Pombiliti™ (cipaglucosidase alfa-atga) plus Opfolda™ (miglustat) – New drug approvals

- On September 28, 2023, Amicus Therapeutics announced the FDA approval of Pombiliti (cipaglucosidase alfa-atga) plus Opfolda (miglustat), for the treatment of adult patients with late-onset Pompe disease (lysosomal acid alpha-glucosidase [GAA] deficiency) weighing ≥ 40 kg and who are not improving on their current enzyme replacement therapy (ERT).

- Pompe disease is an inherited lysosomal disorder caused by deficiency of the enzyme GAA. Pompe disease ranges from a rapidly deteriorating infantile form with significant impact to heart function, to a more slowly progressive, late-onset form primarily affecting skeletal muscle and progressive respiratory involvement.

- Pombiliti provides an exogenous source of GAA and Opfolda is an enzyme stabilizer.

    — Opfolda will be available as a 65 mg capsule of miglustat. Miglustat is also available generically as a 100 mg capsule. The 100 mg strength is approved for Gaucher disease.

- The efficacy of Pombiliti plus Opfolda was established in a randomized, double-blind, active-controlled study in patients ≥ 18 years old diagnosed with late-onset Pompe disease. Patients were randomized to receive Pombiliti in combination with Opfolda or a non-U.S.-approved alglucosidase alfa product with placebo every other week for 52 weeks. The efficacy population included a total of 123 patients of whom 77% had received prior treatment with U.S.-approved alglucosidase alfa or a non-U.S.-approved alglucosidase alfa product (ERT-experienced) and 28 (23%) were ERT-naïve. Key efficacy endpoints included assessment of sitting forced vital capacity (FVC) (% predicted) and 6-minute walk distance (6MWD).

    — Patients treated with Pombiliti in combination with Opfolda showed a mean change in sitting FVC from baseline at week 52 of -1.1% as compared with patients treated with a non-U.S.-approved alglucosidase alfa product with placebo of -3.3%; the estimated treatment difference was 2.3% (95% CI: 0.02, 4.62). The ERT-experienced patients treated with Pombiliti in combination with Opfolda showed a numerically favorable change in sitting FVC from baseline at week 52.
    — Patients treated with Pombiliti in combination with Opfolda walked on average 21 meters farther from baseline as compared to those treated with a non-U.S.-approved alglucosidase alfa product with placebo who walked 8 meters farther from baseline; the estimated treatment difference was 14 meters (95% CI: -1, 28). The ERT-experienced patients treated with Pombiliti in combination with Opfolda showed a numerically favorable change in 6MWD from baseline at week 52.

- Pombiliti carries a boxed warning for severe hypersensitivity reactions, infusion-associated reactions, and risk of acute cardiorespiratory failure in susceptible patients.

- Pombiliti in combination with Opfolda is contraindicated in pregnancy.

- An additional warning and precaution for Pombiliti and Opfolda is embryo-fetal toxicity.

- The most common adverse reactions (≥ 5%) with Pombiliti plus Opfolda use were headache, diarrhea, fatigue, nausea, abdominal pain, and pyrexia.

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- The recommended dosage of Pombiliti is 20 mg/kg (of actual body weight) administered every other week as an intravenous infusion over approximately 4 hours.
- The recommended dosage of Opfolda is based on actual body weight. For patients weighing ≥ 50 kg, the recommended dosage is 260 mg orally every other week. For patients weighing ≥ 40 kg to < 50 kg, the recommended dosage is 195 mg orally every other week.
- Pombiliti in combination with Opfolda should be started 2 weeks after the last ERT dose.
- Amicus Therapeutics plans to launch Pombiliti plus Opfolda immediately. Pombiliti will be available as a 105 mg lyophilized powder in a single-dose vial for reconstitution. Opfolda will be available as a 65 mg capsule.

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