Kanuma, approved by the FDA in 2015, is a recombinant human lysosomal acid lipase (a lysosomal enzyme) indicated for the treatment of Lysosomal Acid Lipase (LAL) deficiency.

LAL deficiency is a lysosomal storage disorder caused by a genetic defect of the LIPA gene that results in decreased or absent activity of the LAL enzyme. Deficient LAL enzyme activity results in progressive complications due to the lysosomal accumulation of cholesteryl esters and triglycerides in multiple organs, including the liver, spleen, intestine, and the walls of blood vessels. Accumulation of lipids in the liver can lead to fibrosis and cirrhosis. Lipid accumulation in the intestinal walls can lead to malabsorption and growth failure. Dyslipidemia and accelerated atherosclerosis also occur.

Kanuma works as an enzyme replacement therapy and catalyzes the lysosomal hydrolysis of cholesteryl esters and triglycerides to break them down. It is the first drug to be approved for LAL-D and the first treatment to target the underlying pathology. Previous management focused on strategies like lipid lowering medications, diet modification, liver transplant, or stem cell transplant.

Wolman disease is the early infantile-onset phenotype of LAL-D which is more severe and rapidly progressive, with survival not expected beyond infancy. Kanuma significantly prolongs the life expectancy of these patients. Cholesterol ester storage disease (CESD) has a more variable phenotype with onset during childhood or adulthood. Kanuma has proven benefits for these patients as well.

Kanuma (sebelipase alfa) will be considered for coverage when the following criteria are met:

Lysosomal Acid Lipase (LAL) Deficiency

For **initial** authorization:

- 1. Member is at least 1 month of age; AND
- 2. Medication must be prescribed by or in consultation with a hepatologist, cardiologist, metabolic specialist, or geneticist; AND
- 3. Member has a diagnosis of LAL deficiency confirmed by <u>at least one</u> of the following methods:
 - a) Deficient LAL enzyme activity (assay)
 - b) Identification of biallelic pathogenic mutations of the LIPA gene (genetic testing); AND
- 4. Member demonstrates at least one clinical feature of LAL-D such as dyslipidemia, elevated transaminases (ALT, AST), impaired growth or failure to thrive, malabsorption, hepatomegaly, adrenal calcification (in Wolman's disease), or advanced liver disease.
- 5. **Dosage allowed/Quantity limit:**

Infants with rapidly progressive LAL-D within first 6 months of life: Starting dose of 1 mg/kg once weekly via IV infusion. If clinical response is suboptimal, may increase to 3 mg/kg once weekly, and further to 5 mg/kg once weekly if needed.

Pediatric and adult: 1 mg/kg IV infusion every other week. If clinical response is suboptimal, may increase to 3 mg/kg every other week.



If all the above requirements are met, the medication will be approved for 6 months.

For **reauthorization**:

1. Chart notes must document a positive clinical response to treatment such as improved lipid profile (LDL-c, triglycerides), liver biomarkers c(001 Tw7d[4)Tj0.0z1 Tw 0503cLs-1.7 (er)0.7 (os)3.8 (pon4.4 (y)3.7 (c)3.4 (v)3.7 (c)3.7 (c