

## **1 NAME OF THE MEDICINAL PRODUCT**

Benzylamine Hydrochloride 0.15% w/v Mouthwash

Oral Soothe and Sore Throat 0.15% w/v Mouthwash

## **2 QUALITATIVE AND QUANTITATIVE COMPOSITION**

Benzylamine hydrochloride 0.15% w/v

Each 15ml dose contains 22.5mg benzylamine hydrochloride.

Each 1ml of mouthwash contains 1.5mg benzylamine hydrochloride.

### Excipients with known effect

Ethanol (96%) and methyl parahydroxybenzoate (E 218)

For the full list of excipients, see section 6.1

## **3 PHARMACEUTICAL FORM**

Mouthwash.

Clear, green liquid with a characteristic mint odour with a pH between 5 – 7

## **4 CLINICAL PARTICULARS**

### **4.1 Therapeutic indications**

Benzylamine Mouthwash is a locally acting analgesic and anti-inflammatory treatment for the relief of painful inflammatory conditions of the mouth and throat including:

Traumatic conditions: Pharyngitis following tonsillectomy or the use of a naso-gastric tube.

Inflammatory conditions: Pharyngitis, aphthous ulcers and oral ulceration due to radiation therapy.

Dentistry: For use after dental operations.

## 4.2 Posology and method of administration

### Posology

*Adults and elderly:* Rinse or gargle with 15ml (approximately 1 tablespoonful) every 1½-3 hours as required for pain relief

*Children:* Not suitable for children aged 12 years or under

*Elderly:* No special dosage recommendations are made for elderly patients.

### Method of administration

Rinse or gargle

The solution should be expelled from the mouth after use.

Benzydamine Mouthwash should generally be used undiluted, but if ‘stinging’ occurs the rinse may be diluted with water.

Uninterrupted treatment should not exceed seven days, except under medical supervision.

## 4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1

## 4.4 Special warnings and 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.

Benzydamine Mouthwash should generally be used undiluted, but if ‘stinging’ occurs the rinse may be diluted with water.

Avoid contact with the eyes.

Contains methyl parahydroxybenzoate which may cause allergic reactions (possibly delayed)

This medicinal product contains 10.1 vol % ethanol (alcohol), i.e. up to 1200mg per dose, equivalent to 30ml beer, 12.5ml wine per dose. Harmful for those suffering from alcoholism.

To be taken into account in pregnant or breast-feeding women, children and high-risk groups such as patients with liver disease, or epilepsy.

This medicine contains less than 1 mmol sodium (23 mg) per 15 ml dose, that is to say essentially 'sodium-free'.

#### **4.5 Interaction with other medicinal products and other forms of interaction**

None known

#### **4.6 Fertility, pregnancy and lactation**

##### Pregnancy

There are no clinical data from the use of Benzydamine Mouthwash during pregnancy.

During the third trimester of pregnancy, systemic use of prostaglandin synthetase inhibitors may induce cardiopulmonary and renal toxicity in the fetus. At the end of the pregnancy prolonged bleeding time in both mother and child may occur, and labour can be delayed.

It is not known if the systemic Benzydamine Mouthwash exposure reached after topical administration can be harmful to an embryo/fetus.

Therefore, Benzydamine Mouthwash should not be used during pregnancy unless clearly necessary. If used, the dose should be kept as low and duration of treatment as short as possible.

There is no evidence of a teratogenic effect in animal studies (see section 5.3).

From the 20th week of pregnancy onward, Benzydamine Mouthwash use may cause oligohydramnios resulting from foetal renal dysfunction. This may occur shortly after treatment initiation and is usually reversible upon discontinuation. In addition, there have been reports of ductus arteriosus constriction following treatment in the second trimester, most of which resolved after treatment cessation. Therefore, during the first and second trimester of pregnancy, Benzydamine Mouthwash should not be given unless clearly necessary. If Benzydamine Mouthwash is used by a woman attempting to conceive, or during the first and second trimester of pregnancy, the dose should be kept as low and duration of treatment as short as possible. Antenatal monitoring for oligohydramnios and ductus arteriosus constriction should be considered after exposure to Benzydamine Mouthwash for several days from gestational week 20 onward. Benzydamine Mouthwash should be discontinued if oligohydramnios or ductus arteriosus constriction are found. During the third trimester of pregnancy, all prostaglandin synthesis inhibitors may expose the foetus to:

- cardiopulmonary toxicity (premature constriction/closure of the ductus arteriosus and pulmonary hypertension);
- renal dysfunction (see above);

the mother and the neonate, at the end of pregnancy, to:

- possible prolongation of bleeding time, an anti-aggregating effect which may occur

even at very low doses;

- inhibition of uterine contractions resulting in delayed or prolonged labour.

Consequently, Benzydamine Mouthwash is contraindicated during the third trimester of pregnancy (see sections 4.3).

#### Breast-feeding

It is not known whether benzydamine hydrochloride / metabolites are excreted in human milk. Benzydamine Mouthwash should not be used during breastfeeding unless considered essential by the physician.

#### Fertility

There is no evidence of a teratogenic effects in studies (see section 5.3). It is not known whether treatment with Benzylamine Mouthwash affected fertility in humans.

#### **4.7 Effects on ability to drive and use machines**

None

#### **4.8 Undesirable effects**

Within each frequency grouping, undesirable effects are presented in order of the decreasing seriousness

The following frequency categories are used: 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  $<1/1,000$ ) and Very rare ( $<1/10,000$ ), not known (cannot be estimated from the available data).

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

##### Respiratory, thoracic and mediastinal disorders

*Very rare:* Laryngospasm or bronchospasm

##### Gastrointestinal disorders

*Uncommon:* Oral numbness (hypoesthesia) and a stinging feeling in the mouth (oral pain)

##### Skin and subcutaneous tissue disorders

*Very rare:* pruritus, urticaria, photosensitivity reaction and a rash

*Frequency not known:* Angioedema

##### Immune system disorders

*Frequency not known:* Anaphylactic reaction which can be potentially life-threatening. Hypersensitivity reactions.

Methyl parahydroxybenzoate may cause allergic reactions (possibly delayed).

##### 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

Yellow card Scheme at: [www.mhra.gov.uk/yellowcard](http://www.mhra.gov.uk/yellowcard) or search for MHRA Yellow Card in the Google Play or Apple App Store.

## 4.9 Overdose

Benzydamine is unlikely to cause adverse systemic effects, even if accidental ingestion should occur. Intoxication is only to be expected if large quantities of benzydamine are swallowed (>300mg).

Symptoms associated with ingested overdose of 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.

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.

#### Mechanism of action

The indazole analogue benzydamine has physicochemical properties and pharmacological activities which differ from those of the aspirin-like NSAIDs. Unlike aspirin-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 pro-inflammatory cytokines including tumour necrosis factor-alpha (TNF- $\alpha$ ) and Interleukin-1 $\beta$  (IL-1 $\beta$ ) 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 compound 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 Difflam 0.15% 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 30ml 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 water control for the first 24 hours whereas aspirin 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 Difflam cream 3% 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**

Oral doses of benzydamine are well absorbed and plasma drug concentrations reach a peak fairly rapidly and then decline with a half-life of about 13 hours. Less than 20% of the drug is bound to plasma proteins.

Although local drug concentrations are relatively large, the systemic absorption of mouthwash-gargle doses of benzydamine is relatively low compared to oral doses. This low absorption should greatly diminish the potential for any systemic drug side effects when benzydamine is administered by this route.

Benzydamine is metabolised primarily by oxidation, conjugation and dealkylation.

### **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.

### **6.1 List of excipients**

Glycerol

Ethanol 96%

Methyl parahydroxybenzoate (E218)

Saccharin sodium (E954)

Sodium hydrogen carbonate

Polysorbate 20

Mint flavour SC-5230-AT (maltodextrin and menthol)

Purified water

### **6.2 Incompatibilities**

None known

### **6.3 Shelf life**

2 years unopened

Use within 12 months of opening

### **6.4 Special precautions for storage**

There are no special requirements for storage

### **6.5 Nature and contents of container**

100ml or 300ml amber glass bottle with an HDPE screw cap with tamper evident band.  
Supplied with a PPc graduated measuring cup.

### **6.6 Special precautions for disposal**

Not applicable

**7      MARKETING AUTHORISATION HOLDER**

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06/03/2025

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28/08/2025