

## PATIENT LEAFLET IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) - 1986

This medicine is dispensed with a doctor's prescription only

**Binocrit 1,000 IU/0.5 ml**

**Binocrit 2,000 IU/1 ml**

**Binocrit 3,000 IU/0.3 ml**

**Binocrit 4,000 IU/0.4 ml**

**Binocrit 5,000 IU/0.5 ml**

**Binocrit 6,000 IU/0.6 ml**

**Binocrit 8,000 IU/0.8 ml**

**Binocrit 10,000 IU/1 ml**

**Binocrit 20,000 IU/0.5 ml**

**Binocrit 30,000 IU/0.75 ml**

**Binocrit 40,000 IU/1 ml**

**Solution for injection in a pre-filled syringe**

**The active ingredient - epoetin alfa**

**Binocrit 1,000 IU/0.5 ml:**

One pre-filled syringe contains 0.5 ml solution for injection which contains 1,000 international units (IU) corresponding to 8.4 micrograms of epoetin alfa.

**Binocrit 2,000 IU/1 ml:**

One pre-filled syringe contains 1 ml solution for injection which contains 2,000 international units (IU) corresponding to 16.8 micrograms of epoetin alfa.

**Binocrit 3,000 IU/0.3 ml:**

One pre-filled syringe contains 0.3 ml solution for injection which contains 3,000 international units (IU) corresponding to 25.2 micrograms of epoetin alfa.

**Binocrit 4,000 IU/0.4 ml:**

One pre-filled syringe contains 0.4 ml solution for injection which contains 4,000 international units (IU) corresponding to 33.6 micrograms of epoetin alfa.

**Binocrit 5,000 IU/0.5 ml:**

One pre-filled syringe contains 0.5 ml solution for injection which contains 5,000 international units (IU) corresponding to 42.0 micrograms of epoetin alfa.

**Binocrit 6,000 IU/0.6 ml:**

One pre-filled syringe contains 0.6 ml solution for injection which contains 6,000 international units (IU) corresponding to 50.4 micrograms of epoetin alfa.

**Binocrit 8,000 IU/0.8 ml:**

One pre-filled syringe contains 0.8 ml solution for injection which contains 8,000 international units (IU) corresponding to 67.2 micrograms of epoetin alfa.

**Binocrit 10,000 IU/1 ml:**

One pre-filled syringe contains 1 ml solution for injection which contains 10,000 international units (IU) corresponding to 84.0 micrograms of epoetin alfa.

**Binocrit 20,000 IU/0.5 ml:**

One pre-filled syringe contains 0.5 ml solution for injection which contains 20,000 international units (IU) corresponding to 168.0 micrograms of epoetin alfa.

**Binocrit 30,000 IU/0.75 ml:**

One pre-filled syringe contains 0.75 ml solution for injection which contains 30,000 international units (IU) corresponding to 252.0 micrograms of epoetin alfa.

**Binocrit 40,000 IU/1 ml:**

One pre-filled syringe contains 1 ml solution for injection which contains 40,000 international units (IU) corresponding to 336.0 micrograms of epoetin alfa.

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

**Read this leaflet carefully in its entirety before using this medicine.** This leaflet contains concise information about the medicine. If you have further questions, refer to the doctor or pharmacist.

This medicine has been prescribed for 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.

**Please note, every time you get this medicine at the pharmacy, it is important that you check that you have been given the same medicine that your specialist has prescribed you. If the medicine you are given looks different from what you usually get or if the instructions for use have changed, please consult your pharmacist immediately to make sure you received the correct medicine. Only your specialist can switch your medicine or change the dosage of medicine that contains epoetin alfa (the active ingredient in this medicine). Please check that the medicine that your specialist prescribed you has the same brand name as the medicine you received from the pharmacist.**

• **Binocrit is a biosimilar medicine. For additional information about biosimilars, refer to the Ministry of Health website: <https://www.health.gov.il/UnitsOffice/HD/MTI/Drugs/Registration/Pages/Biosimilars.aspx>**

### 1. WHAT IS THIS MEDICINE INTENDED FOR?

• Treatment of symptomatic anemia associated with chronic renal failure (CRF):

in adults and children aged 1 to 18 years who are on hemodialysis and adult patients on peritoneal dialysis;

in adults with renal insufficiency not yet undergoing dialysis for the treatment of severe anemia of renal origin accompanied by clinical symptoms.

• Treatment of anemia and reduction of the need for a blood transfusion in adult patients receiving chemotherapy for solid tumors, malignant lymphoma or multiple myeloma, and at risk of transfusion as assessed by the patient's general status (e.g. cardiovascular status, preexisting anemia at the start of chemotherapy).

• Treatment of anemia in adult patients who are in a predonation program to increase the yield of autologous blood before major surgery. Treatment should only be given to patients with moderate anemia (hemoglobin concentration range between 10-13 g/dl (6.2-8.1 mmol/l), no iron deficiency), if 'blood saving' procedures are not available or are insufficient when the scheduled major elective surgery requires a large volume of blood (4 or more units of blood for women or 5 or more units for men).

• For non-iron deficient adult patients with anemia prior to major elective orthopedic surgery, having a high risk for transfusion complications to reduce exposure to allogeneic blood transfusions. Use should be restricted to patients with moderate anemia (hemoglobin concentration range between 10-13 g/dl or 6.2-8.1 mmol/l) who do not have an autologous predonation program available and with an expected blood loss of 900 to 1800 ml.

**Therapeutic group:** human erythropoietin produced in cell culture. Binocrit stimulates the bone marrow to produce red blood cells.

### 2. BEFORE USING THIS MEDICINE

**Do not use this medicine if:**

- you are sensitive (allergic) to epoetin alfa or to any of this medicine's inactive ingredients listed in section 6.
  - you have been diagnosed with pure red cell aplasia (PRCA) (the bone marrow cannot produce enough red blood cells) after previous treatment with any product that stimulates red blood cell production (including Binocrit).
  - you have high blood pressure not adequately controlled with medicines.
  - do not use Binocrit to stimulate the production of your red blood cells (so that it is possible to take more blood from you) if you cannot receive transfusions with your own blood during or after surgery.
  - you are due to have major elective orthopedic surgery (such as hip or knee surgery), and you:
    - have severe heart disease
    - have severe disease of the arteries and veins
    - have recently had a heart attack or stroke
    - can't take medicines to thin the blood
- Binocrit may not be suitable for you. Discuss with your doctor. While being treated with Binocrit, some patients need medicines to reduce the risk of blood clots. If you can't take medicines that prevent blood clots, you must not use Binocrit.

### Special warnings about using this medicine

**Binocrit and other medicines that stimulate production of red blood cells may increase the risk of developing blood clots in all patients. The risk is higher if you have additional risk factors for developing blood clots (a blood clot in the past, if you are overweight, if you have diabetes, if you have heart disease or if you are bedridden for a long time because of surgery or illness). Tell your doctor if one or more of the above conditions apply to you.**

**Before treatment with Binocrit, inform the doctor if you are suffering from:**

- Hypertension
- Epileptic fits or seizures
- Liver disease
- Anemia from other causes
- Porphyria (a rare blood disease)

• If you have chronic renal failure, particularly if you do not respond well to treatment with Binocrit, your doctor will check your dose of Binocrit because repeatedly increasing your dose if you are not responding to treatment may increase the risk of heart or blood vessel problems and may increase the risk of heart attack, stroke and death.

• If you have cancer, be aware that medicines that stimulate red blood cell production (such as Binocrit) may act as a growth factor and therefore may affect progression of your cancer.

Depending on your individual situation, a blood transfusion may be preferable.

If you are a cancer patient, please note: Binocrit may be associated with shorter survival and a higher death rate in head and neck, and metastatic breast cancer patients who are receiving chemotherapy.

Serious skin reactions including Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) have been reported during epoetin treatment.

SJS/TEN can appear initially as a reddish rash, in the form of circular macules/patches, often with blisters on the trunk. Also, ulcers of mouth, throat, nose, genitals and eyes (red and swollen eyes) can occur.

These serious skin reactions may be preceded by fever and/or other flu-like symptoms.

The rash may get worse and spread, with peeling of the skin, resulting in a life-threatening condition.

If you develop a serious rash or skin symptoms as noted above, stop taking Binocrit and contact your doctor or seek medical attention immediately (emergency room).

### Tests and follow-up

Your doctor will monitor your blood pressure frequently while you are being treated with Binocrit.

If you are being treated with erythropoietin, check your blood hemoglobin values regularly, until the values stabilize, and routinely check them after that. There is a potential increased risk of rare thromboembolic events (e.g., heart attacks, stroke, and pulmonary embolism) when hemoglobin levels rise beyond the target range.

Before starting treatment with Binocrit, take into account all other possible causes of anemia such as iron deficiency, destruction of red blood cells (hemolysis), blood loss, vitamin B<sub>12</sub> or folic acid deficiency, and treat them. Your doctor may refer you for blood tests to decide if you need iron supplements to ensure an optimal response to Binocrit.

Your doctor may decide to refer you for routine blood tests to determine platelet counts in the blood during the first 8 weeks of treatment. There may be a moderate dosage-dependent increase in the platelet count, within the normal range, during the course of treatment with Binocrit, that gradually decreases during treatment. It is important to maintain a normal iron level in the blood throughout treatment with Binocrit.

Your doctor may tell you to take iron tablets.

### Interactions with other medicines

**If you are taking or have recently taken other medicines, including nonprescription medicines and dietary supplements, tell your doctor or pharmacist.** Particularly if you are taking:

**If you have hepatitis C and are being treated with interferon and ribavirin**

You should discuss this with your doctor because a combination of epoetin alfa with interferon and ribavirin has led to a loss of effect and development of a condition called pure red cell aplasia (PRCA), a severe and sudden anemia as a result of a depression of the manufacturing center of red blood cells in the bone marrow, in rare cases. Binocrit is not intended for treatment of anemia associated with hepatitis C.

Cyclosporin - a medicine administered to prevent transplant rejection (e.g. after kidney transplant). Your doctor may order blood tests to monitor the level of cyclosporin during treatment with Binocrit.

Iron supplements and other medicines that promote production of red blood cells may increase the effectiveness of Binocrit. Consult your doctor, and they will decide if you should take them.

If you visit the hospital or any clinic or family doctor for treatment/consultation - inform the medical staff that you are being treated with Binocrit as Binocrit may affect other treatments or results of laboratory tests.

### Pregnancy, breastfeeding and fertility

It is important to consult the doctor if you are pregnant, think you are pregnant, are planning to become pregnant, or are breastfeeding. There is no information on the effect of Binocrit on fertility.

**Important information about some of this medicine's ingredients** The product contains a negligible amount of sodium (less than 1 millimole / 23 milligrams per dose) and is defined as "sodium free".

### 3. HOW TO USE THIS MEDICINE?

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

Only your doctor will determine your dose and how you should take this medicine.

Use this medicine at set intervals, as determined by your doctor.

**Do not exceed the recommended dose.**

**Binocrit can be injected in two ways:**

**1. intravenous administration**

**2. or subcutaneous administration.**

Your doctor will decide how it will be injected. In most cases, it will be injected by a doctor, nurse, or other healthcare practitioner.

Binocrit may be self-injected subcutaneously only after appropriate training by a doctor or a nurse.

Do not inject Binocrit in the following cases:

- after the expiry date of the medicine
- if you know or think that the product was accidentally frozen
- if there has been a failure in the refrigerator where the product was stored.

The dose of Binocrit you receive is based on your body weight in kilograms. The cause of your anemia may also be a factor in your doctor's decision about the dose.

### Instructions for subcutaneous injection

When treatment starts, Binocrit is usually injected by a doctor or a nurse. Later, your doctor may suggest that you learn or teach your caregiver how to inject Binocrit under the skin yourself.

• **Do not try to inject yourself unless you have been trained by a doctor or nurse. If you are not sure how to inject the product or if you have any questions, contact your doctor for help.**

• **Use Binocrit exactly according to your doctor's instructions.**

• **Make sure that you only inject the amount of liquid instructed by your doctor or nurse.**

• **Only use Binocrit if it has been stored correctly (see details in section 5- 'How to store the medicine?').**

• **Before use, take the Binocrit syringe out of the refrigerator, and let it reach room temperature before injecting. This usually takes between 15 and 30 minutes. Use the syringe within 3 days of taking it out of the refrigerator.**

**Inject only one dose of Binocrit from each syringe.**

When Binocrit is injected under the skin (subcutaneously), the dose injected is not normally more than 1 ml in a single injection.

Binocrit is given alone and not mixed with other liquids for injection. Do not shake Binocrit syringes. Prolonged vigorous shaking may damage it. If you know that the syringe has been shaken, do not use that syringe.

Detailed instructions on how to inject yourself with Binocrit can be found at the end of this leaflet.

### If you have accidentally taken a higher dose

Tell your doctor or nurse immediately. Side effects from an overdose of Binocrit are unlikely.

If you have taken an overdose or if a child accidentally swallowed some medicine, immediately see a doctor or go to a hospital emergency room and bring the medicine package with you.

### If you forget to inject this medicine

As a rule, inject the next injection as soon as you remember. If you are within a day of your next injection, do not inject when you remember the missed dose. Wait and inject according to your normal schedule. Never inject two doses together!

Adhere to the treatment as recommended by your doctor. Even if your health improves, do not stop the treatment with the 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 further questions about using of this medicine, consult your doctor or pharmacist.**

### 4. SIDE EFFECTS

As with any medicine, using Binocrit may cause side effects in some users. Do not be alarmed by this list of side effects; you may not experience any of them.

Tell your doctor or nurse immediately if you experience any of the side effects listed below.

Serious skin reactions including Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) have been reported during epoetin treatment. These effects can appear as reddish macules or circular patches often with blisters on the trunk, skin peeling, ulcers of mouth, throat, nose, genitals and eyes and can be preceded by fever or flu-like symptoms.

**If you develop these symptoms, stop taking Binocrit, and contact your doctor or seek medical attention immediately (emergency room).**

**Very common side effects (affect more than 1 in 10 patients):**

Diarrhea, vomiting, nausea, fever.

Respiratory tract congestion, such as a stuffy nose and sore throat, has been reported by kidney patients who have not yet undergone dialysis.

**Common side effects (affect 1-10 in 100 patients):**

Increased blood pressure. Headaches, especially sudden, stabbing and migraine-like headaches. Feeling confused or fits may be signs of a sudden increase in blood pressure. This requires immediate treatment. There may be a need to treat a rise in blood pressure with additional medicines (or adjustment to the medicines you are already taking for high blood pressure).

Blood clots (including deep vein thrombosis and embolism) that may require urgent treatment. You may experience chest pain, breathlessness and painful swelling and redness of the leg.

Cough.

Skin rashes, which may be the result of an allergic reaction.

Bone or muscle pain.

Flu-like symptoms, such as headache, joint pain, feeling of weakness, chills, tiredness and dizziness. These symptoms may be more common at the start of treatment. If you experience these symptoms during injection into the vein, a slower injection may help reduce them in the future.

Redness, sensation of burning and pain at the site of the injection.

Swelling of the ankles, feet or fingers.

Arm or leg pain.

**Uncommon side effects (affect up to 1 in 100 patients):**

High levels of blood potassium which can cause heart rate disturbances (this effect is very common in dialysis patients).

Epileptic fits.

Nose or airway congestion.

Allergic reaction.

Hives.

**Rare side effects (affect up to 1 in 1,000 patients):**

Severe and sudden anemia as a result of depression of the manufacturing center of red blood cells in the bone marrow (pure red cell aplasia - PRCA). The symptoms of this condition are unusual tiredness, feeling dizzy and breathlessness.

PRCA has been reported in very rare cases mostly in patients with kidney disease after months or years of treatment with epoetin alfa and other medicines that stimulate red blood cell production.

Increased blood platelet levels, which are normally involved in formation of blood clots, may occur, especially when starting treatment. Your doctor will check on this.

Severe allergic reaction that may include swollen face, lips, mouth, tongue or throat; difficulty swallowing or breathing; itchy rash (hives). Problems with the blood that may cause pain, dark colored urine or increased sensitivity of the skin to sunlight (porphyria).

If you are undergoing hemodialysis:

- Blood clots may form in your dialysis shunt. This is more likely if you have low blood pressure or if you have fistula complications.
- Blood clots may form in your hemodialysis system. Your doctor will decide if the heparin dosage should be increased during dialysis.

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

Side effects can be reported to the Ministry of Health by clicking on the "Reporting Side Effects of Drug Treatment" link on the Ministry of Health home page ([www.health.gov.il](http://www.health.gov.il)) which opens an online form for reporting side effects, or 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 your doctor.

- Do not use the medicine after the expiry date (exp. date) which is stated on the package. The expiry date refers to the last day of that month.

### Storage conditions:

- Store in a refrigerator at a temperature between 2-8°C; do not freeze. Do not shake.

Keep the syringe in the original package in order to protect from light.

The product may be removed from the refrigerator and kept at room temperature (up to 25°C) for no more than 3 days. Once the syringe has been taken out of the refrigerator and has reached room temperature (up to 25°C), use it within 3 days or discard it if not used.

Do not use the product:

- if the solution is cloudy or has particles in it
- if the seal is broken
- if the solution was accidentally frozen or if there has been a refrigerator failure.

Do not throw away medicines via wastewater or household waste. Ask the pharmacist how to dispose of medicines you no longer use. These measures will help protect the environment.

### 6. ADDITIONAL INFORMATION

In addition to the active ingredients, this medicine also contains: glycine, sodium chloride, disodium phosphate dihydrate, sodium dihydrogen phosphate dihydrate, polysorbate 80, hydrochloric acid (for pH adjustment), sodium hydroxide (for pH adjustment), and water for injections.

### What the medicine looks like and the contents of the pack:

Binocrit is a clear, colorless solution in a pre-filled syringe. The syringes are packaged in a blister.

License holder and importer's name and address: Sandoz Pharmaceuticals Israel Ltd., P.O.Box 9015, Tel Aviv.

Revised in June 2024

Registration numbers of the medicine in the Ministry of Health's National Drug Registry:

Binocrit 1,000 IU/0.5 ml – 147-08-33360-00

Binocrit 2,000 IU/1 ml – 147-09-33361-00

Binocrit 3,000 IU/0.3 ml – 147-17-33370-00

Binocrit 4,000 IU/0.4 ml – 147-11-33363-00

Binocrit 5,000 IU/0.5 ml – 147-13-33364-00

Binocrit 6,000 IU/0.6 ml – 147-12-33365-00

Binocrit 8,000 IU/0.8 ml – 147-14-33366-00

Binocrit 10,000 IU/1 ml – 147-15-33367-00

Binocrit 20,000 IU/0.5 ml – 147-16-33368-00

Binocrit 30,000 IU/0.75 ml – 147-10-33362-00

Binocrit 40,000 IU/1 ml – 147-18-33372-00

**Instructions on how to inject yourself (for patients with symptomatic anemia caused by kidney disease, adult patients receiving chemotherapy, or adult patients with moderate anemia scheduled for major orthopedic surgery only)**

This section contains information on how to give yourself an injection of Binocrit. It is important that you do not try to give yourself the injection unless you have received special training from your doctor or nurse. Binocrit is provided with or without a needle safety guard, and you will be shown how to use this by your doctor or nurse. If you are not sure about how to inject the medicine or you have questions, please ask your doctor or nurse for help.

**WARNING:** Do not use if the syringe has fallen onto a hard surface or fell after removing the needle cap. Do not use the Binocrit pre-filled syringe if it is broken or defective. Return the syringe and the package it came in to the pharmacy.

1. Wash your hands.
2. Remove one syringe from the pack and remove the protective cap from the injection needle. Syringes are embossed with graduation rings in order to enable partial use if required. Each graduation ring corresponds to a volume of 0.1 ml. If partial use of a syringe is required, remove unwanted solution before injection.
3. Clean the skin at the injection site using an alcohol wipe.
4. Form a skin fold by pinching the skin between thumb and forefinger.
5. Insert the needle into the skin fold with a quick, firm action. Inject the Binocrit solution as you have been shown by your doctor. You should check with your doctor or pharmacist if you are not sure how to do this.

### Pre-filled syringe without needle safety guard

6. Always keeping your skin pinched, depress the plunger slowly and evenly.

7. After injecting the liquid, remove the needle and let go of your skin. Apply pressure to the injection site with a dry, sterile pad.

8. Discard any unused product or waste material. Only use each syringe for one injection.



### Pre-filled syringe with needle safety guard

6. Always keeping your skin pinched, depress the plunger slowly and evenly until the entire dose has been given and the plunger cannot be depressed any further. Do not release the pressure on the plunger!

7. After injecting the liquid, remove the needle while maintaining pressure on the plunger and only then let go of your skin. Apply pressure to the injection site with a dry, sterile pad.

8. Let go of the plunger. The needle safety guard will rapidly move to cover the needle.

9. Discard any unused product or waste material. Only use each syringe for one injection.

