Omontys (Peginesatide)

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Anaemia, normocytic normochromic is a regular feature of chronic kidney disease (CKD). It is observed as early as stage 3 CKD & is almost universal by stage 4. Primary cause of anaemia in CKD is insufficient production of erythropoietin. It is associated with number of adverse pathophysiologic consequences & is responsible for many of the non specific symptoms.

Prior to the development of erythropoietin stimulating agents (ESA), red blood cell transfusions and androgens were the primary options available for the management of anaemia associated with CKD. The availability of recombinant human EPO and modified EPO products, such as darbepoetin-alpha, has been one of the most significant advances in the care of renal patients since the introduction of dialysis and renal transplantation. The newest addition to these ESA has been Omontys (peginesatide) (1). Omontys has as its main advantage in the fact that it needs less frequent dosing; about once monthly versus weekly or even more regularly for EPO. The less frequent dosing is also an advantage for dialysis centers. Omontys has another advantage. It's quite likely to be less expensive than EPO to manufacture. Omontys was approved by FDA in March 2012.

Description

Omontys is an ESA that is a synthetic, pegylated dimeric peptidecomprised of two identical 21- amino acidchains covalently bonded to a linker derived from iminodiacetic acid and β-alanine. Omontys is manufactured as an acetate salt. It has no amino acid sequence homology to erythropoietin unlike other ESA.

Mechanism of action

Omontys binds to the human erythropoietin receptor to induce erythropoiesis by stimulating the division and differentiation of committed erythroid progenitor cells; induces the release of reticulocytes from the bone marrow into the bloodstream, where they mature to erythrocytes. This results in an increase in reticulocyte counts followed by a rise in hemoglobin levels.(2) Omontys is a synthetic, peptide-based ESA and cross-reactivity of the immune response against either endogenous or recombinant protein-based erythropoietin agents (eg, epoetin, darbepoetin) to Omontys is unlikely.

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Clinical Pharmacology

- The bioavailability and peak plasma time of Omontys following s. c. administration is approximately 46% and 48 hrs respectively.
- The volume of distribution is 34.9ml/kg (i. v.).
- Omontys is not metabolized and urinary excretion is the predominant route of elimination.
- The mean half-life following i. v. administration in healthy subjects is 25 hours and in Dialysis patients it is 47.9 hours. The half life following s. c. administration in healthy patients is 53 hours.

Indications

- Omontys is indicated for the treatment of anemia due to chronic kidney disease (CKD) in adult patients on dialysis

Omontys is not indicated and is not recommended for use:

- In patients with CKD not on dialysis and whose anemia is not due to CKD.
- As a substitute for RBC transfusions in patients who require immediate correction of anemia.

Contraindications

Omontys is contraindicated in patients with:

· Uncontrolled hypertension

Dosage and administration

Evaluation of Iron Stores and Nutritional Factors

- Evaluate the iron status in all patients before and during treatment and maintain iron repletion. Supplemental iron is recommended if serum ferritin <100 mcg/L or serum transferrin saturation <20%.

- Correct or exclude other causes of anemia (e.g., vitamin deficiency, metabolic or chronic inflammatory conditions, bleeding, etc.) before initiating Omontys Initiation of Treatment and Starting Dose (3)
- Initiate Omontys treatment when the hemoglobin level is less than 10 g/dL.
- The recommended starting dose is 0.04 mg/kg body weight administered as a single i. v. or s. c. injection once monthly.
- For patients previously receiving epoetin alfa, the first dose of Omontys should be administered one week after the last epoetin alfa dose was administered.
- For patients previously receiving darbepoetin alfa, the first dose of Omontys should be administered at the next scheduled dose in place of darbepoetin alfa. Maintain the route of administration (i. v. or s. c. injection).

Dosage adjustments:

- If hemoglobin does not increase by >1 g/dL after 4 weeks: Increase dose by 25%; do not increase the dose more frequently than once every 4 weeks
- If hemoglobin increases >1 g/dL in the 2-week period prior to the dose or >2 g/dL in 4 weeks: Reduce dose by 25% (or more) as needed to reduce rapid response
- Inadequate or lack of response over a 12-week escalation period: Further increases are unlikely to improve response and may increase risks; use the minimum effective dose that will maintain a Hgb level sufficient to avoid RBC transfusions and evaluate patient for other causes of anemia. Discontinue therapy if responsiveness does not improve.

Administration

- May be administered as an i. v. injection or s. c. injection. The i. v. route is generally used for hemodialysis patients
- Peritoneal dialysis patients should only administer therapy via the s. c. route.
- For s. c. injections, may inject in either the outer area of the upper arms, the front of the middle thighs, the abdomen (excluding the 2-inch area around the navel), or the upper outer buttocks area.

Dosing in special population:

- Pregnancy – (Category C) Omontys should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.
- Lactation - Excretion in breast milk unknown/use caution
- Pediatric Use - The safety and efficacy of Omontys in pediatric patients have not been established.
- Renal Impairment - No dosage adjustment provided in manufacturer's labeling.
- Hepatic Impairment - No dosage adjustment provided in manufacturer's labeling (has not been studied).

Adverse Reactions

>10% (Significant)

- Cardiovascular: Hypotension (14%), hypertension (13%), procedural hypotension (11%)
- Central nervous system: Headache (15%), fever (12%)
- Endocrine & metabolic: Hyperkalemia (11%)
- Gastrointestinal: Diarrhea (18%), nausea (17%), vomiting (15%)]
- Neuromuscular & skeletal: Muscle spasms (15%), arthralgia (11%), back pain (11%), extremity pain (11%)
- Respiratory: Dyspnea (18%), cough (16%), upper respiratory tract infection (11%)
- Miscellaneous: Arteriovenous fistula site complication (16%) 1% to 10%: Peginesatide-specific binding antibodies (1%) <1% (Limited to important or life-threatening): Allergic reaction, seizures

Warnings/Precautions

- Allergic reactions: Discontinue and treat symptoms appropriately in patients who experience serious allergic/anaphylactic reactions.
- Lack/loss of response: Patients with a sudden loss of hemoglobin response should be evaluated for potential causes of decreased response (eg, iron deficiency, infection, bleeding, inflammation). If common causes are excluded, patient should be evaluated for the presence of peginesatide antibodies. During trials, peginesatide-specific binding antibodies were detected rarely (with a higher incidence noted in patients receiving s. c compared to i. v. administration).
- Drug Interactions: There are no known significant interactions.

References

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2. Macdougall IC, Rossert J, Casadevall N, et al, "A Peptide-Based Erythropoietin-Receptor Agonist for Pure Red-Cell Aplasia," N Engl J Med, 2009, 361(19):1848- 55.
3. Macdougall IC, Wiecek A, Tucker B, et al, "Dose-Finding Study of Peginesatide for Anemia Correction in Chromic Kidney Disease Patients," Clin J Am Soc Nephrol, 2011, 6(11):2579-86.