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Genetics, Pharmacology, FDA Update

FDA Update: FDA approves first drug to treat rare enzyme disorder in infants, children

by from the Food and Drug Administration Office of Pediatric Therapeutics and Division of Pediatric and Maternal Health

The Food and Drug Administration (FDA) has approved sebelipase alfa (Kanuma, Alexion Pharmaceuticals Inc.), the first treatment for a rare genetic disease known as lysosomal acid lipase (LAL) deficiency.

The new drug is a recombinant form of the human LAL enzyme produced in the egg whites of genetically engineered (GE) chickens. It is intended to replace the missing, partially active or inactive LAL protein in patients with LAL deficiency. With the approval of Kanuma in December 2015, these patients have access for the first time to a treatment that may improve their lives and chances of survival.

LAL deficiency causes cholesteryl esters and triglycerides to build up in vital organs leading to life-threatening liver and cardiovascular diseases and other complications. A rapidly progressive form of LAL deficiency, Wolman disease, often presents in infants around 2-4 months of age, and survival is rare beyond 1 year of age. A milder form, cholesteryl ester storage disease (CESD), presents in older children or adults with varying disease severity and associated complications.

The estimated incidence of Wolman disease is one in 350,000 live births (http://ghr.nlm.nih.gov/condition/wolman-disease), while CESD has an estimated prevalence as high as one in 40,000 (Porto AF. *Pediatr Endocrinol Rev*. 2014;12 Suppl 1:125-132).

The FDA determined that sebelipase alfa was safe and effective based on two clinical trials: an open-label, historically controlled trial in infants with Wolman disease and a double-blind, placebo-controlled trial in pediatric and adult patients with CESD.

In the first trial, six of the nine infants (67%) treated with sebelipase alfa were alive at 12 months of age compared with none of the 21 infants in the historical control group.

In the second trial, 20 weeks of treatment resulted in statistically significant improvements over placebo in low-density lipoprotein cholesterol levels and other disease-related parameters. Common adverse effects included diarrhea, vomiting, fever, rhinitis, anemia, cough, headache, constipation and nausea.

The FDA also assessed the safety and effectiveness of the recombinant DNA integrated in the GE chickens and its stability in the animals' genome over several generations. No adverse outcomes were noted in the chickens. These GE chickens and eggs are raised in highly secure indoor facilities, and rigorous steps are taken to ensure that neither the chickens nor the eggs enter the nation's food supply.

Kanuma was granted a rare pediatric disease priority review voucher, which encourages development of new products for prevention and treatment of rare pediatric diseases.

Resources

- Prescribing information for Kanuma (sebelipase alfa)
- Rare Pediatric Disease Priority Review Voucher Program
- Guidance for Industry: Regulation of Genetically Engineered Animals Containing Heritable Recombinant

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