1 PRODUCT NAME

ALUSTAL – SINGLE ALLERGENS
ALUSTAL – DISPENSED MIXTURES

A range of various ALUSTAL allergen extracts are registered in New Zealand either as a single allergen extract or combination allergen extracts. These include mite extracts, pollen extracts and animal extracts.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

ALUSTAL is prepared from freeze-dried allergen extracts adsorbed onto aluminium hydroxide gel. The freeze-dried allergen extracts are prepared by ammonium bicarbonate extraction of the allergen source materials e.g. pollen, mites. Specific allergen(s) are selected by the physician for Specific Immunotherapy Treatment (SIT) for the individual patient.

Each 5mL vial contains specific allergen extract(s) in suspension and are available in various concentrations. Different concentrations are identified by different coloured caps on the vials.

Yellow cap:	**0.1 IR/mL**	**or**	**0.1 IC/mL**
Green cap:	**1.0 IR/mL**	**or**	**1.0 IC/mL**
Blue cap:	**10.0 IR/mL**	**or**	**10.0 IC/mL**

➢ IR (Index of Reactivity): An allergen extract is said to have a titre of 100 IR/mL if in a prick-test performed using a Stallerpoint® in 30 subjects sensitised to the allergen in question, it produces a wheal measuring 7 mm in diameter (geometric mean). Skin reactivity in these subjects is simultaneously demonstrated by a positive response to a prick-test with codeine phosphate 9% or histamine dihydrochloride 10 mg/mL.

➢ IC (Index of Concentration): An allergen extract has an Index of Concentration of 100 IC/mL when its manufacturing parameters lead to the same dilution ratio as those of standardized extracts at 100 IR/mL from the same family, taken as a reference.

When the family does not contain any standardized reference extract, the value 100 IC/mL corresponds to an extract where the dilution ratio is established according to medical experience.

For the full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Suspension for injection

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

ALUSTAL treatment is indicated for patients with Type 1 allergy (Gell and Coombs classification), particularly presenting as seasonal or perennial rhinitis, conjunctivitis, rhinoconjunctivitis with or without associated asthma.

4.2 Dose and method of administration

Treatment is given in two phases:

- Initial treatment at escalating dosage (weekly injections);
- Maintenance treatment at constant dosage (monthly injections)

Before each injection:

- The expiry date on the vial should be checked;
- It should be confirmed that the vial to be used is the same as that prescribed (composition, patient's name, concentration). The vial should be shaken gently before the quantity to be injected is withdrawn
- The normal rules of asepsis should be observed.
- Disposable 1 mL "tuberculin" syringes with 1/100 graduations should be used;
- The injection should be precisely the required dose.

Paediatric population

The dosage for children is the same as for adults. Because of the smaller size of children larger volumes of solution may produce excessive discomfort. Therefore in order to achieve the total dose required, the volume of the dose may need to be divided into more than one injection.

Dosage does not vary with age, but must be adjusted to the reactivity of the individual patient.

1. ***Initial Treatment: Escalation of Dosage***. The product is injected exclusively by the deep subcutaneous route, at progressively escalating dosage, at a rate of one injection per week up to the maximum tolerated, according to the following treatment schedule:

Week	Injection	Vial (concentration)	Volume	Frequency
W1 W2 W3 W4	1 2 3 4	0.1 IR/mL or 0.1 IC/mL (Yellow cap)	0.10 0.20 0.40 0.80	1 injection per week
W5 W6 W7 W8	5 6 7 8	1 IR/mL or 1 IC/mL (Green cap)	0.10 0.20 0.40 0.80	1 injection per week
W9 W10 W11 W12 W13 W14 W16 W19	9 10 11 12 13 14 15 16	10 IR/mL or 10 IC/mL (Blue cap)	0.10 0.20 0.40 0.60 0.80 0.80 0.80 0.80	1 injection per week
W23 (First monthly dose)	Maintenance Therapy	10 IR/mL or 10 IC/mL (Blue cap)	Maximum tolerated dose	Every 2 weeks, then monthly or at longer intervals not exceeding 6 weeks

Important Note: This treatment schedule is a guideline only. It must be modified depending on the patient's condition and any reactions that occur. Ideally, SIT with Pollen allergens should begin before pollen season.

2. ***Maintenance Treatment: Constant dose****.* [Maintenance – 1 vial 10 IR/mL or IC/mL (Blue cap)] The highest tolerated dose (Max. 0.8 mL) in the initial treatment course is then repeated at interval of two weeks, then monthly or at longer intervals, not exceeding 6 weeks between successive injections. If the interval is longer, the dose should be readjusted. It should be remembered that the above treatment schedule is a guideline only. It must be modified depending on the patient's condition and any reactions that occur. When changing vials for a patient on maintenance therapy, the first dose of the new vial should be 50% of the last dose (i.e., last dose given at 0.8mL of 10.0 IR/mL, new vial dose should be 0.4mL of 10.0 IR/mL; then followed by regular monthly doses of 0.8mL). For Pollen allergens, it may be necessary to reduce the maintenance dosage by half during pollen season but only if reactions occur.

Important Note: Administer maintenance therapy only after treatment with the initial allergen set has been completed and within 6 weeks of the previous final dose.

Duration of treatment: As a general rule, SIT with ALUSTAL should be continued for between 3 and 5 years.

Method of administration

Precautions to be taken before handling or administering the medicine

4.3 Contraindications

Hypersensitivity to the active substance(s) or to any of the excipients listed in section 6.1

Do not give SIT to patients with unstable asthma, severe immunodeficiency, malignant disease, or autoimmune disease. SIT is contraindicated for patients on treatment with beta-blockers. Any injections including SIT should be avoided in patients with a bleeding tendency.

4.4 Special warnings and precautions for use

Before starting SIT, patients should have their symptoms controlled, if necessary by administration of adequate symptomatic treatment.

1. Immunotherapy should only be administered by trained personnel familiar with the recognition of early signs of allergic reactions and competent in the management of systemic reactions. A medical practitioner should always be on the premises where immunotherapy is administered. Before giving an SIT injection, the practitioner should ensure that an emergency kit is immediately available, containing aqueous epinephrine hydrochloride (adrenaline) 1:1000, equipment for administering oxygen, equipment for administering intravenous fluids, oral airway, an injectable corticosteroid, an injectable antihistamine, vasopressor, stethoscope and sphygmomanometer, tourniquets, syringes, hypodermic and large-bore needles.

2. SHAKE VIAL GENTLY BEFORE WITHDRAWING DOSE

3. Proper aseptic precautions should be taken during withdrawal of dose including swabbing of bungs with a suitable antiseptic.

4. The injection should be postponed if the patient has a cold, influenza, or febrile illness.

5. Absolute accuracy of dosage is essential. Double-check both the vial strength and amount drawn up every time.

6. Inject slowly using deep subcutaneous route. Always pull back syringe plunger before injecting to ensure needle is not in a blood vessel. DO NOT INJECT INTO A BLOOD VESSEL OR INTRAMUSCULARLY.

7. PATIENTS SHOULD BE KEPT UNDER MEDICAL OBSERVATION FOR AT LEAST 30 MINUTES AFTER TREATMENT.

The majority of serious reactions will begin within 30 minutes after an injection. Patients must be instructed to avoid any activity that may increase blood flow through the injection site e.g. strenuous exercise, hot baths, sauna, application of local heat or rubbing, for the remainder of the day. Patients should be instructed to seek medical advice immediately if symptoms develop after leaving the clinic. The more rapidly symptoms begin, the more severe they are likely to be and the more rapidly treatment measures should begin.

8. Special care should be taken in the treatment of patients with **ASTHMA** as they may be more susceptible to severe adverse reactions. Patients with asthma must be supervised by a specialist with expertise and experience with the administration of immunotherapy to those with asthma. Before considering immunotherapy for patients with asthma, establish serial baseline lung function values. If there has been a recent exacerbation of asthma, as assessed clinically and/or by measurement of Peak Expiratory Flow Rate (PEFR), treatment should be halted and restarted after symptomatic improvement.
9. In many patients with asthma lung function is worst in the morning and therefore in such patients it may be preferable to give the injection in the afternoon.

10. Risk of accumulation of aluminium from aluminium hydroxide preparations (as for any aluminium hydroxide vaccine) into tissues (central nervous system, bones) should be kept in mind, especially in case of renal insufficiency.

Always ask the patient and record any local or systemic reaction that occurred after leaving the clinic after the previous injection. If necessary, adjust the dose of the next injection appropriately.

4.5 Interaction with other medicines and other forms of interaction

No interaction studies have been performed

4.6 Fertility, pregnancy and lactation

Pregnancy (Category B)
It is not advisable to use SIT during pregnancy: pregnancy is not considered as a contraindication to the continuation of immunotherapy but treatment should not be started during pregnancy. If a patient becomes pregnant during initial treatment, stop injections; if a patient becomes pregnant during maintenance therapy, treatment may continue if well tolerated. There is no data available on the excretion of allergen extracts in human milk or any effect on breast-fed infants.

4.7 Effects on ability to drive and use machines
Alustal has no or negligible influence on the ability to drive and use machines

4.8 Undesirable effects
Adverse effects- Post Marketing experience

System Organ Class (SOC)	Frequency	Side effects
Respiratory, thoracic and mediastinal disorders	Common	Dyspnea, asthma, Rhinitis, laryngeal oedema
Skin and subcutaneous tissues disorders Skin and subcutaneous tissues disorders NEC	Common Very rare	Pruritus, urticaria, facial erythema, angioedema Pre-existing atopic eczema outbreaks
Injection site	Common	Local reaction
Immune system disorders	Uncommon	Anaphylactic shock
Eye disorders	Uncommon	Conjunctivitis
Musculoskeletal disorders	Very rare	Myalgia within serum sickness like syndrome
General disorders NEC	Very rare	Headache, asthenia

Adverse effects –Clinical Trial Experience

System Organ Class (SOC)	Frequency	Side effects
Respiratory, thoracic and mediastinal disorders	Common	Asthma, bronchospasm, rhinitis
Skin and subcutaneous tissues disorders	Common	Rash, urticaria
Injection site	Common	Injection site reactions
Eye Disorders	Uncommon	conjunctivitis

As with all forms of hyposensitisation therapy, local and/or systemic reactions may occur. Injections of ALUSTAL may be associated with some itching and redness at the injection site. Prolonged pain, or pain radiating up the arm is usually the result of intramuscular injection. The tolerated dose is not necessarily constant, but may vary over time, depending on the individual's specific reactivity and environment.

Management of adverse reactions:

Local Reactions: Skin reactions due to Aluminium Hydroxide have been reported. Some regress spontaneously, while others, much more rarely, can progress to the formation of subcutaneous

nodules. Local reactions (>2 to 3 cm in diameter) with erythema, oedema and pruritus are relatively common, and do not invariably necessitate modification of the treatment schedule. However, they may still act as a reminder that caution is required.

A major local reaction (≥ 5 cm in diameter) should be treated with an oral antihistamine. Supervision of the patient should be extended, reduce the next dose to that previously tolerated. If necessary, increase the subsequent doses by smaller increments. Another dose should never be given until all local reaction resulting from the previous dose has disappeared.

DISCONTINUE INJECTIONS IF REACTION SIZE INCREASES.

Other Reactions:

Immediate-type reactions:

- A patient experiencing asthma after an injection must be observed until stable.

- If an asthma attack occurs after an injection, bronchodilators must be used, if necessary together with a parenteral corticosteroid.

- Systemic reactions (pruritus, giant urticaria or angioedema) should be treated by intramuscular injection of 0.5 to 1 mL of 1/1000 epinephrine (adrenaline), if necessary together with an intravenous corticosteroid. In view of the possibility of progression to shock, intensive and prolonged monitoring in a hospital setting is required.

- Laryngeal dyspnoea should also be treated with intramuscular injection of epinephrine (adrenaline), admission to hospital is advisable.

- In case of anaphylactic shock, the treatment should be administered as in an emergency and the patient should be admitted to a specialised unit (see Anaphylaxis section below).

Severe Delayed reactions:

- A serum sickness type of reaction may occur, with arthralgia, myalgia, urticarial rashes, nausea, lymphadenopathy, and fever. This is extremely rare; however SIT should be discontinued if any of these occur.

Anaphylaxis

Anaphylactic shock consists of some of the following: widespread urticaria, angio-oedema of the face and glottis, pallor, cough, wheezing, bronchospasm, faintness and hypotension, bradycardia, hyperemesis, shock.

i. Lay patient flat and elevate the legs. Treat immediately.

ii Give 0.5mL 1/1000 epinephrine (adrenaline) intramuscularly, near the injection site at once. If necessary, repeat 1/1000 epinephrine (adrenaline) intramuscularly at 3-5 minute intervals to a maximum of 2.0mL in 15 minutes.

iii Ensure maintenance of adequate airway.

iv Give antihistamine.

v If necessary use full supportive measures such as, intravenous saline or plasma expanders for hypotension, oxygen, external cardiac massage.

vii If bronchospasm is severe, Isoprenaline Sulphate or Salbutamol Inhaler may also be used and if necessary 10-20mL of Aminophylline Injection B.P. by slow intravenous injection at a rate of 2mL per minute.

viii A parenteral steroid such as 200-600mg Hydrocortisone Injection B.P., intravenously, may help to prevent persistent bronchospasm.

ix Patients experiencing an anaphylaxis reaction should be admitted to hospital for close monitoring for at least 24 hours.

STOP TREATMENT IN PATIENTS WITH SEVERE REACTIONS

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 https://nzphvc.otago.ac.nz/reporting/

4.9 Overdose
See above 4.4 Special warnings and precautions for use

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: V (various); C1 Allergy (desensitization); P1 Allergens and Antigens.
ATC classification: V01

Mechanism of action
The precise mechanism of SIT is not known

Pharmacodynamic effects
The following biological changes have been demonstrated:

- appearance of specific antibodies (IgG) which act as blocking antibodies
- reduction of specific plasma IgE levels in some cases
- change in the behaviour of cells involved in allergic reaction
- favourable change in TH2 and TH1 lymphocyte activities, leading to the production of cytokines (decrease in IL-4 and increase in IFNγ) that regulate IgE production.

At the same time Specific Immunotherapy stimulates an immune response which is maintained over long periods by immunological memory.

SIT acts directly upon the patient's immune system, providing lasting hyposensitisation and preventing progression of the allergy to more severe forms.

SIT is more effective if treatment is initiated at an early age. Thus, in children SIT may be started from the age of 5 years. It should be administered to children or young adults as soon as it is justified by the severity of the allergic symptoms. When immunotherapy is contemplated for very young children, consultation with a specialist paediatric immunologist/allergist is essential. The physician who administers the injections should be able to treat a systemic reaction appropriately. In adults aged over 50 years, SIT remains indicated in cases of recent sensitisation.

5.2 Pharmacokinetic properties
There is no information available

5.3 Preclinical safety data
There are no preclinical data

6 PHARMACEUTICAL PARTICULARS
6.1 List of excipients
Aluminium hydroxide, sodium chloride, phenol, mannitol and water for injection**.**

6.2 Incompatibilities
In the absence of compatibility studies, this medicine must not be mixed with other medicines.

6.3 Shelf life
18 months from date of manufacture
The vial may be stored refrigerated between 2° to 8 °C for up to 6 months once opened. Do not use after the expiry date. Do not freeze.

6.4 Special precautions for storage
Store at 2° to 8°C (Refrigerate, do not freeze)
For storage conditions after first opening of the medicine, see section 6.3.

6.5 Nature and contents of container
Initial treatment set: 3 vials, each vial containing either 0.1, 1.0 and 10.0 IR/mL or IC/mL.
Maintenance: a single vial containing 10.0 IR/mL or IC/mL.

Available Concentrations: Vial containing 5 mL of suspension.

Yellow cap:	0.1	IR/mL	or 0.1	IC/mL
Green cap:	1.0	IR/mL	or 1.0	IC/mL
Blue cap:	10.0	IR/mL	or 10.0	IC/mL

6.6 Special precautions for disposal and other handling
Any unused medicine or waste material should be disposed of in accordance with local requirements.

7 MEDICINE SCHEDULE
PRESCRIPTION ONLY MEDICINE

8 SPONSOR
Sponsor in New Zealand
Stallergenes Greer New Zealand
Level 1, 24 Manukau Road,
Epsom, Auckland 1023
New Zealand
Ph: 0800 824 166

9 DATE OF FIRST APPROVAL

Date of publication in the New Zealand Gazette of consent to distribute the medicine:
19 October 2006

10 DATE OF REVISION OF THE TEXT

Date of Datasheet preparation: 6 June 2019
Version 2.5

SUMMARY TABLE OF CHANGES

Section Changed	**Summary of new information**
8 SPONSOR	Sponsor has been changed from EBOS to Stallergenes Greer NZ and hence the updated sponsor details
NA	Reformat to the new Medsafe format (updating headings and/or subheadings, updating numbering and cross-references of tables and figures, and inclusion of standard text)
NA	Update the table below which lists the ALUSTAL products availability in Australia and New Zealand

ALUSTAL ALLERGEN EXTRACT AVAILABILITY IN AUSTRALIA AND NEW ZEALAND

REGISTRATION NAME	**ACTIVE INGREDIENT**	**AUSTRALIA AUST R**	**NEW ZEALAND**
Mites			
ALUSTAL House Dust Mites Extract	*Dermatophagoides pteronyssinus* and *Dermatophagoides farinae* body extracts	AUST R 132680 (M) AUST R 132725 (I)	X
ALUSTAL European Dust Mite Extract	*Dermatophagoides pteronyssinus* body extract	AUST R 132678 (M) AUST R 132723 (I)	TT50-6900a (I) TT50-6900b (M)
ALUSTAL American Dust Mite Extract	*Dermatophagoides farinae* body extract)	AUST R 132679 (M) AUST R 132724 (I)	TT50-6900/1a (I) TT50-6900/1b (M)
Animals			
ALUSTAL Cat Epithelia Extract	Feline epithelium extract	X	TT50-6901a (I) TT50-6901b (M)
ALUSTAL Dog Epithelia Extract	Canine epithelium extract	X	TT50-6901/1a (I) TT50-6901/1b (M)
ALUSTAL Horse Epithelia Extract	Equine epithelium extract	X	X
ALUSTAL Feathers Mix Extract	Chicken feather/ Duck feather/ Goose feather extract	X	X
Pollens			
ALUSTAL Birch Pollen Extract	*Betula alba* pollen extract	X	TT50-6902a (I) TT50-6902b (M)
ALUSTAL Oleaceae Pollen Mix Extract	*Fraxinus excelsior/ Olea europaea/* *Ligustrum vulgare* pollen extracts	X	TT50-6902/1a (I) TT50-6902/1b (M)
ALUSTAL Plantain Pollen Extract	*Plantago lanceolata* extract	AUST R 132838 (M) AUST R 132839 (I)	TT50-6902/3a (I) TT50-6902/3b (M)
ALUSTAL Fat Hen Pollen Extract	*Chenopodium album* extract	X	TT50-6902/4a (I) TT50-6902/4b (M)
ALUSTAL Sorrel Pollen Extract	*Rumex acetosa* pollen extract	X	X
ALUSTAL Wheat Pollen Extract	*Triticum aestivum* pollen extract	X	X
ALUSTAL Bermuda Grass Extract	*Cynodon dactylon* pollen extract	AUST R 132834 (M) AUST R 132835 (I)	X
ALUSTAL Rye Grass Extract	*Lolium perenne* pollen extract	AUST R 132843 (M) AUST R 132844 (I)	X

ALUSTAL Olive Tree Extract	*Olea europea* pollen extract	AUST R 132840 (M) AUST R 132841 (I)	X
ALUSTAL Extract of Three Grasses	*Dactylis glomerata / Lolium perenne/ Phleum pratense* pollen extracts	AUST R 132845 (M) AUST R 132846 (I)	X
ALUSTAL Extract of Five Grasses	*Dactylis glomerata / Poa pratensis / Lolium perenne / Anthoxanthum odoratum / Phleum pratense* pollen extracts	AUST R 132847 (M) AUST R 132848 (I)	TT50-6902/6a (I) TT50-6902/6b (M)
ALUSTAL Extract of Twelve Grasses	*Agrostis tenuis / Cynodon dactylon Bromus inermis / Dactylis glomerata / Festuca elatior / Poa pratensis / Arrhenatherum elatius / Lolium perenne / Anthoxantum odoratum / Phleum pratense / Avena fatua / Holcus latanus* pollen extracts	AUST R 132849 (M) AUST R 132850 (I)	X

X = Not Available; I = Initial treatment; M = Maintenance treatment

Patient Verification

The following table has been provided to allow the patient and physician to verify that the vial specifically for the patient is being used at time of treatment.

	Injection	Date	Vial (concentration)	Physician's Initial	Patient's Initial
Initial Set	1		0.1 IR/mL or 0.1 IC/mL (Yellow cap)		
	2				
	3				
	4				
	5		1 IR/mL or 1 IC/mL (Green cap) 1 IR/mL or		
	6				
	7				
	8				
Maintenance Set	9		10 IR/mL or 10 IC/mL (Blue cap)		
	10				
	11				
	12				
	13				
	14				
	15				
	16				
	17				
	18				
	19				
	20				
	21				
	22				
	23				
	24				
	25				
	26				
	27				
	28				
	29				
	30				
	31				
	32				
	33				
Maintenane Vial	34		10 IR/mL or 10 IC/mL (Blue cap)		
	35				
	36				
	37				
	38				
	39				
	40				
	41				
	42				
	43				
	44				

	Injection	Date	Vial (concentration)	Physician's Initial	Patient's Initial
	45				
	46				
	47				
	48				
	49				
	50				
	51				
	52				
	53				