## Galafold™ (migalastat) – New orphan drug approval

- On August 10, 2018, the FDA announced the approval of Amicus Therapeutics' Galafold (migalastat) for the treatment of adults with a confirmed diagnosis of Fabry disease and an amenable galactosidase alpha gene (GLA) variant based on in vitro assay data.
    - This indication is approved under accelerated approval based on reduction in kidney interstitial capillary (KIC) cell globotriaosylceramide (GL-3) substrate.
    - Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

- Fabry disease is a rare, progressive genetic disorder characterized by a defective GLA gene that causes an enzyme deficiency. This enzyme is responsible for breaking down the disease substrate that builds up in blood vessels, nerves, and major organs, such as the kidneys, in Fabry disease patients. This leads to kidney disease, cardiac hypertrophy, arrhythmias, stroke, and early death.
    - Fabry disease affects both males and females.
    - Classic Fabry disease (the most severe type) affects approximately one in 40,000 males. The later-onset type is more frequent, and in some populations, may occur in one in 1,500 to 4,000 males.
    - An estimated 35% – 50% of Fabry disease patients may have the amenable GLA variant.

- The efficacy of Galafold was demonstrated in a placebo-controlled study of 45 Fabry disease patients with amenable GLA variants. Patients were randomized to Galafold or placebo. The major efficacy outcome measure was the average number of GL-3 inclusions per KIC in renal biopsy samples.
    - Of the 45 evaluable patients (males and females), a greater proportion of patients treated with Galafold demonstrated ≥ 50% reduction from baseline in the major efficacy measure compared to placebo (52% vs. 45%, respectively).
    - Among males in the trial, the major efficacy measure was achieved in 71% of Galafold-treated patients vs. 44% of placebo-treated patients. Among females, the major efficacy measure was achieved in 44% of Galafold-treated patients vs. 46% of placebo-treated patients.
    - Patients with non-amenable GLA variants had no change from baseline in the average number of GL-3 inclusions per KIC after 6 months of treatment.

- The safety of Galafold was further studied in four clinical trials which included a total of 139 patients with Fabry disease.

- The most common adverse reactions (≥ 10%) with Galafold use were headache, nasopharyngitis, urinary tract infection, nausea, and pyrexia.

- The recommended dosage regimen of Galafold is 123 mg orally once every other day at the same time of day.
    - Treatment is indicated for patients with an amenable GLA variant that is interpreted by a clinical genetics professional as causing Fabry disease in the clinical context of the patient.
    - Consultation with a clinical genetics professional is strongly recommended in cases where the amenable GLA variant is of uncertain clinical significance or may be benign.

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- The average price for Galafold is $315,000 per year.
- Amicus Therapeutics plans to launch Galafold immediately and will begin shipping to a limited distribution network in the coming week. Galafold will be available as a 123 mg capsule.