SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Difflam 0.15% w/v Sore Throat Rinse.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Benzydamine Hydrochloride 0.15% w/v.
Excipient(s) with known effects:

Methyl para hydroxy benzoate

Ethanol

Mint flavour with benzyl alcohol, cinnamyl alcohol, citral, citronellol, eugenol,

geraniol, isoeugenol, limonene and linalool.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Liquid for use as mouthwash/gargle.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Benzydamine Sore Throat Rinse is a locally acting analgesic and anti-inflammatory treatment for the relief of painful inflammatory conditions of the 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: Rinse or gargle with 15ml (using measuring cup provided) every 1½ to 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 Sore Throat Rinse 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

Difflam Sore Throat Rinse is contra-indicated in patients with:
Hypersensitivity to the active ingredient, benzydamine hydrochloride 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 Sore Throat Rinse should generally be used undiluted, but if 'stinging' occurs the rinse may be diluted with water. Avoid contact with the eyes.
The amount in 15ml dose of this medicine is equivalent to less than 1126 mg of alcohol. The amount in 15 ml of this medicine is equivalent to less than 30ml beer or 12 ml wine. The small amount of alcohol in this medicine will not have any noticeable effects.
Methyl hydroxybenzoate may cause allergic reactions (possibly delayed)

This medicine contains 2mg benzyl alcohol in each 15 ml dose which is equivalent to 0.14mg/ml. Benzyl alcohol may cause allergic reactions.

This medicinal product contains mint flavour with benzyl alcohol, cinnamyl alcohol, citral, citronellol, eugenol, geraniol, isoeugenol, limonene and linalool. These substances may cause allergic reactions.
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 Sore Throat Rinse 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 Sore Throat Rinse exposure reached after topical administration can be harmful to an embryo/fetus.

Therefore, Benzydamine Sore Throat Rinse 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.

Breast-feeding

Benzydamine Sore Throat Rinse should not be used during lactation unless considered essential by the physician.

4.7 Effects on ability to drive and use machines

Not applicable.

4.8 Undesirable effects

Within the system organ classes, adverse reactions are listed under headings of frequency (number of patients expected to experience the reaction), using the following categories: Very common (≥ 1/10), Common (≥ 1/100 to <1/10),

Uncommon (≥1/1,000 to <1/100), Rare (≥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.

System organ class	Frequency	Adverse reaction
Immune system disorders	Not known	Anaphylactic reactions, Hypersensitivity reactions [20].
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 rash
	Not known	Angioedema

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 or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

Intoxication is only to be expected if large quantities of Difflam Oral Rinse/ Difflam Sore Throat Rinse 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 esophageal 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 anti-inflammatory and antrheumatic agents, non-steroids /Anti-inflammatory preparations, non-steroids for topical use,

ATC code: M01AX07/M02AA05

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 proinflammatory cytokines including tumour necrosis factor-alpha (TNF-α) and Interleukin-1β (IL-1β) 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 Benzydamine 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 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 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 metabolized 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 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Ethanol (96% v/v)
Glycerol
Saccharin
Sodium hydrogen carbonate
Mouthwash Flavour, 52 503/T
Polysorbate 20
Methyl parahydroxybenzoate
Quinoline Yellow (E104)
Patent Blue V (E131)
Purified Water

6.2 Incompatibilities

None known.

6.3 Shelf life

4 years.

6.4 Special precautions for storage

Do not leave uncartoned bottle in direct sunlight.

6.5 Nature and contents of container

Clear glass bottle with screw cap containing 200 ml, with graduated 30 ml measuring cup.

6.6 Special precautions for disposal

No special requirements

7 MARKETING AUTHORISATION HOLDER

Cooper Consumer Health B.V.,
Verrijn Stuartweg 60, 1112 AX Diemen,
The Netherlands

8 MARKETING AUTHORISATION NUMBER(S)

PL 60682/0014

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

20/10/1995 / 31/10/2005

10 DATE OF REVISION OF THE TEXT

17/10/2025