SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Diclofenac Diethylamine 2.32% w/w Gel

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

1 g of gel contains diclofenac as 23.2 mg diclofenac diethylamine corresponding to 20 mg of diclofenac sodium.

Excipient(s) with known effect

1 g of gel contains 54 mg of propylene glycol (E1520), 0.2 mg butylhydroxytoluene (E321) and 1 mg fragrance (contains 0.15 mg benzyl alchohol (E1519), citral, citronellol, coumarin, eugenol, farnesol, geraniol, d-limonene, linalool).

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Gel

White to almost white, homogeneous gel

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For the local symptomatic relief of pain and inflammation in:

- trauma of the tendons, ligaments, muscles and joints, e.g. due to sprains, strains and bruises
- localised forms of soft tissue rheumatism

For the relief of pain of non-serious arthritic conditions.

4.2 Posology and method of administration

For cutaneous use only

Adults and children 14 years and over: The gel should be rubbed gently into the skin**.** Depending on the size of the affected site to be treated, 2-4g (a circular shaped mass approximately 2.0-2.5cm in diameter) of gel should be applied 2 times a day (preferably morning and evening). The maximum daily dose is 8g. Therefore, the maximum weekly dose is 56g.

The gel can be used for up to 14 days under doctor or pharmacy supervision.

After application, the hands should be washed unless they are the site being treated.

If symptoms do not improve by day 7, or if they worsen within the first 7 days, a consultation with a doctor is recommended. Do not use for more than 14 days unless recommended by a doctor.

Use in the elderly: The usual adult dosage may be used.

Children and adolescents: 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 over, 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.

4.3 Contraindications

- Patients with or without chronic asthma in whom asthma, angioedema, urticaria or acute rhinitis are precipitated by aspirin or other non-steroidal anti-inflammatory agents.
- Hypersensitivity to diclofenac, acetylsalicylic acid or other non-steroidal anti-inflammatory drugs.
- Hypersensitivity to any other ingredient of the gel.
- During the last trimester of pregnancy.

4.4 Special warnings and precautions for use

The possibility of experiencing systemic adverse events (those associated with the use of systemic forms of diclofenac) from application of this medicine cannot be excluded if the preparation is used at higher dosage/large amounts over large areas of skin and/or over a prolonged period (see the product information of systemic forms of diclofenac e.g. oral or injection for systemic adverse reactions).

Concomitant use of systemic NSAIDs should be cautioned since the possibility of an increase in incidence of untoward effects, particularly systemic side effects, cannot be ruled out.

This medicine should be applied only to intact, non-diseased skin and not to skin wounds or open injuries. It should not be used with occlusion. It should not be allowed to come into contact with the eyes or mucous membranes, and should never be taken by mouth.

Patients with a history of, or active, peptic ulceration. Some possibility of gastro-intestinal bleeding in those with a significant history of this condition has been reported in isolated cases.

Like other drugs that inhibit prostaglandin synthetase activity, diclofenac and other NSAIDs can precipitate bronchospasm if administered to patients suffering from or with a previous history of, bronchial asthma.

Discontinue the treatment if a skin rash develops after applying the product.

Patients should be warned against excessive exposure to sunlight in order to reduce the incidence of photosensitivity.

Diclofenac Diethylamine Gel contains butylhydroxytoluene which may cause local skin reactions (e.g. contact dermatitis) or irritation to the eyes and mucous membranes.

This medicinal product contains fragrance with benzyl alcohol (0.15 mg/g, E1519), citral, citronellol, coumarin, eugenol, farnesol, geraniol, d-limonene and linalool which may cause allergic reactions.

In addition, benzyl alcohol may cause mild local irritation.

Instruct patients not to smoke or go near naked flames - risk of severe burns. Fabric (clothing, bedding, dressings etc) that has been in contact with this product burns more easily and is a serious fire hazard. Washing clothing and bedding may reduce product build-up but not totally remove it.

4.5 Interaction with other medicinal products and other forms of interaction

Since systemic absorption of diclofenac from a topical application is very low such interactions are very unlikely. There are no known interactions with this medicine, but for a list of interactions known with oral diclofenac the SPCs for oral dosage forms should be consulted.

4.6 Fertility, pregnancy and lactation

There are no data available on the use of topical formulations of diclofenac and its effects on fertility in humans.

Pregnancy

The systemic concentration of diclofenac 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/fetal 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-fetal 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, diclofenac should not be given unless clearly necessary. If diclofenac 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.

Lactation

Like other NSAIDs, diclofenac passes into breast milk in small amounts. However, at therapeutic doses of this medicine 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, this medicine 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

This medicine has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Undesirable effects include mild and passing skin reactions at the site of application. In very rare instances, allergic reactions may occur.
Adverse reactions are ranked under heading of frequency, the most frequent first, using the following convention: Very common (> 1/10); Common (>1/100, <1/10); Uncommon (> 1/1,000, > 1/100); Rare (≥ 1/10,000, <1/1000); Very rare (< 1/10,000), Not known: cannot be estimated from the available data.

Infections and infestations:	
Very rare:	Rash pustular
Immune system disorders:	
Very rare:	Hypersensitivity (including urticaria), angioedema

Respiratory, thoracic and mediastinal disorders:	
Very rare:	Asthma
Skin and subcutaneous tissue disorders:	
Common:	Dermatitis (including contact dermatitis), rash, erythema, eczema, pruritus
Rare:	Dermatitis bullous
Very rare:	Photosensitivity reaction
Not known:	Desquamation, skin discolouration, burning sensation at the application site, dry skin

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

Signs and symptoms

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 this medicine is inadvertently ingested (e.g. 1 tube of 50 g contains the equivalent of 1 g diclofenac sodium).

Treatment

If the recommended dose is significantly exceeded, this medicinal product should be removed from the skin and washed off with water.

Management of overdosage with NSAIDs essentially consists of supportive and symptomatic measures. There is no typical clinical picture resulting from diclofenac overdosage. Supportive and symptomatic treatment should be given for complications such as hypotension, renal failure, convulsions, gastro-intestinal irritation, and respiratory depression; specific therapies such as forced diuresis, dialysis or haemoperfusion are probably of no help in eliminating NSAIDs due to their high rate of protein binding and extensive metabolism.

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. The use of activated charcoal should be considered, especially within a short time (within one hour) of ingestion of a toxic dose.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Topical products for joint and muscular pain. Anti-inflammatory preparations, non-steroids for topical use, ATC code: M02A A15

Mechanism of action and pharmacodynamic effects: Diclofenac is a potent non-steroidal anti-inflammatory drug (NSAID) with pronounced analgesic, anti-inflammatory and antipyretic properties. Diclofenac exerts its therapeutic effects primarily through inhibition of prostaglandin synthesis by cyclo-oxygenase 2 (COX-2).

This medicine is an anti-inflammatory and analgesic preparation designed for topical application. In inflammation and pain of traumatic or rheumatic origin, this medicine relieves pain, decreases swelling, and shortens the time to return to normal function. In one ankle sprain study (VOPO-P-307), this medicine significantly decreased pain on movement scores versus placebo treated subjects within three days of starting treatment, including a subgroup of patients with severe pain. In addition treatment with this medicine also significantly improved ankle joint function within 3 days of beginning treatment.

Due to an aqueous-alcoholic base the gel also exerts a cooling effect.

5.2 Pharmacokinetic properties

Absorption

The quantity of diclofenac absorbed through the skin is proportional to the size of the treated area, and depends on both the total dose applied and the degree of skin hydration. After topical application to approximately 400 cm^2 of skin, the extent of systemic exposure as determined by plasma concentration of this medicine (2 applications/day) was equivalent to diclofenac 1.16% gel (4 applications/day). The relative bioavailability of diclofenac (AUC ratio) for this medicine versus tablet was 4.5% on day 7 (for equivalent diclofenac sodium dose). Absorption was not modified by a moisture and vapour permeable bandage.

Distribution

Diclofenac concentrations have been measured from plasma, synovial tissue and synovial fluid after application of topical diclofenac to hand and knee joints. Maximum plasma concentrations were approximately 100 times lower than after oral administration of the same quantity of diclofenac. 99.7 % of diclofenac is bound to serum proteins, mainly albumin (99.4 %).

From the skin and underlying tissue, diclofenac penetrates inflamed areas, preferentially distributing to and persisting in deep inflamed tissues (such as joints), rather than in the bloodstream. Diclofenac is found in concentrations up to 20 times higher than in plasma.

Biotransformation

Biotransformation of diclofenac involves partly glucuronidation of the intact molecule, but mainly single and multiple hydroxylation resulting in several phenolic metabolites, most of which are converted to glucuronide conjugates. Two of the phenolic metabolites are biologically active, however, to a much smaller extent than diclofenac.

Elimination

The total systemic clearance of diclofenac from plasma is 263 ± 56 ml/min. The terminal plasma half-life is 1-2 hours. Four of the metabolites, including the two active ones, also have short plasma half-lives of 1-3 hours. One metabolite, 3'-hydroxy-4'-methoxy-diclofenac, has a longer half-life but is virtually inactive. Diclofenac and its metabolites are excreted mainly in the urine.

Characteristics in patients

No accumulation of diclofenac and its metabolites is to be expected in patients suffering from renal impairment. In patients with chronic hepatitis or non-decompensated cirrhosis, the kinetics and metabolism of diclofenac are the same as in patients without liver disease.

5.3 Preclinical safety data

This medicine was well tolerated in a variety of studies. There was no potential for phototoxicity and diclofenac-containing gel caused no skin sensitisation or irritation.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Isopropyl alcohol

Propylene glycol (E1520)

Cocoyl Caprylocaprate

Paraffin, Liquid

Carbomer

Macrogol cetostearyl ether

Diethylamine

Oleic acid (E570)

Butylhydroxytoluene (E321)

Fragrance (contains citronellol, geraniol, benzyl alcohol (E1519), linalool, limonene, citral, farnesol, coumarin, eugenol)

Purified water

6.2 Incompatibilities

None Stated.

6.3 Shelf life

30 months

6.4 Special precautions for storage

Store in the original tube in order to protect from light.

This medicinal product does not require any special temperature storage conditions.

This medicine should be kept out of the sight and reach of children.

6.5 Nature and contents of container

The gel is packed in aluminium laminated tubes, closed with PE seal and PP screw caps in pack sizes: 30g, 50g, 60g, 100g, 150g, 180g per tube.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

None.

7 MARKETING AUTHORISATION HOLDER

Teva UK Limited,
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