Dipoetin

Darbepoetin Alfa INN

Composition:
Dipoetin 40 microgram solution for injection in pre-filled syringe: Each 0.40 ml pre-filled syringe contains recombinant Darbepoetin Alfa INN 40 microgram.
Dipoetin 60 microgram solution for injection in pre-filled syringe: Each 0.30 ml pre-filled syringe contains recombinant Darbepoetin Alfa INN 60 microgram.

Pharmacology:
Dipoetin (Darbepoetin Alfa) is an erythropoiesis-stimulating agent that is produced in Chinese Hamster Ovary (CHO) cells by recombinant DNA technology. **Dipoetin** (Darbepoetin Alfa) is a 165-amino acid protein containing 5 N-linked oligosaccharide chains, whereas recombinant human erythropoietin contains 3 chains. Erythropoietin is a glycoprotein that is the primary regulator of erythropoiesis through specific interaction with the erythropoietin receptor on the erythroid progenitor cells in the bone marrow. The production of erythropoietin primarily occurs in and is regulated by kidney in response to change in tissue oxygenation. Hypoxia and anemia generally results in an increase in endogenous erythropoietin production, which in turn stimulates erythropoiesis. **Dipoetin** (Darbepoetin Alfa) stimulates erythropoiesis by the same mechanism as endogenous erythropoietin.

Indications:
Dipoetin is indicated for the treatment of anemia due to -
- Chronic Kidney Disease (CKD) in patients on dialysis and patients not on dialysis.
- The effects of concomitant myelosuppressive chemotherapy, and upon initiation, there is a minimum of two additional months of planned chemotherapy.

Dosage & Administration:
For adult patients with CKD on dialysis:
- Initiate **Dipoetin** treatment when the hemoglobin level is less than 10 g/dL.
- 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.
- If the hemoglobin level approaches or exceeds 11 g/dL, reduce or interrupt the dose of **Dipoetin**.

For adult patients with CKD not on dialysis:
- Initiate **Dipoetin** treatment when the hemoglobin level is less than 10 g/dL
- The recommended starting dose is 0.45 mcg/kg intravenously or subcutaneously given once at four week intervals as appropriate.
- If the hemoglobin level exceeds 10 g/dL, reduce or interrupt the dose of **Dipoetin** & use the lowest dose of **Dipoetin** sufficient to reduce the need for RBC transfusions.

For pediatric patients with CKD:
- Initiate **Dipoetin** treatment when the hemoglobin level is less than 10 g/dL.
- The recommended starting dose for pediatric patients (less than 18 years) is 0.45 mcg/kg given as a single subcutaneous or intravenous injection once a week; patients not receiving dialysis may be initiated at 0.75 mcg/kg once every 2 weeks.
- If the hemoglobin level approaches or exceeds 12 g/dL, reduce or interrupt the dose of of **Dipoetin**.

Dose adjustment for CKD patients:
If a dose adjustment is required to maintain hemoglobin at the desired level, it's advised that the dose is adjusted approximately by 25%. If the increase in hemoglobin is inadequate (less than 1 g/dL in four weeks), increase the dose by 25%. Dose increases must not be made more frequently than once every four weeks. Decreases in dose can occur more frequently. Avoid frequent dose adjustments. If the hemoglobin rises rapidly (more than 1 g/dL in any 2-week period), reduce the dose of Darbepoetin Alfa by 25% or more as needed to reduce rapid response.

Conversion of Erythropoietin Alfa to Darbepoetin Alfa (**Dipoetin**) in patients with CKD on dialysis.
Dipoetin is administered less frequently than Erythropoietin Alfa.
- Initiate **Dipoetin** once weekly in patients receiving Erythropoietin Alfa 2 to 3 times weekly.
- Initiate **Dipoetin** once every 2 weeks in patients who were receiving Erythropoietin Alfa once weekly.

Estimated Darbepoetin Alfa (Dipoetin) Starting Doses (mcg/week) for patients with CKD on Dialysis Based on Previous Erythropoietin Alfa Dose (Units/week)

(Table -1)

Previous Weekly Erythropoietin Alfa Dose (Units/week)	Darbepoetin Alfa (Dipoetin) Dose (mcg/week)	
	Adult	Pediatric
<1,500	6.25	*
1,500 to 2,499	6.25	6.25
2,500 to 4,999	12.5	10
5,000 to 10,999	25	20
11,000 to 17,999	40	40
18,000 to 33,999	60	60
34,000 to 89,999	100	100
≥ 90,000	200	200

* For pediatric patients receiving a weekly Erythropoietin Alfa dose of <1,500 units/week, the available data are insufficient to determine the **Dipoetin** conversion dose.

Conversion of Erythropoietin Alfa to Darbepoetin Alfa (**Dipoetin**) in patients with CKD not on dialysis.
- Refer to Table-1. the dose conversion depicted in Table-1 does not accurately estimate the once monthly dose of **Dipoetin**.

Treatment of anemia in cancer patients on chemotherapy:
- Initiate **Dipoetin** treatment when the hemoglobin level is less than 10 g/dL, and if there is a minimum of two additional months of planned chemotherapy.
- The recommended starting dose & schedules are 2.25 mcg/kg every week subcutaneously until completion of a chemotherapy or 500 mcg every 3 weeks subcutaneously until completion of a chemotherapy course.

Dose adjustment for cancer patients:
(Table-2)

Dose Adjustment	Weekly Schedule	Every 3 Week Schedule
• If hemoglobin increases greater than 1g/dL in any 2-week period or • If hemoglobin reaches a level needed to avoid RBC transfusion	Reduce dose by 40%	Reduce dose by 40%
If hemoglobin exceeds a level needed to avoid RBC transfusion	• Withhold dose until hemoglobin approaches a level where RBC transfusions may be required • Reinitiate at a dose 40% below the previous dose	• Withhold dose until hemoglobin approaches a level where RBC transfusions may be required • Reinitiate at a dose 40% below the previous dose
If hemoglobin increases by less than 1 g/dL and remains below 10 g/dL after 6 weeks of therapy	Increase dose to 4.5 mcg/ kg/week	No dose adjustment
• If there is no response as measured by hemoglobin levels or if RBC transfusions are still required after 8 weeks of therapy • Following completion of a chemotherapy course	Discontinue Darbepoetin Alfa	Discontinue Darbepoetin Alfa

Preparation and Administration:
- Do not shake. Do not use Darbepoetin Alfa that has been shaken frozen.
- Protect pre-filled syringe from light.
- Do not use any pre-filled syringes exhibiting particulate matters or discoloration.
- Discard unused portion of Darbepoetin Alfa.
- Do not dilute and do not administer in conjunction with others drug solutions.

Contraindications:
Darbepoetin Alfa is contraindicated in patients with uncontrolled hypertension, Pure Red Cell Aplasia (PRCA) that begins after treatment with Darbepoetin Alfa or other Erythropoietin protein drugs, serious allergic reactions to Darbepoetin Alfa.

Warnings and Precautions:
The use of Darbepoetin Alfa & others ESA may increase risk of mortality, myocardial infraction, stroke, thromboembolism, congestive heart failure, thrombosis of hemodialysis vascular access and other thromboembolic events in higher target groups.

Drug Interaction:
No drug interaction studies have been conducted with Darbepoetin Alfa.

Adverse Reactions:
Patients with CKD: Hypertension, dyspnea, peripheral edema, cough & procedural hypotension.
Patients with cancer receiving chemotherapy: Abdominal pain, edema, thrombovascular events.

Use in Special Population:
Pregnancy: There are no adequate well-controlled studies of Darbepoetin Alfa in pregnant women. Animal studies do not indicate direct harmful effects with respect to pregnancy. Caution should be exercised when prescribing Darbepoetin Alfa to pregnant women. *Nursing mothers:* There is no information regarding the presence of Darbepoetin Alfa in human milk, the effects on the breastfed child or the effects on milk production. Caution should be exercised when Darbepoetin Alfa is administered to nursing mother. *Pediatric use: Pediatric patients with CKD:* The safety and effectiveness of Darbepoetin Alfa with CKD receiving and not receiving dialysis have been established in the age groups 1 months to 16 years old. No data are available in pediatric patients less than 1 month old. *Pediatric patients with cancer:* The safety and efficacy of Darbepoetin Alfa in pediatric patients with cancer have not been established.

Overdose:
Darbepoetin Alfa overdosage can cause hemoglobin levels above the desired level, which should be managed with discontinuation or reduction of Darbepoetin Alfa dosage and/or with phlebotomy, as clinically indicated. Severe hypertension has been observed by ESAs overdose.

Storage:
Store at 2-8° C, protect from light. Do not shake or don't keep in deep freez. Keep out of the reach of children.

How Supplied:
Dipoetin 40 microgram solution for injection in pre-filled syringe: Each box contains 0.40 ml pre-filled syringe injection containing recombinant Darbepoetin Alfa INN 40 microgram.
Dipoetin 60 microgram solution for injection in pre-filled syringe: Each box contains 0.30 ml pre-filled syringe injection containing recombinant Darbepoetin Alfa INN 60 microgram.

Manufactured by:
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