Recormon®

1. Pharamcology / Use of Drug

Recormon® is a biological product containing recombinant human erythropoietin (rHuEPO) and is indicated for the treatment of anaemia of chronic disease, including chronic kidney disease and cancer chemotherapy-induced anaemia.

2. Dosage and Administration

Recormon® is administered twice weekly over 4 weeks. On those occasions where the patient's PCV allows blood donation, i.e. PCV ≥ 33 %, Recormon is used to support the asymptomatic patient to enable blood donation. Recormon® should be used following the patient's PCV allows blood donation as the individual response cannot be predicted (see section 2.5.4 Pediatric use).

3. Contraindications

- Known hypersensitivity to the active substance or any of the excipients.
- Poorly controlled hypertension (see section 2.4.1 General, Warnings and Precautions).

4. Special Precautions for Use

In patients in an autologous blood pre-donation program, there may be a slight rise in platelet count, mostly within the normal range. Therefore, it is recommended that the platelet count be determined at least once a week in these patients. If there is an increase in platelets of more than 150 x 10^9/l, treatment should be discontinued.

5. Adverse Drug Reactions

Recormon® has been shown to be effective in the treatment of anaemia of chronic disease, including chronic kidney disease and cancer chemotherapy-induced anaemia. The most frequent adverse drug reactions are:

- Nervous system disorders: Headache
- Vascular disorders: Hypertension

6. Overdose

In case of overdosage, normal supportive measures should be taken. In patients with chronic kidney disease and cancer chemotherapy-induced anaemia, the administration of Recormon® should be continued at the next dose interval, unless there are signs of adverse effects.

7. Interaction Studies

No dedicated clinical interaction studies have been performed. It is not known if Recormon® interacts with other substances. However, the concomitant use of other substances is probably not contraindicated. Recormon® should be used with caution in patients with existing or developing hypertension.

8. Laboratory Tests

In patients with chronic kidney disease, serum potassium elevation has been reported to be a potentially serious adverse effect. Therefore, serum potassium levels should be monitored regularly.

In patients with cancer receiving chemotherapy, there may be an increase in platelet count due to the effects of chemotherapy. Therefore, platelet counts should be monitored regularly.

In patients with chronic kidney disease, the administration of Recormon® may cause a rise in blood pressure. Therefore, blood pressure should be monitored regularly.

9. Special Instructions for Use, Handling and Disposal

Syringes and needles for each administration should be used (see section 4.2 Special Instructions for Use, Handling and Disposal).

10. Storage

Recormon® should be stored at a temperature of 2°C to 8°C. The product should be protected from light.

11. Clinical Studies

Clinical studies have shown a higher frequency of thromboembolic events in cancer patients or can be an aggravation of existing hypertension (see section 2.4.1 General, Warnings and Precautions).

12. Pregnancy

Recormon® is not recommended for use in pregnancy due to the potential risk of harm to the fetus. However, in the absence of convincing evidence, it may be used in pregnancy to correct severe anaemia when other measures are inadequate.

13. Breast-feeding

Endogeneous erythropoietin is excreted in breast milk and therefore breast-feeding or to continue or discontinue therapy with epoetin beta should be made taking into account the benefit of the product.

14. Other Information

In patients with chronic kidney disease, serum potassium elevation has been reported to be a potentially serious adverse effect. Therefore, serum potassium levels should be monitored regularly.

15. References

Clinical studies have shown a higher frequency of thromboembolic events in cancer patients or can be an aggravation of existing hypertension (see section 2.4.1 General, Warnings and Precautions).

16. Patient Information

In patients with chronic kidney disease, serum potassium elevation has been reported to be a potentially serious adverse effect. Therefore, serum potassium levels should be monitored regularly.
4. Take the reconstitution and withdrawal device (which allows sterile air file in these populations and the ADR profile of epoetin beta (see sections 2.4.1 General, Warnings and Precautions, 2.5 Use in Special Populations, 2.6 Undesirable Effects).

8. Penetrate the seal with the needle to a depth of about 1 cm and slowly inject the solution for injection into the syringe provided with the vial. The vial should be held horizontally and the needle should be directed towards the base of the vial. The needle should remain in place for at least 2 seconds to ensure complete injection of the contents into the syringe. After injection, the needle should be quickly withdrawn and the site of injection should be cleaned with aseptic technique using an alcohol wipe. The site of injection should be observed for any signs of bleeding or inflammation for at least 5 minutes. If any signs of bleeding or inflammation are noted, the injection should be stopped and the patient should be repositioned in a sitting or supine position, with the head elevated, until the bleeding or inflammation subsides.

9. Swirl the vial gently until the powder has dissolved. Do not shake. Check that the solution is clear and that no particulate matter is present. If particulate matter is present, the vial should be discarded. The solution should be reconstituted immediately before use, and the reconstituted solution should be used within 24 hours of preparation. If the reconstituted solution is not to be used immediately, it should be refrigerated at +4°C to +8°C (refrigerator).

2.7 Overdose

The therapeutic range of Recormon is wide and individual response to therapy must be monitored throughout the treatment period.

4. Replace the needle by a new one (the new needle should have the size which is recommended by the manufacturer).

5. Pharmacokinetic Properties

Pharmacokinetic investigations in healthy volunteers and uremic patients show that the half-life of intravenously administered epoetin beta is about 10 hours in healthy volunteers and about 15 hours in uremic patients. The distribution volume corresponds to one to two times the plasma volume. Analogous results have been found in animal experiments in uremic and normal rats. After single dose administration of epoetin beta no effects on behavior or locomotor activity were observed. The biological effective increase in hemoglobin was significantly shorter in patients receiving epoetin beta (HR=1.62, p=0.0008). The results and interpretation of this study were confounded by imbalances between the treatment groups, especially with regard to tumor localization, smoking status and the heterogeneity of the study population.

5.2.1 Absorption

After subcutaneous administration of epoetin beta to uremic patients, the protracted absorption results in a serum half-life of 23-42 hours as compared with intravenous administration. The terminal half-life is about 6-8 hours. The maximum concentration of epoetin beta (Cmax) after subcutaneous administration is reached at about 12 hours after injection. The time to reach Cmax (tmax) is about 12 hours after injection. The mean area under the plasma concentration-time curve (AUC) after subcutaneous administration is about 23-42% of the area under the plasma concentration-time curve after intravenous administration of epoetin beta.

5.2.2 Distribution

Pharmacokinetic investigations in healthy volunteers and uremic patients show that the distribution volume corresponds to one to two times the plasma volume. Analogous results have been found in animal experiments in uremic and normal rats. After single dose administration of epoetin beta no effects on behavior or locomotor activity were observed. The biological effective increase in hemoglobin was significantly shorter in patients receiving epoetin beta (HR=1.62, p=0.0008). The results and interpretation of this study were confounded by imbalances between the treatment groups, especially with regard to tumor localization, smoking status and the heterogeneity of the study population.

5.2.3 Metabolism and excretion

Pharmacokinetic investigations in healthy volunteers and uremic patients show that the half-life of intravenously administered epoetin beta is about 10 hours in healthy volunteers and about 15 hours in uremic patients. The distribution volume corresponds to one to two times the plasma volume. Analogous results have been found in animal experiments in uremic and normal rats. After single dose administration of epoetin beta no effects on behavior or locomotor activity were observed. The biological effective increase in hemoglobin was significantly shorter in patients receiving epoetin beta (HR=1.62, p=0.0008). The results and interpretation of this study were confounded by imbalances between the treatment groups, especially with regard to tumor localization, smoking status and the heterogeneity of the study population.

5.2.4 Other

Penetration of the seal with the needle to a depth of about 1 cm and slowly inject the solution for injection into the syringe provided with the vial. The vial should be held horizontally and the needle should be directed towards the base of the vial. The needle should remain in place for at least 2 seconds to ensure complete injection of the contents into the syringe. After injection, the needle should be quickly withdrawn and the site of injection should be cleaned with aseptic technique using an alcohol wipe. The site of injection should be observed for any signs of bleeding or inflammation for at least 5 minutes. If any signs of bleeding or inflammation are noted, the injection should be stopped and the patient should be repositioned in a sitting or supine position, with the head elevated, until the bleeding or inflammation subsides.

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