Agalsidase beta (Fabrazyme®) Criteria for Non-Formulary Use

VA Pharmacy Benefits Management and Medical Advisory Panel

The following recommendations are based on current medical evidence and expert opinion from clinicians. The content of the document is dynamic and will be revised as new clinical data becomes available. The purpose of this document is to assist practitioners in clinical decision-making, to standardize and improve the quality of patient care, and to promote cost-effective drug prescribing. The clinician should utilize this guidance and interpret it in the clinical context of individual patient situations.

Indications for Use in Veteran Patients

- Agalsidase beta is restricted for use in patients with a diagnosis of classic Fabry disease. Treatment in patients with the cardiac variant may also be appropriate although the use of agalsidase beta in patients with this form of Fabry disease has not been adequately studied.

Dosage and Administration

Dosage and infusion rate:

- The recommended dosage is 1.0mg/kg by IV infusion every 2 weeks.
- Initial infusion rate should not exceed 0.25mg/min (15mg/hr). The infusion rate should be slowed if the patient develops infusion-associated reactions. Once patient tolerance has been determined, the infusion rate may be increased by increments of 0.05 to 0.08 mg/min (3 to 5 mg/hr) for each infusion thereafter. The manufacturer's prescribing information states that 31 of 58 patients (53%) received infusions of rates $\geq$ 33mg/hr.
- Due to the high potential for infusion reactions, the patient should be given antipyretics (and possibly, antihistamines) prior to infusion (see **Monitoring**).

Instructions for reconstitution and dilution:

- Reconstitution and dilution should be performed by aseptic technique.
- The product is supplied as a single-use 20ml vial with 37mg agalsidase beta (5mg/ml with a total 35mg per vial upon reconstitution). The number of vials needed should be determined based on the patient's weight. The vial should be stored in the refrigerator and allowed to come to room temperature (approximately 30 minutes) prior to reconstitution.
- Each vial should be reconstituted by slowly injecting 7.2ml Sterile Water for Injection, USP down the inside wall of the vial. Gently roll and tilt each vial. Avoid shaking or agitating the product.
- The reconstituted solution should be clear and colorless. Do not use the solution if there is particulate matter or if it is discolored.
- Upon reconstitution, each vial will contain 5mg/ml agalsidase beta with 7ml total for extraction (35mg).
- The reconstituted solution should then be diluted to a final total volume of 500ml with 0.9% Sodium Chloride Injection, USP. The volume of 0.9% Sodium Chloride for Injection, USP equal to the volume of the reconstituted agalsidase beta patient dose should first be removed from 500ml infusion bag and then the dose can be added for dilution.
  - Example: Patient weight = 80kg; dose =80mg
  - 80mg divided by 5mg/ml = 16ml agalsidase beta
  - Therefore, remove 16ml Sodium Chloride solution from bag
- Slowly withdraw reconstituted agalsidase beta from each vial to obtain total patient dose. Inject dose directly into Sodium Chloride solution (do not inject into airspace).
- Invert bag gently to mix solution.
- Do not infuse solution in the same IV line with other products.
- The solution should be used immediately. If it is not possible to use immediately, the reconstituted and diluted solution may be stored at 36°-46°F for up to 24 hours. Discard any unused portion.
- It is recommended not to use filter needles during preparation.
- The manufacturer's product information states that an in-line low protein-binding 0.2μm filter may be used to filter the diluted solution during administration.

Adverse Events

The most common and severe adverse effects with agalsidase beta are infusion reactions. The reactions were reported to include fever, rigors, tachycardia, hypertension, hypotension, chest pain, dyspnea, pruritus, urticaria, rash, throat tightness, lip or ear edema, headache, nausea, vomiting, abdominal pain. Patients were pretreated with acetaminophen and an antihistamine. Some patients experienced reactions despite pretreatment with an antipyretic, antihistamine, and oral steroid. The frequency of infusion reactions decrease with chronic therapy, although serious reactions may still occur after prolonged duration of therapy.

Monitoring

Due to the common occurrence of infusion reactions with agalsidase beta (see Adverse Events), it is recommended that patients receive antipyretics prior to infusion. If a patient experiences a reaction, recommended interventions include decreasing the rate of or temporarily stopping the infusion, and/or giving antipyretics (regardless of pretreatment), antihistamines, and/or steroids. Since some infusion reactions have been severe, it is important to have appropriate medical support available when administering agalsidase beta. It has yet to be determined if monitoring plasma GL-3 concentrations will prove useful. Patients should be informed of the established Registry to evaluate disease progression and chronic treatment with agalsidase beta. The effects of agalsidase beta on pregnant women and their offspring are being monitored as well as whether agalsidase beta is excreted in breast milk. Information is available at **www.fabryregistry.com** or (800) 745-4447.

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