

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Medispray oromucosal spray, solution Chlorhexidine digluconate 2 mg/ml Lidocaine hydrochloride 0.5 mg/ml

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

1 spray contains 177 micrograms chlorhexidine digluconate and 42 micrograms lidocaine hydrochloride.

Excipients with known effect: 1 spray contains 28 mg ethanol.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Oromucosal spray, solution

Clear, colourless solution

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Medispray is indicated for the symptomatic relief of painful, irritated sore throats in adults, adolescents and children over 12 years.

4.2 Posology and method of administration

Adults, adolescents and children over 12 years

The dose is 3 to 5 sprays (0.3 - 0.5 ml). This can be repeated 6 to 10 times per day.

The lowest effective dose should be used for the shortest duration necessary to relieve symptoms.

Repeat the dose every hour as needed up to a maximum of ten times in 24 hours.

The stated dose should not be exceeded.

Children under 12 years

Should not be used in children under 12 years of age.

Short term use

This medicine is intended as symptomatic treatment and should not be used on a long-term basis.

Method of administration

Oromucosal use

Aim nozzle at back of throat and spray on to the affected area.

Do not inhale whilst using the spray.

Please note that prior to first use or re-use 8 actuations must be fired to waste.

It is advisable to clean the nozzle preventively on a daily basis with the following procedure:

1. Turn the spray upside down and press the spray head until no more liquid comes out.
2. Remove the nozzle from the spray pump and place it in a hot water bath for a few minutes.
3. Take the nozzle out of the water and let it dry.
4. Place the dry nozzle on the spray pump by turning it downwards so that it blocks the spray pump.

4.3 Contraindications

- Hypersensitivity to the active substances or to any of the excipients listed in section 6.1.
- History of possible chlorhexidine-related allergic reactions (see sections 4.4 and 4.8).
- History of allergic reaction to local anaesthetics.
- Use in children under 12 years old.

4.4 Special warnings and precautions for use

- Disinfecting substances do not make sterile; they temporarily reduce the number of micro-organisms at the oral cavity and pharynx.
- Treatment with Medispray should be limited to the relief of existing pain and irritation when strictly necessary. It is not intended for prolonged use, either continuously or repeatedly.
- The lowest effective dose should be used for the shortest duration necessary to relieve symptoms.
- A doctor should be consulted if symptoms worsen during use, do not improve after 2 days or are accompanied by high fever, headache, nausea or vomiting.
- Patients should not inhale whilst using the spray.
- Contact with eyes and ears should be avoided; if the spray inadvertently comes into contact with the eye, immediate rinsing with water is required.
- Medispray should be used with caution in patients with asthma.
- Medispray should be used with caution in patients who have a history of or are suspected to have methaemoglobinaemia.
- Medispray should be used with caution in patients with severe shock or heart block.
- Patients should be advised not to use and to seek medical advice if they have difficulty in swallowing.
- Excessive doses (more than 1 bottle a day) can cause a small risk of loss of sensitivity of the glottis area. This can cause a diminished control on the swallowing reflex and food aspiration in the airways can occur.
- Medispray should be used with caution in patients with wounds or traumatised mucosa in the region of the proposed application.
- Medispray contains chlorhexidine. Chlorhexidine is known to very rarely induce hypersensitivity, including generalised allergic reactions and anaphylactic shock (see sections 4.3 and 4.8).
- This medicine contains 139 mg of alcohol (ethanol) in each dose (5 sprays of 0.425 ml) which is equivalent to 41.6% (v/v). The amount in each dose (5 sprays) of this medicine is equivalent to 3.5 ml of beer or 1.5 ml of wine. The small amount of alcohol in this medicine will not have any noticeable effects.
- Medispray contains less than 1 mmol sodium (23 mg) per dose unit, that means that it is essentially 'sodium-free'.
- Medispray is a sugar free preparation and can be used by patients with diabetes.

4.5 Interaction with other medicinal products and other forms of interaction

Chlorhexidine is not known to interact with other drugs.

Whilst a number of interactions are theoretically possible with lidocaine, such interactions should be of no clinical importance following short term treatment with low dose lidocaine (Medispray) administered topically at recommended doses. Lidocaine is known to inhibit drug metabolism by CYP1A2. A reduced rate of lidocaine metabolism may result from an inhibition of CYP3A4.

The toxicity of oral lidocaine may be increased when the drug is taken in combination with the following drugs:

- CYP3A4 inhibitor drugs (e.g. erythromycin, itraconazole and ketoconazole)
- CYP1A2 inhibitor drugs (e.g. fluvoxamine and cimetidine)
- Beta blockers
- Other antiarrhythmic drugs (e.g. mexiletine)

4.6 Fertility, pregnancy and lactation

Pregnancy

There is inadequate evidence of the safety of lidocaine and chlorhexidine in human pregnancy.

Pregnant women must take into account that Medispray contains 41.6 vol % alcohol.

This medicine is intended for local treatment. No effects during pregnancy are anticipated, since systemic exposure to the active substance is negligible at therapeutic dose levels, however Medispray should only be used in pregnancy under the direction of a physician.

Breast-feeding

Women who are breast-feeding must take into account that Medispray contains 41.6 vol % alcohol. This medicine is intended for local treatment. No effects on the breastfed newborn/infant are anticipated since the systemic exposure of the breast-feeding woman to the active substance is negligible, at therapeutic dose levels, however Medispray should only be used during breast feeding under the direction of a physician.

Fertility

There are no relevant data on fertility available.

4.7 Effects on ability to drive and use machines

The use of Medispray has no influence on the ability to drive and use machines.

4.8 Undesirable effects

Classification of undesirable effects is made according to the MedDRA-system organ classes and frequency convention.

Very common ($\geq 1/10$)

Common ($\geq 1/100$ to $<1/10$)

Uncommon ($\geq 1/1,000$ to $<1/100$)

Rare ($\geq 1/10,000$ to $<1/1,000$)

Very rare ($< 1/10,000$)

Not known (the frequency cannot be estimated from the available data).

System organ class	Frequency	Undesirable effects
Immune system disorders	Rare	Hypersensitivity including anaphylactic shock have been reported following the topical use of chlorhexidine. Hypersensitivity reactions to lidocaine hydrochloride following local injection have presented as localised oedema with slight difficulty in breathing or as a generalised rash. Local anaesthetic preparations have been associated with allergic reactions.
Skin and subcutaneous tissue disorders	Not known	Skin hypersensitivity to chlorhexidine has been reported. Allergic skin reactions such as dermatitis, pruritus, erythema, eczema, rash, urticaria, skin irritation, and blisters.
General disorders and administration site conditions	Not known	Taste disorders. A burning feeling on the tongue and occasional parotid gland swelling. Prolonged and continuous use of chlorhexidine can cause brown-discoloration of the teeth and tongue. However, this brown-discoloration is removable.

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:

HPRA Pharmacovigilance

Website: www.hpra.ie

4.9 Overdose

Although this medicine contains only a fraction of the toxic dose and although the foreseen use of this composed medicine is limited to local use, the possibility of an overdose by mistake or carelessness should be taken into account, especially in children.

Chlorhexidine is resorbed in very little amounts from the gastrointestinal tract. Lidocaine is absorbed more quickly, and its bioavailability is 35 per cent. When excessive doses are used, difficulty when swallowing and an increased risk of aspiration can occur.

Excessively high blood concentrations of lidocaine may produce CNS and/or cardiovascular effects. Early CNS effects may consist of nervousness, dizziness, tinnitus, nystagmus, restlessness, excitation, paraesthesia, blurred vision, nausea, vomiting, and tremors which may progress to medullary depression and tonic and clonic convulsions. Cardiovascular reactions are depressant and may be characterised by hypotension, myocardial depression, bradycardia and possibly cardiac arrest.

Although the bioavailability of lidocaine is low it may be sufficient to result in significant toxicity when swallowed. CNS toxicity, seizures and death have been reported following the ingestion of topical preparations. However, in the case of Medispray

more than one litre would have to be swallowed to be equivalent to the ingestion of sufficient lidocaine (0.5 g or more) to cause significant toxicity.

Systemic toxicity from chlorhexidine is rare. The main consequence of ingestion is mucosal irritation.

Very rarely, methaemoglobinaemia may occur with excessive exposure to some local anaesthetics. This is much more commonly seen with benzocaine and prilocaine than with lidocaine. Risk is increased in patients with hereditary methaemoglobinaemia and when used with other oxidising agents.

Treatment of lidocaine overdose consists of ensuring adequate ventilation and arresting convulsions. Ventilation should be maintained with oxygen by assisted or controlled respiration as required.

Convulsions may be treated with thiopentone, diazepam or succinylcholine. As succinylcholine will arrest respiration it should only be used if the clinician has the ability to perform endotracheal intubation and to manage a totally paralysed patient. If ventricular fibrillation or cardiac arrest occurs, effective cardiovascular resuscitation must be instituted. Adrenaline in repeated doses and sodium bicarbonate should be given as rapidly as possible.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: throat preparations, ATC code: R02AA05

Lidocaine hydrochloride is a local peripheral anaesthetic of the amide group, which has a superficial analgesic effect. Lidocaine as a local anaesthetic has the same mechanism of action as other medicines from this group in that it prevents generation and conduction of nerve impulses in sensoric, motoric and autonomous nerves. It primarily affects the cell membrane where it blocks the ion channels and thereby reduces the permeability of sodium ions. Due to the progressive propagation of the anaesthetic effect in the nerve, the electric stimulation threshold is increased, impulse conduction is slowed down and the propagation of the action potential is contracted. Finally, the conductivity is interrupted completely. In principle, local anaesthetics block autonomous nerve fibres, small non-myelinated (sensation of pain) and small myelinated (sensation of pain and temperature), more quickly than large myelinated fibres (sensation of touch and pressure).

On a molecular level, lidocaine specifically blocks sodium ion channels in the inactive state, thereby preventing the formation of an action potential. This mechanism prevents the conduction of stimuli when lidocaine is used locally in the vicinity of nerves. Chlorhexidine is a bisbiguanide cationic antiseptic. It is effective against Gram-positive (e.g. *Micrococcus* sp., *Staphylococcus* sp., *Streptococcus* sp., *Bacillus* sp.) and to a lesser extent against Gram-negative bacteria, especially in the vegetative form (it is not effective against spores at normal temperature). It also has an antimycotic effect on dermatophytes and fungi. It quickly inactivates the infectiousness of certain lipophilic viruses (influenza virus, herpes virus, HIV).

In smaller concentrations, it has a bacteriostatic effect, while in larger concentrations, it functions as a bactericide.

The chlorhexidine molecule has a strong positive charge, and therefore adsorbs to the negatively charged areas on the cell surface. The adsorption is specific and takes place in special parts of the bacterial cell wall containing phosphates. This damages the cell membrane, increasing permeability.

It is also adsorbed onto the surfaces of the teeth, plaque or the oral mucosa, thereby persisting in the oral cavity.

The effectiveness of antiseptics and disinfectants depends on the concentration, temperature and exposure time.

5.2 Pharmacokinetic properties

Small amounts may enter the digestive system if some of the Medispray solution or saliva is swallowed.

Chlorhexidine

Absorption

In oral or topical use, absorption of chlorhexidine is insignificant.

In topical use on intact skin, chlorhexidine is adsorbed on the outside layers of the skin, providing long-term antimicrobial effect. After rinsing the oral cavity, approximately 30% of chlorhexidine is retained, which is then slowly released into the saliva. In view of the insignificant bioavailability of chlorhexidine after oral or topical administration, the following elements are just for information:

Distribution

Chlorhexidine tightly binds to saliva proteins. It was shown that chlorhexidine is stable in the oral cavity for at least 9 h and high concentrations of the drug (2 µg/ml total) are still present in saliva even after 8 h from mouth rinsing.

Biotransformation

Chlorhexidine is not accumulated in the body and is only minimally metabolised.

Elimination

In a case of ingestion of a massive dose (300 mg) of chlorhexidine gluconate, approximately 90 % was excreted in faeces via biliary routes and less than 1 % was eliminated into urine.

Lidocaine

Absorption

Lidocaine absorption varies, depending on the site and the method of use. It is quickly resorbed from the digestive organs, mucous membranes and through damaged skin. In healthy adults, no detectable plasma lidocaine levels were noted after use of a 2 % mouth rinse. Children and immune impaired adults do resorb lidocaine from the oral mucosa into the plasma. The levels were approximately 0.2 micrograms/ml but the toxic plasma concentration is 5 micrograms/ml. The anaesthetic effect is limited to the surface and does not extend to the submucosal structures.

Distribution

Lidocaine is distributed well in the tissues (kidneys, lungs, liver, heart, skeletal muscle and adipose tissue). Lidocaine passes through the blood-brain barrier and placenta and into mother's milk.

Biotransformation

It is metabolised during the first pass through the liver and the bioavailability is about 35 % after oral administration. 90 % is deethylated in the liver to monoethylglycinexylide and glycinexylide. Both primary metabolites are pharmacologically active. Further cleavage of the amide bonds forms the metabolites xylidine and 4-hydroxyxylidine.

Elimination

Lidocaine is eliminated in the form of metabolites through the kidneys. Approximately 10% is eliminated unchanged. The biological half life of lidocaine is one and a half to two hours in adults. The biological half life of the primary metabolites is two to ten hours.

5.3 Preclinical safety data

No data available.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Ethanol
Glycerol
Levomenthol
Cineole
Saccharin sodium
Citric acid monohydrate
Purified water

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months.
After first opening: 3 months.

6.4 Special precautions for storage

Store below 25°C. Do not refrigerate or freeze.

6.5 Nature and contents of container

Bottle with spray pump with 30 ml oromucosal spray solution.

Bottle: Glass bottle, amber

Closure: Synthetic pump dip tube, tamper proof cap and cannula (polypropylene, polyethylene, stainless steel, butyl and acetalic resin).

6.6 Special precautions for disposal and other handling

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Clonmel Healthcare Ltd
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8 MARKETING AUTHORISATION NUMBER

PA0126/300/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 25th March 2022

10 DATE OF REVISION OF THE TEXT

July 2022