NEW ZEALAND DATA SHEET – ALDURAZYME® (LARONIDASE-RCH CONCENTRATE FOR SOLUTION FOR INFUSION)

1 NAME OF THE MEDICINE

Laronidase -rch

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

The extractable volume of 5.0 mL from each vial provides 2.9 mg (500 U) laronidase, 43.9 mg sodium chloride, 63.5 mg monobasic sodium phosphate monohydrate, 10.7 mg dibasic sodium phosphate heptahydrate, and 0.05 mg polysorbate 80. Aldurazyme does not contain preservatives; vials are for single use only. See section 6.1 LIST OF EXCIPIENTS.

3 PHARMACEUTICAL FORM

Aldurazyme is intended for intravenous infusion. It is supplied as a sterile, nonpyrogenic, colourless to pale yellow, clear to slightly opalescent solution that must be diluted prior to administration.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

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

4.2 DOSE AND METHOD OF 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 clinical emergencies would be readily available.

The recommended dosage regimen of Aldurazyme is 100 U/kg (0.58 mg/kg) of actual body weight administered once weekly as an intravenous infusion.

Pretreatment with antipyretics and/or antihistamines is recommended 60 minutes prior to the start of the infusion. In the Phase 3 studies, all patients were pretreated prior to each infusion with age-appropriate dosages of antihistamines and antipyretics, such as diphenhydramine or hydroxyzine and paracetamol or ibuprofen, respectively (see section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE, General).

The total volume of the infusion is determined by the patient's actual body weight and should be delivered over approximately 3 to 4 hours. Patients with an actual body weight of 20 kg or less should receive a total volume of 100 mL. Patients with an actual body weight of greater than 20 kg should receive a total volume of 250 mL. The initial infusion rate of 2 U/kg/hr (equivalent to 2 mL/hr in patients with an actual body weight of 20 kg or less or 5 mL/hr in patients with an actual body weight of greater than 20 kg) may be incrementally increased (doubled) every 15 minutes during the first hour, as tolerated, until a maximum infusion rate of 43 U/kg/hr is reached. The maximum rate is then maintained for the remainder of the infusion (2-3 hours).

Each vial of Aldurazyme contains 500 U (100 U/mL; 0.58 mg/mL) of laronidase and is intended for single use only. The concentrate for solution for infusion must be diluted with 0.9% Sodium Chloride for Injection, using aseptic techniques. In the absence of stability studies using glass containers, it is recommended that Aldurazyme be prepared and administered using PVC containers. It is recommended that the Aldurazyme solution be administered with a PVC infusion set equipped with an in-line, low protein-binding 0.2 micrometre (μm) filter.

Studies in patients with hepatic or renal insufficiency have not been performed.

Instructions for reconstitution and use (Aseptic Techniques)

The Aldurazyme solution should not be shaken, as this may cause a decrease in the potency of the product.

1. Prepare an infusion bag of 0.9% Sodium Chloride for Injection. Determine the total volume of the infusion to be used based on the patient's body weight. The total final volume should be either 100 mL (if weight is less than or equal to 20 kg) or 250 mL (if weight is greater than 20 kg).

2. Determine the number of vials to be diluted based on the individual patient's weight and the recommended dose of 100 U/kg. (Patient's weight (kg) x 1 mL/kg Aldurazyme = number mL of Aldurazyme). Remove the required number of vials from the refrigerator to allow them to reach room temperature. Do not heat or microwave vials.

3. Before dilution, visually inspect each vial for particulate matter and discolouration. The Aldurazyme solution should be clear to slightly opalescent and colourless to pale yellow. A few translucent particles may be present. Do not use if the solution is discoloured.

4. Withdraw and discard a volume of the 0.9% Sodium Chloride for Injection from the infusion bag, equal to the volume of Aldurazyme concentrate to be added.

5. Slowly withdraw the calculated volume of Aldurazyme (laronidase) from the appropriate number of vials, using caution to avoid excessive agitation.

6. Slowly add the Aldurazyme solution to the 0.9% Sodium Chloride for Injection, using care to avoid agitation of the solutions.

7. Gently rotate the infusion bag to ensure proper distribution of Aldurazyme. Prior to use, visually inspect the solution for particulate matter. Only clear and colourless solutions, practically free of visible particles, should be used. Do not shake the solution.

8. It is recommended that the diluted solution be filtered through an in-line low protein-binding 0.2μm filter during administration.

Aldurazyme does not contain any preservatives, therefore, after dilution with saline in the infusion bags, any unused product or waste material should be disposed of in accordance with local requirements.

Aldurazyme must not be mixed with other medicinal products in the same infusion.

4.3 CONTRAINDICATIONS

Aldurazyme is contraindicated in patients with known, severe, life-threatening hypersensitivity (anaphylactic reaction) to laronidase or any of the components of the formulation.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Hypersensitivity Reactions/Risk of Anaphylaxis

Life-threatening anaphylactic reactions have been observed in some patients during Aldurazyme infusions. Therefore, appropriate medical support should be readily available when Aldurazyme is administered. Patients with compromised respiratory function or acute respiratory disease may be at risk of serious acute exacerbation of their respiratory compromise due to infusion reactions, and require additional monitoring.

Patients treated with Aldurazyme may develop infusion-associated hypersensitivity reactions (including anaphylaxis). Some of these reactions were life-threatening and included respiratory failure, respiratory distress, stridor, tachypnea, bronchospasm, obstructive airways disorder, hypoxia, hypotension, bradycardia, and urticaria.

If severe allergic or anaphylactic reactions occur, immediate discontinuation of the administration of Aldurazyme should be considered and an appropriate treatment initiated (see section 4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)). The risks and benefits of re-administering Aldurazyme following a severe hypersensitivity or anaphylactic reaction should be considered. Extreme care should be exercised, with appropriate resuscitation measures available, if the decision is made to re-administer the product.

Caution should be used if considering the administration of adrenaline to MPS I patients due to the increased prevalence of coronary artery disease in these patients.

General

Patients with an acute illness at the time of Aldurazyme infusion appear to be at greater risk for infusion-related reactions. Careful consideration should be given to the patient's clinical status prior to administration of Aldurazyme. One patient with acute bronchitis and hypoxia experienced increased tachypnoea during the first Aldurazyme infusion that resolved without intervention. The patient's respiratory symptoms returned within 30 minutes of completing the infusion and responded to bronchodilator therapy. Approximately 6 hours after the infusion, the patient experienced coughing, then respiratory arrest and died.

The diagnosis, assessment and management of MPS I should only be undertaken by physicians with experience and training in the treatment of inherited diseases of metabolism. Aldurazyme

therapy should be initiated by a physician with experience in the management of patients with MPS I.

As with any intravenously administered protein product, patients may develop reactions associated with the administration of the protein (infusion-associated reactions, IARs) (see section 4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)). These patients should be treated with caution when re-administering Aldurazyme. In the Phase 3 clinical studies with Aldurazyme, most IARs were successfully treated by slowing the rate of infusion and by administering antihistamines and antipyretics, thus enabling the continuation of treatment (see section 4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS) and section 4.2 DOSE AND METHOD OF ADMINISTRATION).

Immunogenicity

During the clinical studies, almost all patients treated with Aldurazyme developed IgG antibodies to Aldurazyme, which tended to decrease over time. The presence of high IgG levels has been associated with variable urinary GAG reduction. The clinical significance of antibodies to Aldurazyme and of their potential for in-vitro neutralisation is not known.

Overall, a small number of patients have tested positive for IgE, 1 of whom experienced a severe anaphylactic reaction with urticaria and airway obstruction. These IgE-positive patients discontinued Aldurazyme treatment. Testing for IgE antibodies was rarely indicated during the clinical studies and its significance has not been established.

In the Phase 3 double-blind study and the open-label extension study, almost all of the patients developed Aldurazyme-specific IgG antibodies; thus, seroconversion is expected to occur in the majority of patients treated with Aldurazyme. In the Phase 3 double-blind study, the safety profiles for Aldurazyme and placebo were similar. In the open-label extension study, 2 of the patients who received a total of 50 weeks of Aldurazyme treatment no longer had detectable IgG antibodies to Aldurazyme. Patients who have developed antibodies or symptoms of IARs should be treated with caution when administering Aldurazyme.

It is suggested that patients be monitored as clinically indicated for Aldurazyme-specific IgG antibody formation.

Use in the Elderly

Clinical studies of Aldurazyme did not include patients aged 65 and over to determine whether they respond differently from younger patients. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

Paediatric Use

Safety and effectiveness of Aldurazyme in paediatric patients from ages 5 to 16 have been studied in the 3 clinical studies. Safety and effectiveness in patients below the age of 5 have not been established.

Effect on Laboratory Tests

No effects on laboratory tests have been identified.

4.5 INTERACTIONS WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTIONS

No drug interaction studies have been conducted. Based on its metabolism, laronidase is an unlikely candidate for cytochrome P450-mediated drug-drug interactions. Interaction studies with food and drinks have not been performed; interactions are unlikely given the mechanism of action and the IV route of administration.

Aldurazyme should not be administered simultaneously with chloroquine or procaine due to a theoretical risk of interference with the intracellular uptake of laronidase.

Aldurazyme must not be mixed with other medicinal products in the same infusion.

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on fertility

There are no clinical data on the effects of laronidase on fertility.

Reproductive studies showed no impairment of mating or fertility after rats received daily IV doses of 0, 0.036, 0.36 or 3.6 mg/kg/day Aldurazyme from 28 days before cohabitation until

sacrifice after 7 days of cohabitation (males) or from 15 days before cohabitation until gestation Day 7 (females; sacrificed at gestation Day 21.) There were no treatment-related effects on sperm parameters, litter parameters, or foetal gross external development at exposure levels equivalent to ca. 9 times the proposed human weekly dose on a body surface area basis.

Use in pregnancy – Pregnancy Category B2

Studies in rats at IV doses of 1.3 times the proposed human doses on a body surface area basis (9.3 times when calculated on a weekly basis), did not indicate direct or indirect harmful effects on embryofoetal development. However, there are no data for the use of Aldurazyme in pregnant women and Aldurazyme should not be used during pregnancy unless clearly necessary.

Use in lactation

It is not known whether the drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Aldurazyme is administered to a nursing woman.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

No studies on the effects on the ability to drive and use machines have been performed.

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

The most serious adverse reactions reported with Aldurazyme during clinical trials and the postmarketing period were anaphylactic and allergic reactions (see section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE, Hypersensitivity Reactions/Risk of Anaphylaxis). In the clinical studies, one patient developed a severe anaphylactic reaction approximately 3 hours after the initiation of the infusion (at Week 62 of treatment) which consisted of urticaria and airway obstruction. Resuscitation required emergency tracheostomy. The patient's pre-existing upper airway obstruction may have contributed to the severity of the reaction. In addition, a 3 year-old, severely affected patient who was treated in the post-marketing setting experienced an anaphylactic reaction and respiratory arrest during an Aldurazyme infusion requiring ventilatory support, adrenaline and corticosteroids. Both patients subsequently discontinued Aldurazyme treatment.

The most common adverse reactions associated with Aldurazyme treatment in the clinical studies were upper respiratory tract infection, rash, and injection site reaction.

The most common adverse reactions requiring intervention were infusion-related reactions, particularly flushing. Most infusion-related reactions requiring intervention were ameliorated with slowing of the infusion rate, temporarily stopping the infusion, and/or administering additional antipyretics and/or antihistamines.

Overall infusion site reactions with laronidase administration are very common. During clinical trials and post-marketing experience, infusion/injection site reactions included: extravasation, swelling, pain, erythema, edema, discomfort, urticaria, pallor, macule, and warmth.

The data described below reflect exposure to 100 U/kg (0.58 mg/kg) of Aldurazyme for 26 weeks in a placebo-controlled, double-blind study in 45 patients with MPS I (n=22 Aldurazyme, and n=23 placebo). All 45 patients continued into an open-label study of Aldurazyme treatment for an additional 36 weeks. An additional 10 patients participated in a Phase 1 open-label study with continued infusions for up to 3 years. The population in the placebo-controlled study was evenly distributed for gender (n=23 females and n=22 males) and ranged in ages from 6 to 43 years. Of the 45 patients in the placebo-controlled study, 1 was clinically assessed as having Hurler form, 37 Hurler-Scheie, and 7 Scheie. All patients were treated with antipyretics and antihistamines prior to the infusions.

Because clinical trials are conducted under widely varying and controlled conditions, the observed adverse reaction rates may not predict the rates observed in patients in clinical practice.

Table 1 enumerates adverse events and selected laboratory abnormalities that occurred during the placebo-controlled trial in at least 2 patients more in the Aldurazyme group than was observed in the placebo group. Reported adverse events have been classified using standard WHOART terms. Observed adverse events in the Phase 1 study and the open-label treatment period following the controlled study were not different in nature or severity.

Table 1 - Number and (%) of Patients with Adverse Events and Selected Laboratory Abnormalities in the Placebo-Controlled Study

Adverse Event	Placebo (n = 23)	Aldurazyme ® (n = 22)
Respiratory System		
Upper respiratory tract infection	4 (17)	7 (32)
Body as a Whole		
Chest pain	0	2 (9)
Nervous System		
Hyperreflexia	0	3 (14)
Paresthesia	1 (4)	3 (14)
Skin and Appendages		
Rash	5 (22)	8 (36)
Resistance Mechanism		
Abscess	0	2 (9)
Liver and Biliary System		
Bilirubinaemia	0	2 (9)
Vascular		
Vein disorder	1 (4)	3 (14)
Urinary System		
Facial oedema	0	2 (9)
Cardiovascular, General		
Hypotension	0	2 (9)
Dependent oedema	0	2 (9)
Vision		
Corneal opacity	0	2 (9)
Application Site		
Injection site pain	0	2 (9)
Injection site reaction	2 (9)	4 (18)
Platelet, Bleeding and Clotting		
Thrombocytopenia	0	2 (9)

In the post-marketing experience, the most frequently reported adverse reactions (using MedDRA terminology) included chills, vomiting, nausea, arthralgia, diarrhoea, tachycardia, abdominal pain, blood pressure increase and oxygen saturation decrease. Additional significant adverse drug reactions included serious reports of infusion-related bronchospasm that required treatment adrenaline, corticosteroids and/or oxygen therapy. Some of these patients were successfully re-challenged with Aldurazyme.

Infusion-Associated Reactions

In a clinical study, infusion-associated reactions (IARs) were reported in 7 of 22 patients treated with Aldurazyme. IARs were not significantly different between the Aldurazyme treatment group and the placebo group who received infusions of diluent and all components of

Aldurazyme except the laronidase enzyme. The most common IARs included flushing, fever, headache and rash. Flushing occurred in 5 patients (23%) receiving Aldurazyme; other reactions were less frequent. There was one case of anaphylaxis during the open-label extension setting and one additional case received for a patient treated in the post-marketing setting. Less common IARs include cough, bronchospasm, dyspnoea, urticaria, angioedema and pruritus.

All reactions were mild to moderate in severity. The frequency of IARs decreased with continued use during the open-label extension use.

Post Marketing Experience

In addition to the infusion reactions reported in clinical trials, the following infusion reactions have been reported in patients during post-marketing use of Aldurazyme: cough, dyspnoea, oxygen saturation decreased/hypoxia, tachypnoea, cyanosis, respiratory failure, drug specific antibody, neutralising antibodies, hypersensitivity, bradycardia and manifestations of angioedema such as facial oedema and laryngeal oedema. Additional significant adverse drug reactions (ADRs) have included serious reports of infusion-associated bronchospasm that required treatment with adrenaline, corticosteroids and/or oxygen therapy. Some patients were successfully re-challenged.

Other infusion reactions reported patients during post marketing experience include: pallor, fatigue, erythema, oedema peripheral, paresthesia, feeling hot, and feeling cold.

There have been a small number of reports of extravasation in patients treated with Aldurazyme. There have been no reports of tissue necrosis associated with extravasation.

Reporting suspected adverse effects

Reporting suspected adverse reactions after registration 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 at https://nzphvc.otago.ac.nz/reporting/.

4.9 OVERDOSE

Inappropriate administration of laronidase (overdose and/or infusion rate higher than recommended) may be associated with adverse drug reactions. An excessively fast administration of laronidase may result in nausea, abdominal pain, headache, dizziness and dyspnea.

If signs or symptoms occur associated with overdose or an infusion rate higher than recommended, the infusion must be stopped immediately. If medically appropriate, further intervention may be indicated.

For information on the management of overdose, contact the New Zealand National Poisons Information Centre (telephone 0800 POISON or 0800 764 766).

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Mechanism of Action

Mucopolysaccharide storage disorders are caused by the deficiency of specific lysosomal enzymes required for the catabolism of glycosaminoglycans (GAGs). Mucopolysaccharidosis I (MPS I) is characterised by the deficiency of α-l-iduronidase, a lysosomal hydrolase which catalyses the hydrolysis of terminal α-l-iduronic acid residues of dermatan sulfate and heparan sulfate. Reduced or absent α-l-iduronidase activity results in the accumulation of the GAG substrates, dermatan sulfate and heparan sulfate, throughout the body and leads to widespread cellular, tissue, and organ dysfunction.

The rationale for enzyme replacement therapy is to restore a level of enzymatic activity sufficient to hydrolyse the accumulated substrate and to prevent further accumulation. After intravenous infusion, laronidase is rapidly removed from the circulation and taken up by cells into lysosomes, most likely by the mannose-6 phosphate receptors.

Clinical trials

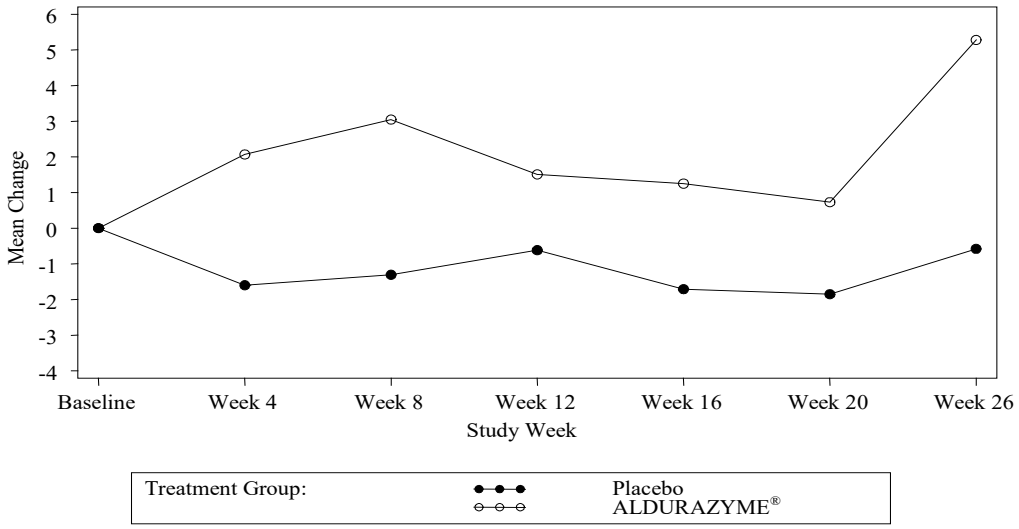
Three clinical studies have assessed the somatic manifestations of MPS I during treatment with Aldurazyme. No clinical data exist demonstrating a benefit on the neurological manifestations of the disorder.

The safety and efficacy of Aldurazyme were assessed in a randomised, double-blind, placebo-controlled, multicentre Phase 3 study of 45 MPS I patients. Patients received either 100 U/kg (0.58 mg/kg) of Aldurazyme or placebo once weekly for a total of 26 consecutive weeks. All patients were pretreated with antipyretics and antihistamines.

The 2 primary efficacy variables were forced vital capacity (FVC) and the 6-minute walk test (6MWT). After 26 weeks of treatment, Aldurazyme-treated patients showed a significant improvement in lung function as measured by the change in percent of predicted normal FVC (mean difference from placebo 5.9 percentage points; median difference from placebo 3.0 percentage points, p=0.016). Patients who received Aldurazyme (n=22) improved from a mean of 48.4 to 53.7 percent of predicted normal FVC, whereas patients receiving placebo (n=23) declined from a mean of 54.2 to 53.6 percent of predicted normal FVC (Figure 1). In Aldurazyme-treated patients there was an improvement in walking ability, as measured by the distance traveled in the 6MWT (mean difference from placebo 38.1 metres; median difference from placebo 38.5 metres, p=0.066). Patients who received Aldurazyme (n=22) improved from a mean of 319.1 to 338.8 metres, whereas patients receiving placebo (n=23) showed a mean decline from 366.7 to 348.3 metres (Figure 2).

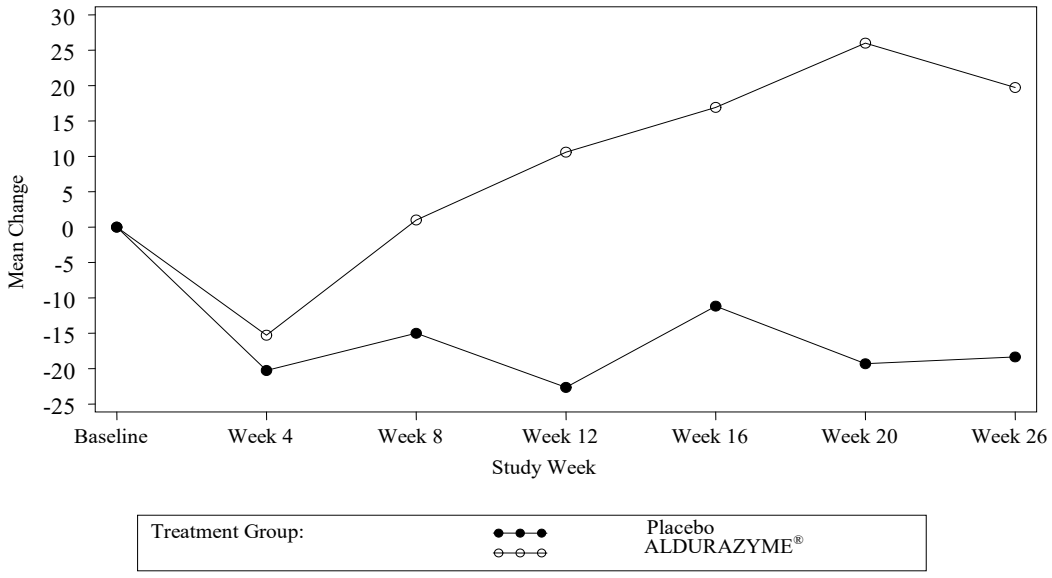
In addition, a significant reduction in liver size, as measured by MRI, was observed when compared to placebo (p=0.001). Normalisation of liver volume occurred in 72% of the Aldurazyme-treated patients who had hepatomegaly at baseline. Urinary GAG excretion showed a rapid decline in Aldurazyme-treated patients that was maintained through the remainder of the study (p<0.001). No significant improvement was captured in the course of the study with the quality of life instruments used. These instruments were not specifically adapted for patients with MPS I. Apnoea-Hypopnoea Index and joint range of motion did not show statistically significant improvement in the intent-to-treat population. However, the study was not powered for these secondary variables and many patients had normal values at baseline.

Figure 1 - Mean Change from Baseline to Week 26 in Percent of Predicted Normal FVC by Study Visit (ITT Population)



Note: The percent of predicted normal FVC was calculated using baseline standing height.

Figure 2 - Mean Change in Distance Walked in 6 Minutes at Each Study Visit (ITT Population)



All 45 patients who participated in the Phase 3 Double-Blind Study were enrolled in an Open-Label Extension Study. For patients previously treated with Aldurazyme, after an additional 24 weeks of treatment, the mean increase from baseline in distance walked during the 6MWT was 42.9 metres (an additional 23.2 metres from start of the Phase 3 Open-Label Extension Study). Improvements seen in percent of predicted FVC and GAG excretion during the Phase 3 Double-Blind Study were maintained. Reductions in liver size continued to be observed through Week 24 of the Open-Label Extension Study and normalisation of liver volume occurred in 80% of the patients who had hepatomegaly at baseline.

For patients previously treated with placebo, after 24 weeks of Aldurazyme treatment, the increase in the mean distance walked during the 6MWT (23.8 m), and the improvements seen in GAG excretion were similar to those noted in the Aldurazyme group in the Phase 3 Double-Blind Study. Reductions in liver size were observed after 24 weeks of treatment and normalisation of liver volume occurred in 50% of the patients who had hepatomegaly at entry into the Open-Label Extension Study. The change in percent of predicted FVC was not significant after 24 weeks of treatment.

In a Phase 1/2 Open-Label Study, 10 MPS I patients received 100 U/kg of Aldurazyme every week for up to 1 year. Subsequently, through a continuation of the study, patients received treatment for up to 3 years. The primary endpoints for this study were reductions in hepatosplenomegaly and urinary GAG excretion. After 1 year of treatment with Aldurazyme, the mean reductions in liver and spleen size were 26% and 21%, respectively, resulting in the normalisation of liver size in 9 of 10 patients. The mean reductions in liver and spleen size were maintained over the additional year of follow-up treatment. Urinary GAG excretion showed a mean decrease of 63% after 1 year, which decreased further with continued treatment; there was a 74% reduction at Week 104 and a 79% reduction at Week 152.

5.2 PHARMACOKINETIC PROPERTIES

Pharmacokinetics of laronidase were evaluated in 12 MPS I patients following the 1st, 12th and 26th infusions. After intravenous administration of laronidase with a mean infusion time of 4 hours and at a dose of 100 U/kg (0.58 mg/kg) body weight, once weekly, the mean maximum plasma concentrations (Cmax) ranged from 0.20 to 0.30 U/mL for the 3 time points. The mean area under the plasma concentration-time curve (AUC∞) ranged from 0.93 to 1.19 h•U/mL. The mean volume of distribution (Vz) ranged from 0.24 to 0.60 L/kg, and the mean volume of distribution at steady state (Vss) ranged from 0.22 to 0.44 L/kg. Mean plasma clearance (CL) ranged from 1.7 to 2.3 mL/min/kg, and the mean elimination half-life (t1/2) ranged from 1.94 to 3.61 hours. Cmax showed an increase over time. The volume of distribution decreased with continued treatment, possibly related to antibody formation and/or decreased liver volume.

Laronidase is a protein and is expected to be metabolically degraded through peptide hydrolysis. Consequently, impaired liver function is not expected to affect the pharmacokinetics of laronidase in a clinically significant way. Renal elimination of laronidase is considered to be a minor pathway for clearance.

5.3 PRECLINICAL SAFETY DATA

Genotoxicity

No data is available.

Carcinogenicity

Studies to assess the mutagenic and carcinogenic potential of laronidase have not been conducted.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Sodium chloride 43.9 mg

Monobasic sodium phosphate monohydrate 63.5 mg

Dibasic sodium phosphate heptahydrate 10.7 mg

Polysorbate 80; 0.05 mg

6.2 INCOMPATIBILITIES

Aldurazyme must not be mixed with other medicinal products in the same infusion except those mentioned in section 4.2 DOSE AND METHOD OF ADMINISTRATION.

6.3 SHELF LIFE

The expiry date can be found on the packaging.

From a microbiological point of view, the diluted solution should be used immediately. If not used immediately, in-use storage and conditions prior to use are the responsibility of the user and should not be longer than 24 hours when refrigerated (2°C to 8°C).

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store Aldurazyme under refrigeration at 2°C to 8°C. DO NOT FREEZE OR SHAKE. Protect from light. DO NOT USE Aldurazyme after the expiration date on the vial. This product contains no antimicrobial agent. Product is for single use in one patient only. Discard any residue.

6.5 NATURE AND CONTENTS OF CONTAINER

Aldurazyme is supplied in a sterile solution in clear Type I glass 5 mL vials. The closure consists of a siliconised butyl stopper and an aluminium seal with a plastic flip-off cap.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

Any unused medicine or waste material should be disposed of by taking to your local pharmacy.

Aldurazyme does not contain any preservatives, therefore, after dilution with saline in the infusion bags, any unused product or waste material should be disposed of in accordance with local requirements.

6.7 PHYSICOCHEMICAL PROPERTIES

Aldurazyme is produced by recombinant DNA technology and is a replacement therapy for the human enzyme, α-L-iduronidase. Purified laronidase is a glycoprotein with a molecular weight of approximately 83 kD. The predicted amino acid sequence of the recombinant form, as well as the nucleotide sequence that encodes it, are identical to human α-l-iduronidase. The recombinant protein is comprised of 628 amino acids after cleavage of the N-terminus and contains 6 N-linked oligosaccharide modification sites. Laronidase is produced by a genetically engineered Chinese hamster ovary cell line. The protein is purified by a column chromatography process that includes steps to inactivate and remove potential viruses, resulting in a highly purified, active protein.

The Aldurazyme solution has a nominal laronidase concentration of 100 U/mL (0.58 mg/mL) and a pH of approximately 5.5.

CAS Number

210589-09-6

7 MEDICINE SCHEDULE (POISONS STANDARD)

S4, Prescription only medicine

8 SPONSOR

Pharmacy Retailing (NZ) Ltd t/a Healthcare Logistics
PO Box 62027
Sylvia Park Auckland 1644
Freecall: 0800 283 684
Email: medinfo.australia@sanofi.com

9 DATE OF FIRST APPROVAL

21 December 2017

10 DATE OF REVISION

15 February 2023

SUMMARY TABLE OF CHANGES

Section Changed	Summary of new information
All	Minor editorial changes throughout
4.4	Addition of infusion-associated hypersensitivity reactions
4.6	Inclusion of statement saying there are no clinical data on the effects of laronidase on fertility.
4.8	Addition of ADRs on hypersensitivity reactions and infusion associated reactions
4.9	Addition of overdose information, including signs, symptoms and management

Aldurazyme® is a registered trademark of BioMarin/Genzyme LLC.