Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Benzydamine Hydrochloride 0.15% w/v Oromucosal Spray

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each metered dose pump spray delivers Benzydamine hydrochloride 0.15 % w/v, approximately 180 microlitres per puff.

Excipient(s) with known effect: methyl parahydroxybenzoate, 1.000 mg/ml and ethanol, 81.0008 mg/ml. Each puff (0.18 ml) of the spray delivers 0.18 milligrams of methyl parahydroxybenzoate and 14.58 milligrams of ethanol 96%.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Oromucosal spray, solution

Colorless and clear solution with mint odor.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Benzydamine Hydrochloride 0.15 % w/v Oromucosal Spray is a locally acting analgesic and anti-inflammatory treatment for the throat and mouth.
It is used to treat various painful oropharyngeal conditions such as mouth ulcers, sore throat, sore mouth or gums, dental pain.

4.2 Posology and method of administration

Posology
Adults adolescents and elderly **:** 4 - 8 puffs every 1.5 – 3 hourly.
Children (6 - 12): 4 puffs every 1.5 – 3 hourly.
Children under 6: One puff to be administered per 4 kg of body weight, up to a maximum of 4 puffs, 1.5 – 3 hourly.
Elderly: Because of the small amount of drug applied, elderly patients can receive the same dose as adults.

Method of administration
Prior to use, the pump should be actuated a maximum of 5 times to release an even spray mist. After not having used the spray for a longer time, the pump should be actuated once before applying the product again. For application the spray bottle should be used in an upright position with the nozzle targeted at the affected area whilst pushing down the pump head completely.

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

4.3 Contraindications

Benzydamine Hydrochloride 0.15 % w/v Oromucosal Spray is contra-indicated in patients with known hypersensitivity to the active substance 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.
Avoid contact with the eyes.
If the condition is aggravated or not improved use should cease.
This medicinal product contains 9.87 vol % ethanol.
Benzydamine Hydrochloride 0.15 % w/v Oromucosal Spray contains E218 methyl parahydroxybenzoate 1 mg/ml, which may cause allergic reactions (possibly delayed).

4.5 Interaction with other medicinal products and other forms of interaction

None known.

4.6 Fertility, pregnancy and lactation

Pregnancy
There is limited amount of data from the use of benzydamine hydrochloride in pregnant women. There is no evidence of a teratogenic effect in animal studies (see section 5.3). Benzydamine Hydrochloride 0.15 % w/v Oromucosal Spray should not be used in pregnancy unless the clinical condition of the woman requires treatment with benzydamine hydrochloride.

Breastfeeding
It is unknown whether benzydamine hydrochloride /metabolites are excreted in human milk. Benzydamine Hydrochloride 0.15 % w/v Oromucosal Spray should not be used during breastfeeding unless considered essential by the physician.

Fertility
It is not known whether treatment with Benzydamine Hydrochloride 0.15 % w/v Oromucosal Spray 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 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
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 HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie.

4.9 Overdose

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 antirheumatic agents, non-steroids,
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 proinflammatory (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 hydrochloride 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 benzydamine hydrochloride 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

Absorption
Following oral administration, Benzydamine is rapidly absorbed from the gastrointestinal tract and maximum plasma levels reached after 2-4 hours.

Distribution
The most important aspect of the tissue distribution of Benzydamine is its tendency to concentrate at the site of inflammation.

Biotransformation and 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.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium bicarbonate
Polysorbate 20
Ethanol 96 %
Glycerol
Saccharin sodium
Methyl parahydroxybenzoate (E218)
Peppermint oil
Water, purified

6.2 Incompatibilities

None.

6.3 Shelf life

3 years.

After first opening of the medicinal product: 6 months.

6.4 Special precautions for storage

This medical product does not require any special storage condition. Do not freeze.

For storage conditions after first opening of the medicinal product, see section 6.3.

6.5 Nature and contents of container

Amber glass bottle (Type III) with metered dose pump.

Pack size: 30 ml

6.6 Special precautions for disposal and other handling

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Abdi Farma, Unip. Lda.
Quinta da Fonte, Rua dos Malhões
Edifício D. Pedro I
2770-071 Paço de Arcos
Portugal

8 MARKETING AUTHORISATION NUMBER

PA2158/001/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 9th February 2018

10 DATE OF REVISION OF THE TEXT

April 2018