Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Difflam Spray, 0.15% w/v, Oromucosal Spray

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each puff (175 microlitres) contains 262. 5 micrograms of benzydamine hydrochloride (0.15% w/v).

Excipients: Each puff contains 0.17 mg of Methyl parahydroxybenzoate (E218), 14 mg of Ethanol and mint flavour (see section 4.4 for details).

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Oromucosal spray.
Difflam Spray is a metered dose pump oromucosal spray solution.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

As an adjunct in the symptomatic relief of painful inflammatory conditions of the throat and mouth.

4.2 Posology and method of administration

For oromucosal administration.

ADULTS AND ELDERLY: 4 to 8 puffs, 1½-3 hourly.

CHILDREN (6-12):4 puffs, 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.

The spray should be directed onto the affected area. Uninterrupted treatment should not exceed seven days, except under medical supervision.

4.3 Contraindications

Use in patient with a known hypersensitivity (eg bronchospasm, rhinitis, urticaria) to this product.

4.4 Special warnings and precautions for use

Avoid contact with the eyes.

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

This medicinal product contains:

- 14 mg of alcohol (ethanol) in each puff. The small amount of alcohol in this medicine will not have any noticeable effects.

- less than 1 mmol sodium (23 mg) per dose of 8 puffs, that is to say essentially 'sodium-free'.
- methyl parahydroxybenzoate (E218) which may cause allergic reactions (possibly delayed)
- mint flavour with benzyl alcohol, cinnamyl alcohol, citral, citronellol, eugenol, geraniol, isoeugenol, limonene and linalool. These substances may cause allergic reactions. 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.

4.5 Interaction with other medicinal products and other forms of interactions

None known.

4.6 Fertility, pregnancy and lactation

Difflam Spray 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

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) 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
Frequency not known: Angioedema

Immune system disorders
Frequency not known: Anaphylactic reactions (which can be potentially life-threatening), hypersensitivity 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. Healthcare professionals are asked to report any suspected adverse reactions via HPRA Pharmacovigilance, Website: www.hpra.ie.

4.9 Overdose

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.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 antiinflammatory and antirheumatic agents, nonsteroids / 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 pro-inflammatory cytokines including tumor 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
Benzydamine was evaluated topically as spray or rinse for the relief of painful inflammatory conditions of the mouth and throat through its local analgesic, anaesthetic, and anti-inflammatory action. In clinical studies Difflam spray or rinse have shown benefit in traumatic conditions such as pharyngitis following tonsillectomy or the use of an endotracheal tube. Difflam further showed efficacy in the relief of inflammatory conditions including pharyngitis relieving pain and dysphagia. In clinical studies benzydamine reduced pain, inflammation and ulceration of the oral mucosa associated with radiation therapy. Rinsing with benzydamine after dental surgery reduced pain and inflammation and improved healing of the surgical site. Patients with aphthous ulcer reported pain relief after rinsing with benzydamine solution.

5.2 Pharmacokinetic properties

Following oral administration, Benzydamine is rapidly absorbed from the gastrointestinal tract and maximum plasmalevels 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

Glycerol
Saccharin

Sodium hydrogen carbonate
Ethanol (96%)
Methyl parahydroxybenzoate (E218)
Mint flavour
Polysorbate 20
Purified Water

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Do not store above 30°C. Do not refrigerate or freeze. Store in the original package.

6.5 Nature and contents of container

Difflam spray is presented in a box containing a 30 ml HDPE bottle with a 170 microlitre metering valve spray pump.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Mylan IRE Healthcare Limited
Unit 35/36
Grange Parade
Baldoyle Industrial Estate
Dublin 13
Ireland

8 MARKETING AUTHORISATION NUMBER

PA2010/030/003

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 20 November 1987

Date of last renewal: 06 September 2007

10 DATE OF REVISION OF THE TEXT

March 2021