AUSTRALIAN PRODUCT INFORMATION – MINIMS OXYBUPROCAINE HYDROCHLORIDE (OXYBUPROCAINE HYDROCHLORIDE) EYE DROPS

1 NAME OF THE MEDICINE

Oxybuprocaine Hydrochloride

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Minims Oxybuprocaine Hydrochloride Eye Drops contain oxybuprocaine hydrochloride 0.4% (4 mg/mL). No preservatives are included in the formulation.

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

3 PHARMACEUTICAL FORM

A single-use eye drops, solution.

Minims Oxybuprocaine Hydrochloride Eye Drops are clear, colourless sterile ophthalmic solution. No preservatives are included in the formulation.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

To produce local anaesthesia in the eye for short opthalmological procedures.

4.2 DOSE AND METHOD OF ADMINISTRATION

All patients
One drop of 0.4% oxybuprocaine solution instilled into each eye has been shown sufficient for tonometry after one minute. Addition of a further drop after 90 seconds provides adequate anaesthesia for fitting of a contact lens. To obtain a deeper anaesthetic effect, further drops may be instilled at intervals of no less than 90 seconds. For most procedures one to two drops is sufficient, however for removal of foreign bodies or minor surgery, three to six drops is suggested.

One drop a minute for 10 minutes was shown to provide adequate anaesthesia for patients undergoing pterygium surgery.

One drop instilled in each eye of a 0.2% oxybuprocaine solution prior to tonometry, was shown to be sufficient in patients over 40 years, suggesting that older patients may achieve sufficient anaesthetic effect with a lower dose of drug.

Corneal sensitivity is normal again after about 1 hour.

Each Minims unit should be discarded after a single use.

4.3 CONTRAINDICATIONS

Known hypersensitivity to anaesthetics in this group.
Concomitant infection of the eye.
Patient instillation of drug. To be given only by a clinician.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Identified precautions

The anaesthetized eye should be protected from dust and bacterial contamination.

Systemic absorption may be reduced by compressing the lacrimal sac at the medial canthus for a minute during and following the instillation of the drops. This blocks the passage of the drops via the naso-lacrimal duct to the wide absorptive area of the nasal and pharyngeal mucosa. It is especially advisable in children.

This preparation may cause transient blurring of vision. Patients should be advised not to drive or operate hazardous machinery until their vision is clear.

Oxybuprocaine has the potential to cause severe corneal damage and morbidity.

Use of oxybuprocaine 1% solution for long term ventilator bronchoscopy had no effect on cardiovascular function, but produced a decline in mean arterial oxygen pressure (paO_2) from 100 to 78, which persisted for over 30 minutes in one patient.

Anaesthesia of the respiratory system with oxybuprocaine has rarely resulted in hypersensitivity reactions including lung oedema.

Warnings
Oxybuprocaine eye drops should not be used for prolonged periods. Frequent or chronic use may result in severe corneal damage, keratitis and acquired tolerance. NOT FOR INJECTION – Topical ophthalmic use only.

Use in the elderly

No data available

Paediatric use

No data available

Effects on laboratory tests

No data available

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

Metabolism of local anaesthetics derived from esters may be inhibited by anticholinesterases and thus prolong the effects of oxybuprocaine. Ester - type local anaesthetics may competitively enhance the neuromuscular blocking action of suxamethonium.

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on fertility

No data available.

Use in pregnancy – Pregnancy Category D

Safety for use in pregnancy has not been established. The use of Minims Oxybuprocaine eye drops should be used only when it is considered essential by a physician

Use in lactation.

No studies have established the safety of Minims Oxybuprocaine eye drops during lactation. This medication should therefore be used only when it is considered essential by a physician.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

The effects of this medicine on a person's ability to drive and use machines were not assessed as part of its registration.

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

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.

In rare cases, local anaesthetic preparations have been associated with allergic reactions (in the most severe instances, anaphylactic shock).

Ocular

Instillation of drops commonly causes a transient stinging or burning sensation.

Stromal infiltration, oedema, candida keratitis, disciform keratitis and peripheral corneal ring formation have all been reported as a result of the frequent use of oxybuprocaine.

Frequent or chronic use can also result in acquired tolerance, epithelial cell damage irreversible apical cell damage at the level of the corneal endothelial cells and keratitis.

Local anaesthetics are known to inhibit the rate of movement of corneal epithelial cells migrating to cover wounds.

Reductions in tear film stability have also been documented as a result of oxybuprocaine treatment.

A fibrinousiritis has been observed in two patients following minor surgery, believed to be the result of drug entering the anterior chamber.

Frequency unknown: eye allergy, allergic blepharitis.

Cardiovascular

One incidence of sinus bradycardia after one drop of 0.4% oxybuprocaine solution was instilled into each eye occurred in one patient.

Central Nervous System

Abuse or overdose of oxybuprocaine may cause sedation, confusion, agitation, euphoria, disorientation, hearing, visual or speech disorders, paraesthesia, muscle twitching and if severe enough seizures, respiratory depression and coma. These symptoms would be very rare in therapeutic doses.

Gastrointestinal

Occasional nausea, vomiting and dysphagia have been observed during therapy.

Immunological

Use of local anaesthetics of the ester type, especially when frequent, has the potential to cause allergic reactions including contact allergy, urticaria and angioneurotic oedema.

Frequency unknown: hypersensitivity, anaphylactic reaction/shock.

4.9 OVERDOSE

Overdose of any local anaesthetic may cause various serious neurological, cardiovascular and respiratory events. These are overwhelmingly associated with oral and parenteral use/abuse, and are unlikely to occur in therapeutic, topical doses. Treatment for the various clinical effects is complex, however cessation of drug and supportive management including oxygen, intravenous fluids and management of any seizures is essential.

For information on the management of overdose, contact the Poisons Information Centre on 13 11 26 (Australia).

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Mechanism of action

Surface or topical anaesthesia blocks conduction of sensory, motor and autonomic nerve fibres, the excitability of nociceptors and the conducting system of the heart. A 0.4 % solution of oxybuprocaine has been shown to give effective surface anaesthesia in short opthalmological procedures. Sensation of pain is locally and reversibly reduced, with the possibility of temperature and pressure sensitivity also affected. Anaesthetic activity is ten times that of cocaine and twice that of tetracaine (amethocaine).

Surface anaesthesia occurs in approximately one minute with 0.4% intra-ocular solution, and peak response is between 1 and 15 minutes. Anaesthesia persists for about 20 to 30 minutes, with full corneal sensitivity taking 40 minutes or more to return.

Oxybuprocaine has demonstrated a concentration-related inhibition of platelet-activating- factor-induced aggregation of human blood samples taken from volunteers. 50% inhibition was demonstrated at 170 micromoles.

A 1% oxybuprocaine solution demonstrated significant bactericidal activity against Pseudomonas aeruginosa, Escherichia coli, Haemophilus influenza and Streptococcus pneumonia.

Oxybuprocaine, like several local anaesthetics, competitively inhibits the exchange transport of glucose in human erythrocytes.

Clinical trials

No data available

5.2 PHARMACOKINETIC PROPERTIES

Absorption

Most local anaesthetics are readily absorbed through mucous membranes and through damaged skin.

Distribution

Local anaesthetics at tissue pH can diffuse through connective tissue and cellular membranes to reach the nerve fibre where ionisation can occur.

Metabolism

Oxybuprocaine is metabolized by esterases in the plasma and, to a lesser extent, in the liver. There are at least nine metabolites, with 3-butoxy-4-aminobenzoic acid making up 70 – 90 %. Their activity is unknown.

Excretion

Urinary excretion of the drug and its metabolites at 9h after an oral dose is approximately 90%.

5.3 PRECLINICAL SAFETY DATA

Genotoxicity

No data is available regarding the mutagenicity of oxybuprocaine in humans.

Carcinogenicity

No data is available regarding the carcinogenicity of oxybuprocaine in humans.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Hydrochloric Acid
Purified Water

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

Store at 2°C to 8°C. (Refrigerate. Do not freeze.) Do not expose to strong light.

6.5 NATURE AND CONTENTS OF CONTAINER

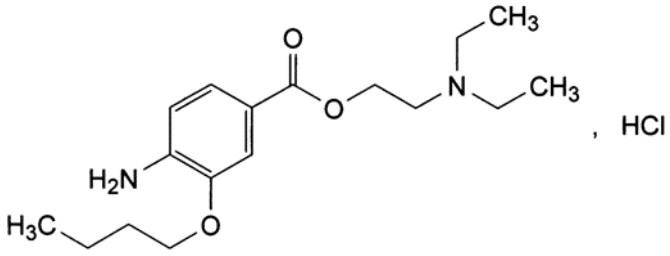
Minims Oxybuprocaine Hydrochloride Eye Drops are supplied in a single use polypropylene tube (unit) overwrapped in a polyester/paper blister. The blisters are packed in cartons of 20 units. Each unit contains approximately 0.5 mL of solution.

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



Chemical name:2-Diethylaminoethyl-4-amino-3-butoxybenzoate hydrochloride
Molecular formula: C17H28N2O3.HCl
Molecular weight: 344.9

Oxybuprocaine hydrochloride is a local, surface anaesthetic of the ester type. It is a white or off-white crystal or crystalline powder, odourless or with a slight characteristic odour. It is freely soluble in water, alcohol and chloroform and practically insoluble in ether. Aqueous solutions have a pH of 4.5 to 6.

CAS number

5987-82-6

7 MEDICINE SCHEDULE (POISONS STANDARD)

S4 - Prescription Only Medicine

8 SPONSOR

Bausch & Lomb (Australia) Pty Ltd
Level 2, 12 Help Street
Chatswood, NSW 2067

9 DATE OF FIRST APPROVAL

19 June 2000

10 DATE OF REVISION

13 August 2019

SUMMARY TABLE OF CHANGES

Section Changed	Summary of new information
All	New PI format
4.8	As a result of Signal Assessment report's recommendation this section was updated with the terms: "allergic reactions, eye allergy, blepharitis allergic, hypersensitivity, anaphylactic reaction/shock" with unknown frequency.