Lamzede® (velmanase alfa-tycv) – New orphan drug approval

- On February 16, 2023, Chiesi Global Rare Diseases announced the FDA approval of Lamzede (velmanase alfa-tycv), for the treatment of non-central nervous system manifestations of alpha mannosidosis in adult and pediatric patients.

- Alpha mannosidosis is an ultra-rare, progressive lysosomal storage disorder caused by deficiency in the enzyme α-mannosidase. Alpha mannosidosis results in the body's cells being unable to properly break down certain groups of complex sugars. The buildup of sugars can affect many of the body's organs and systems.

    - The prevalence of alpha mannosidosis is approximately one in every 500,000 to one in every 1,000,000 babies born worldwide.

- Lamzede is the first enzyme replacement therapy approved for alpha mannosidosis.

- The efficacy of Lamzede was established in Trial 1, a randomized, double-blinded, placebo-controlled study in 25 adult and pediatric patients with alpha-mannosidosis. Patients received Lamzede or placebo for 52 weeks. The endpoints evaluated included 3-minute stair climbing test (3MSCT), 6-minute walking test (6MWT), forced vital capacity (FVC), and serum oligosaccharide concentrations.

    - The mean relative change (%) from baseline in 3MSCT (steps/min) was 0.5 for Lamzede vs. -3.6 for placebo (treatment difference 3.4, 95% CI: -9.5, 16.3).
    - The mean relative change (%) from baseline in 6MWT (meters) was 1.2 for Lamzede vs. -0.8 for placebo (treatment difference 1.6, 95% CI: -7.2, 10.4).
    - The mean relative change (%) from baseline in FVC (% predicted) was 11.4 for Lamzede vs. 1.9 for placebo (treatment difference 7.4, 95% CI: -5.7, 20.5).
    - The mean relative change (%) from baseline in serum oligosaccharide concentration (µmol/L) was -75.8 for Lamzede vs. -20.3 for placebo (treatment difference -55.6, 95% CI: -69.3, -41.9).

- The efficacy of Lamzede was also evaluated in Trial 2, a single arm study in 5 pediatric alpha mannosidosis patients less than 6 years of age. The mean (standard deviation) absolute and percentage changes from baseline for serum oligosaccharides at 24 months were -7.7 (4.27) µmol/L and -65.8% (23.1%) respectively.

- Lamzede carries a boxed warning for severe hypersensitivity reactions.

- Additional warnings and precautions for Lamzede include infusion-associated reactions and embryo-fetal toxicity.

- The most common adverse reactions (> 20%) with Lamzede use were hypersensitivity reactions including anaphylaxis, nasopharyngitis, pyrexia, headache, and arthralgia.

- The recommended dosage of Lamzede is 1 mg/kg (actual body weight) administered once every week as an intravenous infusion.

    - The total volume of infusion is determined by the patient's actual body weight and should be administered over a minimum of 60 minutes for patients weighing up to 49 kg. Patients

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weighing 50 kg and greater should be infused at a maximum infusion rate of 25 mL/hour to control the protein load.
  - Prior to Lamzede administration, pre-treatment with antihistamines, antipyretics, and/or corticosteroids should be considered.

- Chiesi Global Rare Diseases' launch plans for Lamzede are pending. Lamzede will be available as a 10 mg lyophilized powder in a single-dose vial for reconstitution.