NEW ZEALAND DATA SHEET

1 PRODUCT NAME

Zemaira® 1000 mg, powder and diluent for solution for infusion.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Active substance:

Zemaira® is a highly purified, pasteurised, nanofiltered, lyophilised, stable human plasma alpha1-proteinase inhibitor (A_1-PI) concentrate.

One vial contains approximately 1000 mg of A_1-PI, as determined by its capacity to neutralise human neutrophil elastase (NE). Zemaira® is produced from the plasma of human donors.

The specific activity of Zemaira® is ≥0.7 mg of functional A_1-PI per milligram of total protein. The purity is ≥90% A_1-PI.

The total protein content is approximately 1100 mg per vial.

After reconstitution with 20 mL of diluent (Sterile Water for Injection [WFI]), the solution contains approximately 50 mg/mL of A_1-PI.

Excipients with known effect:

Zemaira® contains approximately 37 mg of sodium per vial.

Zemaira® contains no preservatives.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Powder and diluent for solution for infusion.

The powder is white to off-white. The diluent is a clear and colourless solution.

The reconstituted solution has an approximate osmolality of 223–335 mOsm/kg and a pH of 7.0.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Zemaira® is indicated for maintenance treatment, to slow the progression of emphysema in adults with documented severe A_1-PI deficiency (A_1-PI <11 µM) and progressive lung disease. Patients are to be under optimal pharmacologic and non-pharmacologic treatment.

4.2 Dose and method of administration

Treatment should be initiated and supervised by a healthcare professional experienced in the use of A_1-PI or in the treatment of A_1-PI deficiency.

Zemaira® is administered intravenously by a doctor or nurse. If self-administration and home-treatment is considered appropriate, refer to **Home-treatment / self-administration** below and in section 4.4.

Dose

The recommended dose of Zemaira® is 60 mg/kg body weight (bw) administered once weekly.

To achieve the desired serum A_1-PI level and clinical response the dosage can be adjusted over time. Dose ranging studies using efficacy endpoints have not been performed with Zemaira® or any A_1-PI product. In the RAPID and RAPID extension studies, the trough mean serum A_1-PI levels, based on the 60 mg/kg dose, were maintained >15 µM (see section 5.1).

Paediatric population

The safety and efficacy of Zemaira® in the paediatric population (below 18 years) have not been established.

Elderly population

The safety and efficacy of Zemaira® in elderly patients (65 years of age or older) is limited. No clinical study has determined whether elderly patients respond differently from younger subjects.

Patients with renal or hepatic impairment

No special investigations have been performed. No alternative dose regimen can be recommended in these patients.

Method of administration

Zemaira® should only be administered intravenously by infusion after reconstitution.

The powder must be reconstituted with water for injection (see instructions on reconstitution in section 6.6) and filtered during administration using an intravenous administration set with a suitable infusion filter (recommended pore size 5 µm).

The reconstituted product has to be inspected visually. It should be clear, colourless to slightly yellow and free of visible particles).

Zemaira® does not contain an antimicrobial preservative. It must, therefore, be used immediately after reconstitution. If product is not used immediately after reconstitution, protect from light and use within 3 hours. Use in one patient on one occasion only. Any unused solution should be discarded appropriately. Do not use if the product has been frozen. Aseptic conditions are to be kept during administration.

It should be administered at an infusion rate of about 0.08 mL/kg bw/min using a separate dedicated infusion line. The infusion rate may be adjusted, based upon patient tolerability. The recommended dose of 60 mg/kg bw will take approximately 15 minutes to infuse.

Aseptic conditions are also to be kept during withdrawal.

For further detailed information regarding the administration of the reconstituted solution, follow the instructions in section 6.6.

Home-treatment / self-administration

If deemed appropriate by the treating physician, Zemaira® may be self-administered by the patient (or carer) following adequate training. This includes its administration in the home or other appropriate setting.

If self-administration/home-treatment is deemed appropriate, ensure that the patient/carer receives clear instructions, adequate training on intravenous administration and has demonstrated the ability to perform intravenous infusions.

4.3 Contraindications

Zemaira® is contraindicated in patients with a history of anaphylaxis or severe systemic reactions to the active substance or to any of its excipients.

Zemaira® is contraindicated in immunoglobulin A (IgA)-deficient patients with antibodies against IgA, due to the risk of severe hypersensitivity.

4.4 Special warnings and precautions for use

The recommended infusion rate should be adhered to. During the first infusions, patient's clinical state, including vital signs, should be closely monitored throughout the infusion period. If any reaction takes place that might be related to the administration of Zemaira®, the rate of infusion should be decreased or the administration should be stopped, as required by the clinical condition of the patient. If symptoms subside promptly after stopping, the infusion may be resumed at a lower rate that is comfortable for the patient.

Hypersensitivity / Anaphylaxis

Caution should be used when administering Zemaira® to patients with known hypersensitivity to an A_1-PI product.

Zemaira® may contain trace amounts of IgA. Patients with selective or severe IgA deficiency can develop antibodies to IgA and, therefore, have a greater risk of developing potentially severe hypersensitivity and anaphylactic reactions.

Suspected allergic or anaphylactic type reactions may require immediate discontinuation of the infusion, depending on the nature and severity of the reaction. In case of shock, emergency medical treatment should be administered.

Home-treatment / self-administration

There are limited data regarding the use of this medicinal product in home-treatment / self-administration.

Potential risks associated with home-treatment / self-administration are related to the handling and administration of the medicinal product as well as to the handling of adverse reactions, particularly hypersensitivity. Patients should be informed of signs of hypersensitivity reactions.

The decision of whether a patient is suitable for home-treatment / self-administration is made by the treating doctor, who should ensure appropriate training is provided (e.g. regarding reconstitution, use of transfer device or filter, assembly of intravenous tubing, infusion techniques, maintenance of a treatment diary, identification of adverse reactions and measures to be taken in case such reactions occur) and the use is reviewed at regular intervals.

Pathogen safety

Standard measures to prevent infections resulting from the use of medicinal products prepared from human blood or plasma include selection of donors, screening of individual donations and plasma pools for specific markers of infection, and the inclusion of effective manufacturing steps for the inactivation / removal of viruses. The Zemaira® manufacturing process includes two virus inactivation / removal steps, pasteurisation (60°C for 10 hours) and nanofiltration, to reduce the possibility of pathogen transmission. Despite this, when medicinal products prepared from human blood or plasma are administered, the possibility of transmitting infective agents cannot be totally excluded. This also applies to unknown or emerging viruses and other pathogens.

The measures taken are considered effective for enveloped viruses such as human immunodeficiency virus (HIV), hepatitis B virus (HBV) and hepatitis C virus (HCV) and for the non-enveloped hepatitis A (HAV) and parvovirus B19 virus.

Vaccination for patients in receipt of medicinal products from human plasma should be considered where appropriate.

It is strongly recommended that every time that Zemaira® is administered to a patient, the name and batch number of the product are recorded in order to maintain a link between the patient and the batch of the product.

4.5 Interaction with other medicines and other forms of interaction

No interaction studies have been performed.

4.6 Fertility, pregnancy and lactation

Pregnancy

No animal reproduction studies have been conducted with Zemaira® and its safety for use in human pregnancy has not been established in controlled clinical trials. Since A_1-PI is an endogenous human protein, it is considered unlikely that Zemaira® will cause harm to the foetus when given at recommended doses. However, Zemaira® should be given with caution to pregnant women.

Breast-feeding

It is unknown whether Zemaira® / metabolites are excreted in human milk. The excretion of human A_1-PI in milk has not been studied in animals. A decision on whether to continue/discontinue breast-feeding or to continue/discontinue therapy with Zemaira® should be made, taking into account the benefit of breast-feeding to the child and the benefit of human A_1-PI therapy to the woman.

Fertility

No animal fertility studies have been conducted with Zemaira® and its effect on human fertility has not been established in controlled clinical trials. Since human A_1-PI is an endogenous human protein, no adverse effects on fertility are expected when given at recommended doses.

4.7 Effects on ability to drive and use machines

Zemaira® may have a minor influence on the ability to drive and use machines. Adverse reactions such as dizziness may occur following administration of Zemaira®.

4.8 Undesirable effects

Tabulated list of adverse reactions

The adverse reactions (ARs) collected from six clinical studies in 221 patients and post-marketing experience are presented in **Table 1** according to the MedDRA System Organ Class (SOC and Preferred Term Level). Frequency per patient (based on six months of exposure during clinical trials) has been evaluated according to the following convention: common (≥1/100 to <1/10), uncommon (≥1/1,000 to <1/100), rare (≥1/10,000 to <1/1000) and very rare (<1/10,000). The frequency of ARs during post-marketing only is considered as “not known (cannot be estimated from the available data)”.

Table 1: Frequency of Adverse Reactions (ARs) in clinical studies and post-marketing experience with Zemaira®

System Organ Class (SOC)	Frequency of ARs			
	Common (≥1/100 to <1/10)	Uncommon (≥1/1,000 to <1/100)	Very rare (<1/10,000)	Not known
Blood and lymphatic system disorders				Lymph node pain
Immune system disorders		Hypersensitivity reactions (including tachycardia, hypotension, confusion, syncope, oxygen consumption decreased and pharyngeal oedema)	Anaphylactic reactions	
Nervous system disorders	Dizziness, headache	Paraesthesia	Hypoaesthesia	
Eye disorders				Eye swelling
Vascular disorders		Flushing		
Respiratory, thoracic and mediastinal disorders	Dyspnoea			
Gastrointestinal disorders	Nausea			Lip swelling
Skin and subcutaneous tissue disorders		Urticaria, rash (including exfoliative and generalised)	Hyperhidrosis, pruritus	Face swelling
General disorders and administration site conditions		Asthenia, infusion-site reactions (including infusion site haematoma)	Chest pain, chills, pyrexia	

Paediatric population

Safety and effectiveness in the paediatric population have not been established. No data are available.

Elderly

The safety and efficacy of Zemaira® in elderly patients (65 years of age or older) have not been established in clinical trials.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions via https://nzphvc.otago.ac.nz/reporting/

4.9 Overdose

Consequences of an overdose are not known.

For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antihaemorrhagics, proteinase inhibitor
ATC code: B02AB02

Human alpha1-proteinase inhibitor is a normal constituent of human blood. It belongs to the family of serine protease inhibitors.

Mechanism of action

The A_1-PI is a 52 kDa single polypeptide glycoprotein produced by hepatocytes and mononuclear phagocytes and is understood to be the primary anti-protease in the lower respiratory tract, where it inhibits neutrophil elastase (NE). Lung tissue can be degraded by neutrophil proteases, which have been activated by infection and / or inflammation. Normal healthy individuals produce sufficient A_1-PI to control the NE produced by activated neutrophils and are thus able to prevent inappropriate proteolysis of lung tissue by NE. Conditions that increase neutrophil accumulation and activation in the lung, such as respiratory infection and smoking, will in turn increase the levels of NE.

Individuals deficient in endogenous A_1-PI are unable to maintain appropriate anti-protease defence and experience more rapid proteolysis of the alveolar walls starting prior to the development of clinically evident chronic obstructive lung disease in the third or fourth decade. Over time, the progressive loss of lung tissue results in the decline in lung function characterised by dyspnoea and its sequelae. The normal range for A_1-PI is 20–53 µM.

Approximately 100 genetic variants of A_1-PI deficiency can be identified electrophoretically (e.g. genotypes PiZZ, PiZ(null), Pi(null,null), PiSZ), only some of which are associated with the clinical disease. Ninety-five percent of clinically symptomatic A_1-PI deficient individuals are of the severe PiZZ phenotype.

Pharmacodynamic effects

Augmenting the levels of functional A_1-PI by intravenous infusion and correcting the imbalance between NE and protease inhibitors is an approach to therapy for patients with A_1-PI deficiency. The administration of Zemaira® increases and maintains the antigenic and functional serum levels as well as the lung epithelial lining fluid (ELF) levels of A_1-PI in the lower lung, leading to a slowdown in the progression of emphysema.

The efficacy of augmentation therapy in affecting the progression of emphysema has been demonstrated in randomised, controlled clinical studies by CT scan densitometry.

Clinical efficacy and safety

RAPID studies

The safety and efficacy of Zemaira® was evaluated in a randomised, double-blind, placebo-controlled, multi-centre study (RAPID) followed by a 2-year open-label extension study (RAPID extension study).

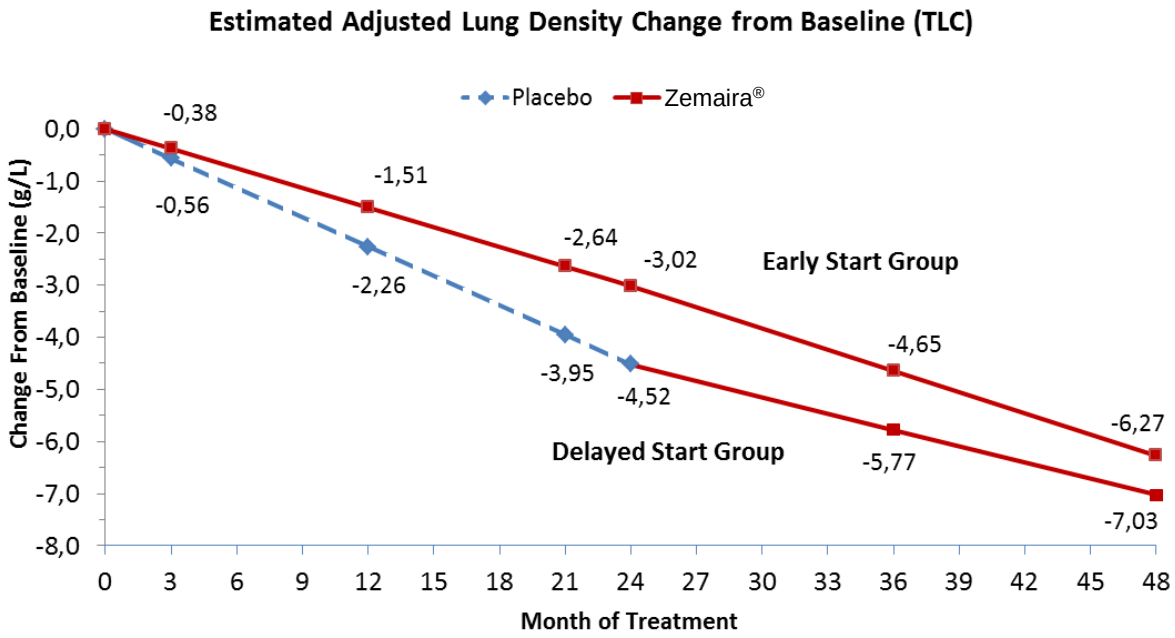
A total of 180 subjects with A_1-PI deficiency characterised by a serum A_1-PI level <11 µM (i.e. <50 mg/dL as determined by nephelometry) and clinical evidence of emphysema (progressive lung disease, e.g. lower forced expiratory volume per second (FEV_1) predicted, impaired walking capacity or increased number of exacerbations), were randomised to receive a weekly 60 mg/kg bw intravenous dose of either Zemaira® or placebo for up to 24 months.

One-hundred and forty subjects (76 Zemaira®-treated subjects and 64 subjects treated with placebo in the RAPID Study) continued into the RAPID extension study and were treated with a weekly 60 mg/kg bw intravenous dose of Zemaira® for up to 24 months.

The study investigated the effect of Zemaira® on the progression of emphysema, assessed by the decline of lung density, measured by computer tomography (CT). The subjects ranged in age from 31 to 67 years (median age 54 years) with average baseline A_1-PI levels of approximately 6.15 µM, and average volume-adjusted CT lung density of 47 and 50 g/L for Zemaira® and placebo subjects, respectively.

Zemaira®-treated subjects demonstrated a consistent pattern of slower lung density decline than those receiving placebo (see **Figure 1**). The annual rate of lung density decline, as measured by CT scan at total lung capacity over 2 years was lower with Zemaira® (-1.45 g/L) as compared with placebo (-2.19 g/L), reflecting a 34% reduction ($p = 0.017$, 1-sided). Higher CT lung density measurements correlated with higher forced expiratory volume in 1 second (0.31, $p < 0.001$), higher diffusion capacity of carbon monoxide (0.46, $p < 0.001$), higher exercise capacity (0.26, $p = 0.002$), and lower St. George's Respiratory Questionnaire activity score (-0.26, $p = 0.002$) throughout the study.

Figure 1: Changes in Lung Density from baseline in the RAPID study



The final analysis of the 24-month, open-label, RAPID extension study, has been performed on 140 subjects in the ITT population. The analysis showed that the reduced rate in lung density decline was maintained for subjects continuously treated with Zemaira® (Early Start group). Subjects who originally received placebo in the RAPID study and then received Zemaira® in the RAPID extension study also exhibited a comparable, reduced rate of decline in lung density (Delayed Start group). Comparison of the annual lung density decline rates at TLC between Zemaira® and placebo in this limited population within the RAPID study demonstrated similar reductions in the annual rate of lung density decline: Zemaira® (-1.51 g/L) as compared with placebo (-2.26 g/L), reflecting a 33% reduction (p = 0.021, 1-sided). Furthermore a statistically significant inflection point favouring Zemaira® was established for Delayed start subjects by comparing the response from Baseline to Month 24 with Month 24 and Month 48 both in terms of the absolute changes in lung density and the annual rate of lung density decline. The lung density loss during the first 2 years of placebo treatment was not regained during the subsequent 2 years of treatment (see **Figure 1**).

In the RAPID study, Zemaira® demonstrated a similar safety and tolerability profile compared to placebo.

Single doses of 120 mg/kg have been administered to 137 subjects treated with Zemaira®.

5.2 Pharmacokinetic properties

Four clinical studies were conducted with Zemaira® in 89 subjects (59 males and 30 females) to evaluate the effect of Zemaira® on serum levels of A_1-PI. The subjects ranged in age from 29 to 68 years (median age 49 years). At screening, serum A_1-PI levels were between 3.2 and 10.1 μM (mean of 5.6 μM).

A double-blind, randomised, active-controlled, crossover pharmacokinetic study was conducted in 13 males and 5 females with A_1-PI deficiency, ranging in age from 36 to 66 years. Nine subjects received a single 60 mg/kg bw dose of Zemaira® followed by a comparator product, and 9 subjects received comparator product followed by a single 60 mg/kg bw dose of Zemaira®, with a wash-out period of 35 days between doses. A total of 13 post-infusion serum samples were taken at various time points up to Day 21. **Table 2** shows the mean results for the Zemaira® pharmacokinetic parameters.

Table 2: Pharmacokinetic parameters for A_1-PI following a single 60 mg / kg bw dose of Zemaira®

Pharmacokinetic Parameter	Mean (standard deviation)*
Area under the curve ($AUC_{0-\infty}$)	144 (±27) µM x day
Maximum concentration (C_{max})	44.1 (±10.8) µM
Terminal half-life ($t_{1/2ß}$)	5.1 (±2.4) days
Total clearance	603 (±129) mL/day
Volume of distribution at steady state	3.8 (±1.3) L

* n=18 subjects.

A population pharmacokinetic analysis was conducted using data from 90 Zemaira®-treated subjects from the RAPID trial. The population estimate of mean half-life was 6.8 days. The model predicted mean steady state concentration was 21.8 µM after a 60 mg/kg bw / week dose. The population pharmacokinetic analysis did not indicate that there were any significant effects of age, gender, weight, or baseline serum antigenic A_1-PI concentrations on the clearance of Zemaira®.

Pharmacokinetic / pharmacodynamic relationship

In a double-blind, active-controlled clinical study to evaluate the safety and biochemical efficacy of Zemaira® 44 subjects were randomised to receive 60 mg/kg bw intravenous dose of Zemaira® once weekly for 24 weeks. The mean trough serum A_1-PI levels at steady state (weeks 7–11) were maintained above 11 µM. The mean of the steady state trough serum A_1-PI level for Zemaira®-treated subjects was 17.7 µM (standard deviation: 2.5), thus providing evidence that Zemaira® raises A_1-PI levels.

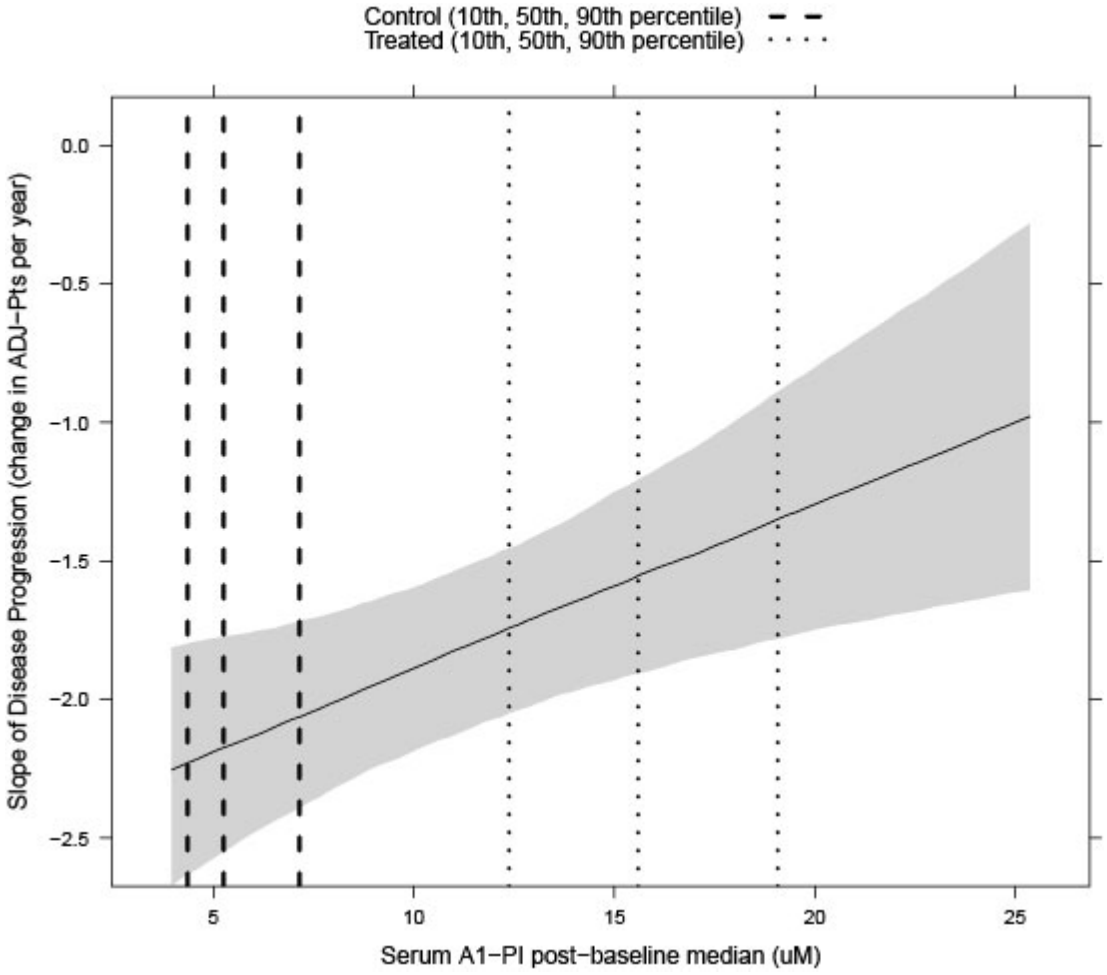
In a subgroup of subjects enrolled in this study (10 Zemaira®-treated subjects) bronchoalveolar lavage have been performed. ELF measurements of A_1-PI levels showed a consistent increase following treatment. ELF levels of antigenic A_1-PI and A_1-PI : NE complexes increased from baseline. Free elastase was unmeasurably low in all samples.

The RAPID and RAPID extension study evaluated serum antigenic A_1-PI levels over 48 months. The post-baseline trough mean (SD) concentration in subjects receiving Zemaira® for 24 months was 15.9 µM, (2.7) and in subjects treated with Zemaira® for an additional 24 months, the mean serum antigenic A_1-PI concentration was 15.1 µM (2.5) (see section 5.1).

An exposure response analysis of the RAPID / RAPID extension data revealed an inverse linear relationship between trough serum A_1-PI levels and the annual decline in lung density as measured by

volume adjusted CT scans for subjects receiving 60 mg/kg bw intravenous dose of Zemaira® or placebo (see **Figure 2**).

Figure 2: Expected Lung Density Decline Rate as a Function of Trough Serum A_1-PI Level



The area in grey represents 90% confidence intervals based on annual rate of change in adjusted lung density from a bootstrapping method.

5.3 Preclinical safety data

The safety of Zemaira® has been assessed in several preclinical studies. Preclinical data reveal no special risk for humans based on safety pharmacology and short term toxicity studies. At the recommended therapeutic dose of 60 mg/kg bw, no toxicity was observed.

Since human A_1-PI is a protein and a physiological constituent of human blood, it is not expected to present carcinogenic, genotoxic, or teratogenic effects.

Repeat dose toxicity studies longer than 5 days or long-term safety, in general, can not be investigated in animals because of the formation of antibodies against heterologous human proteins.

The local tolerance of Zemaira® was evaluated in rabbits following intravenous, perivenous, and intraarterial administration. No treatment-related local adverse reactions were observed.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium chloride
Sodium dihydrogen phosphate monohydrate
Mannitol
HCl or NaOH (for pH-adjustment)
Water for injection

6.2 Incompatibilities

This medicinal product must not be mixed with other medicinal products, diluents, or solvents except those mentioned in section 6.6, and should be administered by a separate infusion line.

The reconstituted solution should not be mixed with other medicinal products.

6.3 Shelf life

3 years

Stability after reconstitution

From a microbiological point of view, the product should be used immediately after reconstitution. However, chemical and physical in-use stability has been demonstrated for 3 h at room temperature (up to 25°C). Do not freeze the reconstituted solution.

6.4 Special precautions for storage

Store below 25°C (Do not freeze). Do not use after the expiry date. Protect from light.

For storage conditions after reconstitution of the medicinal product, see section 6.3.

6.5 Nature and contents of container

1000 mg of powder in a glass vial (type I), closed with a rubber (butyl) stopper and an aluminium seal with a plastic flip off cap.

20 mL of water for injection in a glass vial (type I), closed with a rubber (butyl) stopper and an aluminium seal with a plastic flip off cap.

Zemaira® is presented in packs containing:

- 1 vial with powder for infusion: A_1-PI 1000 mg
- 1 vial with 20 mL Sterile Water for Injection
- 1 vented transfer device.

6.6 Special precautions for disposal and other handling

The product must be reconstituted, administered and handled with caution using aseptic technique to maintain product sterility.

Reconstitution using the transfer device and diluent vial:

The powder must be reconstituted with 20 mL of diluent (water for injection). Total reconstitution should be obtained within 5 minutes.

Please follow the instructions given below:

Notes on using the transfer device (see **Figure 3**) (in steps 3–7)

- The transfer device provided in the Zemaira® carton has a white end (for WFI) with a double orifice and green end (for the powder) with a single orifice.
- Incorrect use of the transfer device will result in loss of vacuum and prevent transfer of the WFI, thereby prolonging or preventing reconstitution of Zemaira®.
- The transfer device is sterile. Once the protective covers have been removed (steps 3 and 4), do not touch the exposed ends of the spikes.

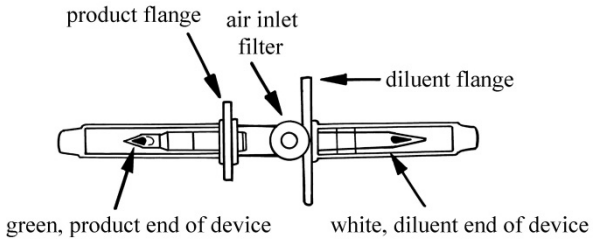


Figure 3

1. Ensure that powder vial (green cap) and WFI vial (white cap) are at room temperature (up to 25°C).
2. Remove the plastic flip-top caps from each of the vials being used. Treat each of the rubber stoppers with disinfectant and allow them to dry.
3. Remove the protective cover from the white end of the transfer device. Place the WFI vial on a flat surface and insert the white end of the transfer device into the centre of the stopper of the upright WFI vial (see **Figure 4**).

Figure 4

4. Place the powder vial (green cap) on a flat surface. Remove the protective cover from the green end of the transfer device. Invert the WFI vial with the attached transfer device and, gently, insert the green end of the transfer device into the centre of the rubber stopper of the upright powder vial (green top). The flange of the transfer device should rest on the surface of the stopper so that the WFI flows into the powder vial (see **Figure 5**).

Figure 5

5. Allow the WFI to flow into the powder. This happens automatically because of a vacuum in the powder vial. If there is no vacuum in the vial, the WFI will not flow into the powder vial. In this case, do not use the product.
6. During WFI transfer, wet the powder completely by gently tilting the powder vial. Do not allow the air inlet filter to face downward. Care should be taken not to lose the vacuum, as this will prolong or prevent reconstitution (see **Figure 6**).

Figure 6

7. When WFI transfer is complete, withdraw the transfer device from the powder vial and discard the WFI vial and transfer device.
8. Gently swirl the powder vial until the powder is completely dissolved. **DO NOT SHAKE TO AVOID FOAMING** (see **Figure 7**).

Figure 7

9. Inspect visually the reconstituted solution. The solution should be clear, colourless to slightly yellow, and free from visible particles. Do not use solutions that are discoloured, cloudy or have particles.
10. As more than 1 vial of powder is needed to achieve the required dose, repeat steps 1 to 9 using an additional package containing a transfer device. Do not reuse the transfer device.
11. Use aseptic technique to transfer the reconstituted solution from the vials into the administration container (such as empty intravenous bag or glass bottle; not supplied) via a commercially available intravenous tubing transfer set (not supplied).

Administration

The reconstituted solution must be filtered during administration using a suitable infusion filter (recommended pore size 5 µm) and administered using an IV administration set (not supplied).

1. Attach the administration set to the administration container.
   Make sure that the roller clamp on the administration set is closed.
2. Elevate the administration container (if IV bag, hang on an IV pole).
3. Prime the chamber by squeezing the drip chamber until Zemaira® has filled the chamber half-way.
4. Slowly open the roller clamp on the administration set and let Zemaira® flow until it reaches the end of the tubing with no air bubbles.
5. Close the roller clamp.
6. Attach a filter (recommended pore size 5 µm) onto the end of the administration set (not supplied). Again open the roller clamp and let Zemaira® flow until the filter is saturated.
7. Connect the other end of the filter to the injection set (e.g. butterfly / winged infusion needle or infusion catheter).
8. Inject / infuse the reconstituted solution into the vein following the instructions given to you by your doctor. The solution should be infused at an infusion rate of about 0.08 mL/kg bw/min, as determined by your response and your comfort. The recommended dose of 60 mg/kg bw will take approximately 15 minutes to infuse.
9. If you notice that the infusion stops or slows, you may need to change the filter as it can become clogged. Repeat then the steps 6–8.

7 MEDICINE SCHEDULE

Prescription Medicine

8 SPONSOR

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9 DATE OF FIRST APPROVAL

14 June 2018

10 DATE OF REVISION OF THE TEXT

Not applicable

NEW ZEALAND DATA SHEET

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SUMMARY TABLE OF CHANGES

Section changed	Summary of new information
All	Data sheet reformatted to the SPC format
4.1	Indication reworded to reflect the clinical trial outcomes
4.2	Additional administration instructions included
5.1	New clinical trial data added
6.6	Additional administration steps included