days during the 24-week period

Key exclusion criteria:[1]

- Hemoglobin S/β-thalassemia or α-thalassemia
- Major organ damage (liver disease, heart disease, lung disease, renal insufficiency)
- Recent (within past 24 weeks) deep vein thrombosis or stroke
- Recent use (within past 24 weeks) of ESA, immunosuppressant, or hydroxyurea therapy

Randomized 2:1

REBLOZYL + BSC

REBLOZYL 1 mg/kg SC every 3 weeks* + BSC for 48 weeks (n = 224)†

Placebo + BSC

Placebo SC every 3 weeks + BSC for 48 weeks (n = 112)†

All patients in both arms were eligible to receive BSC as needed, including:[1]

- RBC transfusions
- Iron-chelating agents
- Use of antibiotic, antiviral, and antifungal therapy
- Nutritional support

Adapted from the REBLOZYL Product Monograph.

Primary endpoint[1]

- ≥ 33% reduction from baseline in RBC transfusion burden with a reduction of ≥ 2 units from Weeks 13-24

Key secondary endpoints[1]

- ≥ 33% reduction from baseline in RBC transfusion burden with a reduction of ≥ 2 units from Weeks 37–48
- ≥ 50% reduction from baseline in RBC transfusion burden with a reduction of ≥ 2 units at:
  - Weeks 13-24
  - Weeks 37-48

ESA: Erythropoiesis-stimulating agent; RBC: Red blood cell; SC: Subcutaneous injection.
* REBLOZYL was administered once every 3 weeks as long as a reduction in transfusion requirement was observed or until unacceptable toxicity.
† The study was unblinded when all patients received at least 48 weeks of treatment or had discontinued treatment.

BASELINE **CHARACTERISTICS**

Disease characteristics of patients with β-thalassemia in the BELIEVE trial[1]

Disease characteristics	REBLOZYL (n = 224)	Placebo (n = 112)
β-thalassemia diagnosis, n (%)		
β-thalassemia	174 (77.7)	83 (74.1)
HbE/β-thalassemia	31 (13.8)	21 (18.8)
β-thalassemia combined with α-thalassemia	18 (8)	8 (7.1)
Missing*	1 (0.4)	0
Baseline transfusion burden 12 weeks prior to randomization		
Median units/12 weeks (min, max)	6.12 (3, 14)	6.27 (3, 12)
β-thalassemia gene mutation grouping, n (%)		
β0/β0	68 (30.4)	35 (31.3)
Non-β0/β0	155 (69.2)	77 (68.8)
Missing*	1 (0.4)	0
Baseline serum ferritin level (µg/L)		
Median (min, max)	1441.25† (88, 6400)	1301.50‡ (136, 6400)
Splenectomy, n (%)		
Yes	129 (57.6)	65 (58)
No	95 (42.4)	47 (42)
Age patient started regular transfusions (years)		
Median (min, max)	2§ (0, 52)	2¶ (0, 51)

Adapted from the REBLOZYL Product Monograph.

Patient population characteristics[1]

- The median age was 30 years (range between 18 to 66)
- 42% of patients enrolled were male
- 54.2% of patients were Caucasian, 34.8% were Asian, and 0.3% were African American

α-thalassemia: Alpha thalassemia; HbE: Hemoglobin E.
* "Missing" category includes patients in the population who had no result for the parameter listed.
† n = 220.
‡ n = 111.
§ n = 169.
¶ n = 85.

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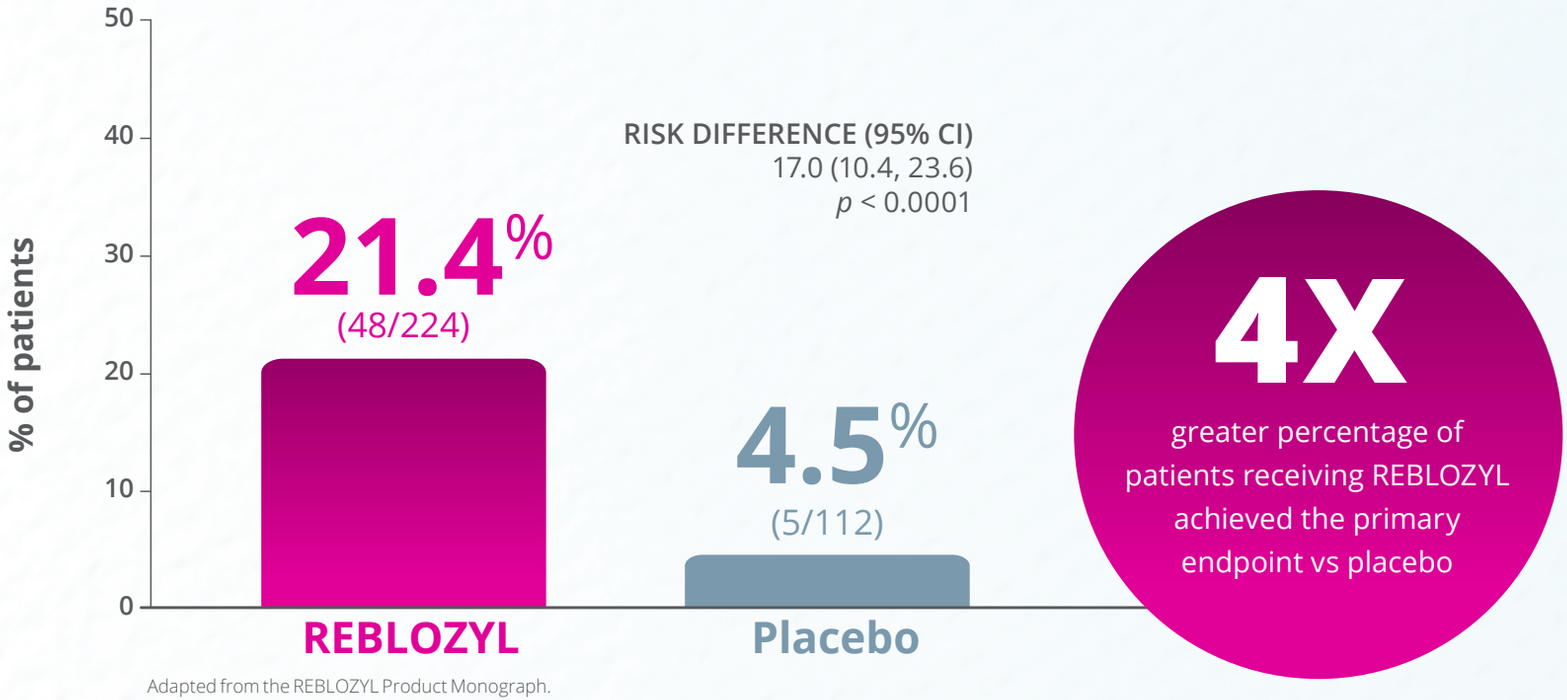
REBLOZYL PROVIDED SIGNIFICANT REDUCTIONS IN **RBC TRANSFUSION BURDEN COMPARED TO PLACEBO**[1]

PRIMARY ENDPOINT:

≥ 33% REDUCTION FROM BASELINE IN RBC TRANSFUSION BURDEN WITH A REDUCTION OF ≥ 2 UNITS FROM WEEKS 13 TO 24[1]



Adapted from the REBLOZYL Product Monograph.

Subgroup analysis on the primary endpoint hazard ratio were generally consistent across the predefined subgroups in:[1]

- Patients with the β0/β0 gene mutation
- Patients with a high transfusion burden (> 6 units/12 weeks) at baseline

CI: Confidence Interval; RBC: Red blood cell.

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SIGNIFICANT REDUCTIONS IN **RBC TRANSFUSION BURDEN WERE ACHIEVED AT WEEKS 13 TO 24 WITH REBLOZYL COMPARED TO PLACEBO**[1]

≥ 50% **REDUCTION FROM BASELINE IN RBC TRANSFUSION BURDEN WITH A REDUCTION OF ≥ 2 UNITS FROM WEEKS 13–24**

7.6%
(n = 17/224)
REBLOZYL

VS

1.8%
(n = 2/112)
Placebo

RISK DIFFERENCE (95% CI)
5.8 (1.6, 10.1)
p = 0.0303

Adapted from the REBLOZYL Product Monograph.

CI: Confidence Interval; RBC: Red blood cell.

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SIGNIFICANT REDUCTIONS IN RBC **TRANSFUSION BURDEN WERE ALSO SEEN AT WEEKS 37 TO 48 WITH REBLOZYL COMPARED TO PLACEBO**[1]

≥ 33% **REDUCTION FROM BASELINE IN RBC TRANSFUSION BURDEN WITH A REDUCTION OF ≥ 2 UNITS FROM WEEKS 37–48**

19.6%
(n = 44/224)
REBLOZYL

VS

3.6%
(n = 4/112)
Placebo

RISK DIFFERENCE (95% CI)
16.1 (9.8, 22.4)
$p < 0.00017$

Adapted from the REBLOZYL Product Monograph.

CI: Confidence interval; RBC: Red blood cell.

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SIGNIFICANT REDUCTIONS IN RBC **TRANSFUSION BURDEN WERE ALSO SEEN AT WEEKS 37 TO 48 WITH REBLOZYL COMPARED TO PLACEBO**[1]

≥ 50% **REDUCTION FROM BASELINE IN RBC TRANSFUSION WITH A REDUCTION OF ≥ 2 UNITS FROM WEEKS 37–48**

10.3%
(n = 23/224)
REBLOZYL

VS

0.9%
(n = 1/112)
Placebo

RISK DIFFERENCE (95% CI)
9.4 (5.0, 13.7)
p = 0.0017

Adapted from the REBLOZYL Product Monograph.

CI: Confidence interval; RBC: Red blood cell.

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ADVERSE **EVENTS**

- TEAEs in the BELIEVE trial reflected a median treatment duration of 64.1 weeks (range 3–97) in the REBLOZYL arm vs 64.0 weeks (range 9–92) in the placebo arm[1]

All TEAEs observed in ≥ 5% of REBLOZYL-treated patients including Grades 3 or 4 TEAEs reported in ≥ 1% of REBLOZYL-treated patients[1]*†

System organ class/preferred term	REBLOZYL N = 223		Placebo N = 109	
	All Grades n (%)	Grades 3–4* n (%)	All Grades n (%)	Grades 3–4 n (%)
Gastrointestinal disorders	**80 (36)**	**4 (2)**	**36 (33)**	**0 (0)**
Abdominal pain§	31 (14)	0 (0)	13 (12)	0 (0)
Diarrhea	27 (12)	1 (< 1)	11 (10)	0 (0)
Nausea	20 (9)	0 (0)	6 (6)	0 (0)
General disorders and administration site conditions	**105 (47)**	**4 (2)**	**45 (41)**	**0 (0)**
Fatigue	30 (14)	0 (0)	14 (13)	0 (0)
Pain	13 (6)	0 (0)	4 (4)	0 (0)
Metabolism and nutrition disorders	**34 (15)**	**10 (5)**	**7 (6.4)**	**1 (1)**
Hyperuricemia‖	19 (9)	9 (4)	1 (1)	0 (0)
Musculoskeletal and connective tissue disorders	**137 (61)**	**9 (4)**	**61 (56)**	**1 (1)**
Bone pain	44 (20)	3 (1)	9 (8)	0 (0)
Arthralgia	43 (19)	0 (0)	13 (12)	0 (0)
Pain in extremity	21 (9)	0 (0)	9 (8)	0 (0)

TEAE: Treatment emergent adverse event.
* Grade 3 or 4 TEAEs included have ≥ 1% greater frequency versus placebo.
† TEAEs are included without regard to causality.
‡ Limited to Grade 3 reactions with the exception of 4 events of Grade 4 hyperuricemia.
§ Grouped term includes abdominal pain and abdominal pain upper.
‖ Grouped term includes hyperuricemia and blood uric acid increase.

System organ class/preferred term	REBLOZYL N = 223		Placebo N = 109	
	All Grades n (%)	Grades 3–4* n (%)	All Grades n (%)	Grades 3–4 n (%)
Infections and infestations	**141 (63)**	**15 (7)**	**63 (58)**	**6 (6)**
Influenza	19 (9)	0 (0)	6 (6)	0 (0)
Viral upper respiratory tract infection	14 (6)	1 (0.4)	2 (2)	0 (0)
Nervous system disorders	**90 (40)**	**9 (4)**	**39 (29)**	**1 (1)**
Headache	56 (26)	1 (< 1)	26 (24)	1 (1)
Dizziness	25 (11)	0 (0)	5 (5)	0 (0)
Respiratory, thoracic and mediastinal disorders	**71 (32)**	**0 (0)**	**29 (27)**	**0 (0)**
Cough	32 (14)	0 (0)	12 (11)	0 (0)
Oropharyngeal pain	28 (13)	0 (0)	12 (11)	0 (0)
Vascular disorders	**25 (11)**	**4 (2)**	**6 (6)**	**0 (0)**
Hypertension†	18 (8)	4 (2)	3 (3)	0 (0)

Adapted from the REBLOZYL Product Monograph.

- The most common TEAEs in patients treated with REBLOZYL (≥ 10% and with ≥ 1% frequency compared to placebo) were:[1]
  - Headache (26%)
  - Fatigue (14%)
  - Diarrhea (12%)
  - Bone pain (20%)
  - Cough (14%)
  - Dizziness (11%)
  - Arthralgia (19%)
  - Abdominal pain (14%)
- Serious TEAEs occurred in 15.2% of patients treated with REBLOZYL compared to 5.2% of patients treated with placebo
  - Serious TEAEs of infections occurred in 5.8% of patients treated with REBLOZYL compared to 2.8% of patients treated with placebo

TEAE: Treatment emergent adverse event.
* Limited to Grade 3 reactions with the exception of 4 events of Grade 4 hyperuricemia.
† Grouped term includes essential hypertension, and hypertensive crisis.

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TREATMENT DISCONTINUATION AND **DOSE MODIFICATIONS DUE TO ADVERSE EVENTS**[1]

5.4% REBLOZYL vs **0.9%** Placebo

PERMANENT DISCONTINUATIONS DUE TO AN ADVERSE EVENT

Most common adverse events leading to discontinuation of REBLOZYL included arthralgia (0.9%), back pain (0.9%), and deep vein thrombosis (0.9%)

2.7% REBLOZYL vs **2.8%** Placebo

DOSE REDUCTIONS DUE TO AN ADVERSE EVENT

The most common adverse event leading to dose reduction of REBLOZYL was hypertension (0.9%)

15.2% REBLOZYL vs **10.1%** Placebo

DOSE DELAY/INTERRUPTIONS DUE TO AN ADVERSE EVENT

Most common adverse events leading to dose delay/interruption of REBLOZYL included upper respiratory tract infection (1.8%), ALT increase (1.3%), and cough (1.3%)

Adapted from the REBLOZYL Product Monograph.

ALT: Alanine aminotransferase.

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SELECTED LABORATORY ABNORMALITIES REPORTED IN THE BELIEVE TRIAL[1]

Lab shift	REBLOZYL N = 223 n (%)	Placebo N = 109 n (%)
ALT ≥ 3 x ULN	26 (12)	13 (12)
AST ≥ 3 x ULN	25 (11)	5 (5)
ALP ≥ 2 x ULN	17 (8)	1 (1)
Total bilirubin ≥ 2 x ULN	143 (64)	51 (47)
Direct bilirubin ≥ 2 x ULN	13 (6)	4 (4)
Creatine > 2 x baseline	6 (3)	0
Creatinine clearance < 0.5 x baseline	7 (3)	0
Leukocytes > 2 x baseline and > ULN	11 (5)	2 (2)

Adapted from the REBLOZYL Product Monograph.

Immunogenicity

Among 284 patients with β-thalassemia treated with REBLOZYL and evaluable for the presence of anti-luspatercept antibodies, 4 patients (1.4%) tested positive for treatment-emergent anti-luspatercept antibodies, including 2 patients (0.7%) who had neutralizing antibodies.[1]

There were no severe acute systemic hypersensitivity reactions reported for patients with anti-luspatercept antibodies in REBLOZYL clinical trials, and there was no association between hypersensitivity type reaction or injection site reaction and presence of anti-luspatercept antibodies.[1]

ALP: Alkaline phosphate; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; ULN: Upper limit of normal.

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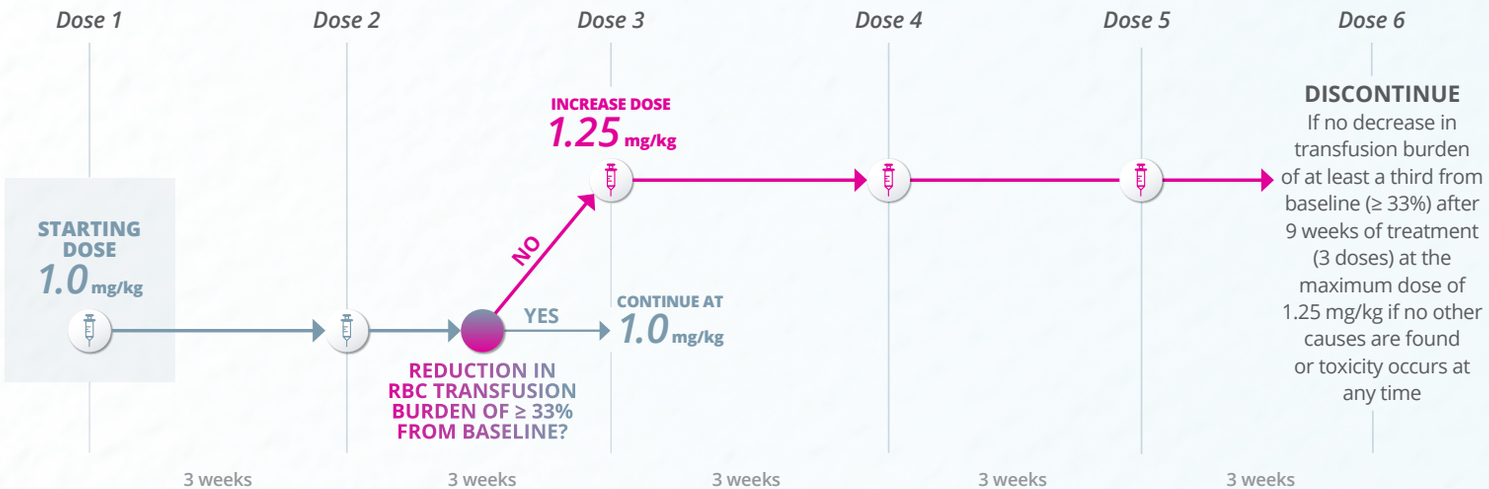
REBLOZYL DOSING **RECOMMENDATIONS**

Assess and review Hgb results prior to each administration[1]

- Start patients at the recommended starting dose of 1 mg/kg by subcutaneous (SC) injection once every 3 weeks
- Hemoglobin results prior to each administration must be considered for dosing purposes. If an RBC transfusion occurred prior to dosing, the pre-transfusion Hgb must be considered for dosing purposes
- If the pre-dose Hgb is ≥ 115 g/L and the Hgb level is not influenced by recent transfusion, delay dosing until the Hgb is ≤ 110 g/L

No reduction in transfusion burden after at least 6 weeks?

Increase dose to 1.25 mg/kg (maximum dose) if patient does not achieve a response, which is defined as a reduction in transfusion burden of at least a third from baseline (≥ 33%) after at least 2 consecutive doses at 1 mg/kg (6 weeks)[1]



Adapted from the REBLOZYL Product Monograph.

Dosing considerations[1]

- There are no dosing recommendations available for patients with severe renal impairment (estimated glomerular filtration rate [eGFR] < 30 mL/min/1.73 m^2) due to limited clinical data
- Consider the risk of REBLOZYL use in β-thalassemia patients excluded from clinical trials, i.e., patients with uncontrolled hypertension, a deep vein thrombosis or stroke in the previous 24 weeks, or use of an ESA within the previous 24 weeks
- Discontinue REBLOZYL in case of extramedullary hematopoietic (EMH) masses causing serious complications

If a planned administration of REBLOZYL is missed, administer REBLOZYL as soon as possible and continue dosing as prescribed, with at least 3 weeks between doses.[1]

ESA: Erythropoiesis-stimulating agent; Hgb: Hemoglobin.

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DOSAGE ADJUSTMENT **RECOMMENDATIONS***

Pre-dose hemoglobin ≥ 115 g/L or rapid hemoglobin rise

- If the pre-dose Hgb is ≥ 115 g/L in the absence of transfusions, delay dose and restart only when Hgb is ≤ 110 g/L[1]

Reduce dose if there is an increase in Hgb > 20 g/L within 3 weeks of previous dose, and in the absence of transfusion[1]

REBLOZYL DOSE RECOMMENDATIONS FOR β-THALASSEMIA

Current dose	Dosing recommendation
1.25 mg/kg	1 mg/kg
1 mg/kg	0.8 mg/kg
0.8 mg/kg	0.6 mg/kg
0.6 mg/kg	Discontinue REBLOZYL

Dose modifications to help manage adverse events[1]

Adverse events†	Dose modification
Any Grade 2 event	Delay dose until resolved to ≤ Grade 1
Grade 3 or 4	
Hypersensitivity reactions	Discontinue REBLOZYL
Leukocytosis‡ or suspected hematologic malignancy	Delay dose until resolved. Discontinue if hematologic malignancy is confirmed.
Other adverse reactions	Delay dose until resolved

Please refer to the Product Monograph for complete dosing recommendations and administration instructions.

Hgb: Hemoglobin; NCI-CTCAE: National Cancer Institute-Common Terminology Criteria for Adverse Events.
* A dose increase to 1.25 mg/kg may occur at any time during treatment after patients have received at least 2 consecutive doses of 1 mg/kg.
† Grades as per NCI-CTCAE or when not defined Grade 1 is mild, Grade 2 is moderate, Grade 3 is severe, and Grade 4 is life-threatening.
‡ Leukocytosis is defined as > 100,000 white blood cell/μL.

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REBLOZYL SHOULD BE RECONSTITUTED **AND ADMINISTERED BY A HEALTHCARE PROFESSIONAL**[1]

REBLOZYL is available in 2 strengths as single-use vials for reconstitution[1]

RECONSTITUTION VOLUMES

Vial size	Amount of sterile water for injection, USP required for reconstitution	Approximate deliverable volume	Nominal concentration per mL
25-mg vial	0.68 mL	0.5 mL	25 mg/0.5 mL (50 mg/mL)
75-mg vial	1.6 mL	1.5 mL	75 mg/1.5 mL (50 mg/mL)

Adapted from the REBLOZYL Product Monograph.

Healthcare professionals should reconstitute[1]:

- Using sterile water for injection, USP only
- The number of REBLOZYL vials to achieve the appropriate dose based on the patient's weight
- Using a syringe with suitable graduations for reconstitution to ensure accurate dosage
- Once reconstituted, the solution has a pH of 6.5

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REBLOZYL **RECONSTITUTION INSTRUCTIONS**

Adhere to the following steps to properly reconstitute REBLOZYL[1]

1 **Add sterile water for injection, USP.** Reconstitute with sterile water for injection, USP using volumes described in the reconstitution volumes table on page 16 with the stream directed onto the lyophilized powder. Allow to stand for 1 minute.

2 **Discard the needle and syringe used for reconstitution.** The needle and syringe used for reconstitution should not be used for SC injections.

3 **Mix and wait.** Gently swirl the vial in a circular motion for 30 seconds. Stop swirling and let the vial sit in an upright position for 30 seconds.

4 **Inspect.** Inspect the vial for undissolved particles in the solution. If undissolved powder is observed, repeat step 3 until the powder is completely dissolved.

5 **Mix and wait.** Invert the vial and gently swirl in an inverted position for 30 seconds. Bring the vial back to the upright position, and let it sit for 30 seconds.

6 **Repeat.** Repeat step 5 seven more times to ensure complete reconstitution of material on the sides of the vial.

7 **Inspect.** Parenteral drug products should be inspected visually for particulate matter and discolouration prior to administration whenever solution and container permit. REBLOZYL is a colourless to slightly yellow, clear to slightly opalescent solution, which is free of foreign particulate matter. Do not use if undissolved product or foreign particulate matter is observed.

8 **Storage.** If the reconstituted solution is not used immediately:

- Store at room temperature at 20°C to 25°C in the original vial for up to 8 hours. Discard if not used within 8 hours of reconstitution.
- Alternatively, the reconstituted solution can be refrigerated at 2°C to 8°C for up to 24 hours in the original vial. Remove from refrigerated conditions 15–30 minutes prior to injection to allow solution to reach room temperature for a more comfortable injection. Discard if not used within 24 hours of reconstitution.
  - **Do not freeze the reconstituted solution.**

Adapted from the REBLOZYL Product Monograph.
SC: Subcutaneous.

REBLOZYL **SC ADMINISTRATION**

- Prior to injection, allow the solution to reach room temperature for a more comfortable injection[1]

STEP 1

Verify correct dose for the patient

- Calculate the exact total dosing volume of 50 mg/mL solution required for the patient according to the table on page 16

STEP 2

Plan and prep for injection

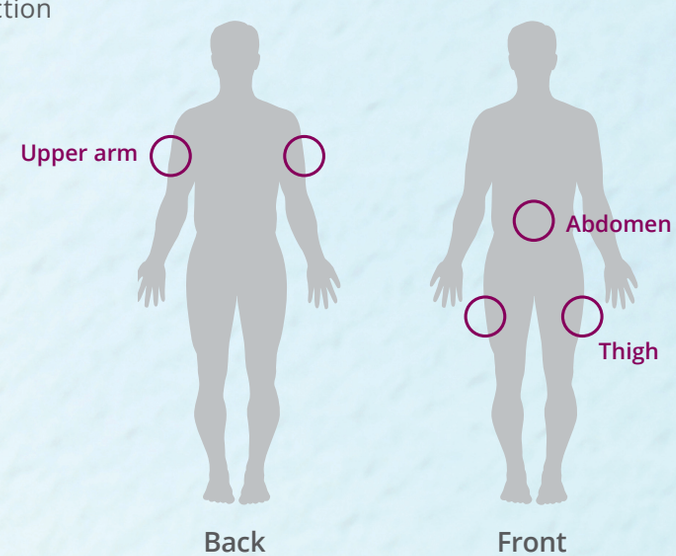
- Slowly withdraw the dosing volume of the reconstituted REBLOZYL solution from the single-use vial(s) into a syringe
- Divide doses requiring larger reconstituted volumes (i.e., > 1.2 mL) into separate similar volume injections and inject into separate sites

STEP 3

Perform SC administration

- If multiple injections are required, use a new syringe and needle for each SC injection
- Administer the SC injection into the upper arm, thigh, and/or abdomen

NOTE: ***Discard any unused portion. Do not pool unused portions from the vials. Do not administer more than 1 dose from a vial. Do not mix with other medications.***[1]



Adapted from the REBLOZYL Product Monograph.

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REBLOZYL **REQUIRES REFRIGERATED STORAGE**[1]

Storage of unreconstituted vial

- Store unreconstituted vials refrigerated at 2°C to 8°C in original carton to protect from light
- Do not freeze

Storage of reconstituted solution

- If the reconstituted solution is not used immediately, store at room temperature at 20°C to 25°C in the original vial for up to 8 hours. Discard if not used within 8 hours of reconstitution
- Alternatively, the reconstituted solution can be refrigerated at 2°C to 8°C for up to 24 hours in the original vial
  - Remove from refrigerated conditions 15–30 minutes prior to injection to allow the solution to reach room temperature for a more comfortable injection
  - Discard if not used within 24 hours of reconstitution
- Do not freeze the reconstituted solution

PATIENT PROFILE

Pr Reblozyl® luspatercept for injection

MEET GISELLE*

GISELLE IS 21 YEARS OLD

Diagnosis

- Diagnosed with β-thalassemia intermedia (β0β+) at age 8 after assessment of growth delay[6]
- Has received regular transfusions since her diagnosis and, in addition, has been on iron chelation therapy since age 10
- Transitioned from pediatric to adult care one year ago

Giselle has β-thalassemia intermedia with low pre-transfusion hemoglobin levels

Lab values at follow-up†

- Pre-transfusion hemoglobin levels: 85 g/L
- Post-transfusion hemoglobin levels: 110 g/L
- Serum ferritin levels: 1900 µg/L
- Liver iron concentration: 6.5 mg/g dry weight

Treatment

Red blood cell (RBC) transfusions, 3 units every 4 weeks, with an average of 4 hours for administration[7]

- Transfusions suppress the underlying ineffective erythropoiesis in β-thalassemia–associated anemia[6,8]

Iron chelation therapy taken once daily

- Iron chelation therapy helps manage iron overload[9]

Consider REBLOZYL for RBC transfusion-dependent anemia associated with β-thalassemia.[1]

* Giselle is a hypothetical patient and not from a clinical trial. Actual patient experiences may vary.
† Normal range in women for serum hemoglobin is 121–151 g/L and for serum ferritin, 12–150 µg/L.[10,11]

PATIENT **JOURNEY**

Pr Reblozyl® luspatercept for injection

1 **Diagnosis**
21-year-old patient diagnosed with β-thalassemia at age 8

2 **Lab values at follow-up***
- Pre-transfusion hemoglobin levels: 85 g/L
- Post-transfusion hemoglobin levels: 110 g/L
- Serum ferritin levels: 1900 µg/L
- Liver iron concentration: 6.5 mg/g dry weight

3 **Treatment**
RBC transfusions (3 units every 4 weeks), and iron chelation therapy

4 **A new option**
Physician prescribed REBLOZYL as a new treatment option that may reduce her RBC transfusion burden[1]

Clinical use:

Pediatrics (< 18 years of age): Health Canada has not authorized an indication for pediatric use.

Geriatrics (> 65 years of age): No differences in safety or effectiveness were observed between older (≥ 65 years) and younger patients when compared to placebo. Clinical studies in β-thalassemia did not include sufficient numbers of patients aged ≥ 65 to determine whether they respond differently.

Relevant warnings and precautions:
- Extramedullary hematopoietic (EMH) masses: Monitor patients with β-thalassemia. Not recommended for patients requiring treatment for EMH masses.[1]
- Hypertension: Monitor blood pressure prior to each administration.[1]
- Thrombosis/thromboembolic events (TEEs), including deep vein thrombosis, pulmonary emboli, and ischemic stroke. Consider thromboprophylaxis in patients at higher risk for developing TEE.[1]
- Monitoring and laboratory testing: Assess and review Hgb results prior to each administration of REBLOZYL.[1]
- Pregnancy: Potential for fetal harm when administered to pregnant women. Females of childbearing potential should be advised to avoid becoming pregnant while receiving REBLOZYL treatment. They are also advised to use effective contraception during treatment and for at least 3 months after the last dose.[1]
- The safe use of REBLOZYL during breast-feeding has not been established.[1]

For more information:

Consult the REBLOZYL Product Monograph for important information relating to adverse reactions, drug interactions, and dosing information, which has not been discussed in this piece. The Product Monograph is also available by calling our medical department at: **1-866-463-6267**.

Hgb: Hemoglobin; RBC: Red blood cell.
* Normal range in women for serum hemoglobin is 121–151 g/L and for serum ferritin, 12–150 µg/L.[10,11]

INTRODUCING **REBLOZYL**

Pr Reblozyl®
luspatercept for injection

REBLOZYL promoted erythroid maturation through differentiation of late-stage erythroid precursors (normoblasts) in mice[1]*

- REBLOZYL binds several endogenous TGF-β superfamily ligands, thereby diminishing SMAD2/3 signalling
- In models of β-thalassemia, REBLOZYL decreased abnormally elevated SMAD2/3 signalling and improved hematology parameters associated with ineffective erythropoiesis

REBLOZYL provided significant reductions in RBC transfusion burden compared to placebo[1]

- 21.4% of patients achieved a ≥ 33% reduction in transfusion burden from baseline of ≥ 2 units from Weeks 13 to 24 vs 4.5% with placebo ($p < 0.0001$).
- 7.6% of patients achieved ≥ 50% reduction in transfusion burden from baseline of ≥ 2 units from Weeks 13 to 24 vs 1.8% with placebo ($p = 0.0303$).

REBLOZYL safety profile was assessed in the phase 3 BELIEVE trial[1]

- The most common TEAEs in patients treated with REBLOZYL (≥ 10% and with ≥ 1% frequency compared to placebo) were headache (26%), bone pain (20%), arthralgia (19%), fatigue (14%), cough (14%), abdominal pain (14%), diarrhea (12%), and dizziness (11%)
- Serious TEAEs occurred in 15.2% of patients treated with REBLOZYL vs 5.2% of patients treated with placebo

Patients should discontinue REBLOZYL if response is not achieved after 9 weeks of treatment at the maximum dose level if no other causes are found or if unacceptable toxicity occurs[1]

- The recommended starting dose of REBLOZYL is 1 mg/kg once every 3 weeks by SC injection
- Doses can be increased to 1.25 mg/kg (maximum dose) if there is no reduction in transfusion burden of at least a third from baseline (≥ 33%) after at least 2 consecutive doses at 1 mg/kg (6 weeks)

RBC: Red blood cell; SC: Subcutaneous; TEAE: Treatment emergent adverse event; TGF-β: Transforming growth factor.
* Clinical significance is unknown.

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