Juvobin | Darbepoetin Alfa Injection 25 mcg/ 40 mcg

Description:

- Juvobin is an erythropoiesis stimulating protein, closely related to erythropoietin that is produced in Chinese hamster ovary (CHO) cells by recombinant DNA technology.
- Juvobin is a 165-amino acid protein that differs from recombinant human erythropoietin in containing 5 N-linked oligosaccharide chains, whereas recombinant human erythropoietin contains 3 chains.
- The 2 additional N-glycosylation sites result from amino acid substitutions in the erythropoietin peptide backbone. The additional carbohydrate chains increase the approximate molecular weight of the glycoprotein from 30,000 to 37,000 Da.

Mechanism of Action:

- Juvobin stimulates erythropoiesis by the same mechanism as endogenous erythropoietin.
- A primary growth factor for erythroid development, erythropoietin is produced in the kidney and released into the bloodstream in response to hypoxia.
- In responding to hypoxia, erythropoietin interacts with progenitor stem cells to increase red cell production. Production of endogenous erythropoietin is impaired in patients with chronic renal failure (CRF), and erythropoietin deficiency is the primary cause of their anemia.
- Increased hemoglobin levels are not generally observed until 2 to 6 weeks after initiating treatment with Juvobin.

Indication:

Juvobin is indicated for the treatment of anemia associated with chronic renal failure, including patients on dialysis and patients not on dialysis.

Dosage and Administration

Juvobin is administered either IV or SC as a single weekly injection.

- **For patients with CKD on dialysis:**
- Initiate Juvobin treatment when the hemoglobin level is less than 10 g/dL.
- If the hemoglobin level approaches or exceeds 11 g/dL, reduce or interrupt the dose of Juvobin.
- The recommended starting dose is 0.45 mcg/kg intravenously or subcutaneously as a weekly injection or 0.75 mcg/kg once every 2 weeks as appropriate. The intravenous route is recommended for patients on hemodialysis.

For patients with CKD not on dialysis:

- Consider initiating Juvobin treatment only when the hemoglobin level is less than 10 g/dL and the following considerations apply:
- The rate of hemoglobin decline indicates the likelihood of requiring a RBC transfusion and,
- Reducing the risk of alloimmunization and/or other RBC transfusion-related risks are a goal.

The recommended starting dose is 0.45 mcg/kg body weight intravenously or subcutaneously given once at four weeks intervals as appropriate.

(*Please refer pack insert for further clarity on Dosage and Administration)

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Darbepoetin alfa in dialysis patients with Anemia

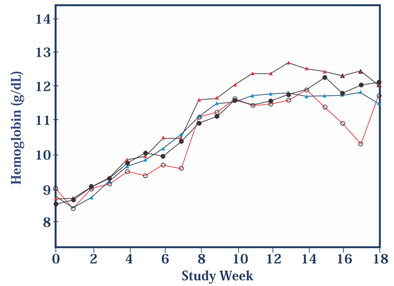

Figure 1

Mean hemoglobin values over the initial 16 weeks of the study, presented by dose level and route of administration. Solid circles, i.v. darbepoetin alfa, 0.45 µg/kg/week (n=10). Open circles, s.c. darbepoetin alfa, 0.45 µg/kg/week (n=12). Red triangles, i.v. darbepoetin alfa, 0.75 µg/kg/week (n=56). Blue triangles, s.c. darbepoetin alfa, 0.75 µg/kg/week (n=30).

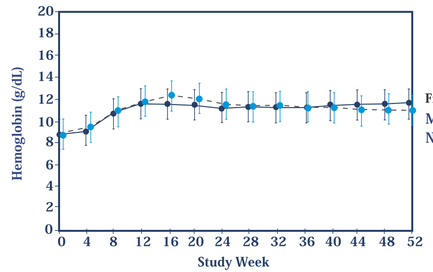

Figure 2

Mean hemoglobin values for patients who continued treatment after 16 weeks of the study. Navy blue circles, i.v. Darbepoetin Alfa (n=41). Blue circles, s.c. Darbepoetin Alfa (n=26).

- **After the first 4 weeks of the study, patients' hemoglobin values progressively increased from a mean baseline value of 8.4 g/dL in patients receiving i.v. darbepoetin alfa and 8.7 g/dL in patients receiving s.c. darbepoetin alfa, reaching a plateau of 11–13 g/dL at 16 weeks (Fig-1).**
- **After this time, hemoglobin was maintained between 10 and 13 g/dL for up to 52 weeks.(Fig-2)**

Reference-Nephrol Dial Transplant (2003) 18: 576–581

Epoetin Alfa versus Darbepoetin Alfa

Characteristic	Epoetin Alfa	Darbepoetin Alfa
Structural	Identical to endogenous human EPO 165 amino acids 3 N-linked carbohydrate chains ≤ 14 sialic acid residues ≈ 40% Carbohydrate MW= 30.4 kDa	Differs from endogenous human EPO 165 amino acids, with 5 substitutions via site-directed mutagenesis 5 N-linked carbohydrate chains ≤ 22 sialic acid residues ≈ 51% Carbohydrate MW= 37.1 kDa
Distribution	Volume of distribution similar to plasma volume	No published data are available, but assumed similar to Epoetin Alfa
Metabolism	Metabolism believed to occur in Kidney, Liver and Bone marrow	
Half-life (I.V.)	8.5 h	25.3 h
Half-life (S.C.)	16-19 h	33-48 h
Bioavailability	20-30 %	37%
Tmax	18 h	54.1 ± 5.1 h
Dose	TIW	QW (Denovo) or Q2W (Conversion)

Conversion from Epoetin Alfa to Darbepoetin Alfa

Due to the longer serum half-life, Darbepoetin Alfa should be administered less frequently than Epoetin Alfa. Darbepoetin Alfa should be administered once a week if a patient is receiving Epoetin alfa 2 to 3 times weekly. Darbepoetin Alfa should be administered once every 2 weeks if a patient is receiving Epoetin Alfa once weekly.

Previous Weekly Epoetin Alfa Dose (Units/week)	Weekly Darbepoetin Alfa Dose (mcg/week)
< 1,500	6.25
1,500 to 2,499	6.25
2,500 to 4,999	12.5
5,000 to 10,999	25
11,000 to 17,999	40
18,000 to 33,999	60
34,000 to 89,999	100
≥ 90,000	200