AUSTRALIAN PRODUCT INFORMATION
3% Citanest® DENTAL with Octapressin®
(prilocaine hydrochloride and felypressin)

1 NAME OF THE MEDICINE
prilocaine hydrochloride
felypressin

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
3% Citanest DENTAL with Octapressin is a clear, colourless sterile aqueous 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 injection solution in a standard and self-aspirating glass cartridge.
The finished product is a clear and colourless solution packed in a carton containing either 50 or 100 units of 1.8 mL and 2.2 mL Type I 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.

4 CLINICAL PARTICULARS
4.1 THERAPEUTIC INDICATIONS
3% Citanest DENTAL with Octapressin is indicated for the production of local anaesthesia in routine dental procedures and oral surgery by means of infiltration and nerve block techniques.

4.2 DOSE AND METHOD OF ADMINISTRATION
The lowest dosage that results in effective anaesthesia should be used. The dosage will also depend on the area of the oral cavity to be anaesthetised, the vascularity of the oral tissues and the technique of anaesthesia.
RECOMMENDED DOSAGE FOR 3% CITANEST DENTAL WITH OCTAPRESSIN (0.03 IU/mL or 0.54 μg/mL felypressin) SOLUTION FOR DENTAL ANAESTHETIC PROCEDURES IN THE AVERAGE, HEALTHY, 70KG ADULT PATIENT
### 3% Citanest® DENTAL with Octapressin®

<table>
<thead>
<tr>
<th></th>
<th>Infilt</th>
<th>Block</th>
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<tbody>
<tr>
<td><strong>Suggested Dose</strong></td>
<td>1 mL</td>
<td>1.5 – 2 mL</td>
</tr>
<tr>
<td><strong>Onset of Action</strong></td>
<td>2 min</td>
<td>4 min</td>
</tr>
<tr>
<td><strong>Duration of Action</strong></td>
<td></td>
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</tr>
<tr>
<td>Pulp</td>
<td>40 min</td>
<td>90 min</td>
</tr>
<tr>
<td>Soft Tissue</td>
<td>2.5 hrs</td>
<td>3.5 hrs</td>
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**Note:**

1. **Recommended doses**

   Toxic doses vary widely between patients and toxic effects may occur after any local anaesthetic procedure. Careful observation of the patient must therefore be maintained. It is recommended that the dose of prilocaine at any one time should not exceed 9 mg/kg. However, the dose administered must be tailored to the individual patient and procedure, and the maximum doses here quoted should be used as a guide only.

2. **Safe dose**

   The safe dose for people with acute or chronic disease, especially those on medications, may be substantially less.

### 4.3 CONTRAINDICATIONS

1) Allergy or hypersensitivity to amide type local anaesthetics or other components of the injection solution which may be present (see note under Section 6.5 Nature and Contents of Container). Detection of suspected sensitivity by skin testing is of limited value.

2) Congenital or idiopathic methaemoglobinaemia.

3) Local anaesthetic techniques must not be used when there is inflammation and/or sepsis in the region of the proposed injection.

See also Section 4.5 Interactions with Other Medicines and Other Forms of Interactions.

### 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

1) **WHEN ANY LOCAL ANAESTHETIC AGENT IS USED, RESUSCITATIVE EQUIPMENT AND MEDICINES, INCLUDING OXYGEN, SHOULD BE IMMEDIATELY AVAILABLE IN ORDER TO MANAGE POSSIBLE ADVERSE EFFECTS INVOLVING THE CARDIOVASCULAR, RESPIRATORY OR CENTRAL NERVOUS SYSTEMS.**

2) **INJECTION SHOULD ALWAYS BE MADE SLOWLY WITH FREQUENT ASPIRATIONS TO AVOID INADVERTENT INTRAVASCULAR INJECTION WHICH CAN PRODUCE TOXIC EFFECTS. MULTIPLE INJECTIONS SHOULD BE ADMINISTERED AT SPACED INTERVALS.**

3) **The safety and effectiveness of 3% Citanest DENTAL with Octapressin depends on proper dosage, correct technique, adequate precautions and readiness for emergencies. Standard textbooks should be consulted for specific techniques and precautions regarding various anaesthetic procedures.**
4) Prilocaine should be given with great caution to patients with severe bradycardia, cardiac conduction disturbances or severe digitalis intoxication.

5) Prilocaine and/or its metabolites may accumulate during prolonged or repeated administration in patients with hepatic, renal or cardiac disease, the elderly and patients in poor general condition. However, this is unlikely to occur at the doses normally used in dentistry.

6) Prilocaine should be used with caution in patients with known medicine sensitivities. Patients allergic to ester derivatives of para-aminobenzoic acid (procaine, tetracaine, benzocaine etc.) have not shown cross sensitivity to agents of the amide type.

7) Prilocaine should be used with caution in patients with genetic predisposition to malignant hyperthermia as the safety of amide local anaesthetic agents in these patients has not been fully established.

8) In patients with hypoxaemia there is the potential for further hypoxic embarrassment as large doses of prilocaine may produce methaemoglobinaemia (see Section 4.8 Adverse Effects (Undesirable Effects).

9) 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.

10) 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 returns.

11) In the head and neck area the intravascular injection of even small doses of local anaesthetics may cause systemic adverse effects similar to those seen after the inadvertent intravascular injection of larger doses in other areas.

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

Use in the elderly

Even if the dose of 3% Citanest DENTAL with Octapressin used in dental practice is generally small, the elderly may require special attention to reduce the risk of dangerous side effect.

Paediatric use

For children, the dose may have to be reduced commensurate with body weight. The dosage should be calculated for each patient individually and modified in accordance with the dentist’s experience and knowledge of the patient.

Effects on laboratory tests

No data available.
4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

1. Anti-arrhythmic medicines
   Local anaesthetics of the amide type should be used with caution in patients receiving anti arrhythmic medicines, e.g. mexiletine, since the toxic effects may be additive.

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

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on fertility
No data available.

Use in pregnancy
Category A
Medicines which have been taken by a large number of pregnant women and women of childbearing age without any proven increase in the frequency of malformations or other direct or indirect harmful effects on the foetus having been observed.

Although the safe use of prilocaine during pregnancy has not been established with respect to possible adverse effects upon foetal development, prilocaine has been used extensively for dental procedures during pregnancy with no reports of ill effects to mother or foetus. In large doses prilocaine may cause maternal and foetal methemoglobinemia which could lead to foetal hypoxia.

Use in lactation
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 the dose, local anaesthetics may have a very mild effect on mental function and may temporarily impair locomotion and coordination.

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

Reactions to prilocaine are rare in the doses used in dental procedures. If adverse effects occur, they are similar in character to those observed with other local anaesthetics of the amide type. Psychogenic reactions in anticipation of or during the dental procedures are, however, common and may mimic the symptoms of generalised systemic reaction to local anaesthetics.

Adverse effects may be due to high plasma levels as a result of excessive dosage, rapid absorption, delayed elimination or metabolism, or inadvertent intravascular injection. Such reactions are systemic in nature and involve the central nervous system.
and/or the cardiovascular system (see Section 4.9 Overdose). Pronounced acidosis or hypoxia may increase the risk and severity of toxic reactions.

The following adverse effects are rare when associated with dental use of prilocaine.

Nervousness, dizziness, blurred vision, tremor, drowsiness, tinnitus, numbness, disorientation, nausea, vomiting, headache, palpitations, and tachycardia.

More serious reactions that reflect an overdosage of prilocaine are convulsions, unconsciousness, respiratory depression or arrest, hypotension, cardiovascular collapse and bradycardia which may lead to cardiac arrest.

Regarding methaemoglobinaemia, see below.

**Allergy**

Allergy to amide type local anaesthetics is very rare but may present as allergic dermatitis, bronchospasm or anaphylaxis.

**Methaemoglobinaemia**

Methaemoglobinaemia and cyanosis may occur following the administration of prilocaine solutions, particularly following a high dose. This is caused by the metabolite o-toluidine. Cyanosis of the nails and lips are clinical signs of methaemoglobinaemia.

In the dental dosage of prilocaine (1-5 mL 3% Citanest DENTAL with Octapressin, i.e. 30-150 mg prilocaine hydrochloride 3% with felypressin 0.03 IU/mL (0.54-2.7 μg/mL), the occurrence of methaemoglobinaemia in dental practice appears remote. However, gross overdosage in dental practice has been reported to cause methaemoglobinaemia.

A dose-response relationship appears to exist between the amount of prilocaine administered and the degree of methaemoglobin formation. In studies conducted in man, the incidence of methaemoglobinaemia at a dose of 400 mg prilocaine is not statistically significant. Cases of cyanosis at doses between 400 mg and 600 mg prilocaine are extremely rare.

At a dose of 600 mg prilocaine, methaemoglobin forms at levels less than 15% of the total haemoglobin content. This degree of methaemoglobinaemia is not associated with any adverse respiratory, cardiovascular or CNS symptoms. However, cyanosis has been reported at this dosage level.

If methaemoglobinaemia does occur, it may be treated by a single intravenous injection of a 1% methylene blue solution, given at a dose of 1 mg/kg body weight over a 5 minute period. This dose normally reverses methaemoglobinaemia within 15 minutes and should not be repeated as methylene blue in high concentrations acts as a haemoglobin oxidant.

In most patients receiving doses of 3% Citanest DENTAL with Octapressin within the recommended range, the appearance of clinical signs and symptoms of hypoxia may be due to cardiac or respiratory insufficiency and should be treated with oxygen and/or other appropriate measures. If cyanosis persists, methaemoglobinaemia should be suspected and methylene blue treatment initiated.

The reduction of 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.

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

**Neurological Reactions**

The incidence of adverse neurological reactions directly caused by the use of local anaesthetics is very low.

Neurological reactions may be related to the total dose of the local anaesthetic administered and are also dependent upon the particular medicine used, the route of administration and the physical status of the patient. Many of these effects may be related to local anaesthetic techniques, with or without contribution from the medicine.

Neurological reactions following regional nerve blocks have included persistent numbness, paraesthesia and sensory disturbances.

**Reporting suspected adverse effects**

Reporting suspected adverse reactions after registration of the medicinal product is important. It allows continued monitoring of the benefit-risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions at www.tga.gov.au/reporting-problems.

**4.9 OVERDOSE**

For information on the management of overdose, contact the Poisons Information Centre on 13 11 26 (Australia) and 0800 764 766 (New Zealand).

Systemic toxicity is initially manifested as CNS excitation and may be characterised by nervousness, dizziness, blurred vision and tremors followed by drowsiness, convulsions, unconsciousness and possibly respiratory arrest.

Toxic cardiovascular reactions to local anaesthetics are usually depressant in nature, may occur rapidly and with little warning and can lead to peripheral vasodilation, hypotension, myocardial depression, bradycardia and possibly cardiac arrest.

**Treatment of Overdosage**

Treatment of a patient with toxic symptoms consists of ensuring a patent airway and supporting ventilation with oxygen and assisted or controlled respiration as required. This usually will be sufficient in the management of most reactions.

Further treatment depends on diagnosis. Medical assistance should be summoned.

If ventricular fibrillation or cardiac arrest occurs, effective cardiovascular resuscitation treatment must be instituted and maintained for a prolonged period if necessary.

For treatment of reactions caused by adrenaline, consult standard textbooks.

For treatment of methaemoglobinaemia, see Section 4.8 Adverse Effects (Undesirable Effects).
5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Mechanism of action
Prilocaine is a membrane stabilising agent and a local anaesthetic of the amide type. Prilocaine stabilises the neuronal membrane and reversibly prevents the initiation and conduction of nerve impulses thereby producing local anaesthesia.

Prilocaine has a similar time of onset and potency to lignocaine. Prilocaine has a lower toxicity than lignocaine.

The onset and duration of anaesthesia depend on the route of administration, status of the patient and the dosage (volume and concentration) employed. The addition of felypressin reduces the rate of absorption of prilocaine from the site of injection thereby increasing its duration of action.

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.

Clinical trials
No data available.

5.2 PHARMACOKINETIC PROPERTIES
No data available.

5.3 PRECLINICAL SAFETY DATA

Genotoxicity
No data available.

Carcinogenicity
No data available.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS
3% Citanest DENTAL with Octapressin contains the excipients sodium chloride and water for injections and may also contain sodium hydroxide and/or hydrochloric acid for pH adjustment to 3.5-5.2.

6.2 INCOMPATIBILITIES
Incompatibilities were either not assessed or not identified as part of the registration of this medicine.
6.3 SHELF LIFE
In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

6.4 SPECIAL PRECAUTIONS FOR STORAGE
3% Citanest DENTAL with Octapressin should be stored below 25°C. Protect from light.

Local anaesthetics react with certain metals and cause the release of their respective ions which, if injected, may cause severe local irritation. Adequate precautions should be taken to avoid prolonged contact between 3% Citanest DENTAL with Octapressin solutions and metal surfaces, e.g. cartridges should not be preloaded and connected to needles until just prior to use.

Cartridges showing discolouration or cracks should be discarded. 3% Citanest DENTAL with Octapressin solutions should not be autoclaved. Surface sterilisation using pure, undiluted isopropyl alcohol (91%) or 70% ethyl alcohol (USP) may be carried out if desired.

6.5 NATURE AND CONTENTS OF CONTAINER

<table>
<thead>
<tr>
<th>Presentation</th>
<th>Fill size</th>
<th>Pack Size</th>
<th>Cartridge type*</th>
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</thead>
<tbody>
<tr>
<td>3% Citanest DENTAL with Octapressin, Prilocaine hydrochloride 66 mg/2.2 mL + felypressin (0.066 IU)</td>
<td>2.2 mL</td>
<td>50, 100</td>
<td>Standard and self-aspirating cartridges</td>
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<tr>
<td>3% Citanest DENTAL with Octapressin, Prilocaine hydrochloride 54 mg/1.8 mL + felypressin (0.054 IU)</td>
<td>1.8 mL</td>
<td>50, 100</td>
<td>Standard and self-aspirating cartridges</td>
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*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.

Note:
1. All Dentsply Sirona dental cartridges are paraben-free and for single use in a single patient only. Remaining unused contents should be discarded.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL
In Australia, any unused medicine or waste material should be disposed of in accordance with local requirements.
6.7 PHYSICOCHEMICAL PROPERTIES

Chemical structure

The chemical structure of prilocaine hydrochloride is:

\[
\text{Me} \quad \text{H} \quad \text{N} \quad \text{H} \quad \text{Me} \quad \text{NHPr}^n \quad \text{HCl}
\]

and enantiomer

The chemical name of prilocaine hydrochloride is 2-(propylamino)-o-propionotoluidide hydrochloride; and it is also known as propitocaine hydrochloride. It has a molecular weight of 256.8.

The structure of felypressin is:

\[
\text{Cys-Phe-Phe-Gln-Asn-Cys-Pro-Lys-GlyNH}_2
\]

The chemical name of the vasoconstrictor octapressin is 2-(phenylalanine)-8-lysine vasopressin; also known as felypressin. It has a molecular weight of 1040.2.

CAS number

The CAS number of prilocaine hydrochloride is 1786-81-8.

The CAS number for octapressin is 56-59-7.

7 MEDICINE SCHEDULE (POISONS STANDARD)

S4 - Prescription Only Medicine
New Zealand Medicine Classification: Prescription Medicine

8 SPONSOR

Australia
Dentsply Sirona Pty Ltd
11-21 Gilby Road
Mount Waverley, VIC 3149
Australia
www.dentsplysirona.com.au

New Zealand
Dentsply Sirona (NZ) Limited
c/o- Lowndes Jordan
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Auckland 1010
New Zealand
www.dentsplysirona.co.nz
9 DATE OF FIRST APPROVAL
28 February 2008

10 DATE OF REVISION
15 November 2018

SUMMARY TABLE OF CHANGES

<table>
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<tr>
<th>Section changed</th>
<th>Summary of new information</th>
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<tr>
<td>All sections</td>
<td>Updated PI format according to the new requirements</td>
</tr>
<tr>
<td>Section 8</td>
<td>Updated sponsor information</td>
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