

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF MEDICINAL PRODUCT, STRENGTH AND PHARMACEUTICAL DOSAGE FORM

ORALSEPT, 0.15%, solution, oromucosal spray

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 ml solution contains 1.5 mg benzydamine hydrochloride, excipients.

* For full list of excipients see section 6.1.

3. PHARMACEUTICAL DOSAGE FORM

Solution, oromucosal spray

Oralsept is a yellow-green, low viscous solution, with mint flavour.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Oralsept spray is a locally acting analgesic and anti-inflammatory treatment for the throat and mouth.

It is especially useful for the relief of pain in traumatic conditions such as following tonsillectomy or the use of a naso-gastric tube; dental surgery.

4.2 Posology and method of administration

Posology

Adults and elderly: 4 to 8 puffs, 1½ - 3 hourly.

Paediatric population

Children (6-12): 4 puffs, 1½ - 3 hourly.

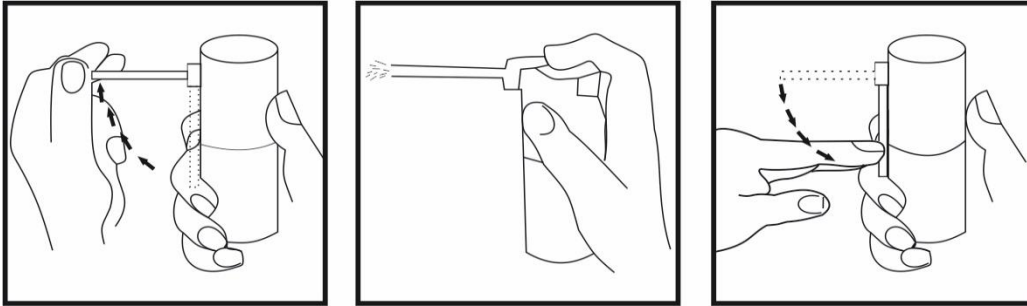
Children under 6: 1 puff to be administered per 4 kg body weight, up to a maximum of 4 puffs, 1½ - 3 hourly.

Method of administration

Oromucosal spray

Instructions for use

NOTICE: Before first use, puff once of the spray in the air.



Picture 1: Hold the bottle in upright position with the extension facing you. Lift the spray extension to a horizontal position (90° angle).

Picture 2: Bring the spray extension close to your mouth and spray the required number of puffs. The time interval between two puffs should not be shorter than 5 seconds.

Picture 3: Return the spray extension to its original position (with the top down).

4.3 Contraindications

Known hypersensitivity to the active substance or to any of the excipients of the medicine.

4.4 Special warnings and special precautions for use

Benzydamine use is not advisable in patients with hypersensitivity to acetylsalicylic acid or other NSAIDs.

Bronchospasm may be precipitated in patients suffering from or with a previous history of bronchial asthma. Caution should be exercised in these patients.

Avoid contact with the eyes.

If the condition is aggravated or not improved use should cease.

Oralsept spray contains methyl parahydroxybenzoate which may cause allergic reactions (possible delayed reactions).

Also, this medicine contains small amount of ethanol (alcohol), less than 100 mg per dose.

4.5 Interaction with other medicinal products and other forms of interaction

No interactions known.

4.6 Use during pregnancy and lactation

Pregnancy

Oralsept spray should not be used during pregnancy.

Breast-feeding

Oralsept spray should not be used during breast-feeding unless considered essential by the physician.

Fertility

There is no evidence of a teratogenic effect in animal studies.

4.7 Effects on ability to drive and use machines

Oralsept spray has no or negligible influence on the ability to drive or use machines.

4.8 Undesirable effects

Adverse events are listed by System Organ Class.

Frequencies are defined using the following convention: very common ($\geq 1/10$), common ($\geq 1/100$, $< 1/10$), uncommon ($\geq 1/1000$, $< 1/100$), rare ($\geq 1/10000$, $< 1/1000$), very rare ($< 1/10000$), not known (cannot be estimated from available data).

The most common side effects are numbness and a stinging feeling in the mouth.

System organ class	Frequency	Undesirable effects
Immune system disorders	Not known	Anaphylactic reaction which can be potentially lifethreatening and hypersensitivity reactions*
Respiratory, thoracic and mediastinal disorders	Very rare	Laryngospasm or bronchospasm
Gastrointestinal disorders	Uncommon	Oral numbness and a stinging feeling in the mouth**
Skin and subcutaneous tissue disorders	Very rare	Pruritus, urticaria, photosensitivity reaction and rash
	Not known	Angiodema

* The stinging has been reported to disappear upon continuation of the treatment, however if it persists it is recommended that treatment be discontinued.

** Methyl parahydroxybenzoate may cause allergic reactions (possible delayed reactions).

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.

4.9 Overdose

Symptoms

Oralsept spray is unlikely to cause adverse systemic effects, even if accidental ingestion should occur. No special measures are required. Intoxication is only expected in case of accidental ingestion of large quantities of benzydamine (> 300 mg).

Symptoms associated with overdose of ingested benzydamine are mainly gastrointestinal symptoms and symptoms of the central nervous system. Most frequent gastrointestinal symptoms are nausea, vomiting, abdominal pain and oesophageal irritation. Symptoms of the central nervous system include dizziness, hallucinations, agitation, anxiety and irritability.

Treatment

In acute overdose only symptomatic treatment is possible. Patients should be kept under close observation and supportive treatment should be given. Adequate hydration must be maintained.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Other agents for local oral treatment

ATC code: A01AD02

Benzydamine exerts an anti-inflammatory and analgesic action by stabilising the cellular membrane and inhibiting prostaglandin synthesis.

Mechanism of action

The indazole analogue benzydamine has physicochemical properties and pharmacological activities which differ from those of the acetylsalicylic acid-like NSAIDs. Unlike acetylsalicylic acid-like NSAIDs which are acids or metabolised to acids, benzydamine is a weak base. In further contrast, benzydamine is a weak inhibitor of the prostaglandin synthesis. Only at concentration of 1mM and above benzydamine effectively inhibits cyclooxygenase and lipooxygenase enzyme activity. It mostly exerts its effects through inhibition of the synthesis of proinflammatory cytokines including tumour necrosis factor-alpha (TNF- α) and Interleukin-1 β (IL-1 β) without significantly affecting other pro-inflammatory (IL-6 and 8) or anti-inflammatory cytokines (IL-10, IL-1 receptor antagonist). Further mechanisms of action are hypothesised including the inhibition of the oxidative burst of neutrophils as well as membrane stabilisation as demonstrated by the inhibition of granule release from neutrophils and the stabilization of

lysosomes. The local anaesthetic activity of the benzydamine has been related to an interaction with cationic channels.

Pharmacodynamic effects

Benzydamine specifically acts on the local mechanisms of inflammation such as pain, oedema or granuloma.

Benzydamine topically applied demonstrates anti-inflammatory activity reducing oedema as well as exudate and granuloma formation. Further, it exhibits analgesic properties if pain is caused by an inflammatory condition and local anaesthetic activity. Hyperthermia, which is indicative of systemic functional involvement, is poorly affected by benzydamine.

Clinical efficacy and safety

In a clinical study in 24 patients with pharyngitis following tonsillectomy rinsing with benzydamine 5 times a day for 6 days significantly better and more rapidly relieved throat pain, difficulty in swallowing and improved clinical signs including hyperaemia and oedema versus placebo on day 7. Similar results were found in other studies in patients with tonsillitis or pharyngitis or following dental surgery. The gargling with 30 ml 0.075% benzydamine prior to the induction of anaesthesia in 58 adults undergoing general anaesthesia with endotracheal tube intubation significantly reduced postoperative sore throat versus control group that gargled with water for the first 24 hours whereas acetylsalicylic acid gargles reduced it for 4 hours.

In a clinical study with 48 patients rinsing four times daily with 0.15% benzydamine during a 3 to 5 week radiotherapy of oral cancer provided significant pain relief and reduction of size and severity of mucositis in the oropharynx. Similar effects were seen in a study in patients undergoing chemotherapy for oral cancer. In a study in 67 patients with severe oropharyngeal mucositis following radiotherapy who rinsed with benzydamine solution pain with swallowing, hyperaemia and severity of mucositis were significantly reduced compared to placebo treatment within the first three treatment days. A higher incidence of transient numbness and stinging was noted among the patients using benzydamine that was attributed to the medication's local anaesthetic effect.

The topical application of benzydamine 3 times daily for 6 days in 50 patients with soft tissue injuries significantly better relieved pain, tenderness, erythema, functional impairment and swelling compared to placebo on day 6.

Overall, benzydamine was well tolerated in clinical trials.

5.2 Pharmacokinetic properties

Absorption

Following oral administration, benzydamine is rapidly absorbed from the gastrointestinal tract and maximum plasma levels reached after 2-4 hours. The most important aspect of the tissue distribution of benzydamine is its tendency to concentrate at the site of inflammation.

Elimination

About half of the benzydamine is excreted unchanged via the kidney at a rate of 10% of the dose within the first 24 hours. The remainder is metabolised, mostly to N-Oxide.

5.3 Preclinical safety data

Non-clinical data reveal no special hazards for humans based on conventional studies of safety pharmacology, repeated toxicity, genotoxicity, cardiogenic potential, and toxicity to reproduction and development.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Methyl parahydroxybenzoate, glycerol, ethanol 96%, saccharin sodium, sodium hydrogen carbonate, polysorbate 60, peppermint flavour, color quinoline yellow E 104, color indigotine E 132, water purified.

6.2 Incompatibilities

None known.

6.3 Shelf life

4 years in original package.

Should not be administered after the expiry date!

6.4 Special precautions for storage

Should be kept at temperature up to 25°C, in original package.

MEDICINE SHOULD BE KEPT OUT OF THE REACH OF CHILDREN!

6.5 Nature and contents of container

Box with HDPE plastic container with dosing spray pump with 30 ml oromucosal spray.

6.6 Special precautions for disposal of unused products/waste materials

No special measures are required.

Any unused medicine or waste materials should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

REPLEK FARM Ltd. Skopje, 188 Kozle str., 1000 Skopje, Republic of North Macedonia

8. MARKETING AUTHORISATION NUMBER

9. DATE OF ISSUE OF THE FIRST MARKETING AUTHORISATION/RENEWAL

10. DATE OF LAST REVISION OF THE TEXT

January

2026