Prescribing Information: Aldurazyme (laronidase) 100 U/ml concentrate for solution for infusion

Please refer to the Summary of Product Characteristics (SmPC) before prescribing.

Presentation: 1 ml contains 100 U (approximately 0.58 mg) of laronidase. Each vial of 5 ml contains 500 U of laronidase.

Indication: Aldurazyme is indicated for long-term enzyme replacement therapy in patients with a confirmed diagnosis of Mucopolysaccharidosis I (MPS I; α-L-iduronidase deficiency) to treat the non-neurological manifestations of the disease.

Dosage and administration: Aldurazyme treatment should be supervised by a physician experienced in the management of patients with MPS I or other inherited metabolic diseases. Administration of Aldurazyme should be carried out in an appropriate clinical setting where resuscitation equipment to manage medical emergencies would be readily available. The recommended dosage regimen of Aldurazyme is 100 U/kg bodyweight administered once every week as an intravenous (IV) infusion. The initial infusion rate of 2 U/kg/h may be incrementally increased every 15 minutes, if tolerated, to a maximum of 43 U/kg/h. The total volume of the administration should be delivered in approximately 3 – 4 hours. Home infusion: Infusion of Aldurazyme at home may be considered for patients who are tolerating their infusions well and have no history of moderate or severe infusion-associated reactions (IARs) for a few months. The decision to have a patient move to home infusion should be made after evaluation and upon recommendation by the treating physician. Home infusion should be supervised by a healthcare professional who should be always available during the home infusion and for a specified time after infusion. (Please refer to SmPC for full guidance).

Special populations: Paediatric population: No dose adjustment necessary. Elderly (≥65 years), renal and hepatic impairment: No data therefore no dosage can be recommended.

Contraindications: Severe hypersensitivity (e.g. anaphylactic reaction) to the active substance or to any of the excipients.

Warnings and Precautions: Hypersensitivity reactions (including anaphylaxis): Hypersensitivity reactions, including anaphylaxis have been reported in patients treated with Aldurazyme. Some of these reactions were life threatening and included respiratory failure/distress, stridor, obstructive airways disorder, hypoxia, hypotension, bradycardia, and urticaria. Appropriate medical support measures, including cardiopulmonary resuscitation equipment should be readily available when Aldurazyme is administered. If anaphylaxis or other severe hypersensitivity reactions occur, the infusion of Aldurazyme should be discontinued immediately Caution should be exercised if epinephrine is being considered for use in patients with MPS I due to the increased prevalence of coronary artery disease in these patients. In patients with severe hypersensitivity, desensitization procedure to Aldurazyme may be considered. If the decision is made to re-administer the product, extreme care should be exercised, with appropriate resuscitation measures available. If mild or moderate hypersensitivity reactions occur, the infusion rate may be slowed or temporarily stopped. Once a patient tolerates the infusion, the dose may be increased to reach the approved dose. Infusion-associated reactions (IARs): IARs**,** defined as any related adverse event occurring during the infusion or until the end of the infusion day, were reported in patients treated with Aldurazyme. Patients with an acute underlying illness at the time of Aldurazyme infusion appear to be at greater risk for IARs. Careful consideration should be given to the patient's clinical status prior to administration of Aldurazyme. With initial administration of Aldurazyme or upon re-administration following interruption of treatment, it is recommended that patients be administered pre-treatment medicines (antihistamines and/or antipyretics) approximately 60 minutes prior to the start of the infusion, to minimise the potential occurrence of IARs. If clinically indicated, administration of pre-treatment medications with subsequent infusions of Aldurazyme should be considered. As there is little experience on resumption of treatment following prolonged interruption, use caution due to the theoretical increased risk of hypersensitivity reaction after treatment interruption. Severe IARs have been reported in patients with pre-existent severe underlying upper airway involvement and therefore specifically these patients should continue to be closely monitored and only be infused with Aldurazyme in an appropriate clinical setting where resuscitation equipment to manage medical emergencies would be readily available. In case of a single severe IAR, the infusion should be stopped until the symptoms are resolved and symptomatic treatment (e.g. with antihistamines and antipyretics/anti-inflammatories) should be considered. The benefits and risk of re-administering Aldurazyme following severe IARs should be considered. The infusion can be restarted with a reduction of the infusion rate to 1/2 – 1/4 the rate of the infusion at which the reaction occurred. In case of a recurrent moderate IAR or re-challenge after a single severe IAR, pre-treatment should be considered (antihistamines and antipyretics/anti-inflammatories and/or corticosteroids) and a reduction of the infusion rate to 1/2 – 1/4 the rate of the infusion at which the previous reaction occurred. In case of a mild or moderate IAR symptomatic treatment (e.g. with antihistamines and antipyretics/anti-inflammatories) should be considered and/or a reduction in the infusion rate to half the infusion rate at which the reaction occurred. Once a patient tolerates the infusion, the dose may be increased to reach the approved dose. Immunogenicity: Based on the randomized, double-blind, placebo-controlled Phase 3 clinical trial, almost all patients are expected to develop IgG antibodies to laronidase, mostly within 3 months of initiation of treatment. As with any IV protein medicinal product, severe allergic-type hypersensitivity reactions are possible. IARs and hypersensitivity reactions may occur independently of the development of anti-drug antibodies (ADAs). Patients who have developed antibodies or symptoms of IARs should be treated with caution when administering Aldurazyme. Patients treated with Aldurazyme should be closely monitored and all cases of IARs, delayed reactions and possible immunological reactions reported. Antibody status, including IgG, IgE, neutralizing antibodies for enzyme activity or enzyme reuptake, should be regularly monitored and reported. In clinical studies IARs were usually manageable by slowing the rate of infusion and by (pre-) treating the patient with antihistamines and/or antipyretics (paracetamol or ibuprofen), thus enabling the patient to continue treatment. In patients with clinical decline, assessing urinary GAGs, ADA and neutralising antibodies should be considered. Excipients of known effect This medicinal product contains 30 mg sodium per vial, equivalent to 1.5% of the WHO recommended maximum daily intake of 2 g sodium for an adult and is administered in 0.9% sodium chloride IV solution.

Interactions: No interaction studies have been performed. Aldurazyme is an unlikely candidate for cytochrome P450 mediated interactions. Aldurazyme should not be administered

simultaneously with chloroquine or procaine due to a potential risk of interference with the intracellular uptake of Aldurazyme.
Fertility, pregnancy and lactation: There are inadequate data on the use of Aldurazyme in pregnant women, thus the potential risk for humans is unknown. Aldurazyme should not be used in pregnancy unless clearly necessary. Aldurazyme may be excreted in milk. It is recommended to stop breast-feeding during Aldurazyme treatment.
Adverse Reactions: Very common: *Adults and paediatric patients ≥5 years:* Headache, flushing, nausea, abdominal pain, rash, arthropathy, arthralgia, back pain, pain in the extremity, pyrexia, infusion site reactions (during clinical trials and post-marketing experience, infusion/injection site reactions notably included: swelling, erythema, oedema, discomfort, urticaria, pallor, macule, and warmth*). Paediatric population <5 years:* Tachycardia, pyrexia, chills, blood pressure increased, oxygen saturation decreased. Common: *Adults and paediatric patients ≥5 years:* Anaphylactic reaction, restlessness, paraesthesia, dizziness, tachycardia, hypotension, pallor, peripheral coldness, respiratory distress, dyspnoea, cough, vomiting, diarrhoea, angioedema, swelling face, urticaria, pruritis, cold sweat, alopecia, hyperhidrosis, musculoskeletal pain, chills, feeling cold, feeling hot, fatigue, influenza-like illness, injection site pain, body temperature increased, oxygen saturation decreased. Other Serious Adverse Drug Reactions (frequency not known): Hypersensitivity (including bradycardia, hypoxia, respiratory failure, stridor, obstructive airways disorder – this list is not exhaustive, see the SmPC for more details), drug specific antibody, neutralising antibodies. *Prescribers should consult the SmPC in relation to other adverse reactions.*
Legal category: POM.
List Price: £444.70 for 1 vial**.**
Marketing authorisation number: PLGB 04425/0760
Marketing authorisation holder: Sanofi, 410 Thames Valley Park Drive, Reading, Berkshire, RG6 1PT, UK.
Further information available from: Sanofi, 410 Thames Valley Park Drive, Reading, Berkshire, RG6 1PT, UK. uk-medicalinformation@sanofi.com.
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Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

Adverse events should also be reported to the Sanofi drug safety department on Tel: 0800 0902 314. Alternatively, send via email to UK-drugsafety@sanofi.com