NEW ZEALAND DATA SHEET

1. PRODUCT NAME

ARDANEST 4% with adrenaline (epinephrine) 1:100,000 solution for injection
ARDANEST 4% with adrenaline (epinephrine) 1:200,000 solution for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

ARDANEST 4% with adrenaline (epinephrine) 1:100,000

1 mL of solution for injection contains articaine hydrochloride 40.00 mg and adrenaline (epinephrine, as tartrate) 0.01 mg.

One cartridge (1.8 mL) contains articaine hydrochloride 72.00 mg and adrenaline (epinephrine, as tartrate) 0.018 mg.

Each 1.8 mL cartridge contains: 0.71 mg of sodium.

For the full list of excipients, see section 6.1.

ARDANEST 4% with adrenaline (epinephrine) 1:200,000

1 mL of solution for injection contains articaine hydrochloride 40.00 mg and adrenaline (epinephrine, as tartrate) 0.005 mg.

One cartridge (1.8 mL) contains articaine hydrochloride 72.00 mg and adrenaline (epinephrine, as tartrate) 0.009 mg.

Each 1.8 mL cartridge contains: 0.71 mg of sodium.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection, for local and regional dental anaesthesia.

The solution is a clear, non-opalescent, colourless liquid with a pH ranging from 3.0 to 4.3. The osmolality of the solution is approximately 267 mOsm/kg.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

ARDANEST 4% with adrenaline (epinephrine) 1:100,000 and **ARDANEST 4% with adrenaline (epinephrine) 1:200,000** are indicated for infiltration anaesthesia and nerve block anaesthesia in dentistry. **ARDANEST 4% with adrenaline (epinephrine) 1:100,000** is especially indicated for more complex dental procedures requiring prolonged anaesthesia.

4.2 Dose and method of administration

Dose

The smallest possible volume of solution that will lead to effective anaesthesia should be used.

For extraction of maxillary teeth, 1.7 mL **ARDANEST 4% with adrenaline (epinephrine) 1:100,000** or **ARDANEST 4% with adrenaline (epinephrine) 1:200,000** per tooth suffices in most cases, thereby avoiding painful palatal injections. A smaller injection volume is often possible for serial extractions of neighbouring teeth.

If a cut or suture is required in the palate, a palatal injection of approximately 0.1 mL per puncture is indicated.

For smooth extractions of mandibular premolar teeth, infiltration anaesthesia of 1.7 mL **ARDANEST 4% with adrenaline (epinephrine) 1:100,000** or **ARDANEST 4% with adrenaline (epinephrine) 1:200,000** per tooth is mostly sufficient; in single cases a buccal re-injection of 1 – 1.7 mL is required. In rare cases an injection into the mandibular foramen can be indicated.

Vestibular injections of 0.5 – 1.7 mL per tooth enable cavity and crown stump preparations.

Nerve-block anaesthesia should be used in the treatment of mandibular molar teeth.

Paediatric population
Generally, in children weighing about 20 – 30 kg, a dose of 0.25 – 1 mL is sufficient; and in children weighing 30 – 40 kg, a dose of 0.5 – 2 mL. **ARDANEST 4% with adrenaline (epinephrine) 1:100,000** or **ARDANEST 4% with adrenaline (epinephrine) 1:200,000** must not be used in children under the age of 4 years.

Dosing in elderly patients and patients with underlying diseases
Increased plasma levels can occur in older patients due to diminished metabolic processes and lower distribution volume. The risk of accumulation is increased, in particular after repeated administration (e.g. re-injection). A similar effect can ensue where the general condition of the patient is poor, and in severely impaired hepatic and renal function (see section 4.4). In these cases, a lower dose range (minimum quantity for sufficient anaesthetic depth) is recommended.

The dose should also be reduced in patients with certain pre-existing diseases (angina pectoris, arteriosclerosis) (see section 4.4).

Maximum Recommended Dose

Adults:
For healthy adults the maximum dose is 7 mg/kg body weight articaine (500 mg for a 70 kg patient), equivalent to 12.5 mL **ARDANEST 4% with adrenaline (epinephrine) 1:100,000** or **ARDANEST 4% with adrenaline (epinephrine) 1:200,000**. The maximum dose represents 0.175 mL of solution per kg.

Children:
The quantity to be injected should be determined by the age and weight of the child and the magnitude of the operation. Do not exceed the equivalent of 7 mg articaine/kg (0.175 mL/kg) of body weight.

ARDANEST 4% with adrenaline (epinephrine) 1:100,000 may be more appropriate for procedures of longer duration and when there is a risk of significant bleeding into the operative field (see section 5.1 for information on duration of analgesia). The duration of anaesthesia during which an operation can be performed using **ARDANEST 4% with adrenaline (epinephrine) 1:100,000** is up to 75 minutes.

Method of Administration

For injection / oromucosal use in dental anaesthesia only.

To avoid intravascular injection, aspiration control in at least two planes (rotation of the needle by 180^{o}) must always be carefully undertaken, although a negative aspiration result does not rule out an unintentional and unnoticed intravascular injection.

The injection rate should not exceed 0.5 mL in 15 seconds, i.e. 1 cartridge per minute.

Major systemic reactions resulting from accidental intravascular injection can in most cases be avoided by the injection technique: after aspiration slow injection of 0.1 – 0.2 mL followed by slow injection of the remainder no sooner than 20 – 30 seconds later.

For single use only. Opened cartridges must not be used in other patients. Any unused solution must be discarded.

Instructions for use
1. Open the package (plate with 10 cartridges).
2. Take a cartridge and place it in the barrel of the syringe.
3. Move the plunger of the syringe into position on the rubber stopper of the cartridge.
4. Carefully introduce the short end of the double-end needle in the needle hit and screw it.
5. Remove the protective cover of the long end of the needle and carry out the injection.

4.3 Contraindications

Use in children under the age of 4 years.

Hypersensitivity to any ingredients (see section 2 and 6.1). In general, patients with demonstrated hypersensitivity to articaine and other amides should receive an ester-group local anaesthetic for subsequent procedures.

Due to the local anaesthetic ingredient articaine, do not use in the event of:
- known allergy or hypersensitivity to local anaesthetics of the amide type;
- severe impairment of the nerve impulses and conduction system of the heart (e.g. grade II and III AV block, pronounced bradycardia);
- acutely decompensated cardiac insufficiency;
- severe hypotension;
- patients who are known to have a deficiency in plasma cholinesterase activity;
- haemorrhagic diatheses, particularly with nerve-block anaesthesia.

Do not inject into inflamed or infected areas.

Due to the content of adrenaline as a vasoconstrictor admixture, do not use in the event of:
- heart disease such as unstable angina pectoris, recent myocardial infarction, recent coronary artery bypass surgery, refractory arrhythmias and paroxysmal tachycardia or high-frequency continuous arrhythmia, untreated or uncontrolled hypertension, arterial hypertension, untreated or uncontrolled congestive heart failure, valvular cardiac disease (particularly sequelae to acute rheumatic fever), untreated thyrotoxicosis;
- concomitant treatment with monoamine oxidase (MAO) inhibitors or tricyclic antidepressants (see section 4.5).

ARDANEST 4% with adrenaline (epinephrine) 1:100,000 and **ARDANEST 4% with adrenaline (epinephrine) 1:200,000** must not be used in persons who are allergic or hypersensitive to sulfite, as well as in persons with severe bronchial asthma. **ARDANEST 4% with adrenaline (epinephrine)**

1:100,000 and **ARDANEST 4% with adrenaline (epinephrine) 1:200,000** can provoke acute allergic reactions with anaphylactic symptoms (e.g. bronchospasm).

4.4 Special warnings and precautions for use

Special warnings

Use with particular caution in the event of:
- severe impairment to renal function;
- angina pectoris (see sections 4.2 and 4.3);
- arteriosclerosis;
- considerably impaired blood coagulation (see section 4.5);
- thyrotoxicosis;
- narrow-angle glaucoma;
- diabetes mellitus;
- lung diseases, particularly allergic asthma;
- pheochromocytoma.

Accidental intravenous injection may be associated with convulsions, followed by central nervous system or cardiorespiratory arrest. Resuscitative equipment, oxygen and other resuscitative drugs should be available for immediate use.

Since amide-type local anaesthetics are metabolised in the liver, use with caution in patients with hepatic disease. Patients with severe hepatic disease are at greater risk of developing toxic plasma levels.

Administer with caution in patients with impaired cardiovascular function since they may be less able to compensate for functional changes associated with the prolongation of A-V conduction produced by these drugs.

Administer with caution to patients with a history of epilepsy.

There is the possibility of a positive doping test result.

Inadvertent vasopuncture can lead to serious bleeding during treatment with anticoagulants (e.g. heparin or acetylsalicylic acid), and in general haemorrhagic tendency is increased.

Avoid inadvertent intravascular injection (see section 4.2).

In the case of cavity or crown preparations the risk of overlooking an opened pulp must be taken into account since adrenaline reduces blood flow in the pulp tissue.

Precautions for Use

Before a local anaesthetic is used the following drugs/therapy should be available:
anti-convulsant medicines (benzodiazepines or barbiturates), myorelaxants, atropine and vasopressors or adrenaline for a severe allergic or anaphylactic reaction; resuscitating equipment (in particular a source of oxygen) enabling artificial ventilation if necessary.

Cardiovascular and respiratory vital signs and the patient's state of consciousness should be monitored after each local anaesthetic injection. Restlessness, anxiety, tinnitus, dizziness, blurred vision, tremors, depression or drowsiness may be early signs of central nervous system toxicity and require rapid corrective measures to prevent possible worsening (see section 4.9).

Although age-dependent adjustments are not required, it is advisable to take particular care when giving an injection to elderly patients and children.

Patients taking phenothiazines
Phenothiazines may reduce or reverse the pressor effect of adrenaline. Concurrent use of these agents should generally be avoided. In situations where concurrent therapy is necessary, careful patient monitoring is essential.

Patients taking non-selective beta-blockers
The concomitant administration of non-cardioselective beta-blockers can lead to an increase in blood pressure due to adrenaline (see section 4.5).

The administration of large doses of articaine may produce methaemoglobinaemia in patients with subclinical methaemoglobinaemia.

This medicinal product contains sodium metabisulfite, which can cause allergic reactions (possibly delayed) and, on occasions, bronchospasm.

This medicinal product also contains 0.71 mg of sodium per cartridge. This may be harmful for patients on low-sodium diets.

Paediatric population
Carers of small children must be informed that due to prolonged soft tissue insensitivity there is a risk that children may accidentally bite themselves.

4.5 Interaction with other medicinal products and other forms of interaction

The sympathomimetic effect of adrenaline can be intensified by the simultaneous intake of MAO inhibitors or tricyclic antidepressants (see section 4.3).

Adrenaline can inhibit insulin release in the pancreas and thus diminish the effect of oral anti-diabetics.

Phenothiazines can reduce the pressor effect of adrenaline (see section 4.4).

Concomitant administration of antiarrhythmic drugs (e.g. quinidine) can increase the potential cardiac effects of local anaesthetics.

The concomitant administration of non-cardioselective beta-blockers can lead to an increase in blood pressure due to the adrenaline component of **ARDANEST 4% with adrenaline (epinephrine) 1:100,000** and **ARDANEST 4% with adrenaline (epinephrine) 1:200,000**.

Certain inhalational anaesthetics, such as halothane, can sensitise the heart to catecholamines and therefore induce arrhythmias following administration of **ARDANEST 4% with adrenaline (epinephrine) 1:100,000** and **ARDANEST 4% with adrenaline (epinephrine) 1:200,000**.

Haemorrhagic tendency is increased during treatment with anti-coagulants (see section 4.4).

Cross-reactivity to articaine has been reported in a patient with delayed hypersensitivity to prilocaine.

4.6 Fertility, pregnancy and lactation

No clinical experience of use in pregnant and lactating women is available.

Fertility

No information available.

Pregnancy
Safe use of local anaesthetics during pregnancy with respect to adverse effects on foetal development has not been established. The medicine should only be used if the expected benefit to the patient outweighs the risk to the foetus.

Breastfeeding
The excretion of articaine and its metabolites in human milk is unknown. Preclinical safety data suggests that the amount of articaine in breast milk does not reach clinically relevant levels. It is recommended that nursing mothers express and discard the first mother's milk following anaesthesia with articaine.

4.7 Effects on ability to drive and use machines

It has been observed that local anaesthesia with articaine does not perceivably hinder normal ability to drive a vehicle. The dentist has to decide whether the patient is capable of returning to operate a machine or drive a vehicle. The possible apprehension and stress resulting from the intervention could affect the patient´s ability to function as usual.

4.8 Undesirable effects

Adverse reactions as a result of the local anaesthetic component articaine

Cardiovascular disorders:
Rare (≥1/10,000 to <1/1,000)
Decreased heart rate, hypotension.
Drop in blood pressure, cardiac impulse conduction disorders, bradycardia, asystole, cardiovascular arrest.

Nervous system disorders:
Rare (≥1/10,000 to <1/1,000)
Metallic taste, tinnitus, vertigo, nausea, vomiting, restlessness, anxiety, yawning, agitation, nervousness, nystagmus, logorrhea, headache, increased respiratory rate.
Paresthesia (loss of sensitivity, burning, tingling) of the lips, tongue or both.
When these signs appear, rapid corrective measures are required to prevent possible worsening.
Drowsiness, confusion, tremors, muscle spasms, tonic-clonic seizure, coma and respiratory paralysis.

Respiratory disorders:
Rare (≥1/10,000 to <1/1,000)
Tachypnea, after bradypnea, which can lead to apnoea.

Allergic reactions:
Very rare (<1/10.000), unknown frequency (cannot be estimated based on the data available)
Manifestations of hypersensitivity to articaine such as: rash, pruritus, edematous pruritus and erythema, as well as nausea, diarrhoea, wheezing or anaphylaxis. Cross-reactivity to articaine has been reported in a patient with delayed hypersensitivity to prilocaine.
In general, patients who have demonstrated hypersensitivity to articaine or other amides should receive an ester local anaesthetic for subsequent procedures.
Administration of large doses of articaine may produce methaemoglobinaemia in patients with subclinical methaemoglobinaemia.

Adverse reactions as a result of the content of adrenaline as a vasoconstrictor component

Cardiovascular disorders:
Rare (≥1/10,000 to <1/1,000)
Hot sensation, sweating, accelerated pulse, migraine headaches, increased blood pressure, angina pectoris disorders, palpitations, tachyarrhythmias and cardiac arrest; oedematous swelling of the thyroid should also not be excluded.

Adverse reactions in isolated cases as a result of the content of sulfite as excipient

Particularly in bronchial asthmatics, allergic or hypersensitivity reactions which are manifested as vomiting, diarrhoea, wheezing, acute asthma attack, clouding of the consciousness or shock may occur.

Adverse reactions as a result of the articaine and adrenaline content

Nervous system disorders:
Two weeks after use of articaine/epinephrine, the appearance of facial nerve paralysis has been reported, persisting up to 6 months after the event.

The simultaneous occurrence of several complications and adverse reactions may interfere with the clinical picture.

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

Adverse reactions (showing an abnormally high concentration of local anaesthetic in the blood), may appear either immediately, as a result of accidental intravascular injection or abnormal absorption conditions, for example in inflamed or intensely vascularised tissue, or later, caused by true overdose following injection of an excessive amount of the anaesthetic solution, manifesting itself as central nervous and/or vascular symptoms.

Symptoms caused by the local anaesthetic component articaine:
Mild central nervous symptoms include metallic taste, tinnitus, vertigo, nausea, vomiting, restlessness, anxiety, initial increase in respiratory rate.
More serious symptoms are: drowsiness, confusion, tremors, sudden muscle spasms, tonic-clonic seizures, coma and respiratory paralysis.
Severe cardiovascular episodes may occur in the form of a drop in blood pressure, cardiac impulse conduction disorders, bradycardia, cardiovascular arrest.

Symptoms caused by adrenaline as vasoconstrictor:
Cardiovascular symptoms such as hot sensation, sweating, accelerated heart rate, headaches, increased blood pressure, angina pectoris disorders, tachycardia, tachyarrhythmias and cardiovascular arrest.

The simultaneous occurrence of several complications and adverse reactions may interfere with the clinical picture.

Therapy

Basic general measures:
In the event of an adverse reaction, application of the local anaesthetic must be interrupted. Diagnosis (respiration, circulation, consciousness), maintenance/restoration of the respiratory and circulatory vital signs, administration of oxygen, intravenous access.

Special measures:
Hypertension: Raise the upper part of the body, sublingual administration of nifedipine if necessary.

Convulsions: Protect the patient from concomitant damage, administer benzodiazepines (for example iv diazepam) if necessary.

Hypotension: Horizontal position, intravascular infusion of a whole electrolyte solution, vasopressor (for example iv ethilefrine), if necessary.

Bradycardia: Atropine iv.

Anaphylactic shock: Contact an emergency doctor, in the meantime place the patient in the shock position, give generous infusion of a complete electrolyte solution, iv adrenaline and/or iv cortisone if necessary.

Cardiovascular arrest: Immediate cardiopulmonary resuscitation, contact an emergency doctor.

For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764 766).

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Anaesthetics, local, amides; ATC-Code: N01B B58

Articaine is a local anaesthetic of the amide type. Local anaesthetics produce reversible loss of sensation by preventing or diminishing the conduction of sensory nerve impulses by decreasing the permeability of the nerve cell membrane to sodium ions. Articaine is thought to act by blocking the voltage-dependent Na^+ channels on the membrane of the nerve fibre.

Adrenaline is a vasoconstrictor added to retard diffusion and limit absorption of the local anaesthetic, thereby prolonging the duration of effect and lessening the danger of toxicity.

Complete anaesthesia can be achieved within 1-3 minutes of administration. The mean duration of effect in pulpal anaesthesia is 48 – 54 minutes for **ARDANEST 4% with adrenaline (epinephrine) 1:200,000** and at least 75 minutes for **ARDANEST 4% with adrenaline (epinephrine) 1:100,000**. For surgical interventions in soft tissue the mean duration of effect is 120 – 240 minutes.

Clinical efficacy and safety

Three randomised, double-blind, active-controlled studies were designed to evaluate effectiveness of articaine hydrochloride 4% with adrenaline 1:100,000 as a dental anaesthetic. A total of 882 patients received articaine hydrochloride 4% with adrenaline 1:100,000. Of these, 7% were between 4 and 16 years old, 87% were between 17 and 65 years old, and 6% were at least 65 years old. In addition, 53% of patients were female and 47% were male, with a racial/ethnic distribution of 73% white, 11% Hispanic, 8% black, 5% Asian and 3% ‘other’ races/ethnicities. These patients underwent simple

dental procedures, single apical resections and single crown procedures, and complex dental procedures such as multiple extractions, multiple crowns and/or bridge procedures, multiple apical resections, alveolectomies, muco-gingival operations, and other surgical procedures on the bone. Articaine hydrochloride 4% with adrenaline 1:100,000 was administered as submucosal infiltration and/or nerve block. Efficacy was measured immediately following the procedure by having the patient and investigator rate the patient's procedural pain using a 10 cm visual analog scale (VAS), in which a score of zero represented no pain, and a score of 10 represented the worst pain imaginable. Mean patient and investigator VAS pain scores were 0.3 – 0.4 cm for simple procedures and 0.5 – 0.6 cm for complex procedures. These values are summarised in Table 1 below.

Table 1. Summary of VAS Pain Scores

	Articaine HCl 4% with adrenaline acid tartrate 1:100,000	
	Simple procedures	Complex procedures
Number of patients	674	207
Investigator score (cm)		
Mean	0.3	0.5
Median	0.0	0.2
Range	0 – 9.0	0 – 7.3
Patient score (cm)		
Mean	0.4	0.6
Median	0.0	0.2
Range	0 – 8.0	0 – 8.7

In clinical trials, 61 paediatric patients between the ages of 4 and 16 years received articaine hydrochloride 4% with adrenaline 1:100,000. Among these paediatric patients, doses from 0.76 mg/kg to 5.65 mg/kg (0.9 to 5.1 mL) were administered safely to 51 patients for simple procedures and doses between 0.37 mg/kg and 7.48 mg/kg (0.7 to 3.9 mL) were administered safely to 10 patients for complex procedures. However, there was insufficient exposure to articaine hydrochloride 4% with adrenaline 1:100,000 at doses greater than 7.00 mg/kg in order to assess its safety in paediatric patients. No unusual adverse events were noted in these patients. Approximately 13% of these paediatric patients required additional injections of anaesthetic for complete anaesthesia.

In the clinical trials 54 patients between the ages of 65 and 75 years, and 11 patients 75 years and over received articaine hydrochloride 4% with adrenaline 1:100,000. Among all patients between 65 and 75 years, doses from 0.43 mg/kg to 4.76 mg/kg (0.9 to 11.9 mL) were administered safely to 35 patients for simple procedures and doses from 1.05 mg/kg to 4.27 mg/kg (1.3 to 6.8 mL) were administered safely to 19 patients for complex procedures. Among the 11 patients ≥ 75 years old, doses from 0.78 mg/kg to 4.76 mg/kg (1.3 to 11.9 mL) were administered safely to 7 patients for simple procedures and doses of 1.12 mg/kg to 2.17 mg/kg (1.3 to 5.1 mL) were administered to 4 patients for complex procedures.

5.2 Pharmacokinetic properties

Absorption and distribution
ARDANEST 4% with adrenaline (epinephrine) 1:100,000 and **ARDANEST 4% with adrenaline (epinephrine) 1:200,000** are rapidly and almost completely absorbed.

The peak plasma concentration of articaine, after an intraoral injection, is reached after about 10-15 minutes.

The distribution volume is 1.67 l/kg, the elimination half-life is approximately 20 minutes and the Cmax value is between 400 and 2100 µg/l.

Up to 95 % of articaine is bound to plasma proteins.

Metabolism and excretion
Articaine is rapidly hydrolysed by plasma cholinesterases to its primary metabolite, articainic acid, which is subsequently metabolised to articainic acid glucoronide. Articaine and its metabolites are eliminated primarily in the urine.

Adrenaline is catabolised rapidly in the liver and other tissues. The metabolites are excreted via the kidneys.

5.3 Preclinical safety data

The toxic symptoms of articaine were independent of the administration route (iv, im, sc or oral) or the animal species, and included tremors, vertigo and tonic-clonic seizures. The duration and intensity of these symptoms were dose-dependent; at high doses (single dose of approximately 50-100 mg/kg) convulsions led to death and at low doses, all symptoms disappeared in 5 - 10 minutes. Lethal doses of articaine produced a pulmonary oedema in mice (iv and sc) and in rats (iv, im, and sc and oral).

In rats, rabbits and cats, it showed no effect on embryo or foetal development in the uterus and there were no organ or skeletal abnormalities. Young being weaned by mothers who received a high dose (80 mg/kg/day) of articaine, which led to maternal toxicity, showed delayed eye opening and were more likely to fail the passive avoidance test.

Adrenaline was potentially teratogenic in albino rats at doses 25 times the human therapeutic dose.

After iv administration, the presence of 1:100,000 adrenaline increased articaine toxicity in rats and mice but not in rabbits.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium metabisulfite (E223)
Sodium chloride
Citric acid
Hydrochloric acid (for pH adjustment)
Sodium hydroxide (for pH adjustment)
Water for injections.

6.2 Incompatibilities

Not applicable.

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

24 months.

6.4 Special precautions for storage

Store below 30^{o}C. Keep the cartridge in the outer carton in order to protect from light.

6.5 Nature and contents of container

Cartridge made of colourless and neutral glass I. Plunger is made of bromobutyl rubber. Aluminium cap with a bromobutyl disc.

Container with 50 and 100 cartridges of 1.8 mL each. Not all pack sizes may be marketed.

6.6 Special precautions for disposal

This product must be visually inspected to detect particles, discoloration or damage to the container prior to administration. The product must not be used if these defects are detected.

The product is for single use only. Any amount of unused product should be discarded immediately after use.

The disposal of unused product and any material that has been in contact with it should be carried out in accordance with local regulations.

7. MEDICINE SCHEDULE

Prescription Medicine

8. SPONSOR

DE Healthcare Limited
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Albany
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Phone: +64 21 035 1588

9. DATE OF FIRST APPROVAL

10 September 2015

10. DATE OF REVISION OF THE TEXT

6 January 2022

SUMMARY TABLE OF CHANGES

Section changed	Summary of new information
8	Sponsor change