Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Voltarol Emulgel 1% w/w Gel

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Voltarol Emulgel contains diclofenac diethylammonium 1.16% w/w corresponding to diclofenac sodium 1% w/w.

Excipients with known effect: Contains propylene glycol (5% w/w) and benzyl benzoate (0.003% w/w)

For a full list of excipients, see Section 6.1.

3 PHARMACEUTICAL FORM

Gel.
Voltarol Emulgel is a white, pleasantly perfumed, homogeneous, non-greasy emulsion in an aqueous gel.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

In adults, the elderly and adolescents aged 14 years and over 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.

4.2 Posology and method of administration

For cutaneous use only.

Adultsand children aged 14 years and over: Voltarol Emulgel 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) should be applied 3-4 times daily. After application, the hands should be washed unless they are the site being treated.

If the condition does not improve or worsens within 7 days of starting treatment, patient should consult their doctor to exclude an alternative underlying cause of pain.

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

Children and adolescents below 14 years: There are insufficient data on efficacy and safety available for children and adolescents below 14 years of age (see also contraindications section 4.3).

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.
During the last trimester of pregnancy.
Hypersensitivity to diclofenac, aspirin or other non-steroidal anti-inflammatory drugs or to any of the excipients contained in the gel (see 6.1, list of excipients)

The use in children and adolescents aged less than 14 years is contraindicated.

4.4 Special warnings and precautions for use

Precautions
The possibility of systemic adverse events from application of Voltarol Emulgel cannot be excluded if the preparation is used at higher dosage or over a prolonged period. These include gastrointestinal disturbances and bleeding, irritability, fluid retention, rash, hepatitis, renal dysfunction, anaphylaxis and rarely blood dyscrasias, bronchospasm and erythema multiforme. This product should only be used with great caution in patients with a history of peptic ulcer, gastrointestinal bleeding, hepatic or renal insufficiency, or bleeding diathesis, or intestinal inflammation. Circulating levels of the active drug substance are low but the theoretical risk in these patients should be considered.
Discontinue the treatment if a skin rash develops after applying the product.
Voltarol Emulgel can be used with non-occlusive bandages but should not be used with an airtight occlusive dressing.

Voltarol Emulgel 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 ingested.

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.

Voltarol Emulgel is usually well tolerated. Local irritation, erythema, pruritus or dermatitis, desquamation and discoloration commonly occur. Bullous or vesicular eruptions are rarely reported. Skin photosensitivity has very rarely been reported. Patients should be warned against excessive exposure to sunlight in order to reduce the incidence of photosensitivity.

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.

Information concerningexcipients

Voltarol Emulgel contains propylene glycol and benzyl benzoate, which may cause skin irritation.

4.5 Interaction with other medicinal products and other forms of interaction

Since systemic absorption of diclofenac from topical application is very low, such interactions are very unlikely.

4.6 Fertility, pregnancy and lactation

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 fetus 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 Voltarol Emulgel 1% 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, Voltarol Emulgel 1% 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 topical diclofenac has no influence on the ability to drive and use machines.

4.8 Undesirable effects

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), not known: cannot be estimated from the available data. Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

Table 1

Infections and infestations:		
	Very rare:	Rash pustular.
Immune system disorders:-		
	Very rare:	Hypersensitivity (including urticaria), angioneurotic oedema.
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

Voltarol Emulgel is usually well tolerated. Local irritation, erythema, pruritus or dermatitis, desquamation and discoloration commonly occur. Bullous or vesicular eruptions are rarely reported. Skin photosensitivity has very rarely been reported.

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

Signs and symptoms

The low systemic absorption of topical diclofenac renders overdosage unlikely. However, undesirable effects, similar to those observed following an overdose of diclofenac tablets can be expected if topical diclofenac is ingested (1 tube of 100g contains the equivalent of 1000mg diclofenac sodium). In the event of accidental ingestion, resulting in significant systemic side-effects, general therapeutic measures normally adopted to treat poisoning with non-steroidal anti-inflammatory drugs should be used.

Treatment

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.

Further management should be as clinically indicated or as recommended by the national poisons centres, where available.

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).

Mode of action:
Diclofenac is a potent non-steroidal anti-inflammatory (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).

Voltarol Emulgel is an anti-inflammatory and analgesic preparation designed for topical application. In inflammation and pain of traumatic or rheumatic origin, Voltarol Emulgel relieves pain, decreases swelling, and shortens the time to return to normal function. Due to an aqueous-alcoholic base the gel exerts a soothing and cooling effect.

Clinical data have demonstrated that Voltarol Emulgel 1% reduces acute pain one hour after initial application ($p < 0.0001$ versus placebo gel). Ninety-four percent (94%) of patients responded to Voltarol Emulgel 1% after 2 days of treatment versus 8% with placebo gel ($p < 0.0001$) Resolution of both pain and functional impairment were achieved after 4 days of treatment with Voltarol Emulgel 1% ($p < 0.0001$ versus placebo gel).

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. Absorption amounts to about 6 % of the applied dose of diclofenac after topical application of 2.5 g Voltarol Emulgel on 500 cm^2 skin, determined by reference to the total renal elimination, compared with Voltarol tablets. A 10-hour occlusion leads to a three-fold increase in the amount of diclofenac absorbed.

Distribution:
Diclofenac concentrations have been measured from plasma, synovial tissue and synovial fluid after topical administration of Voltarol Emulgel to hand and knee joints. Maximum plasma concentrations are 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 %).

Diclofenac accumulates in the skin which acts as a reservoir from where there is a sustained release of drug into underlying tissues. From there, diclofenac preferentially distributes and persists in deep inflamed tissues (such as the joint) 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

Preclinical studies conducted with Voltarol Emulgel did not reveal any clinical relevant toxicological effects.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Diethylamine
Carbomer
Macrogol Cetostearyl Ether
Cocoyl Caprylocaprate
Isopropyl Alcohol
Liquid paraffin
Perfume (including benzyl benzoate)
Propylene glycol
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.

6.5 Nature and contents of container

Sealed aluminium tubes with protective inner coating, closed with a polypropylene screw cap incorporating a built-in point to pierce the aluminium seal, available in packs of 10 g and 30 g.

or

Aluminium laminated tubes consisting of:
[Low density polyethylene / aluminium / high density polyethylene (internal layer) or LDPE / aluminium / LLDPE, HDPE and Antiblock Masterbatch blend (internal layer)] fitted with a high density polyethylene shoulder and closed by a moulded seal. The tube is closed with a polypropylene screw cap, in blue or white, incorporating a moulded feature used to insert, twist and remove the seal before first use, available in packs of 30 g, 50 g & 100 g.

or

Aluminium laminated tubes consisting of:
[Low density polyethylene / aluminium / high density polyethylene (internal layer) or LDPE / aluminium / LLDPE, HDPE and Antiblock Masterbatch blend (internal layer)] fitted with a high density polyethylene shoulder and closed by a moulded seal. The tube is closed with a push / pull cap applicator comprised of a white HDPE head, orange polypropylene (PP) body and a non-coloured PP over-cap, incorporating a moulded feature used to insert, twist and remove the seal before first use, available in packs of 100 g.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Haleon Ireland Limited
12 Riverwalk
Citywest Business Campus
Dublin 24
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8 MARKETING AUTHORISATION NUMBER

PA0678/140/002

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10 DATE OF REVISION OF THE TEXT

July 2023