Clinical Policy Title:	sebelipase alfa
Policy Number:	RxA.186
Drug(s) Applied:	Kanuma®
Original Policy Date:	02/07/2020
Last Review Date:	04/18/2022
Line of Business Policy Applies to:	All lines of business

Background

Sebelipase alfa (Kanuma®) is a hydrolytic lysosomal cholesteryl ester and triacylglycerol-specific enzyme. Kanuma® is indicated for the treatment of patients with a diagnosis of Lysosomal Acid Lipase (LAL) deficiency.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
sebelipase alfa (Kanuma®)	Infants with LAL deficiency: rapidly progressive disease presenting within first 6 months of life	Recommended dose:1 mg/kg intravenous once weekly For patients with a suboptimal clinical response*, increase the dosage to 3 mg/kg once weekly. For patients with continued suboptimal clinical response on the 3 mg/kg once weekly dosage, further increase the dosage to 5 mg/kg once weekly.	5 mg/kg/week
	Pediatric and Adult Patients with LAL deficiency	Recommended dose: 1 mg/kg intravenous every other week For patients with a suboptimal clinical response*, increase the dosage to 3 mg/kg once every other week.	3 mg/kg every other week

* A suboptimal clinical response is defined as any of the following: poor growth, deteriorating biochemical markers, or persistent or worsening organomegaly.

Dosage Forms

- Single-use vial: 20 mg/10 mL

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the provisions of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

I. Initial Approval Criteria

A. Lysosomal Acid Lipase Deficiency (must meet all)**:**

1. Diagnosis of LAL deficiency confirmed by one of the following (a or b):
   a. Enzyme assay demonstrating a deficiency of LAL activity;
   b. LIPA gene mutation;
2. Age ≥ 1 month;
3. Dose does not exceed (a or b)
   a. 5 mg per kg every other week for Infants with rapidly progressive LAL deficiency presenting within the first 6 months of life, For patients with a suboptimal clinical response, increase the dosage to 3 mg/kg once weekly. For patients with continued suboptimal clinical response on the 3 mg/kg once weekly dosage, further increase the dosage to 5 mg/kg once weekly.
   b. 3 mg per kg every other week for Pediatric and Adult Patients with LAL deficiency. For patients with a suboptimal clinical response, increase the dosage to 3 mg/kg once every other week.

Approval Duration
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

A. Lysosomal Acid Lipase Deficiency (must meet all)**:**

1. Member is currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy;
2. Member is responding positively to therapy as evidenced by documentation of clinical response which may include, but is not limited to:
   a. For members with rapidly progressive disease presenting within first 6 months of life: continued survival;
   b. For all other members: decrease in low-density lipoprotein cholesterol (LDL-c), non-high-density lipoprotein cholesterol (non-HDL-c), or triglycerides; increase in HDL-c; normalization of alanine aminotransferase (ALT) or aspartate aminotransferase (AST); reduction in hepatic fat content, steatosis, or liver volume;
3. If request is for a dose increase, new dose does not exceed (a or b):
   a. 5 mg per kg every other week for Infants with rapidly progressive LAL deficiency presenting within the first 6 months of life, For patients with a suboptimal clinical response, increase the dosage to 3 mg/kg once weekly. For patients with continued suboptimal clinical response on the 3 mg/kg once weekly dosage, further increase the dosage to 5 mg/kg once weekly.
   b. 3 mg per kg every other week for Pediatric and Adult Patients with LAL deficiency. For patients with a suboptimal clinical response, increase the dosage to 3 mg/kg once every other week.

Approval Duration
Commercial: 12 months
Medicaid: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key

ALT: alanine aminotransferase
AST: aspartate aminotransferase
FDA: Food and Drug Administration
HDL-c: high-density lipoprotein cholesterol
LAL: lysosomal acid lipase
LDL-c: low-density lipoprotein cholesterol

APPENDIX B: Therapeutic Alternatives

Not applicable

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - None Reported.

- Boxed Warning(s):
  - None Reported.

APPENDIX D: General Information

Measures of Therapeutic Response

- LAL normally causes the breakdown of lipid particles, including LDL-c. A lack of LAL results in accumulation of cholesteryl esters and triglycerides. Therefore, LDL-c, non-HDLc, triglycerides, and HDL-c are clinical parameters that can indicate therapeutic response to Kanuma®. In clinical trials, there were initial increases in LDL-c and triglycerides within the first 2-4 weeks of treatment; however, this was followed by a decrease to below pre-treatment values within 8 weeks of treatment.
- In addition, the lipid accumulation seen in LAL deficiency can occur in multiple organs, including the liver. This results in increased liver fat content and progression of liver disease, including fibrosis and cirrhosis. In clinical trials, patients receiving Kanuma® had normalization of ALT and AST levels, reduction in hepatic fat content and steatosis (defined as the absolute decrease of ≥ 5% from baseline in assessment of hepatic fat content)*, and decrease in baseline liver volume* when compared to patients receiving placebo. As such, improvement in these areas may also indicate positive response to Kanuma®. *Not statistically significant

References

1. Kanuma® Prescribing Information. Boston MA : Alexion Pharmaceuticals, Inc.; November 2021. Available at http://www.kanuma.com/. Accessed January 13, 2022.
2. Zhang B, Porto AF. Cholesteryl ester storage disease: protean presentations of lysosomal acid lipase deficiency. J Pediatr Gastroenterol Nutr. 2013; 56(6): 682-5. Available at: https://journals.lww.com/jpgn/Fulltext/2013/06000/Cholesteryl_Ester_Storage_Disease__Protean.20.aspx . Accessed January 13, 2022.
3. Clinical Pharmacology [database online] powered by Clinical Key. Tampa, FL: Elsevier, 2020. Accessed with subscription at: http://www.clinicalkey.com . Accessed January 13, 2022.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	03/2020	02/07/2020
Policy was reviewed: 1. Policy title table was updated	06/28/2020	09/14/2020

2. Dosing information was updated 3. Clinical policy was updated: updated verbiage to “Currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy” in Continued Therapy Approval, Approval Duration was updated 4. Appendices were updated 5. References were updated		
Policy was reviewed: 1. Statement about provider sample, ‘‘The provision of provider samples does not guarantee coverage…” was added to Clinical Policy 2. References were reviewed and updated	03/01/2021	06/10/2021
Policy was reviewed: 1. Dosing Information, Dosing Regimen, Kanuma®: a. Updated dosing information from 1 mg/kg IV once weekly to Recommended dose:1 mg/kg intravenous once weekly, For patients with a suboptimal clinical response*, increase the dosage to 3 mg/kg once weekly, For patients with continued suboptimal clinical response on the 3 mg/kg once weekly dosage, further increase the dosage to 5 mg/kg once weekly for indication Infants with LAL deficiency: rapidly progressive disease presenting within first 6 months of life. b. Updated dosing information from 1 mg/kg IV every other week to Recommended dose: 1 mg/kg intravenous every other week, For patients with a suboptimal clinical response*, increase the dosage to 3 mg/kg once every other week for indication Pediatric and Adult Patients with LAL deficiency. 2. Dosing Information, Maximum Dose, Kanuma®: a. Updated to maximum dosing information from 3 mg/kg/week to 5 mg/kg/week for indication Infants with LAL deficiency: rapidly progressive	01/13/2022	04/18/2022

disease presenting within first 6 months of life. b. Updated to maximum dosing information from 1 mg/kg every other week to 3 mg/kg every other week for indication Pediatric and Adult Patients with LAL deficiency. 3. Initial Approval Criteria, I.A.3: Updated dosing criteria from Dose does not exceed 1 mg per kg every other week (1 mg per kg per week for members with rapidly progressive disease presenting within first 6 months of life; may be increased to 3 mg per kg per week upon documentation of suboptimal clinical response to 1 mg per kg per week) to Dose does not exceed (a or b) a. 5 mg per kg every other week for Infants with rapidly progressive LAL deficiency presenting within the first 6 months of life, For patients with a suboptimal clinical response, increase the dosage to 3 mg/kg once weekly. For patients with continued suboptimal clinical response on the 3 mg/kg once weekly dosage, further increase the dosage to 5 mg/kg once weekly. b. 3 mg per kg every other week for Pediatric and Adult Patients with LAL deficiency. For patients with a suboptimal clinical response, increase the dosage to 3 mg/kg once every other week. 4. Continued Therapy Approval Criteria II.A.3: Updated dosing criteria from If request is for a dose increase, new dose does not exceed 1 mg per kg every other week (1 mg per kg per week for members with rapidly progressive disease presenting within first 6 months of life; may be increased to 3 mg per kg per week upon documentation of suboptimal clinical response to 1 mg per kg per week) to If request is for a dose increase, new dose does not exceed (a or b): a. 5 mg per kg every other week for Infants with rapidly progressive LAL deficiency presenting within the first 6 months of life, For patients with a suboptimal clinical response, increase the dosage to		

3 mg/kg once weekly. For patients with continued suboptimal clinical response on the 3 mg/kg once weekly dosage, further increase the dosage to 5 mg/kg once weekly. b. 3 mg per kg every other week for Pediatric and Adult Patients with LAL deficiency. For patients with a suboptimal clinical response, increase the dosage to 3 mg/kg once every other week. 5. References were reviewed and updated.		