Kanuma™ (sebelipase alfa) – New Orphan Drug Approval

- On December 8, 2015, the FDA announced the approval of Alexion's Kanuma (sebelipase alfa), for the treatment of patients with a diagnosis of lysosomal acid lipase (LAL) deficiency.

- LAL deficiency (also known as Wolman disease and cholesteryl ester storage disease [CESD]) is a genetic, chronic, and progressive metabolic disease associated with significant multi-organ damage and premature mortality.

    - Wolman disease occurs in 1-2 infants per million births. People have no LAL enzyme activity that causes a build-up of fats in cells and leads to liver and cardiovascular disease as well as other complications. People normally do not survive beyond the first year of life.
    - CESD occurs in 25 individuals per million births. Onset is usually in childhood or later. People have decreased LAL enzyme activity that leads to similar consequences as Wolman disease but at a slower rate.

- Kanuma is enzyme replacement therapy that provides a recombinant form of LAL to act in place of missing or absent LAL. The recombinant form of LAL is produced in genetically engineered chicken egg whites.

    - Kanuma was granted priority review, orphan drug status, breakthrough therapy status for Wolman disease, and a rare pediatric disease priority review voucher.

- The approval of Kanuma was based on two clinical studies and an open-label extension study. A total of 9 infants (< 6 months of age) were enrolled in an open-label trial. In a randomized, double-blind trial, 66 patients were enrolled to receive Kanuma or placebo for 20 weeks. In the open-label extension trial, patients in the double-blind trial received Kanuma for up to 36 weeks.

    - 67% (6 of 9 patients) with the infant form of LAL deficiency survived beyond 12 months of age compared to 0 out of 21 patients in an historical cohort.
    - In the double-blind study, a statistically significant improvement in low density lipoprotein-cholesterol (LDL-c) was observed in the Kanuma-treated group vs. the placebo group (mean difference: -22%; $p < 0.0001$). There were also larger reductions in alanine aminotransferase (ALT) values and liver fat content in patients treated with Kanuma vs. placebo.
    - In the open-label extension trial, patients treated with Kanuma continued to experience improvements in lipid parameters, including LDL-c and high density lipoprotein (HDL)-c levels, and ALT.

- Warnings and precautions of Kanuma are hypersensitivity reactions including anaphylaxis and hypersensitivity to eggs or egg products.

- The most common adverse events (≥ 30%) with Kanuma use in patients with rapidly progressive disease presenting within the first 6 months of life were diarrhea, vomiting, fever, rhinitis, anemia, cough, nasopharyngitis, and urticaria.

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- The most common adverse events (≥ 8%) with Kanuma use in pediatric and adult patients were headache, fever, oropharyngeal pain, nasopharyngitis, asthenia, constipation, and nausea.
- The recommended dose of Kanuma in patients with rapidly progressive disease presenting within the first 6 months of life is 1 mg/kg intravenously once weekly.
    - For patients who do not achieve an optimal clinical response, increase to 3 mg/kg intravenously once weekly.
- The recommended dose of Kanuma in pediatric and adult patients is 1 mg/kg intravenously once every other week.
- Alexion expects to launch Kanuma the first week of January 2015. Kanuma will be available as 20 mg/10 mL (2 mg/mL) solution in single-use vials.
- Alexion will offer support to patients with LAL deficiency through its OneSource™ program.
    - The OneSource™ program helps patients navigate insurance co-pays and receive assistance with out-of-pocket expenses.
    - The Alexion Access Foundation helps patients with no insurance receive free Kanuma.