

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 (A₁-PI) concentrate.

One vial contains approximately 1000 mg of A₁-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 A₁-PI per milligram of total protein. The purity is $\geq 92\%$ A₁-PI of total protein.

The total protein content is approximately 1100 mg per vial.

After reconstitution with 20 mL of diluent (Water for Injection [WFI]), the solution contains approximately 50 mg/mL of A₁-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.

Powder: white to off-white

Diluent (WFI): clear, colourless

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 A₁-PI deficiency (A₁-PI <11 µM) and progressive lung disease. Patients are to be under optimal pharmacologic and non-pharmacologic treatment.

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4.2 Dose and method of administration

Treatment should be initiated and supervised by a healthcare professional experienced in the use of A₁-PI or in the treatment of A₁-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 A₁-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 A₁-PI product. In the RAPID and RAPID extension studies, the trough mean serum A₁-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 administered using an intravenous administration set.

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.

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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 A₁-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.

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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 set, 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 A₁-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.

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Breast-feeding

It is unknown whether Zemaira® / metabolites are excreted in human milk. The excretion of human A₁-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 A₁-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 A₁-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 ($\geq 1/100$ to $< 1/10$), uncommon ($\geq 1/1,000$ to $< 1/100$), rare ($\geq 1/10,000$ 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)”.

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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/>

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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: Antihemorrhagics, 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 A₁-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 A₁-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 A₁-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 A₁-PI is 20–53 µM.

Approximately 100 genetic variants of A₁-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 A₁-PI deficient individuals are of the severe PiZZ phenotype.

Pharmacodynamic effects

Augmenting the levels of functional A₁-PI by intravenous infusion and correcting the imbalance between NE and protease inhibitors is an approach to therapy for patients with A₁-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 A₁-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.

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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 A₁-PI deficiency characterised by a serum A₁-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 (FEV₁) 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.

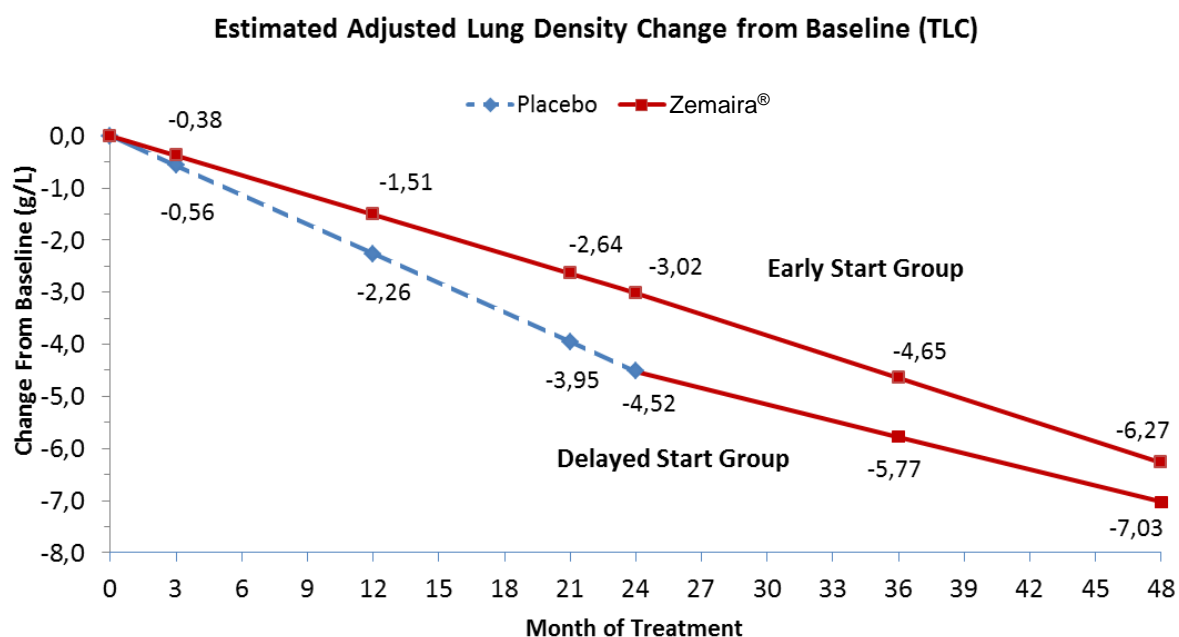
One-hundred and forty subjects (76 Zemaira[®]-treated subjects and 64 subjects treated with placebo in the RAPID Study) continued into the RAPID extension study and were treated with a weekly 60 mg/kg bw intravenous dose of Zemaira[®] for up to 24 months.

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 A₁-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.

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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 A₁-PI. The subjects ranged in age from 29 to 68 years (median age 49 years). At screening, serum A₁-PI levels were between 3.2 and 10.1 µM (mean of 5.6 µM).

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A double-blind, randomised, active-controlled, crossover pharmacokinetic study was conducted in 13 males and 5 females with A₁-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 A₁-PI following a single 60 mg / kg bw dose of Zemaira[®]

Pharmacokinetic Parameter	Mean (standard deviation)*
Area under the curve (AUC _{0-∞})	144 (±27) μM x day
Maximum concentration (C _{max})	44.1 (±10.8) μM
Terminal half-life (t _{1/2B})	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 A₁-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 A₁-PI levels at steady state (weeks 7–11) were maintained above 11 μM. The mean of the steady state trough serum A₁-PI level for Zemaira[®]-treated subjects was 17.7 μM (standard deviation: 2.5), thus providing evidence that Zemaira[®] raises A₁-PI levels.

In a subgroup of subjects enrolled in this study (10 Zemaira[®]-treated subjects) bronchoalveolar lavage have been performed. ELF measurements of A₁-PI levels showed a consistent increase following treatment. ELF levels of antigenic A₁-PI and A₁-PI : NE complexes increased from baseline. Free elastase was unmeasurably low in all samples.

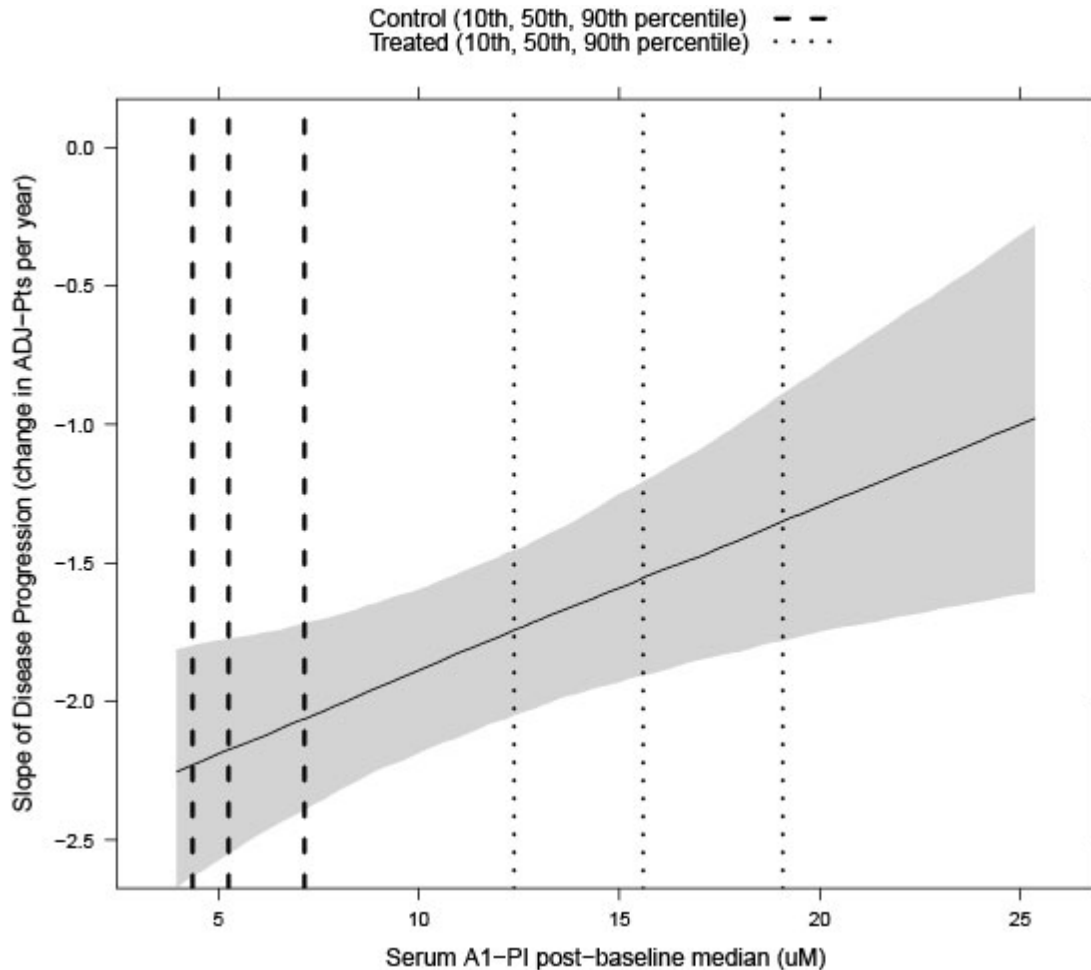
The RAPID and RAPID extension study evaluated serum antigenic A₁-PI levels over 48 months. The post-baseline trough mean (SD) concentration in subjects receiving Zemaira[®] for 24 months was 15.9 μM, (2.7) and in subjects treated with Zemaira[®] for an additional 24 months, the mean serum antigenic A₁-PI 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 A₁-PI levels and the annual decline in lung density as measured by

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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 A₁-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 A₁-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.

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6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Powder:

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

Diluent:

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

Zemaira® 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: A₁-PI 1000 mg
- 1 vial with 20 mL Water for Injection
- 1 Mix2Vial™ transfer set for reconstitution.

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6.6 Special precautions for disposal and other handling

General instructions

The reconstitution should be performed according to the instructions provided below.

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

Do not use provided sterile ancillaries for reconstitution if their package is opened or if they are damaged.

The powder must be reconstituted with 20 mL of diluent (water for injection [WFI]).

Reconstitution

Follow the steps provided below for the preparation and reconstitution of Zemaira®:

1. Bring the Zemaira® vial and WFI vial to room temperature.
2. Remove the plastic flip-top cap from the **WFI** vial.
3. Wipe the rubber stopper of the **WFI** vial with antiseptic solution and allow it to dry.
4. Open the Mix2Vial™ package by peeling off the lid (**Figure 3**). Do not remove the Mix2Vial™ from the blister package.

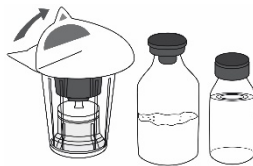


Figure 3

5. Place the **WFI** vial on a level, clean surface and hold the vial tight. Take the Mix2Vial™ together with the blister package and push the spike of the **blue** adapter end straight down through the **WFI** vial (**Figure 4**).

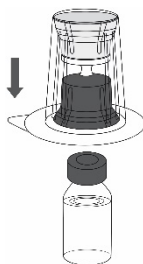


Figure 4

6. Carefully remove the blister package from the Mix2Vial™ set by holding at the rim, and pulling vertically upwards. Make sure that you only pull away the blister package and not the Mix2Vial™ set (**Figure 5**).

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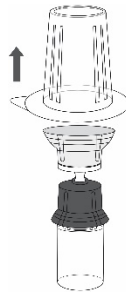


Figure 5

7. Remove the plastic flip-top cap from the **Zemaira®** vial.
8. Wipe the rubber stopper of the **Zemaira®** vial with antiseptic solution and allow it to dry.
9. Place the **Zemaira®** vial on a level and firm surface. Invert the WFI vial with the Mix2Vial™ set attached and push the spike of the **transparent** adapter end straight down through the **Zemaira®** vial stopper (**Figure 6**). The WFI will automatically flow into the Zemaira® vial.

NOTE: Ensure all water has transferred into the Zemaira® vial.

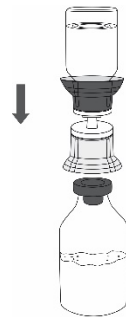


Figure 6

10. Follow steps below to remove entire Mix2Vial™ from Zemaira® vial:
 - With one hand tightly grasp the Zemaira® vial as shown in **Figure 7**.
 - With the other hand tightly grasp the WFI vial and the blue Mix2Vial™ set.
 - Bend **the entire Mix2Vial™ set** to the side until it disconnects from the Zemaira® vial (**Figure 7**).

Discard the WFI vial with the entire Mix2Vial™ set.



Figure 7

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11. Gently swirl the Zemaira[®] vial until the powder is completely dissolved (**Figure 8**). DO NOT SHAKE TO AVOID FOAMING. Take care not to touch the rubber vial stopper. Total reconstitution of a vial should be obtained within 5 minutes.



Figure 8

12. 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.
13. If more than 1 vial of Zemaira[®] is needed to achieve the required dose, repeat steps 1 to 11 above using an additional package containing an unused Mix2Vial[™] transfer set.

Use a separate, unused Mix2Vial[™] transfer set and a WFI vial for each Zemaira[®] vial.

14. Use aseptic technique to transfer the reconstituted solution into the administration container (e.g. empty intravenous bag or glass bottle; not supplied) via a commercially available intravenous fluid tubing transfer set (not supplied).

Administration

The reconstituted solution must be 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. Connect the administration set to the injection set (e.g. butterfly / winged infusion needle or infusion catheter).
7. 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.

Any unused solution should be discarded appropriately.

7 MEDICINE SCHEDULE

Prescription Medicine

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8 SPONSOR

CSL Behring (NZ) Ltd
666 Great South Road
Penrose
Auckland
New Zealand

For Medical/Technical Enquiries: TOLL FREE: 0800 640 677

For Customer Service Enquiries: TOLL FREE: 0800 841 532

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www.cslbehring.com.au

9 DATE OF FIRST APPROVAL

14 June 2018

10 DATE OF REVISION OF THE TEXT

16 October 2018

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SUMMARY TABLE OF CHANGES

Section changed	Summary of new information
6.5	Replacement of transfer device with Mix2Vial™ transfer set
6.6	Replacement of transfer device with Mix2Vial™ transfer set for reconstitution