KANUMA® ▼(sebelipase alfa)
2 mg/mL concentrate for solution for infusion

A GUIDE FOR HEALTHCARE PROFESSIONALS

Important Safety Information:

Please read this guide carefully and use it when prescribing sebelipase alfa as it contains essential safety and efficacy information.

The guide was created as part of the sebelipase alfa Risk Management Plan and includes risk-minimising measures for the safe and effective use of this medicinal product.

The guide is a mandatory part of the approval process for sebelipase alfa to help ensure that healthcare professionals take into account the special safety requirements of prescribing this medicinal product.

▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. For further information on the reporting of adverse reactions, see page 6.

Read the Summary of Product Characteristics (SmPC) carefully before you prescribe or administer sebelipase alfa.

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ALEXION®

INTRODUCTION

Sebelipase alfa is indicated for long-term enzyme replacement therapy (ERT) in patients of all ages with lysosomal acid lipase (LAL) deficiency.

Please read the Summary of Product Characteristics (SmPC) carefully before prescribing or administering sebelipase alfa. The complete and current text of this SmPC is available in the UK on **www.medicines.org.uk** and in Ireland on **www.medicines.ie** and **www.hpra.ie.**

LAL DEFICIENCY REGISTRY

To provide additional data on long-term safety of sebelipase alfa administration, healthcare professionals are strongly encouraged to participate in and enrol all patients diagnosed with LAL deficiency in the LAL deficiency registry. Please note that the registry is a general disease registry not restricted to patients treated with sebelipase alfa and aims to generate information on disease progression and treatment effects not restricted to exposure to sebelipase alfa. For information on how to participate, see page 6.

HYPERSENSITIVITY REACTIONS, INCLUDING ANAPHYLAXIS

In clinical studies of patients being treated with sebelipase alfa, hypersensitivity reactions occurred in 59 of 125 patients (47%) and anaphylactic reactions in 5 of 125 patients (4%). The frequency of the reactions decreased with an increased treatment period, but they were also observed one year after the start of treatment.

The signs and symptoms of the hypersensitivity/anaphylactic reactions included the following:

- Chest discomfort, dyspnea, tachypnea, severe respiratory distress
- Pruritus, rash, eczema, lip swelling, urticaria
- Bronchospasm, rhinorrhea, flushing
- Conjunctival hyperaemia, hyperaemia
- Stridor, hypoxia
- Facial oedema, oedema of the eyelid, laryngeal oedema, oedema
- Tachycardia, hypertension
- Pallor
- Abdominal pain, nausea, diarrhea, vomiting
- Agitation, irritability
- Pyrexia, chills
- Body temperature increased

The majority of these reactions occurred during or within 4 hours of the end of infusion.

PREVENTION AND TREATMENT OF HYPERSENSITIVITY REACTIONS, INCLUDING ANAPHYLAXIS

1. Ensure that **appropriate medical support,** including any required medicine, is readily available when sebelipase alfa is administered.

2. **Observe patients for 1 hour** in order to monitor for any signs or symptoms of anaphylaxis or a severe hypersensitivity reaction following the first sebelipase alfa infusion, including the first infusion after a dose escalation.

3. If, during administration of sebelipase alfa, signs of hypersensitivity occur, the infusion can be slowed or discontinued at the discretion of the healthcare professional.

4. **In case of anaphylaxis, the infusion must be stopped immediately!** Leave the cannula in place for the potential administration of drugs.

5. Initiate the **standard appropriate medical treatment** for the management of hypersensitivity reactions, this may include treatment with:

    - Antihistamines
    - Antipyretics
    - Corticosteroids

6. For patients who have experienced allergic reactions during infusion, **caution should be exercised upon re-administration.** Start with a lower infusion rate and increase until the tolerance limit of the patient is reached.

7. **After severe reactions the risks and benefits** of a further sebelipase alfa administration should be considered.

8. **Consider pre-treatment** with antipyretics and/or antihistamines to prevent subsequent reactions in those cases where symptomatic treatment was required.

Contact information for adverse event reporting is provided on page 6.

IMMUNOGENICITY

In pivotal clinical studies, anti-drug antibodies (ADA), have been observed in 15% (19/125) of patients receiving sebelipase alfa, at some timepoint after starting treatment. Of these, a total of 11 patients showed the presence of inhibitory antibody activity (NAbs) at some post-baseline time point.

- Collection of information on ADA to sebelipase alfa is important to evaluate the impact of development of ADA on a potential loss of effect or development of potential hypersensitivity, including anaphylaxis, and to support identification of ADA development related risk factors.

- Therefore patients should be tested for ADA to sebelipase alfa in the event of severe infusion reactions and in cases of lack or loss of effect. For patients who are positive for ADA, testing should be repeated every 6 months.

- To date, no conclusion on the relationship between development of ADAs/NAbs and associated hypersensitivity reactions or suboptimal clinical response can be made. In clinical studies, 3 patients homozygous for a deletion affecting both alleles of genes Lipase A, lysosomal acid [LIPA] and cholesterol 25-Hydroxylase developed inhibitory antibody activity associated with a suboptimal clinical response. These patients underwent either immunomodulatory therapy alone or in combination with hematopoietic stem cell transplant (HSCT) or bone marrow transplant (BMT) resulting in improved clinical response to sebelipase alfa.

Anti-drug Antibody Testing

Information on ADA testing is provided in section 4.4 of the SmPC as follows:

- It is recommended that healthcare professionals test their patients for ADA to sebelipase alfa in the event of severe infusion reactions and in cases of lack or loss of effect.

As there are no marketed tests for ADA to sebelipase alfa, the Marketing Authorisation Holder will provide testing free of charge through a central laboratory.

- An ADA testing kit and accompanying instruction manual will be provided by Alexion Pharma UK. Please see page 6 for contact information. The instruction manual contains information on how to collect, process, and ship ADA samples.

- Results will be provided to the healthcare provider via the central laboratory portal of the logistics provider.

- Anonymised ADA testing results will be shared with the Alexion Research and Development team. No patient identifying information will be shared throughout the process.

- In the event of a positive ADA testing result, testing should be repeated every 6 months.

CONTACT INFORMATION

Anti-drug Antibody (ADA) Testing

For information on ADA testing, contact the Alexion Pharma UK Medical Information team (details below).

Adverse Event Reporting

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions.

United Kingdom
Please report suspected adverse drug reactions (ADRs) to the MHRA through the Yellow Card scheme.

You can report via:
- the Yellow Card website www.mhra.gov.uk/yellowcard
- the free Yellow Card app available from the Apple App Store or Google Play Store
- some clinical IT systems (EMIS/SystmOne/Vision/MiDatabank) for healthcare professionals

Alternatively you can report a suspected side effect to the Yellow Card scheme by calling 0800 731 6789 for free, Monday to Friday between 9am and 5pm. You can leave a message outside of these hours. When reporting please provide as much information as possible. By reporting side effects, you can help provide more information on the safety of this medicine.

Ireland
HPRA Pharmacovigilance, www.hpra.ie.

Adverse events should also be reported to Alexion Pharma UK on uk.adverseevents@alexion.com or Freephone (UK): 0800 321 3902 and (Ireland) 1800 936 544.

LAL Deficiency Registry

For information on the LAL deficiency registry and how to participate, contact the Alexion Pharma UK Medical Information team (details below).

For further information please see the Summary of Product Characteristics at www.medicines.org.uk, www.medicines.ie and www.hpra.ie, or contact:

ALEXION PHARMA UK MEDICAL INFORMATION TEAM:

Email: medinfo.EMEA@alexion.com
Telephone: (UK): 0800 028 4394, (Ireland): 1800 882 840

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