Cinnapoietin®

Erythropoietin beta

Erythropoietin beta
2000 IU/ 0.3 ml
4000 IU/ 0.3 ml
10,000 IU/ 0.6 ml
20,000 IU/ 0.6 ml
40,000 IU/ 0.6 ml
Sterile Pre-Filled Syringe

Pharmacological -Therapeutic Category:

Erythropoietic – Hematopoietic

Pharmacokinetic- Pharmacodynamics:

Absorption

Average maximal concentrations is available between 12 and 28 hours after SC dosing.

Distribution

1–2 times the plasma volume after IV dosing.

Elimination half-life

Intravenously administered Erythropoietin is between 4 and 12 hours.
Subcutaneously administered Erythropoietin is between 13 and 28 hours.

Bioavailability

The bioavailability of subcutaneously administered Erythropoietin is between 23% and 42% as compared with intravenous administration. Slightly higher bioavailability occurs on repeated subcutaneous administration.

Pharmacodynamics

Cinnapoietin® stimulates the proliferation and differentiation of the erythroid stem cell compartment, therefore leads to an increase in hemoglobin formation and acceleration of cell maturation with reduction in the cell cycle time. A further effect of Cinnapoietin® is the acceleration of reticulocyte maturation and release into the bloodstream.

Dosage and Administration

- Use the lowest dose of Cinnapoietin® that will gradually increase the hemoglobin concentration.
- Cinnapoietin® dosing regimens are different for each of the indications.
- It is recommended that the first dose of Cinnapoietin® be administered under the supervision of a healthcare professional.

Treatment of Anemia in Patients with Chronic Kidney Disease

Cinnapoietin® may be administered by either IV or SC injection, however, SC should be considered where feasible since lower doses are required. Generally, the SC maintenance dose is approximately 20–35% lower than the IV maintenance dose. In the case of IV administration, the solution should be injected over approximately 2 minutes (in hemodialysis patients via the arteriovenous fistula at the end of dialysis). For nonhemodialysis patients, SC administration is preferred in order to avoid puncture of peripheral veins. The recommended hemoglobin target is 10–12 g/dL. The target hemoglobin should be determined individually in the presence of hypertension or existing cardiovascular, cerebrovascular or peripheral vascular diseases. It is recommended that hemoglobin is monitored at regular intervals until stabilized and periodically thereafter. Treatment with Cinnapoietin® is divided into two stages:

1. Correction phase

SC administration
The recommended starting dose is 60 IU/kg body weight/week, administered as a single weekly injection or in up to 7 divided doses. The dose may be increased every 4 weeks by 60 IU/kg body weight/week if the hemoglobin increase is not adequate (Hb < 0.15 g/ dL per week).
IV administration
The initial dose is 120 IU/kg body weight/week, administered in 3 divided doses. The dose may be raised after 4 weeks to 240 IU/kg body weight/ week. If further increments are needed they should be at 60 IU/kg body weight/week, at monthly intervals.
For both types of injection, the maximum dose should not exceed 720 IU for every 1 kg of your body weight per week

2. Maintenance phase

To maintain hemoglobin between 10–12 g/ dL the dose is initially reduced to half of the previously administered amount. In the case of SC administration, the weekly dose can be given as a single injection or in up to 7 divided doses. Patients who are stable on a once weekly dosing regimen may be switched to once every 2 weeks administration. In this case dose increases may be necessary.

Dose adjustment

- Increases in dose should not be made more frequently than once a month. The dose for each patient should be adjusted so that the hemoglobin concentration does not exceed 12 g/dL.
- If the hemoglobin is increasing and approaching 12 g/dL, the dose should be reduced by approximately 25–50%.
- If the hemoglobin continues to increase, the dose should be temporarily withheld until the hemoglobin begins to decrease, at which point therapy should be reinitiated at a dose approximately 25–50% below the previous dose.
- If the hemoglobin increases by more than 1 g/ dL in any 2 week period, the dose should be decreased by approximately 25–50%.
- The maximum dose should not exceed 720 IU/ kg body weight/week.
- Cinnapoietin® is normally a lifelong therapy. It can however, be interrupted if necessary, at any time.

Use in Children and Adolescents

The results of clinical studies in children and adolescents have shown that on average, the younger the patient, the higher the Cinnapoietin® dose required. Nevertheless, the recommended dosing schedule should be followed as the individual response cannot be predicted.

Treatment for Increasing the Amount of Autologous Blood

- The dose may be administered by either IV or SC injection. In the case of IV administration, the solution should be injected over approximately 2 minutes.
- The dose for autologous blood donation prior to elective surgery is 400–1600 IU/kg body weight/week IV or 300–1200 IU/kg body weight/ week SC administered in 2 divided doses, for a maximum of 4 weeks.
- If the patient's Hematocrit ≥ 33 % or Hb > 11 g/ dL, Cinnapoietin® may be administered at the end of the blood donation.
- Patients with pre-existing cardiac diseases should be monitored carefully.
- The dose must be determined for each patient as a function of the required amount of pre-donated blood and the endogenous red cell reserve.
- The maximum dose should not exceed 1600 IU/kg body weight/week for IV and 1200 IU/kg body weight/ week for SC administration.

Prevention of Anemia of Prematurity

- The solution is administered SC at a dose of 750 IU/kg body weight/week administered in 3 divided doses.
- Cinnapoietin® treatment should be commenced as early as possible, preferably by day 3 of life.
- Premature infants who have already been transfused prior to Cinnapoietin® treatment are not likely to benefit as much as non-transfused infants.
- The treatment should last for 6 weeks. Treatment of Anemia in Patients with Non-Myeloid Malignancies
- Cinnapoietin® treatment should not be commenced unless the hemoglobin falls below 10 - 11 g/dL.
- The recommended initial dose is 450 IU/kg body weight/ week, administered SC as a single weekly injection or in 3 to 7 divided doses.
- If after 4 weeks, a patient does not show a satisfactory response in terms of hemoglobin values, then the dose should be doubled.
- The therapy should be continued up to 4 weeks after the end of chemotherapy.
- The maximum dose should not exceed 900 IU/ kg body weight/week.
- If hemoglobin falls by more than 1 g/dL in the next cycle of chemotherapy despite concomitant Cinnapoietin® therapy, further administration may not be effective.
- Rapid increases in hemoglobin concentrations or the use of erythropoietin in subjects with normal hemoglobin concentrations may result in an increased risk of thrombotic adverse events. Therefore, a rise > 1 g/dL after 2 weeks or hemoglobin concentration >12 g/dL should be voided.
- If the hemoglobin concentration is rising by more than 1 g/dL after 2 weeks, reduce the Cinnapoietin® dose by approximately 25%.
- If the hemoglobin concentration exceeds 12 g/ dL, discontinue Cinnapoietin® until it falls below 12 g/dL and then restart Cinnapoietin® at a dose 25% below the previous dose.
- It is recommended that hemoglobin is monitored at regular intervals until stabilized and periodically thereafter.

Use in Premature Infants

Prognostic factors for successful results are infant birth weight and baseline hematocrit (Hct). Infants with both a birth weight > 1100 g and baseline Hct > 45% benefited most. No success was achieved in those infants with both a birth weight < 1100 g and baseline Hct < 45%.

Contraindication:

Cinnapoietin® is contraindicated in patients with:

- Poorly controlled hypertension
- Known hypersensitivity to the active substance

or any of the excipients
- Who donating their own blood before surgery, and:
  - they had a heart attack or stroke in the month before your treatment
  - they have unstable angina pectoris – new or increasing chest pain
  - they are at risk of blood clots in the veins (deep venous thrombosis) – for example, if you have had clots before.
- Previously developed anti-erythropoietin antibodies and Pure Red Cell Aplasia during prior exposure to any erythropoietic substance.

Precaution / Warning:

Cardiovascular and Thrombotic Events

To reduce cardiovascular risks, use the lowest dose of Cinnapoietin® that will gradually increase the hemoglobin concentration. The hemoglobin concentration should not exceed 12 g/dL and the rate of hemoglobin increase should not exceed 1g/dL in a 2-week period. Hemoglobin levels should be checked at regular intervals and dosages adjusted.

Cancer Patients

Cinnapoietin® should only be used to treat cancer patients with anemia where the anemia has arisen as a result of concomitantly administered chemotherapy.

Hypertension

Patients with uncontrolled hypertension should not be treated with Cinnapoietin® blood pressure should be controlled adequately before initiation of therapy.

Seizures

ESAs should be used with caution in patients with epilepsy. Convulsions have been reported in patients with CKD receiving erythropoietin.

Chronic liver disease

patients with chronic liver diseases should be monitored regularly and take the drug under appropriate dose adjustment.

Phenylketonuria

This medicine contains phenylalanine and May be harmful for people with Phenylketonuria.

General

Cinnapoietin® should be used with caution in the presence of thrombocytosis and chronic liver failure. Anaphylactoid reactions have been observed in isolated cases. Rarely, skin reactions such as rash, pruritus, urticarial, injection site reactions or potential effects on the eye in babies may occur. It is recommended that the first dose be administered under medical supervision.
Evaluation of Iron Status: In order to ensure effective erythropoiesis.
Evaluation of certain B vitamins: folic acid and B12 as a co-factor in RBC production.

Pregnancy Risk Factor: C

Lactation:

Endogenous erythropoietin is excreted into breast milk but it is not known whether it is absorbed by the neonatal gastrointestinal tract in functional form. It should be taken into account the benefit of breastfeeding to the child and the benefit of Cinnapoietin® therapy to the woman by your doctor.

Drug Interactions:

If you are taking another medication concurrently (even OTC or herbal medicines), discuss with your doctor or consult with your pharmacist.

Side effects (or Adverse Reactions):

Skin reactions such as rash, pruritus, urticaria, or injection site reactions. Particularly when starting treatment, flulike symptoms such as fever, chills, headaches, pain in the limbs, malaise and/or bone pain have been reported. These reactions were mild to moderate in nature and subsided after a couple of hours or days.

Your doctor may do regular blood tests to check:

- If you have high or rising potassium levels that cause hyperkalemia.
- If you have slightly to moderately rise in platelets count that cause blood clotting.
- Your haemoglobin level to monitor how your anaemia is responding to Cinnapoietin® treatment.

Do not misuse Cinnapoietin®:

Misuse of Cinnapoietin® by healthy people may lead to an increase in blood cells and consequently thicken the blood.

Do not inject too much Cinnapoietin®:

If you have injected more Cinnapoietin® than you should, contact your doctor. Even at very high blood levels, no symptoms of poisoning have been observed. If you have missed an injection, or injected too little, talk to your doctor. DO NOT take a double dose to make up for any forgotten doses.

Storage:

- Store between 2- 8 °C (in refrigerator)
- Store in the carton to protect from light
- Do not freeze.
- Single use only, discard the remainder.
- Each PFS is for the use of one patient.

The other ingredients are:

Sodium Chloride, Monobasic Sodium phosphate dihydrate, Dibasic Sodium phosphate dihydrate, Calcium chloride dihydrate, Polysorbate 20, L-Phenyl alanine, L-Isoleucine, L-Threonine, Glycine, L-leucine, Glutamic acid, Water for Injections.

Packaging:

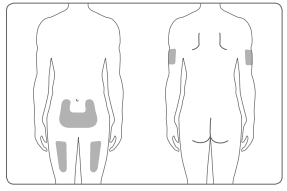
Cinnapoietin® is available in packs containing:
Each pack contains Dosage
6 Sterile Pre-Filled Syringes and PIL 2000 IU/ 0.3 ml
6 Sterile Pre-Filled Syringes and PIL 4000 IU/ 0.3 ml
1 Sterile Pre-Filled Syringe and PIL 10,000 IU/ 0.6 ml
1 Sterile Pre-Filled Syringe and PIL 20,000 IU/ 0.6 ml
1 Sterile Pre-Filled Syringe and PIL 40,000 IU/ 0.6 ml

STEP 1: Setting up for an injection

1. Take the Cinnapoietin® carton containing the pre-filled syringes out of the refrigerator and Remove one prefilled syringe and place it on your working surface and let it to reach room temperature (approximately 15 to 30 minutes). Place the carton containing any remaining pre-filled syringes back into the refrigerator (2° -8°C). Do NOT shake the pre-filled syringe of Cinnapoietin®.
2. Check the expiration date on the pre-filled syringe.
3. Do NOT use the pre-filled syringe if the needle cover is missing or not securely attached.
4. Assemble the additional supplies you will need for your injection (e.g. an alcohol swab)
5. Wash your hands thoroughly with soap and warm water.
6. Do NOT inject the solution if it is cloudy or discolored, or contains visible or colored particles or if the pre-filled syringe appears cracked or broken.

STEP 2: Choosing and Preparing an Injection Site

1. The recommended injection sites for Cinnapoietin® pre-filled syringe is shown in the following picture.

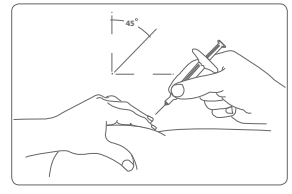


2. Rotate the site of new injection at least one inch from sites of recent injections. Do NOT inject into tender, bruised, red, or hard skin or vein and muscles. Avoid areas with scars or stretch marks.
3. Wipe the injection site with an alcohol swab. Do NOT touch this area again before giving the injection.

STEP 3: Injecting Cinnapoietin® Using a Pre-filled Syringe

Do NOT remove the needle cover from the pre-filled syringe until you are ready to inject.

1. Hold the barrel of the pre-filled syringe and pick it up with one hand and pull the needle cover straight off, there might be a drop of liquid at the end of the needle, this is normal. Do NOT put the needle cover back onto the pre-filled syringe. Do NOT touch the needle or allow it to touch any surface. Do NOT touch or bump the plunger to prevent the liquid leakage.
2. Hold the syringe with the needle pointing up. Remove the larger air bubbles by gently tapping the syringe barrel and slowly pushing the plunger up.
3. Hold the syringe in one hand like a pencil, use the other hand to gently pinch a fold of skin at the cleaned injection.



4. Insert the needle at a slight angle (45 to 90 degrees) to the skin with a quick, “dart like” motion.
5. After the needle is inserted, let go of the skin. Slowly push the plunger all the way down to injects Cinnapoietin®.
6. When the syringe is empty, remove the needle at the same angle as it was inserted.
7. If you have severe bleeding cover the injection site with a bandage.

STEP 4: Disposing of Supplies

1. The syringe should NEVER be reused.
2. Follow any special provincial or local laws regarding the proper disposal of needles and syringes.

If you have any further questions on the use of this medicine, ask your doctor or Pharmacist.

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