PATIENT INFORMATION LEAFLET

Dropoetin Containing 2000 IU/ 0.2 ml SC/IV Solution for Injection, Ready to Use Syringe

It is applied intravenously or under the skin.

- ***Active Substance:*** Epoetin alpha

*** Epoetin alpha is a biosimilar produced using the culture of ovarian cells of the Chinese Hamster, genetically modified with recombinant DNA technology.**

- ***Excipient:*** Polysorbate 20, Propylene glycol, Glycine, D-mannitol, Sodium chloride, Monobasic sodium phosphate monohydrate, Dibasic sodium phosphate heptahydrate, Water for injection.

▼ This medicine is subject to additional monitoring. This triangle will enable the rapid identification of new safety information. You can help by reporting any side effects that occur.

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others.
- Tell your doctor if you go to a doctor or the hospital when you use this medicine.
- Follow strictly to what is written in these instructions. Do not use high or low doses other than the recommended dose for the medication.

What is in this leaflet:

The headlines are involved in.

1. What DROPOETIN is and what it is used for?

• DROPOETIN contains epoetin alpha (A biosimilar that produced by using genetically modified ovarian cells culture of Chinese Hamster with recombinant DNA technology), a protein that stimulates bone marrow to produce more red blood cells. • DROPOETİN is a ready-to-use syringe containing clear, colorless solution. In one package, 6 ready-to-use syringes are provided with needle safety device.

• DROPOETIN is used to treat anemia caused by kidney disease:

- In children who are undergoing hemodialysis (removal of harmful substances in the blood with a machine when the kidneys cannot)
- In adults undergoing hemodialysis or peritoneal dialysis
- In adults with severe anemia who have not yet been on dialysis (deficiency in the number of red blood cells)

• If you have kidney disease, your red blood cells may be insufficient in case of your kidneys are not producing enough erythropoietin (required for red cell production). DROPOETIN is prescribed to stimulate your bone marrow to produce more red blood cells.

2. The things that should be cared before use DROPOETIN;

Do not use DROPOETIN in the following situations.

If;

- If you are allergic (if sensitive) to epoetin alpha or any of the other ingredients of DROPOETIN.
- If you have been diagnosed with pure red cell aplasia (SKHA) after any previous treatment with any product (including DROPOETIN) that stimulates red blood cell production (in this case, the bone marrow cannot produce enough red blood cells). (See section “4. What are the possible side effects?”).
- If you have been diagnosed with pure red cell aplasia (SKHA) (in this case, the bone marrow cannot produce enough red blood cells). after any previous treatment with any product (including DROPOETIN) that stimulates red blood cell production (See section “4. What are the possible side effects?”)
- If you have high blood pressure that is not properly controlled with medicines.
- To stimulate the production of your red blood cells if your own blood cannot be transfused during or after surgery. (for doctors to get more blood from you)

- If you are about to undergo significant elective orthopedic surgery (e.g. hip or knee surgery) and:
  - you have severe heart disease
  - you have severe artery and vein disorders
  - have recently had a heart attack or stroke
  - If you cannot take blood-thinning medications

Cancer, cancer-related and cancer chemotherapy-related anemias,

- DROPOETIN may not be suitable for you. Please talk to your doctor. While using DROPOETIN, some people need medications to reduce the risk of blood clots. If you cannot take medicines that prevent blood clotting, you should not use DROPOETIN.

USE DROPOETIN CAREFULLY in the following cases.

When DROPOETIN and other products that stimulate red blood cell production are administered above the target hemoglobin level of 12 g / dl, it may increase the risk of cancer, worsening in cases of death, heart attack, stroke, vascular occlusion and cancer. For this reason, your doctor will regularly perform blood tests to ensure that your hemoglobin level in your blood remains within the range of 10 to 12 g / dl.

As with all other therapeutic proteins, there is a potential risk of immunogenicity for DROPOETIN.

• DROPOETIN and other products that stimulate red blood cell production may increase the risk of developing blood clots in all patients. If you have other risk factors in terms of blood clot development, this risk may be higher (for example, if you have had a blood clot in the past; if you are overweight; if you have diabetes; if you have heart disease; you have had to lie down for a long time due to surgery or disease). If any of these are involved, please tell your doctor. Your doctor will help you decide whether DROPOETIN is suitable for you.

It is important to tell your doctor if any of the following applies to you. Despite all this, you can use DROPOETIN, but talk to your doctor first.

- If you already know that you are discomforting or have disorder:

• heart disease

• high blood pressure

• epileptic seizure or attack

• liver disease

• anemia from other causes

• porphyria (a rare blood disease)

• If you are a cancer patient, you should be conscious that products that stimulate red blood cell production, such as DROPOETIN, can act as a growth factor and thus theoretically affect the progression of your cancer. In these conditions, depending on your individual situation, blood transfusion may be preferred. Please discuss this with your doctor.

Severe skin reactions, including Stevens-Johnson Syndrome (SJS) and toxic epidermal necrolysis (TEN), have been reported in relation to epoetin treatment. Severe skin reactions, including Stevens-Johnson Syndrome (SJS) and toxic epidermal necrolysis (TEN), have been reported in relation to epoetin treatment.

The SJS / TEN initially appears on the body in the form of a target type red dot, or often circular bubble patches with center. In addition, mouth, throat, nose, genital area and eye (red and bulging eyes) ulcers may occur. Serious skin rashes usually occur before fever and / or flu-like symptoms. Rashes can cause skin peeling and the spread of life-threatening complications.

If you develop a severe rash or any of these skin symptoms, stop using DROPOETIN, contact your doctor immediately, or seek medical help.

Pay special attention to other products that stimulate red blood cell production: DROPOETIN is one of the product groups that stimulate red blood cell production, such as human erythropoietin, a protein. Please make sure exactly what the product you use. If you have been given a product other than DROPOETIN from this product group during your treatment, talk to your doctor or pharmacist.

In order to ensure the traceability of biosimilar products, the trade name and serial number of the applied product must be recorded in the patient file.

If these warnings are valid for you, even at any time in the past, please consult your doctor.

Using DROPOETIN with food and drink

There is no information that suggests that food or beverages have an impact on the efficacy and safety of DROPOETIN.

Pregnancy

Consult your doctor or pharmacist before using this medication.

If you are at an age likely to conceive, consult your doctor for the need to prevent pregnancy.

If you notice that you are pregnant during your treatment, consult your doctor or pharmacist immediately.

Breast-feeding

Consult your doctor or pharmacist before using this medication.

Driving and using machines

No studies on the effect of DROPOETIN on the ability to drive and use machines have been performed. However, you should be careful when performing such activities.

Important information about some of the ingredients of DROPOETIN

DROPOETIN contains less than 1 mmol (23 mg) of sodium in each ready-to-use syringe; in other words, it can be accepted that it does not contain sodium. No warning related to sodium is required.

Using with other medicines

DROPOETIN does not normally react with other medicines, however, if you are using any other medication (or have been using it recently), including those obtained without a prescription, please tell your doctor.

• If you are taking a medicine called cyclosporine (used after kidney transplants), your doctor may order blood tests to check your cyclosporine levels while you are taking DROPOETIN.

• Iron supplements and other drugs that stimulate red blood cell formation may increase the effectiveness of DROPOETIN. Your doctor will decide if it is right to take them.

• Drugs that reduce the production of red blood cells can reduce the response to DROPOETIN. The production of red blood cells decreases with drugs that cause bone marrow suppression, such as azathioprine, which affects chemotherapy and the immune system. Non-steroidal anti-inflammatory drugs can also cause bone marrow suppression in some rare cases.

• If you are visiting a hospital, clinic or family physician, tell them that you are receiving DROPOETIN treatment. DROPOETIN treatment may affect other treatments or test results.

If you are currently using any prescription or non-prescription medication or have used it recently, please inform your doctor or pharmacist about them.

*3.*How to take DROPOETIN?

- **Instructions for proper use and dose / frequency of administration:**

Always use this medicine exactly as your doctor has told you. If you are not sure, consult your doctor.

Your doctor may decide that DROPOETIN treatment is necessary for you after performing the blood tests.

DROPOETIN can be given by injection:

• Either into a vein or into a tube that goes into a vein (intravenously)

• Or under the skin (subcutaneously)

Your doctor will decide how to inject DROPOETIN. Injections will usually be administered by a doctor, nurse, or other healthcare professional. Depending on the reason why they need DROPOETIN treatment, some people can then learn how to inject the product themselves under the skin: See "Instructions on how to inject DROPOETIN" in Chapter 5.

• After the expiration date on the label or outer packaging,

• If you know the product is frozen or you think it may have been frozen by accident,

• If there is a malfunction in your refrigerator.

The dose of DROPOETIN you use is determined based on your body weight in kilograms. The cause of your anemia is also a factor your doctor takes into account when deciding on the right dosage.

Your doctor will regularly monitor your blood pressure while you are taking Dropoetin.

• **Different age groups:**

Use in children (in the treatment of anemia associated with chronic kidney failure): DROPOETIN dose is determined by your doctor based on body weight in kilograms.

Use in the elderly:

There were no differences in safety and efficacy between older patients and younger patients. In order to reach and maintain the target hemoglobin value, dose selection and dose adjustment in elderly patients should be individualized.

• Special use cases:

Kidney failure

Your doctor will keep your hemoglobin level between 10 and 12 g / dl, as high hemoglobin levels can increase the risk of blood clots and death.

The usual starting dose of DROPOETIN for adults and children is 50 International Units per kilogram (kg) of body weight three times a week. DROPOETIN is administered twice a week for patients on peritoneal dialysis.

DROPOETIN is administered to adults and children as an injection into a vein or into a tube that goes into a vein. When it is not possible to easily access this route of administration (via a vein or tube), your doctor may decide that DROPOETIN should be injected under the skin (subcutaneously). This method also includes patients who are on dialysis and not on dialysis yet.

Your doctor will order regular blood tests, usually every four weeks, to see how well your anemia responds to treatment and adjust the dose.

When your anemia improves, your doctor will continue to check your blood regularly, and your DROPOETIN dose and frequency of administration can be adjusted separately to maintain your response to treatment.

If you are taking DROPOETIN at longer intervals (more than once a week), you may not be able to maintain adequate hemoglobin levels, and you may need an increase in DROPOETIN dose or frequency of administration.

To make the treatment more effective, iron supplements may be given to you before and during DROPOETIN treatment.

If you are on dialysis treatment when you start taking DROPOETIN treatment, it may be necessary to adjust your dialysis regimen. Your doctor will decide this.

Liver failure:

DROPOETIN should be used with caution in patients with chronic liver failure.

If you are a patient with hepatitis C and you are using interferon and ribavirin

You should share this with your doctor, as the use of epoetin alpha with interferon and ribavirin leads to loss of effect and the development of a condition called SKHA, which in rare cases is a severe form of anemia. DROPOETIN is not approved for the treatment of hepatitis C-related anemia.

If you have an impression that the effect of DROPOETIN is too strong or weak, talk to your doctor or pharmacist.

If you have used more DROPOETIN than you should:

Side effects from overdose of DROPOETIN are unlikely to occur.

If you have used more than you should use from DROPOETIN, talk to a doctor or pharmacist immediately.

If you forget to use DROPOETIN:

As soon as you remember, apply the next injection. If you are on the day following the next injection, disregard the missed dose and continue your normal schedule.

Do not take a double dose to make up for a forgotten dose.

Effects that may occur when treatment with DROPOETIN is terminated:

When DROPOETIN treatment is discontinued, hemoglobin value may decrease during the following weeks, depending on the patient's underlying medical condition.

4.What are the possible side effects?

Like all medicines, DROPOETIN may cause side effects, but these side effects may not occur in everyone.

Side effects are defined as shown in the following categories:

Very common: It occurs in at least 1 of 10 patients.

Common: Less than one in 10 patients, but more than one in 100 patients.

Uncommon: Less than one in 100 patients, but more than one in 1,000 patients.

Rare: Less than one in 1,000 patients, but more than one in 10,000 patients.

Very rare: Less than one in 10,000 patients can be seen.

Unknown: It cannot be estimated from the available data.

If one of the following occurs, stop using DROPOETIN and report it to your doctor IMMEDIATELY or contact the emergency department of the nearest hospital:

• Severe allergic and anaphylactic reactions (hypersensitivity reactions in the body) such as swelling of the face, lips, mouth, tongue or throat, difficulty swallowing and breathing, itchy rash (hives)

• Life threatening situations

• Blood clots (including deep vein thrombosis and embolism) that require immediate treatment. In this case, you may develop chest pain, shortness of breath, and especially painful swelling and redness of your legs.

Very common

• Diarrhea

• Nausea

• Vomiting

• Fire

Common:

• Increased blood pressure. Headaches, especially sudden, migraine-like headaches, such as stabbing a knife, confusion, or seizures can be symptoms of a sudden increase in blood pressure. This condition requires urgent treatment. An increase in blood pressure may require treatment with medications (or by adjusting any medication you have already taken for high blood pressure).

• Cough

• Skin rashes that may result from an allergic reaction

• Bone or muscle pain

• Flu-like complaints such as headache, pain and hurt in the joints, feeling of weakness, chills, fatigue and dizziness. These are more common at the start of treatment. If you experience these complaints during the injection into the vein, slower administration of the injection may help prevent them in the future.

• Redness, burning and pain at the injection site

• Swelling of the ankle, foot or fingers

• Pain in the arms and legs

Uncommon:

• High blood potassium levels that can lead to abnormal heart rhythm (this is a very common side effect in dialysis patients)

• Seizures

• Blockage in the nose or airway

• Severe allergic reactions such as swelling of the face, lips, mouth, tongue or throat, difficulty swallowing and breathing, itchy rash (hives) (Hypersensitivity in the body)

• Urticaria (rash)

Rare

• Symptoms of pure red blood cell network plasma (SCHA)

SCHA is a condition that means that it cannot produce enough red blood cells in the bone marrow. SCHA causes sudden and severe anemia. Its symptoms are:

• Unusual tiredness,

• Feeling dizzy,

• Shortness of breath

SCHA has been reported very rarely after months-years of treatment with DROPOETIN and other products that stimulate red blood cell production, mostly in patients with chronic renal failure.

• Increased levels of small blood flakes (called platelets) may occur, which are normally involved in the formation of a blood clot, especially when starting treatment.

Your doctor will check this.

• Hypersensitivity to the body

• Blood disease that causes pain during urination, darkening of the urine color or increased sensitivity of the skin to sunlight (Porphyria)

Unknown

• Sudden and severe increase in blood pressure (Hypertensive crisis)

• Edema in the subcutaneous tissues such as lips, tongue, and eyelids and respiratory tract, swelling

• Ineffectiveness of the drug

If you are on hemodialysis treatment:

• Blood clots (thrombosis) may occur in your dialysis shunt. This is more likely if you have low blood pressure or if your fistula has complications.

• Blood clots can also form in your hemodialysis system. Your doctor may decide to increase your dose of heparin, an anti-blood clotting medication during dialysis.

Severe skin rashes such as Stevens-Johnson Syndrome (SJS) and toxic epidermal necrolysis (TEN) have been reported in relation to epoetin treatment. These usually appear in the form of a target-type red spot on the body, or often circular blistering circular patches, skin peels, mouth, throat, nose, genitals, and eye ulcers, and may occur before fever and flu-like symptoms. If you develop a severe rash or any of these skin symptoms, stop using DROPOETIN, contact your doctor immediately, or seek medical help. Also review section 2.

If you notice any of these effects or any other effects during treatment with DROPOETIN, tell your doctor or nurse immediately.

If you encounter any side effects not mentioned in this leaflet, inform your doctor or pharmacist.

Reporting of side effects

If any side effects occur in the instructions for use or not, talk to your doctor, pharmacist or nurse.

5.How to store DROPOETIN?

Keep DROPOETIN in places and in its packaging where children cannot see and reach it.

• Store in the refrigerator (2 °C- 8 °C).

• Do not freeze or shake.

• Store in the original packaging to protect from light.

• Do not use DROPOETIN if you notice that the seal is crumbling or the liquid is colored or you can see particles floating in it.

Do not use DROPOETIN syringes if any of these apply. Talk to your doctor or pharmacist.

How to throw DROPOETIN?

Do not dispose of expired or unused drugs!

DROPOETIN should not be used in the following cases:

- After the expiration date on the label or outer packaging,

- If you know the product is frozen or you think it might have been frozen by accident,

- If there is a malfunction in your refrigerator.

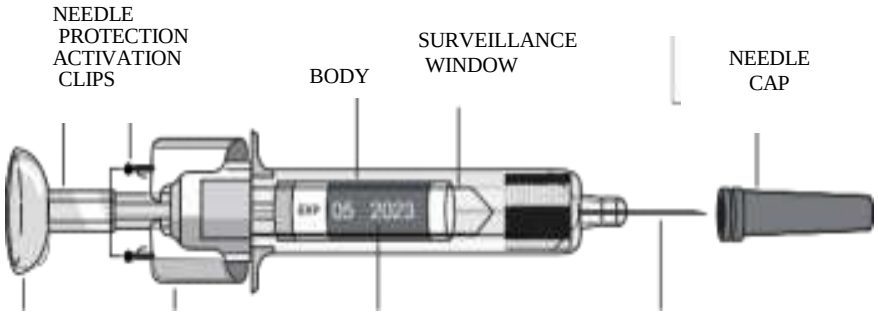
Use in accordance with the expiration date.

Do not use DROPOETIN, which has expired after the EXP (Expiration date) letters on the box and label. The expiry date defines the last day of the specified month.

Instructions on how to inject DROPOETIN into yourself

Figure 1 shows the syringe ready for use.

PISTON



PISTON HEAD
NEEDLE PROTECTION WINGS
LABEL
NEEDLE

Instructions on how to inject DROPOETIN into yourself

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When treatment begins, DROPOETIN injection is usually administered by the medical treatment or care team. Your doctor may then advise you to learn how to inject DROPOETIN under the skin (subcutaneously) or your caregiver to learn.

- **Do not try to inject yourself until you know how to do this from your doctor or nurse.**
- **Always use DROPOETIN strictly according to the instructions of your doctor or nurse.**
- **Only use DROPOETIN if it has been stored correctly "5. See "Storing DROPOETIN".**
- **Allow the DROPOETIN syringe to stand until it reaches room temperature before use. It usually takes 15 to 30 minutes to reach this temperature.**

Take only one dose of DROPOETIN from each syringe.

If DROPOETIN is injected subcutaneously, the amount injected is normally at most one milliliter (1 ml) in a single injection.

DROPOETIN should be applied alone and not mixed with other injection liquids.

Do not shake the DROPOETIN syringe. Shaking quickly for a long time can damage the product.

This product should not be used if it is shaken rapidly.

How can you apply the injection to yourself using a ready-to-use syringe?:

Ready-to-use syringes are equipped with the PROTECS^{TM} needle protection device to help prevent needle-tip injuries after use. This is indicated on the packaging.

- **Take a syringe from the refrigerator.** The liquid should come to room temperature. Do not remove the syringe needle cap while waiting for it to reach room temperature.
- **Check the syringe** to make sure it is the correct dose, the expiration date has not passed, is not damaged, and the liquid is clear and not frozen.
- **Choose an injection site.** Suitable places are the upper part of the thigh and the abdomen; but it should be far from the navel. Change the injection site on each application day.
- **Wash your hands. Apply an antiseptic cotton or gauze bandage over the injection site** to disinfect.
- **Hold the filled syringe ready for use, with the capped needle facing up, from the body of the syringe.**
- **Do not hold the piston head, piston, needle guard flaps, or needle cap.**
- **Never withdraw the piston.**
- **Do not remove the needle cap from the ready-to-use syringe until you are ready to inject your DROPOETIN.**
- **Remove the cap** of the syringe by holding the syringe body and pulling the cap off carefully. Do not push the piston, touch the needle, or shake the syringe.
- **Do not touch the needle activation clips (shown in Figure 1) to prevent the needle from closing prematurely with the needle protector.**
- Hold a **layer of skin** between your thumb and forefinger. Do not squeeze.
- **Push the needle in fully.** Your doctor or nurse may have shown you how to do this.
- **Push the piston with your thumb until all liquid can be injected. While holding** the

skin layer firmly, push it slowly and steadily**. The PROTECS™ needle protection device will not activate unless the entire dose is administered. You may hear a clicking sound when the PROTECS™ needle guard is activated.**

- **When the piston is pushed as far as it can go,** pull the needle out and release the skin.
- **Slowly pull your thumb out of the piston** and allow the syringe to move upward until the entire needle is surrounded by the PROTECSTM needle guard.
- **When the needle is pulled from your skin, there may be some bleeding at the injection site. It's normal.** You can press an antiseptic cotton or bandage over the injection site for a few seconds after the injection.
- **Throw the syringe you are using in a** safe container - “See "5.How to store DROPOETIN?".

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