Patient leaflet in accordance with the Pharmacists' Regulations (Preparations) - 1986
This medicine is dispensed with a doctor's prescription only

Reblozyl® 25 mg
Reblozyl® 75 mg
Powder for solution for injection

Active ingredient and its quantity:
Reblozyl® 25 mg: Each vial contains 25 mg luspatercept
Reblozyl® 75 mg: Each vial contains 75 mg luspatercept
After reconstitution, each mL of solution contains 50 mg luspatercept

Inactive ingredients - see section 6 under 'Additional information' and the section 'Important information about some of this medicine's ingredients' in section 2.

Read the entire leaflet carefully before you start using this medicine. This leaflet contains concise information about this medicine. If you have any further questions, ask your doctor or pharmacist.
This medicine has been prescribed to treat you. Do not pass it on to others. It may harm them, even if it seems to you that their medical condition is similar to yours.

In addition to the leaflet, Reblozyl has a **Patient Card (for women of childbearing potential)**. This card contains important safety information that you should know before starting and during the treatment with Reblozyl and which you should follow. Carefully read the Patient Card (for women of childbearing potential) and patient leaflet before starting treatment with this medicine. Keep the card for further reference if needed.

1. What is this medicine intended for?

- Reblozyl is indicated for the treatment of adult patients with transfusion-dependent anaemia due to very low, low and intermediate-risk myelodysplastic syndromes (MDS) with ring sideroblasts, who had an unsatisfactory response to or are ineligible for erythropoietin-based therapy.
- Reblozyl is indicated in adults for the treatment of anaemia associated with transfusion-dependent and non-transfusion-dependent beta-thalassaemia.

Therapeutic group: anti-anaemic medicines

Myelodysplastic syndromes (MDS)
Myelodysplastic syndromes (MDS) are a collection of many different blood and bone marrow disorders.
- Red blood cells become abnormal and do not develop properly.
- Patients can get a number of signs and symptoms including a low red blood cell count (anaemia) and may need red blood cell transfusions.

Beta-thalassaemia
Beta-thalassaemia is a blood problem that is passed down through genes.
- It affects the production of haemoglobin.
- Patients can get a number of signs and symptoms including a low red blood cell count (anaemia) and may need red blood cell transfusions.

How this medicine works
Reblozyl improves your body's ability to make red blood cells. Red blood cells contain haemoglobin, which is a protein that carries oxygen throughout your body. As your body makes more red blood cells, your haemoglobin level increases.

For MDS and beta-thalassaemia patients in need of regular blood transfusions
Reblozyl treatment can prevent or reduce the need for red blood cell transfusions.
- Red blood cell transfusions can cause abnormally high levels of iron in the blood and in different organs of the body. This can be harmful over time.

For beta-thalassaemia patients not in need of regular blood transfusions
Treatment with Reblozyl can improve your anaemia by increasing your haemoglobin level.

2. Before using this medicine

Do not use this medicine if:

- you are sensitive (allergic) to luspatercept or to any of the other ingredients in this medicine (listed in section 6).
- you are pregnant (see the section 'Pregnancy').
- you require treatment for the control of mass producing blood cells outside the bone marrow (extramedullary haemopoiesis masses, EMH masses).

Special warnings about using this medicine
Before treatment with Reblozyl, tell your doctor if:
- you are a patient with beta-thalassaemia:
  - and you have had your spleen removed. You may have a higher risk of getting a blood clot. Your doctor will talk to you about other possible risk factors that may increase your risk – these include:
    - hormone replacement therapy or
    - a previous blood clot
- you are a patient with MDS:
  - and you have had a stroke or problems with your heart or with blood circulation. You may have a higher risk of getting a blood clot.

  Your doctor may use preventive measures or medicines to reduce the chances of you getting a blood clot.
- you have severe back pain that does not go away, numbness or weakness or loss of voluntary movement in legs, hands or arms, loss of bowel and bladder control (incontinence). They may be symptoms of EMH masses and compression of spinal cord.
- you have ever had high blood pressure – this is because Reblozyl may increase blood pressure. Your blood pressure will be checked before you are given Reblozyl and throughout treatment. You will be given Reblozyl treatment only if your blood pressure is under control.
- you have a medical condition that affects the strength and health of your bones (osteopenia and osteoporosis). You may have a risk of breaking your bones more easily.

Children and adolescents
This medicine is not intended for children and adolescents under 18 years.

Tests and follow-up
You will have a blood test before each dose of Reblozyl. This is because your doctor needs to make sure your haemoglobin level is suitable for you to be given treatment.

If you have kidney problems, your doctor may perform additional tests.

Drug interactions
If you are taking, have recently taken, or might take other medicines, including non-prescription medications and dietary supplements, tell your doctor or pharmacist.

Pregnancy, breast-feeding and fertility

Pregnancy
- Do not use Reblozyl during pregnancy and for at least 3 months before getting pregnant. Reblozyl may cause harm to your unborn baby.
- Your doctor will arrange a pregnancy test before starting treatment and will give you a patient card.
- If you think you may be pregnant or are planning to have a baby, ask your doctor for advice before using this medicine.

Breast-feeding
- Do not breast-feed when using this medicine and for 3 months after your last dose. It is not known if this medicine passes into the mother's milk.

Contraception
- You should use an effective method of contraception during treatment with Reblozyl and for at least 3 months after your last dose.

Talk to your doctor about contraceptive methods that are right for you while you are using this medicine.

Fertility
If you are a woman, this medicine may cause fertility problems. It could affect your ability to have a baby. Consult your doctor before using it.

Driving and using machines
Reblozyl may have a minor influence on your ability to drive and use machines. Your ability to react when performing these tasks may be impaired since you may feel tired, dizzy, or faint, while using Reblozyl. If this happens do not drive or use any tools or machines and contact your doctor straight away.

Important information about some of this medicine's ingredients
This medicine contains less than 1 millimole sodium (23 mg) per dose, that is to say essentially 'sodium-free'.

3. How to use this medicine?

Always use this medicine according to your doctor's instructions.
Check with your doctor or pharmacist if you are not sure about your dose or about how to take this medicine.

Before you are given this medicine, your doctor will carry out blood tests and decide whether you need Reblozyl.
Reblozyl will be given by an injection under your skin (subcutaneously).

Only your doctor will determine your dose and how you should take this medicine. The recommended dosage is usually:
The dose is based on how much you weigh – in kilograms. The injections will be given by a doctor or nurse.
- The recommended starting dose is 1.0 mg for each kilogram of body weight.
- This dose should be given once every 3 weeks.
- Your doctor will check your progress and may change your dose if needed.

Your doctor will monitor your blood pressure while you are using Reblozyl.

Myelodysplastic syndromes
The maximum single dose is 1.75 mg for each kilogram of body weight.

Beta-thalassaemia
The maximum single dose is 1.25 mg for each kilogram of body weight.

Do not exceed the recommended dose.

If an accidental overdose is injected, or if a child has accidentally swallowed some of this medicine, immediately speak to a doctor or go to a hospital. Take the medicine package and this leaflet with you.

If you forget a dose of medicine
If you miss an injection of Reblozyl, or an appointment is delayed, you will receive a Reblozyl injection as soon as possible. Then, your dose will continue as prescribed – with at least 3 weeks between doses.

Adhere to the treatment as recommended by your doctor.

Even if your health improves, do not stop treatment with this medicine without consulting your doctor.

Do not take medicines in the dark! Check the label and dose every time you take medicine. Wear glasses if you need them.

If you have any further questions about using this medicine, consult your doctor or pharmacist.

4. Side effects

Like with all medicines, using the medicine Reblozyl may cause side effects in some users. Do not be alarmed by this list of side effects; you may not experience any of them.

Serious side effects
Tell your doctor or pharmacist straight away if you notice the following effects:
- difficulty in walking or speaking, dizziness, loss of balance and coordination, numbness or paralysis in the face, leg or arm (often on one side of your body), blurred vision. They may all be symptoms of a stroke
- painful swelling and tightness in the leg or arm (blood clots)
- severe back pain that does not go away, numbness or weakness or loss of voluntary movement in legs, hands or arms, loss of bowel and bladder control (incontinence). They may be symptoms of extramedullary haemopoiesis masses (EMH masses) and compression of spinal cord
- swelling of the area around the eyes, the face, lips, mouth, tongue or throat
- allergic reactions
- rashes

Other side effects include:
Very common side effects - affect more than one in ten users:
- cough
- difficulty in breathing or shortness of breath
- swelling of your legs or hands (peripheral oedema)
- high blood pressure without symptoms or associated with headache
- upper respiratory tract infection
- flu or flu like symptoms
- dizziness, headache
- diarrhoea, nausea
- belly pain
- back, joint or bone pain
- feeling tired or weak
- difficulty to sleep or to stay asleep
- changes in blood test results (increase in liver enzymes, increase in blood creatinine levels). These may be signs of liver and kidney problems
- cramps, dizziness, irregular heartbeat, mental confusion. These may be symptoms of too much or not enough of certain minerals in your body (electrolyte abnormalities)

Common side effects - affect 1-10 in 100 users:
- chest infection
- fainting, spinning feeling, feeling confused
- decreased appetite
- abdominal discomfort
- broken bones caused by trauma
- muscle pain
- chest pain
- muscle weakness
- pinpoint, round red/purple spots
- easy bruising, bleeding from the nose or gums
- intense headaches on one side of the head
- rapid heartbeat (tachycardia)
- redness, burning and pain at the site of injection (injection site reactions) or swelling, itchy skin (injection site erythema)
- impaired kidney function
- excessive sweating
- high level of uric acid in the blood (shown in tests)
- not enough fluid in your body (dehydration)
- urinary tract infection
- foamy urine. This may be a sign of too much protein in your urine (proteinuria and albuminuria)
- shortness of breath while you exercise or when you lie down. This may be a sign of heart failure
- anxiety
- irritability

If you experience any side effect, if any side effect gets worse, or if you experience a side effect not mentioned in this leaflet, consult your doctor.

You can report side effects to the Ministry of Health by following the link 'Reporting Side Effects of Drug Treatment' on the Ministry of Health home page (www.health.gov.il) which links to an online form for reporting side effects. You can also use this link: https://sideeffects.health.gov.il

5. How to store the medicine?

- Prevent poisoning! To prevent poisoning, keep this, and all other medicines in a closed place, out of the reach and sight of children and/or infants. Do not induce vomiting unless explicitly instructed to do so by a doctor.
- Do not use the medicine after the expiry date (exp. date) which appears on the vial and carton. The expiry date refers to the last day of that month.

Storage conditions:
- Store the unopened vial in a refrigerator (2°C–8°C). Do not freeze. Store in the original carton in order to protect from light.
- After first opening and reconstitution, Reblozyl should be used immediately. If not used immediately, when held in the original carton the reconstituted medicine may be stored for up to 8 hours at room temperature (≤ 25°C) or for up to 24 hours at 2°C–8°C.
- Do not freeze the reconstituted solution.

6. Additional information

- In addition to the active ingredient, this medicine also contains:
  sucrose, tri-sodium citrate dihydrate, polysorbate 80, citric acid monohydrate, hydrochloric acid and sodium hydroxide.

What the medicine looks like and contents of the pack
Reblozyl is a white to off-white powder for solution for injection. Reblozyl powder is supplied in glass vials containing 25 mg or 75 mg of luspatercept.
Each pack contains one vial.

Registration holder's name and address
Bristol-Myers Squibb (Israel) Ltd.,
18 Aharon Bart St. P.O Box 3361,
Kiryat Arye,
Petach Tikva 4951448

Manufacturer's name and address
Celgene Corporation
86 Morris Avenue,
Summit, New Jersey, 07901, USA

Registration number of the medicine in the Ministry of Health's National Drug Registry:
Reblozyl® 25 mg: 169-03-36646-00
Reblozyl® 75 mg: 169-04-36647-00

Revised in June 2024.

The following information is intended for healthcare professionals only

המידע הבא מיועד לצוות רפואי בלבד

المعلومات التالية معدّة للطاقم الطبيّ فقط

Traceability
In order to improve the traceability of biological medicinal products, the name of the administered product should be clearly recorded.
It is recommended to record the batch number as well.

Incompatibilities
This medicinal product must not be mixed with other injectable medicinal products.

Storage of the product
Unopened vial
Store in a refrigerator (2°C – 8°C). Do not freeze. Store in the original carton in order to protect from light.

Reconstituted solution
When stored in the original carton, chemical and physical in-use stability of the reconstituted medicinal product has been demonstrated for up to 8 hours at room temperature (≤ 25°C) or for up to 24 hours at 2°C – 8°C.

From a microbiological point of view, the medicinal product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and should not be longer than 24 hours at 2°C – 8°C.

Do not freeze the reconstituted solution.

Dose calculation
The total dose, according to the patient's weight (kg) can be calculated as follow:

Total dose (mg) = Dose level (mg/kg) x patient's weight (kg) every three weeks.

Reconstitution instructions
Reblozyl is supplied as a lyophilised powder to be reconstituted with water for injections (WFI). A syringe with appropriate graduations must be used for reconstitution to ensure accurate dosage. See Table 1.

Table 1. Reblozyl reconstitution table

Strength	Amount of WFI required for reconstitution	Post-reconstitution concentration (nominal value)
25 mg vial	0.68 mL	50 mg/mL (0.5 mL)
75 mg vial	1.6 mL	50 mg/mL (1.5 mL)

1. Remove the coloured cap from the vial and wipe the top with an alcohol wipe.
2. Add WFI into the vial by means of a syringe with appropriate graduations with a needle directing the flow onto the lyophilised powder. Allow to stand for one minute.
3. Discard the needle and syringe used for reconstitution. Do not use them for subcutaneous injection.
4. 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.
5. Inspect the vial for undissolved powder in the solution. If undissolved powder is observed, repeat step 4 until the powder is completely dissolved.
6. 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.
7. Repeat step 6 seven more times to ensure complete reconstitution of material on the sides of the vial.
8. Visually inspect the reconstituted solution prior to administration. When properly mixed, Reblozyl reconstituted solution is a colourless to slightly yellow, clear to slightly opalescent solution which is free of visible foreign particulate matter. Do not use if undissolved product or foreign particulate matter is observed.
9. If the reconstituted solution is not used immediately, see *Storage of the product* section above.

Method of administration
If the Reblozyl reconstituted solution has been refrigerated, remove from the refrigerator 15-30 minutes prior to injection to allow it to reach room temperature. This will allow for a more comfortable injection.

The recommended maximum volume of medicinal product per injection site is 1.2 mL. If more than 1.2 mL is required, the total volume of Reblozyl should be divided into separate similar volume injections and administered across separate sites using the same anatomical location but on opposite sides of the body. Reconstitute the appropriate number of Reblozyl vials to achieve the desired dose.

Inject Reblozyl subcutaneously into the upper arm, thigh or abdomen.

If multiple injections are required, use a new syringe and needle for each subcutaneous injection. Discard any unused portion. Do not administer more than one dose from a vial.

Disposal
Dispose of any unused medicinal product or waste material in accordance with local requirements.