Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Difene Spray Gel 4% w/w Cutaneous Spray, Solution

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1g of solution contains 40 mg of diclofenac sodium.
Excipients with known effects: 150 mg propylene glycol (E1520) / gram solution
100 mg Soybean lecithin / gram solution
33,3 mg anhydrous ethanol / gram solution
For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Cutaneous spray, solution.
A golden-yellow, transparent solution, which turns to a gel-like consistency after administration.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For the local symptomatic relief of mild to moderate pain and inflammation following acute blunt trauma of small and medium-sized joints and periarticular structures.
Difene Spray Gel is indicated in adults and for children aged 14 years and older.

4.2 Posology and method of administration

Posology
Adults
Sufficient solution of Difene Spray Gel should be sprayed onto the skin of the affected site. Depending on the size of area to be treated 4-5 pump strokes (0.8-1.0 g of spray containing 32-40 mg of diclofenac sodium) should be applied 3 times daily in regular intervals. A maximum single dose of 1.0 g of the product should not be exceeded. The maximum daily dose is 15 pump strokes (3.0 g of spray containing 120 mg of diclofenac sodium).
Difene Spray Gel should be massaged gently into the skin. After this the hands should be washed unless they are the site to be treated. After application some minutes for drying should be allowed before dressing or binding the treated area.
The treatment may be discontinued when the symptoms (pain and swelling) have subsided. Treatment should not be continued beyond 7-8 days without review. The patient is requested to consult the doctor if no improvement is seen after 3 days or if symptoms worsen.

Paediatric population
There are insufficient data on efficacy and safety available for the children and adolescents below 14 years of age (see also contraindications section 4.3).
In children aged 14 years and older, if this product is required for more than 7 days for pain relief or if the symptoms worsen the patient/parents of the adolescent is/are advised to consult a doctor.

Elderly
No special dose adjustment is required. Due to the possible adverse effect profile the elderly should receive particularly careful monitoring.
Patients with renal impairment
In patients with renal impairment no dose reduction is required.
Patients with hepatic impairment
In patients with hepatic impairment no dose reduction is required.

Method of administration

For cutaneous use only.

4.3 Contraindications

- Hypersensitivity to diclofenac, peanut, soya or to any of the excipients listed in section 6.1.
- Hypersensitivity to acetylsalicylic acid or other non-steroidal anti-inflammatory drugs (NSAIDs).
- Patients in whom attacks of asthma, urticaria or acute rhinitis are precipitated by aspirin or other non-steroidal anti-inflammatory agents (NSAIDs).
- Use on open injuries, inflammations or infections of the skin as well as on eczema or mucous membranes.
- During the third trimester of pregnancy.
- Children and adolescents aged less than 14 years.

4.4 Special warnings and precautions for use

The possibility of systemic adverse events from application of Difene Spray Gel cannot be excluded if the preparation is used on large areas of skin and over a prolonged period (see the product information on systemic forms of diclofenac).
Difene Spray Gel should be applied only to intact non-diseased skin, and not to skin wounds or open injuries. It should not be allowed to come into contact with the eyes or mucous membranes and should not be ingested.
Difene Spray Gel can be used with non-occlusive bandages but should not be used with an airtight occlusive dressing.
Patients should be warned against exposure to sunlight or solarium radiation in order to reduce the incidence of photosensitivity.
Discontinue the treatment if a skin rash develops after applying the product.

The concomitant use of Difene Spray Gel with oral NSAIDs should be cautioned as the incidence of systemic side effects may increase (see section 4.5).
Undesirable effects may be reduced by using the minimum effective dose for the shortest possible duration.
Bronchospasm may be precipitated in patients suffering from or with previous history of bronchial asthma or allergenic disease.
Difene Spray Gel should only be used with caution in patients with a history of peptic ulcer, hepatic or renal insufficiency, bleeding diathesis or inflammatory bowel disease as isolated cases with topical diclofenac have been reported.
Difene Spray Gel contains propylene glycol (E1520) [SK1] which may cause skin irritation in some people.
Difene Spray Gel contains peppermint oil which may cause allergic reactions.
Difene Spray Gel contains 33.3 mg of alcohol (ethanol) per gram, which is equivalent to 3.3% w/w. It can cause a burning sensation on damaged skin. Do not use near an open flame, lit cigarette or some devices (e.g. hairdryers).

4.5 Interaction with other medicinal products and other forms of interaction

Since systemic absorption of diclofenac from a topical application of Difene Spray Gel is very low such interactions are very unlikely. Concurrent acetylsalicylic acid or other NSAIDs may result in an increased incidence of adverse reactions (see section 4.4).

4.6 Fertility, pregnancy and lactation

Pregnancy
The systemic concentration of Difene Spray Gel is lower after topical administration, compared to oral formulations. With reference to experience from treatment with NSAIDs with systemic uptake, the following is recommended:

Inhibition of prostaglandin synthesis may adversely affect the pregnancy and/or the embryo/foetal development. Data from epidemiological studies suggest an increased risk of miscarriage and of cardiac malformation and gastroschisis after use of a prostaglandin synthesis inhibitor in early pregnancy. The absolute risk for cardiovascular malformation was increased from less than 1%, up to approximately 1.5%. The risk is believed to increase with dose and duration of therapy. In animals, administration of a prostaglandin synthesis inhibitor has been shown to result in increased pre- and post-implantation loss and embryo-foetal lethality. In addition, increased incidences of various malformations, including cardiovascular, have been reported in animals given a prostaglandin synthesis inhibitor during the organogenetic period.

During the first and second trimester of pregnancy, Difene Spray Gel should not be given unless clearly necessary. If Difene Spray Gel is used by a woman attempting to conceive, or during the first and second trimester of pregnancy, the dose should be kept as low and duration of treatment as short as possible.

During the third trimester of pregnancy, all prostaglandin synthesis inhibitors may expose the foetus to:
- cardiopulmonary toxicity (with premature closure of the ductus arteriosus and pulmonary hypertension);
- renal dysfunction, which may progress to renal failure with oligo-hydroamniosis;

The mother and the neonate, at the end of pregnancy, to:
- possible prolongation of bleeding time, an anti-aggregating effect which may occur even at very low doses.
- inhibition of uterine contractions resulting in delayed or prolonged labour.

Consequently, diclofenac is contraindicated during the third trimester of pregnancy.
Difene Difene Difene

Lactation
Like other NSAIDs, diclofenac passes into breast milk in small amounts. However, at therapeutic doses of Difene Spray Gel no effects on the suckling child are anticipated. Because of a lack of controlled studies in lactating women, the product should only be used during lactation under advice from a healthcare professional. Under this circumstance, Difene Spray Gel should not be applied on the breasts of nursing mothers, nor elsewhere on large areas of skin or for a prolonged period of time (see section 4.4).

4.7 Effects on ability to drive and use machines

Cutaneous application of Difene Spray Gel has no influence on the ability to drive and use machines.

4.8 Undesirable effects

Skin disorders are commonly reported.
Adverse reactions (Table 1) are ranked under heading of frequency, the most frequent first, using the following convention: 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), or not known (can not to be estimated from available data). Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

Table 1

Immune system disorder	
Very rare	Hypersensitivity (including urticaria), angioneurotic oedema
Infections and infestations	
Very rare	Rash pustular
Respiratory, thoracic and mediastinal disorders	
Very rare	Asthma
Skin and subcutaneous tissue disorders	
Common	Rash, eczema, erythema, dermatitis (including dermatitis contact), pruritus*****
Rare	Dermatitis bullous
Very rare	Photosensitivity reaction
Not known:	Application site reaction, dry skin, burning sensation

* Pruritus has been reported at a frequency of 0.9% in a clinical trial, 236 patients with ankle distortions were treated with 4–5 pump strokes of Difene Spray Gel t.i.d. (120 patients) or placebo (116 patients) for 14 days.

When Difene Sodium Spray Gel is applied on large areas of skin and over a prolonged period, the occurrence of systemic undesirable effects cannot be excluded.

Reactions such as abdominal pain, dyspepsia, gastric, hepatic or renal disorders and systemic hypersensitivity reactions may occur.
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

The low systemic absorption of topical diclofenac renders overdose very unlikely.
However undesirable effects similar to those observed following an overdose of diclofenac tablets can be expected if Difene Spray Gel is inadvertently ingested (i.e. a 15 ml spray bottle containing 500 mg of diclofenac sodium).
In the event of accidental ingestion resulting in significant systemic adverse effects, general therapeutic measures normally adopted to treat poisoning with non-steroidal anti-inflammatory medicines should be used. Gastric decontamination and the use of activated charcoal should be considered, especially within a short time of ingestion.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Topical products for joint and muscular pain; Antiinflammatory preparations, non-steroids for topical use.
ATC code: M02AA 15
Diclofenac is a non-steroidal anti-inflammatory-/analgesic active substance which, via inhibition of prostaglandin synthesis, has been shown to be effective in standard animal models of inflammation. In humans, diclofenac reduces inflammation-related pain and swelling.

5.2 Pharmacokinetic properties

After cutaneous application of 1.5 g Difene Spray Gel a rapid onset of diclofenac absorption can be observed leading to measurable plasma levels of about 1 ng/ml as early as 30 minutes and to maximum levels of about 3 ng/ml at about 24 hours after application.

The achieved systemic concentrations of diclofenac are about 50 times lower than those achieved following oral administration of equivalent amounts of diclofenac. Systemic plasma levels are not supposed to contribute to the efficacy of Difene Spray Gel.

Diclofenac is extensively bound to plasma proteins (about 99 %).

5.3 Preclinical safety data

In rabbit skin, Difene Spray Gel is classified as non-irritant.
Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity and carcinogenic potential of diclofenac.
In rats and rabbits oral doses of diclofenac were not teratogenic but caused embryotoxicity at maternally toxic doses.

Diclofenac did not affect fertility in rats but inhibited ovulation in rabbits and reduced implantation in rats.

In rats, diclofenac resulted in dose-dependent constriction of the fetal ductus arteriosus, dystocia and delayed parturition.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Isopropyl alcohol
Soy bean lecithin
Ethanol
Disodium phosphate dodecahydrate
Sodium dihydrogen phosphate dihydrate
Disodium edetate
Propylene glycol (E1520)
Peppermint oil

Ascorbyl palmitate
Hydrochloric acid concentrated (w/w) for pH-adjustment
Sodium hydroxide 10% (w/w) for pH-adjustment
Purified water.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

Unopened bottle (25g solution in 30 ml bottle and 12.5g solution in 15 ml bottle): 3 years
Unopened bottles (7.5g solution in 10 ml bottle): 2 years
In-use: 6 months.

6.4 Special precautions for storage

Store in the original package.

6.5 Nature and contents of container

Glass bottle with metering pump/nozzle/spray valve and cap.
Pack sizes of 7.5 g (10 ml bottle), 12.5 g (15 ml bottle) and 25 g (30 ml bottle) solution.
Not all pack sizes may be marketed.

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

Glenwood GmbH
Pharmazeutische Erzeugnisse
Arabellastrasse 17
81925 Munich
Germany

8 MARKETING AUTHORISATION NUMBER

PA2256/001/007

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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Date of last renewal: 13 May 2007

10 DATE OF REVISION OF THE TEXT

March 2023