Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Difflam 3 % w/w Cream

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Contains benzydamine hydrochloride 3% w/w.

Difflam Cream also contains Cetyl Alcohol 6%w/w. Methyl hydroxybenzoate (E218) 0.18%w/w, Propyl hydroxybenzoate (E216) 0.02%w/w, Propylene glycol 5%w/wand Eumulgin B1 4%w/w. Eumulgin B1 may contain cetyl and stearyl alcohol.

For a full list of excipients, see 6.1.

3 PHARMACEUTICAL FORM

Cream

Collapsible internally lined aluminium tubes containing a white to ivory-white homogeneous, perfumed cream.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Benzydamine exerts an anti-inflammatory and analgesic effect by stabilising the cellular membrane and inhibiting prostaglandin synthesis.

Benzydamine cream may be used as an anti-inflammatory agent in the treatment of symptoms associated with painful conditions of the musculo-skeletal system such as: myalgia, bursitis, rheumatism and traumatic conditions such as: soft tissue injuries, sprains, strains, contusions and the after effects of fractures.

4.2 Posology and method of administration

May be applied and massaged lightly into the skin up to three times a day, and in more severe conditions up to six times daily.

4.3 Contraindications

Use in patient with a known hypersensitivity to the active ingredient, benzydamine hydrochloride, or to any of the other ingredients.

4.4 Special warnings and precautions for use

This product should not be applied to the eyes or mucosal surfaces.

The excipients methyl hydroxybenzoate, propyl hydroxybenzoate, cetyl alcohol and propylene glycol may cause allergic reactions.

Methyl hydroxybenzoate and propyl hydroxybenzoate may cause allergic reactions (possibly delayed)

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.

4.6 Fertility, 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

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)
Frequency not known (cannot be estimated from the available data)

Skin and subcutaneous tissue disorders
Frequency not known: Photosensitivity reactions have been reported and local skin reactions which have varied from erythema to papular eruption. The skin returned to normal on stopping treatment.

Immune system disorders
Frequency not known: Anaphylactic reactions which can be potentially life-threatening,

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: http://www.hpra.ie/; E-mail: medsafety@hpra.ie.

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 antiinflammatory and antrheumatic agents, nonsteroids / Anti-inflammatory preparations, non-steroids for topical use,
ATC Code: 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 1 mM 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
Difflam cream has been clinically tested as a short-term treatment for the relief of symptoms associated with painful inflammatory conditions of the musculo-skeletal system including myalgia and bursitis. Further, it showed clinical benefit in traumatic condition such as sprains, strains, contusions and post fractures. Difflam Cream is well absorbed through the skin and has been shown to have anti-inflammatory and local anaesthetic actions.

5.2 Pharmacokinetic properties

Following topical administration, Benzydamine is rapidly absorbed through intact skin and reaches peak levels between 24-32 hours, amounting to about 20-25% of the plasma levels obtained after oral administration of the same dose.

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 Monostearate 40-55
Cetyl Alcohol
Decyl Oleate
Eumulgin ^{TM} B1**
Propylene Glycol
Perfume Crematest ^{TM} 0/064060***
Methyl parahydroxybenzoate
Propyl parahydroxybenzoate
Purified water

* Glycerol Monostearate 40-55 contains a mixture of mono and diglycerides of palmitic and stearic acids.
** Eumulgin B1 contains polyglycollic ethers of cetyl and stearyl alcohols (Macrogol Cetostearyl Ether).
*** Perfume Crematest 0/064060 contains perfume in diethyleneglycolmonoether.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Do not store above 25°C. Do not freeze.
Keep the lid tightly closed.

6.5 Nature and contents of container

Collapsible aluminium tube closed with plastic screwcap.
Pack size: 50 g

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

PA2010/030/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 15 April 1981

Date of last renewal: 05 September 2008

10 DATE OF REVISION OF THE TEXT

November 2018