Difflam Spray

Summary of Product Characteristics Updated 01-May-2015 | Meda Pharmaceuticals

1. Name of the medicinal product

Difflam Spray

2. Qualitative and quantitative composition

Each metered dose pump spray delivers Benzydamine hydrochloride 0.15% w/v, approximately 175 microlitres per puff.

Contains methyl parahydroxybenzoate and Ethanol.

For a full list of excipients, see section 6.1.

3. Pharmaceutical form

Difflam Spray is a metered dose pump throat spray.

4. Clinical particulars

4.1 Therapeutic indications

Difflam 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

For oral administration. Adults, adolescents and elderly: 4 to 8 puffs every 1½-3 hourly. Children (6-12): 4 puffs every 1½-3 hourly. Children under 6: One puff to be administered per 4 kg body weight, up to a maximum of 4 puffs, 1½-3 hourly. Because of the small amount of drug applied, elderly patients can receive the same dose as adults.

4.3 Contraindications

Difflam Spray is contra-indicated in patients with known hypersensitivity to any of the ingredients.

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.

Difflam spray SPC (UK 150501)
Avoid contact with the eyes.

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

This medicinal product contains 10 vol % ethanol.

Methyl hydroxybenzoate may cause allergic reactions (possibly delayed)

4.5 Interaction with other medicinal products and other forms of interaction

None known.

4.6 Pregnancy and lactation

Difflam should not be used in pregnancy or lactation unless considered essential by the physician. There is no evidence of a teratogenic effect in animal studies.

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 decreasing seriousness

The following rate values have been used: 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.

Respiratory, thoracic and mediastinal disorders

Very rare: Laryngospasm or bronchospasm.

Gastrointestinal disorders

Uncommon: Oral numbness and a stinging feeling in the mouth.

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

Skin and subcutaneous tissue disorders

Very rare: Hypersensitivity reactions which may be associated with pruritus, urticaria, photosensitivity reaction and rash

Difflam spray SPC (UK 150501)
Frequency not known: Angioedema

Immune system disorders

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

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.

4.9 Overdose

Difflam is unlikely to cause adverse systemic effects, even if accidental ingestion should occur. No special measures are required.

5. Pharmacological properties
5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Other anti-inflammatory and antirheumatic agents, non-steroids /Anti-inflammatory preparations, non-steroids for topical use, ATC code: M01AX07

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 stabilisation 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 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

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. 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.

6. Pharmaceutical particulars

6.1 List of excipients

Difflam spray SPC (UK 150501)

Purified Water Ph. Eur.

6.2 Incompatibilities

None.

6.3 Shelf life

The shelf life expiry date for this product shall not exceed 3 years from the date of its manufacture.

6.4 Special precautions for storage

Do not store above 30°C, do not refrigerate or freeze. Keep out of the reach of children.

6.5 Nature and contents of container

Difflam Spray is presented in a 30 ml HDPE bottle with 170 µl valve pump spray.

6.6 Special precautions for disposal and other handling

The patient should read the instruction leaflet before use.

7. Exceptional Marketing authorization holder

C.G. Papaloisou Ltd, 35 Kilkis Avenue, 2234 Cyprus

8. Exceptional Marketing authorization number(s)

S00004

9. Date of first authorisation/renewal of the authorisation

07/06/2005

10. Date of revision of the text

01 May 2015

Difflam spray SPC (UK 150501)