NEW ZEALAND DATA SHEET

1 PRODUCT NAME

3% Citanest® DENTAL with Octapressin® Injection

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

3% Citanest® DENTAL with Octapressin® injection solution contains 30 mg/mL prilocaine hydrochloride and 0.54 micrograms/mL felypressin.

For the full list of excipients, see Section 6.1 List of excipients.

3 PHARMACEUTICAL FORM

3% Citanest® DENTAL with Octapressin® is a sterile aqueous solution. The pH of the solution is 3.5-5.2.

3% Citanest® DENTAL with Octapressin® injection solution in a standard and self-aspirating glass cartridge.

The finished products is a clear and colourless solution packed in a carton containing 100 units of 1.8 mL or 2.2 mL Type 1 glass cartridges, closed on one end with a self-aspirating bromobutyl rubber plunger and at the other end by a bromobutyl disk covered by an aluminium cap. The ampoules and cartridges are free from preservatives and are intended for single use only.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

- Infiltration anaesthesia in dentistry, where there is no need for profound ischaemia in the injected area.
- Regional nerve block anaesthesia in dentistry.

4.2 Dose and method of administration

3% Citanest® DENTAL with Octapressin® has a rapid onset of action after infiltration anaesthesia, with an average of 2-3 minutes. Inferior alveolar nerve block requires 5 minutes or more to take full effect. The duration of effective anaesthesia varies in individuals and depends on the type of block. The average duration of useful anaesthesia after infiltration is 45 minutes. After successful regional block, e.g. inferior alveolar nerve block, anaesthesia lasts for 2 hours or longer.

Injections should always be made slowly with careful aspiration before and intermittently during injection to avoid inadvertent intravascular injection, which may have toxic effects.

The lowest dose that results in effective anaesthesia should be used. The dose will also depend on the area of the oral tissues to be anaesthetised, the vascularity of the oral tissues and the technique of anaesthesia. The total dose must be adjusted to the age, size and physical status of the patient.

For effective local anaesthesia in most dental procedures, an adequate dose of 3% Citanest® DENTAL with Octapressin® solution injected into the tissue is:

In normally healthy adults: 1-5 mL (equivalent to 30-150 mg prilocaine hydrochloride). For routine dental procedures, a dose of 10 mL (equivalent to 300 mg prilocaine hydrochloride) 3% Citanest® DENTAL with Octapressin® should not be exceeded.

Children under 10 years of age: 1-2 mL (equivalent to 30-60 mg prilocaine hydrochloride).

A rapid rate of injection may lead to complications due to the high concentration (see Section 4.9 Overdose) even after the injection of small amounts. This is more likely following accidental intravascular injection. The injected medicine could be transported in a retrograde manner along a blood vessel and, in cases of intra-arterial injection in the head and neck area, reach the brain.

4.3 Contraindications

- Known history of hypersensitivity to local anaesthetic agents of the amide type.
- Congenital or idiopathic methaemoglobinaemia.

4.4 Special warnings and precautions for use

The safety and effectiveness of the local anaesthetic agent, prilocaine hydrochloride, depends on the proper dosage, the correct injection technique, adequate precautions and readiness for emergencies.

Although largely free of side-effects, as an additive to prilocaine, felypressin may cause a rise in blood pressure or coronary constriction if an overdose is given.

Before administering a local anaesthetic medicine, make sure that resuscitative equipment, such as equipment required for oxygenation and assisted ventilation, and medicine for the treatment of toxic reactions are immediately available.

The patient should be advised to exert caution to avoid inadvertent trauma to the lips, tongue, cheek mucosa or soft palate when these structures are anaesthetised. The ingestion of food should therefore be postponed until normal function and sensation returns.

In the head and neck area, due to the proximity of the CNS, the intravascular injection of even small doses of local anaesthetics may cause systemic adverse reactions similar to those seen after the inadvertent intravascular injection of larger doses in other parts of the body.

Even if the dose of 3% Citanest® DENTAL with Octapressin® used in dental practice is generally small, some patients may require special attention to reduce the risk of dangerous side effects:

- Patients with partial or complete heart block due to the fact that local anaesthetics may depress myocardial conduction.
- Patients with advanced liver disease or severe renal dysfunction.
- The elderly and patients in poor general condition.

Local anaesthetics should be administered with caution to patients with severe or untreated hypertension, severe heart disease, severe anaemia or circulatory failure from whatever cause, or any other pathological condition. Local anaesthetics should be avoided when there is infection in the region of the proposed injection.

Regarding methaemoglobin formation see Section 4.8 Undesirable effects.

4.5 Interaction with other medicines and other forms of interaction

Prilocaine should be used with caution in patients receiving agents structurally related to local anaesthetics, since the toxic effects are additive.

Medicines which may predispose to methaemoglobin formation, e.g. sulphonamides, antimalarials and certain nitric compounds, could potentiate this adverse effect of prilocaine.

Due to its very low acute toxicity, felypressin does not increase the toxicity of a prilocaine solution.

4.6 Fertility, pregnancy and lactation

It is reasonable to assume that 3% Citanest® DENTAL with Octapressin® has been administered to a large number of pregnant women and women of child-bearing age. No specific disturbances to the reproductive process have so far been reported, e.g. an increased incidence of malformations or other direct or indirect harmful effects on the foetus.

Methaemoglobinaemia in the neonate has been reported after the administration of prilocaine to the mother in doses exceeding 600 mg.

Prilocaine may enter the mother's milk, but in such small amounts that there is generally no risk of this affecting the neonate. It is not known whether felypressin is excreted in breast milk.

4.7 Effects on ability to drive and use machines

Depending on dosage, local anaesthetics may have a very mild effect on mental function and may temporarily impair locomotion and co-ordination.

4.8 Undesirable effects

Reactions to 3% Citanest® DENTAL with Octapressin® are very rare in the doses used in dental procedures. If adverse reactions occur, they are similar in character to those observed with other local anaesthetics.

Allergic Reactions
Allergic reactions (in the most severe instances anaphylactic shock) to local anaesthetics of the amide type are rare.

Neurological Complications
The incidence of adverse neurological reactions (e.g. persistent neurological deficit) associated with the use of local anaesthetics is very low. Neurological reactions may be dependent upon the particular medicine used, the route of administration and the physical status of the patient. Many of these effects may be linked to the injection techniques, with or without a contribution by the medicine. Neurological reactions following regional nerve blocks have included persistent numbness, paraesthesia and other sensory disturbances.

Acute Systemic Toxicity
Prilocaine can cause acute toxic effects if high systemic levels occur due to accidental intravascular injection, fast absorption or overdosage. (See Section 5.1 Pharmacodynamic properties and Section 4.9 Overdose.)

Methaemoglobinaemia
Methaemoglobinaemia may occur after the administration of prilocaine. The repeated administration of prilocaine, even in relatively small doses, can lead to clinically overt methaemoglobinaemia (cyanosis).

The conversion of haemoglobin to methaemoglobin is caused by the prilocaine metabolite, σ-toluidine, which has a long half-life and tends to accumulate, and in turn, by its conversion to 4- and 6-hydroxytoluidine. Methaemoglobin has risen to clinically significant levels in patients receiving high doses of prilocaine. Cyanosis occurs when the methaemoglobin concentration in the blood reaches 1-2 g/100 mL (6-12% of the normal haemoglobin concentration). Methaemoglobin oxidises slowly back to haemoglobin, but this process can be greatly accelerated by giving methylene blue IV (see Section 4.9 Overdose).

The reduction in the oxygen-carrying capacity in normal patients is marginal, hence the cyanosis is usually symptomless. However, in severely anaemic patients it may cause significant hypoxaemia. It is important to rule out other more serious causes of cyanosis such as acute hypoxaemia and/or heart failure. With the dental dosage of prilocaine (1-5 mL 3% Citanest® DENTAL with Octapressin®, i.e. 30-150 mg prilocaine hydrochloride 3% with felypressin 0.54 mcg/mL), the occurrence of methaemoglobinaemia in dental practice

appears remote. However, gross overdosage in dental practice has been reported to cause methaemoglobinaemia.

Note. Even low concentrations of methaemoglobin may interfere with pulse oximetry readings, indicating a false low oxygen saturation.

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 adverse reactions http://nzphvc.otago.ac.nz/reporting/

4.9 Overdose

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

Since prilocaine is the least toxic of the amino-amide local anaesthetics, it is particularly useful in situations where a high dosage of the local anaesthetic may be needed. This advantage, however, should be weighed against the risk of causing methaemoglobinaemia.

Acute emergencies are, in general, dose-related and may result from high plasma levels caused by excessive dosage, rapid absorption (i.e. rate of increase of plasma concentration) or unintentional intravascular injection, or may result from hypersensitivity or diminished tolerance on the part of the patient.

Acute Systemic Toxicity
CNS reactions are excitatory or depressant and may be characterised by nervousness, tinnitus, twitching, euphoria, drowsiness, blurred or double vision, dizziness, convulsions, unconsciousness and possibly respiratory arrest. The excitatory reactions may be very brief or may not occur at all, in which case the first manifestation of toxicity is drowsiness merging into unconsciousness and even respiratory arrest.

Cardiovascular reactions are depressant and may be characterised by hypotension, myocardial depression, bradycardia and possibly cardiac arrest. Signs and symptoms of depressed cardiovascular function may commonly result from a vasovagal reaction, particularly if the patient is in an upright position. Less commonly, they may occur as a direct effect of the medicine. Failure to recognise premonitory signs such as sweating, a feeling of faintness, changes in pulse or sensorium may result in progressive cerebral hypoxia and seizure or serious cardiovascular collapse.

Cardiovascular effects are usually only seen in the most severe cases and are generally preceded by signs of toxicity in the central nervous system.

Acidosis or hypoxia in the patient may increase the risk and severity of toxic reactions. Such reactions involve the central nervous system and the cardiovascular system.

Treatment of Overdosage
The immediate treatment of acute systemic toxicity is as follows:

1. Put the patient in a supine position. Raise the legs 30°-45° above the horizontal level.
2. Ensure a patent airway. If ventilation is inadequate, ventilate the patient, with oxygen if available. This is important since toxicity increases with acidosis.
3. The treatment of convulsions consists of ensuring a patent airway and arresting convulsions. Should convulsions persist despite adequate ventilation, diazepam 0.1 mg/kg or thiopentone sodium 1-3 mg/kg should be administered intravenously to arrest the convulsions. Since this treatment may also depress respiration, a means of mechanically supporting or controlling ventilation should be available.
4. Supportive treatment of circulatory depression may require the administration of intravenous fluids and, when appropriate, a vasopressor (e.g. ephedrine 5-10 mg IV and repeated, if necessary, after 2-3 min), as governed by the clinical situation.

5. If the patient is unresponsive and the carotid pulse rate is totally absent, start external cardiac massage and mouth to mouth resuscitation.

Treatment of Acute Methaemoglobinaemia

If clinical methaemoglobinaemia occurs, it can be rapidly treated by a single intravenous injection of a 1% methylene blue solution, 1 mg/kg body weight, over a 5-minute period. Cyanosis will disappear in about 15 minutes. This dose should not be repeated as methylene blue in high concentrations acts as a haemoglobin oxidant.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Amides, ATC code: N01BB54

Prilocaine is a local anaesthetic of the amide type with a potency and duration similar to lidocaine (lignocaine).

Prilocaine, like other local anaesthetics, causes a reversible blockade of impulse propagation along nerve fibres by preventing the inward movement of sodium ions through the nerve membrane. Local anaesthetics of the amide type are thought to act within the sodium channels of the nerve membrane.

Local anaesthetic medicines may also have similar effects on excitable membranes in the brain and myocardium. If excessive amounts of medicine reach the systemic circulation rapidly, symptoms and signs of toxicity will appear, emanating mainly from the central nervous and cardiovascular systems.

Central nervous system toxicity (see Section 4.9 Overdose) usually precedes the cardiovascular effects as it occurs at lower plasma concentrations. Direct effects of local anaesthetics on the heart include slow conduction, negative inotropism and eventually cardiac arrest.

Felypressin is a suitable alternative to adrenaline as a localising agent, provided that local ischaemia is not essential.

Felypressin is a synthetic hormone with similar properties to vasopressin. In contrast to adrenaline, felypressin does not produce ischaemia distal to or at the injection site. 3% Citanest® DENTAL with Octapressin® is therefore indicated for routine use. It is particularly suitable for use in patients for whom the use of solutions containing sympathomimetic agents is contraindicated.

5.2 Pharmacokinetic properties

Prilocaine has a pKa of 7.9 and an N-heptane/pH 7.4 buffer partition coefficient of 0.9.

Prilocaine is between 40% and 55% protein bound in plasma, mainly to alpha 1-acid glycoprotein.

Prilocaine redistributes rapidly from the blood and it has a large apparent distribution volume of between 190 L and 260 L.

The terminal elimination half-life of prilocaine is 1.6 h.

Prilocaine readily passes through the placenta and free plasma concentrations are similar in both foetus and mother. In the presence of fetal acidosis, they may be slightly higher in the foetus, due to ion trapping. Information concerning the elimination half-life of prilocaine in neonates is not available.

In the liver, prilocaine is primarily metabolized by amide hydrolysis to σ-toluidine and N-propylamine. σ-Toluidine is subsequently hydroxylated to 2-amino-3-hydroxytoluene and 2-amino-5-hydroxytoluene, metabolites which are believed to be responsible for the occurrence of methaemoglobinaemia.

Only a small proportion of prilocaine (less than 5%) is excreted unchanged in the urine. In vitro and animal studies have shown metabolism of prilocaine by lung and kidney tissues.

5.3 Preclinical safety data

No data available.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

- Sodium Chloride
- Sodium Hydroxide
- Hydrochloric Acid
- Water for Injections

6.2 Incompatibilities

Incompatibilities were either not assessed or not identified as part of the registration of this medicine.

6.3 Shelf life

24 months

6.4 Special precautions for storage

Store below 25°C. Protect from light. Do not freeze.

6.5 Nature and contents of container <and special equipment for use, administration or implantation>

Presentation	Fill size	Pack Size	Cartridge type*
3% Citanest® DENTAL with Octapressin, Prilocaine hydrochloride 66 mg/2.2 mL + felypressin (0.066 IU) 1.188 µg/2.2 mL	2.2 mL	50, 100	Standard and self-aspirating cartridges
3% Citanest® DENTAL with Octapressin, Prilocaine hydrochloride 54 mg/1.8 mL + felypressin (0.054 IU) 0.972 µg/1.8 mL	1.8 mL	50, 100	Standard and self-aspirating cartridges

*Type I glass cartridges, closed on one end with either a standard or self-aspirating blue chlorobutyl rubber plunger and at the other end by a chlorobutyl disk covered by an aluminium cap.
Not all pack sizes/presentations are being distributed.

6.6 Special precautions for disposal <and other handling>

Additions to 3% Citanest® DENTAL with Octapressin® used in conjunction with dental procedures are not recommended.

Instructions for Use/Handling

Surface sterilisation using pure, undiluted isopropyl alcohol (91%) or 70% ethyl alcohol may be carried out if desired. Do not soak or autoclave.

The solutions which are free from preservative should be used immediately after opening of the container. Any unused solution should be discarded.

Aspiration (preferably by the use of passive-type aspiration systems) prior to injection is recommended since this reduces the possibility of intravascular injection, thereby keeping the incidence of side effects and anaesthetic failure to a minimum.

In order to avoid traumatic nerve injuries leading to paraesthesia in conjunction with dental nerve blocks, an atraumatic technique should be used. Dental cartridge systems may generate high pressures during injection, leading to local anaesthetics distributing in a retrograde manner along a nerve in cases of intraneural injection.

7 MEDICINE SCHEDULE

Prescription Medicine

8 SPONSOR

Dentsply Sirona (N.Z.) Limited
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9 DATE OF FIRST APPROVAL

31 December 1969

10 DATE OF REVISION OF THE TEXT

14 May 2019

SUMMARY TABLE OF CHANGES

Section changed	Summary of new information
All sections	Updated Data Sheet format according to the new requirements
Section 8	Updated sponsor information