Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Oxybuprocaine Agepha 4 mg/ml eye drops, solution

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains 4 mg oxybuprocaine hydrochloride.
Each drop contains approximately 0.133 mg of oxybuprocaine hydrochloride.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Eye drops, solution
Clear, colourless solution

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

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

Oxybuprocaine Agepha 4 mg/ml eye drops, solution is indicated in adults.

4.2 Posology and method of administration

Posology
1 drop before the procedure, repeated as needed.

Since Oxybuprocaine hydrochloride is a fast-acting local anaesthetic, the envisaged intervention should be performed within 10 to 15 minutes following the last application of Oxybuprocaine Agepha 4 mg/ml.

Paediatric population
The safety and efficacy of Oxybuprocaine Agepha in children and adolescents has not been established.

Method of administration
For use on the eye.
Instil dropwise into the eye to be examined.

Avoid touching the tip of the dropper insert with the fingers as well as direct contact with the eye.
Lacrimal sac at the medial canthus should be compressed for 1-2 minutes in order to avoid a potential systemic effect.

For other applicable measures, see section 4.4.

People wearing contact lenses (see section 4.4)

Duration of use
The duration of use must be limited to the intervention.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1
- Known hypersensitivity to topical anaesthetics which belong to the group of active substances of p-aminobenzoic acid

4.4 Special warnings and precautions for use

Not intended for long-term use as this may result in the risk of severe corneal damage.
For external use, not for injection.
Only intended for short-term use in ophthalmic procedures by a physician

Special precaution should be taken in patients with a history of allergies, cardiac diseases, asthma, hyperthyroidism and hepatic diseases as well as in elderly patients.

While the anaesthetic effect persists, the eye must be protected from dust and foreign bodies. Since spontaneous eyelid closure is restrained due to sensory numbness until anaesthesia fully takes effect, the patient should keep his or her eyes closed until the intervention to counter any impairment resulting from dryness of the eyes.
Immediately after the medical intervention, any adverse effects resulting from the lack of normal blink frequency while anaesthesia persists should be countered by specific measures, such as topical administration of artificial tear substitutes.

Systemic absorption may be reduced by compressing the lacrimal sac at the medial canthus for 1-2 minutes 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.

Use with caution on an inflamed eye, as hyperaemia greatly increases the rate of systemic absorption through the conjunctiva.

Notice for people wearing contact lenses
Contact lenses should be removed before instilling the drops into the eye and only be put back on the eye once the anaesthetic effect has fully subsided (at least one hour after instillation). Failure to follow this advice may lead to corneal damage.

4.5 Interaction with other medicinal products and other forms of interaction

Sulfonamides: The antimicrobial effect of sulfonamides may be reduced.

4.6 Fertility, pregnancy and lactation

Pregnancy
There is insufficient data regarding the use of this medicine in pregnant women.
This medicine should therefore only be used during pregnancy when it is considered essential by the physician.

Breastfeeding
It is not known whether the active ingredient passes into the breast milk. Hence, Oxybuprocaine Agepha should only be used during lactation when considered essential by the physician.

4.7 Effects on ability to drive and use machines

Oxybuprocaine Agepha 4 mg/ml eye drops, solution has major influence on the ability to drive and use machines.

Since vision may be impaired, caution must be exercised when driving and operating machines.

4.8 Undesirable effects

The most common side effect is local irritation.
Due to the low systemic absorption, systemic side effects are very rare.

Within each frequency group, undesirable effects are presented in order of decreasing seriousness.

Eye disorders
Common (≥1/100 to <1/10)*:*
short-term burning and stinging sensation may occur on instillation Corneal damage from repeated use.

Rare (≥1/10 000 to <1/1 000):
Blurred vision.

Frequency not known (cannot be estimated from the available data):
Eye allergy, allergic blepharitis

Immune system disorders
Frequency not known (cannot be estimated from the available data):
Hypersensitivity reaction, anaphylactic reaction/shock

Nervous system disorders
Rare (≥1/10 000 to <1/1 000):
Tremor

Cardiac disorders
Rare (≥1/10 000 to <1/1 000)*:*
Bradycardia

Vascular disorders
Rare (≥1/10 000 to <1/1 000):
Hypotension

General disorders and administration site conditions
Rare (≥1/10 000 to <1/1 000):
Dizziness

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation 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 via the national reporting system:

HPRA Pharmacovigilance
Website: www.hpra.ie

4.9 Overdose

Systemic or local intoxication is practically excluded during proper use of Oxybuprocaine Agepha 4 mg/ml eye drops, solution.
Misapplication, such as repeated use in case of pain, may result in severe corneal damage, impaired vision and loss of corneal sensitivity.
If administration is immediately discontinued, in some cases the corneal tissue may regenerate. In other cases, a keratoplasty has to be performed.
After intoxication induced by local anaesthesia, the following systemic symptoms may occur: muscle twitching, seizures, drop in blood pressure, fainting, cardiac arrhythmias, cardiac arrest caused by conduction disturbances, respiratory paralysis.

Therapy
Immediate respiratory and blood circulation management (intubation and artificial ventilation), cardiovascular stimulation, infusions (no adrenaline). In case of cardiac arrest, external cardiac massage and electro-stimulation is to be performed. In case of seizures, ultra-short-acting barbiturates or diazepam should be given (long-acting barbiturates should not be administered due to the risk of respiratory depression).

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: local anaesthetic, oxybuprocaine
ATC code: S01HA02

Mechanism of action
Oxybuprocaine hydrochloride is a local anaesthetic of the ester type and chemically related to procaine. Oxybuprocaine blocks the excitability of nociceptors and the conductivity of sensory nerve fibres in a reversible and locally restricted manner. After reducing the sensation of pain, it diminishes temperature, touch and pressure sensitivity in a descending order.

When using local anaesthetics, thin nerve fibres are blocked before thick nerve fibres. Oxybuprocaine reduces membrane permeability for cations, in particular sodium, and at higher concentrations also for potassium. The excitability of the nerve fibres is reduced depending on concentration, because the sudden increase in sodium permeability necessary for inducing an action potential is diminished.

Pharmacodynamic effects
Efficacy is reduced in inflamed tissue due to its lower pH value.
Oxybuprocaine in solution (4 mg/ml) is a fast-acting local anaesthetic. Its effect sets in approximately 30 to 60 seconds after application. Within the following 15 minutes, anaesthesia is sufficient for pre-planned medical interventions. As a rule, corneal sensitivity is normal again after approximately one hour.

5.2 Pharmacokinetic properties

Absorption and distribution

The rate of loss of local anaesthetics through tear flow is very high as they induce an initial stinging reaction which stimulates reflex lacrimation and leads to dilution of the drugs. It is thought that this is responsible for the very short duration of maximum effect of local anaesthetics.

The non-ionised base of oxybuprocaine is rapidly absorbed from the pre-corneal tear film by the lipophilic corneal epithelium. The drug then passes into the corneal stroma and from there into the anterior chamber where it is carried away by the aqueous flow and diffuses into the blood circulation in the anterior uvea.

Biotransformation
Local anaesthetics of the ester type are broken down by cholinesterase activity in the plasma. Broken-down products are ineffective as local anaesthetics.

Elimination
Oxybuprocaine and its metabolites are rapidly eliminated through the kidneys.

5.3 Preclinical safety data

Systemic
No investigations have been conducted on chronic toxicity, mutagenicity, carcinogenicity and reproduction toxicology.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Chlorhexidine diacetate
Boric acid
Hydrochloric acid (for pH adjustment)
Water for injections

6.2 Incompatibilities

Oxybuprocaine Agepha 4 mg/ml eye drops, solution are incompatible with silver nitrate, mercury salts, fluorescein sodium and alkaline substances.

6.3 Shelf life

2 years
To be used within 4 weeks after first opening.

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

10 ml eye drops solution in LDPE bottle, with LDPE nozzle and HDPE closure.
Pack size: 1 bottle of 10 ml

6.6 Special precautions for disposal

No special requirements.

7 MARKETING AUTHORISATION HOLDER

AGEPHA Pharma s.r.o.
Dialnicná cesta 5,
Senec 90301,
Slovakia

8 MARKETING AUTHORISATION NUMBER

PA22584/002/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 27th January 2023

10 DATE OF REVISION OF THE TEXT