Sample Letter of Medical Necessity for KANUMA® (sebelipase alfa)

in Patients Who Have Lysosomal Acid Lipase Deficiency (LAL-D)

Payers may request a letter of medical necessity to support coverage of KANUMA. The letter should explain why the drug is medically necessary for the specific patient and may include supporting documentation (eg, medical records, peer-reviewed literature, Prescribing Information, clinical treatment history, etc). The letter may be submitted as part of a prior authorization (PA) request, with the claim form, or in response to a payer's request for additional documentation. The letter should include patient-specific information, be on your letterhead, be signed by the prescriber, and be submitted to a payer to support a PA request or claim for KANUMA.

This sample letter of medical necessity is provided for informational purposes only and is not based on legal advice or official guidance from payers. It is not intended to increase or maximize reimbursement by any payer. Alexion does not warrant, promise, guarantee, or make any statement that the use of this information will result in coverage or payment for KANUMA or that any payment received will cover providers' costs.

INDICATION

KANUMA® (sebelipase alfa) is indicated for the treatment of patients with a diagnosis of Lysosomal Acid Lipase (LAL) deficiency.

IMPORTANT SAFETY INFORMATION INCLUDING BOXED WARNING

WARNING: HYPERSENSITIVITY REACTIONS INCLUDING ANAPHYLAXIS

Patients treated with enzyme replacement therapies have experienced life-threatening hypersensitivity reactions, including anaphylaxis. Anaphylaxis has occurred during the early course of enzyme replacement therapy and after extended duration of therapy.

Initiate KANUMA in a healthcare setting with appropriate medical monitoring and support measures, including access to cardiopulmonary resuscitation equipment. If a severe hypersensitivity reaction (e.g., anaphylaxis) occurs, discontinue KANUMA and immediately initiate appropriate medical treatment, including use of epinephrine. Inform patients of the symptoms of life-threatening hypersensitivity reactions, including anaphylaxis and to seek immediate medical care should symptoms occur [see Warnings and Precautions (5.1)].

WARNINGS AND PRECAUTIONS

Hypersensitivity Reactions Including Anaphylaxis

Life-threatening hypersensitivity reactions, including anaphylaxis, have been reported in patients treated with enzyme replacement therapies, including KANUMA. These reactions in KANUMA-treated patients were based on application of Sampson criteria to identify signs/symptoms consistent with anaphylaxis. In clinical trials, 3 (infants) of 106 (3%) patients treated with KANUMA experienced signs and symptoms consistent with anaphylaxis. These patients experienced reactions during infusion with signs and symptoms including chest discomfort, conjunctival injection, dyspnea, generalized and itchy rash, hyperemia, swelling of eyelids, rhinorrhea, severe respiratory distress, tachycardia, tachypnea, and urticaria.

Please see Important Safety Information on pages 1 and 4 and full Prescribing Information for KANUMA (sebelipase alfa), including Boxed WARNING regarding hypersensitivity reactions including anaphylaxis.

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Kanuma® (sebelipase alfa) intravenous infusion 20mg/10mL

[John Doe, MD]
[Address]
[City, State ZIP]
[(888) 555-5555]

[Date]
[Contact Name], [Title] [Name of Health Insurance Plan or PBM]
[Address]
[City, State ZIP Code]

Letter of Medical Necessity for KANUMA® (sebelipase alfa)
[Request for Expedited Review Due to Medical Urgency]
Insured: [Name]; Policy Number: [Number]; Group Number: [Number]
Date(s) of service: [Date(s)]

Dear [Contact Name],

I am writing on behalf of my patient, [First Name] [Last Name], to request that [name of health insurance company] approve coverage and appropriate reimbursement associated with [Mr/Ms/Mrs/other title] [Last Name]'s treatment with KANUMA. KANUMA is indicated for the treatment of lysosomal acid lipase deficiency (LAL-D).

Patient Medical Overview
[First Name] [Last Name] is a[n] [age]-year-old [gender] born [MM/DD/YYYY] who requires treatment with KANUMA after being diagnosed with LAL-D on [date of diagnosis MM/DD/YYYY].

Medical History (Including Clinical Signs, Symptoms, and Laboratory Results) [see page 3 for reference]
[Provide relevant LAL-D clinical signs and symptoms and describe the severity of disease of your patient's current presentation and disease progression based on your medical opinion. Include specific clinical presentations, relevant patient-specific clinical scenarios demonstrating serious medical need].

In my medical opinion, KANUMA is the most appropriate treatment for [First Name] [Last Name]'s LAL-D based on the clinical efficacy and safety data.

Treatment Plan
[Select population and indicated dosage:

- In infants with rapidly progressive LAL-D presenting within the first 6 months of life, the recommended starting dosage is 1 mg/kg as an intravenous infusion once weekly. For patients with a suboptimal clinical response, increase the dosage to 3 mg/kg once weekly, and a further increase of the dosage to 5 mg/kg once weekly for patients with continued suboptimal clinical response

- In pediatric and adult patients with LAL-D, the recommended dosage is 1 mg/kg as an intravenous infusion once every other week. For patients with a suboptimal clinical response, the dose may be increased to 3 mg/kg once every other week]

Summary
Based on the above facts, I am confident you will agree that KANUMA is indicated and medically necessary for this patient. For your convenience, I am enclosing [list enclosures such as supporting clinical documentation, Prescribing Information, Food and Drug Administration (FDA) approval letter for KANUMA in LAL-D, copy of patient's insurance card, etc].

If you have any further questions, please feel free to call me at [physician's phone number] to discuss. Thank you in advance for your immediate attention to this request.

Sincerely,
[Physician's Name], MD
[Physician's Identification Number]
[Physician's Practice Name]
[Physician's Phone Number]
[Physician's Fax Number]
[Physician's Email]

Enclosures
[Supporting clinical documentation, Prescribing Information, FDA approval letter for KANUMA in LAL-D, copy of patient's insurance card, etc]

Medical History (Including Clinical Signs, Symptoms, and Laboratory Results)

Below are some clinical signs and symptoms for LAL-D. Please include any relevant documentation that is applicable to your patient's clinical presentation as well as applicable laboratory or test results.

- ☐ Confirmed diagnosis via **Lysosomal Acid Deficiency (LAL) enzyme assay** demonstrating deficiency in enzyme activity[1-3]
- ☐ **Chart notes and laboratory results** documenting clinical features and biochemical results (eg, alanine aminotransferase [ALT] level, aspartate aminotransferase [AST] level, total cholesterol, triglycerides, bilirubin direct/indirect results, hepatic biopsy, elastography findings, or magnetic resonance imaging and spectroscopy)[1-4]
- ☐ Previous experience, if any, with receiving KANUMA
- ☐ Previous **treatment history of related comorbidities**, including date and dosage (eg, statins, ezetimibe, proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors, nutritional support, and blood transfusions)[1-3]
- ☐ **History of complications leading to emergency room visits**, hospital admissions, and/or intensive care unit stays, including dates (eg, hepatomegaly, splenomegaly, stroke, myocardial infarction, liver transplant, hematopoietic stem cell transplant)[1-3]
- ☐ Diagnosis of **Wolman disease** at birth or **cholesteryl ester storage disease (CESD)** in infancy, childhood, or adulthood[1]
- ☐ **Clinical signs and symptoms** to help describe the patient's current clinical presentation. This list is not all inclusive of LAL-D clinical signs and symptoms.
  - o Hepatic: hepatomegaly, fibrosis, cirrhosis, liver failure[1-3]
  - o Cardiovascular: elevated low-density lipoprotein-cholesterol (LDL-C) and triglyceride levels, low high-density lipoprotein-cholesterol (HDL-C) levels[1,2]
  - o Splenic: splenomegaly[1-3]
  - o Gastrointestinal: abdominal pain, diarrhea, impaired nutrient absorption/malnutrition[1-3]
  - o Other: growth failure, anemia, thrombocytopenia, calcium deposits in the adrenal glands[1,3,4]

References: 1. Bernstein DL, et al. *J Hepatol*. 2013;58(6):1230-1243. **2.** Burton BK, et al. *J Pediatr Gastroenterol Nutr*. 2015;61(6):619-625. **3.** Jones S, et al. *Genet Med*. 2016;18(3):452-458. **4.** Kohli R, et al. *Mol Genet Metab*. 2020;129(2):59-66.

IMPORTANT SAFETY INFORMATION INCLUDING BOXED WARNING (cont.)

WARNINGS AND PRECAUTIONS (cont.)

Hypersensitivity Reactions Including Anaphylaxis (cont.)

In clinical trials, 21 of 106 (20%) KANUMA-treated patients, including 9 of 14 (64%) infants and 12 of 92 (13%) pediatric patients who were 4 years and older and adults, experienced signs and symptoms either consistent with or that may be related to a hypersensitivity reaction. Signs and symptoms of hypersensitivity reactions, occurring in two or more patients, included abdominal pain, agitation, fever, chills, diarrhea, eczema, edema, hypertension, irritability, laryngeal edema, nausea, pallor, pruritus, rash, and vomiting. Most reactions occurred during or within 4 hours of the completion of the infusion. Patients were not routinely pre-medicated prior to infusion of KANUMA in these clinical trials.

Administration of KANUMA should be supervised by a healthcare provider knowledgeable in the management of severe hypersensitivity reactions including anaphylaxis. Observe patients closely during and after the infusion.

The management of hypersensitivity reactions should be based on the severity of the reaction and may include temporarily interrupting the infusion, lowering the infusion rate, and/or treatment with antihistamines, antipyretics, and/or corticosteroids. If interrupted, the infusion may be resumed at a slower rate with increases as tolerated. Pre-treatment with antipyretics and/or antihistamines may prevent subsequent reactions in those cases where symptomatic treatment was required.

Consider the risks and benefits of re-administering KANUMA following a severe reaction. Monitor patients, with appropriate resuscitation measures available, if the decision is made to re-administer the product.

Hypersensitivity to Eggs or Egg Products

Patients with a known history of egg allergies were excluded from the clinical trials. Consider the risks and benefits of treatment with KANUMA in patients with known systemic hypersensitivity reactions to eggs or egg products.

ADVERSE REACTIONS

In clinical trials, the most common adverse reactions were:

- Infants with Rapidly Progressive LAL Deficiency Presenting within the First 6 Months of Life (≥30%): diarrhea, vomiting, fever, rhinitis, anemia, cough, nasopharyngitis, and urticaria.
- Pediatric and Adult Patients with LAL Deficiency (≥8%): headache, fever, oropharyngeal pain, nasopharyngitis, asthenia, constipation, and nausea.

To report SUSPECTED ADVERSE REACTIONS, contact Alexion Pharmaceuticals, Inc. at 1-844-259-6783 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch

Please see full Prescribing Information for KANUMA (sebelipase alfa), including Boxed WARNING regarding hypersensitivity reactions including anaphylaxis.

ALEXION®
AstraZeneca Rare Disease