Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Voltarol Emulgel 1% w/w Gel

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each gram of gel contains 11.6mg of diclofenac diethylammonium corresponding to 10mg of diclofenac sodium (1% w/w).

Also contains propylene glycol.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Gel
Product imported from Greece:
Voltarol Emulgel is a white, pleasantly perfumed, homogenous, non-greasy emulsion in an aqueous gel.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

For 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.

It is recommended that treatment should be reviewed after 14 days in these indications.
These indications should not warrant treatment for more than 6 weeks.

- For the symptomatic treatment of osteoarthritis of superficial joints such as the knee.
- In the symptomatic treatment of osteoarthritis, therapy should be reviewed after 4 weeks.

4.2 Posology and method of administration

Topical application.

Adults*: 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.

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). 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.

* It is recommended that treatment be reviewed after 14 days. These indications should not warrant treatment for more than 6 weeks.

4.3 Contraindications

Hypersensitivity to diclofenac or to any of the excipients contained in the gel (see 6.1, list of excipients).

Patients in whom attacks of asthma, urticaria, or acute rhinitis are precipitated by acetylsalicylic acid or other non-steroidal anti-inflammatory drugs (NSAIDs).

During the last trimester of pregnancy.

Use in patients hypersensitive to propylene glycol or isopropanol or other components of the gel base.

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

4.4 Special warnings and precautions for use

The possibility of systemic adverse events from application of Voltarol Emulgel 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).

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 allowed to come into contact with the eyes or mucous membranes, and should not be ingested.

Side effects include itching, reddening or smarting of the skin or skin rash. Photosensitivity reactions have been observed in isolated cases.

Asthma has been rarely reported in patients using topical non steroidal anti-inflammatory drugs (NSAID) preparations.

Application over extensive areas for prolonged periods or application in excess of recommended dosage may give rise to systemic effects. 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.

Information concerning excipients
Voltarol Emulgel contains propylene glycol, which may cause mild, localised skin irritation in some people.

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. However, the following interactions occur with <u>oral</u> forms of Voltarol:

<u>Lithium and digoxin</u>: Voltarol may increase plasma levels of lithium or digoxin.

<u>Anticoagulants</u>: Although clinical investigations do not appear to indicate that Voltarol has an influence on the effect of anticoagulants, there are isolated reports of an increased risk of haemorrhage with the combined use of diclofenac and anticoagulant therapy.

Therefore to be certain that no change in anticoagulant dosage is required, close monitoring of such patients is required. As with other non-steroidal anti-inflammatory agents, diclofenac in a high dose can reversibly inhibit platelet aggregation.

Antidiabetic agents: Clinical studies have shown that Voltarol can be given together with oral antidiabetic agents without influencing their clinical effect. However there have been isolated reports of hypoglycaemic and hyperglycaemic effects which have required adjustment to the dosage of hypoglycaemic agents.

Ciclosporin: Cases of nephrotoxicity have been reported in patients receiving concomitant ciclosporin and NSAIDs, including Voltarol. This might be mediated through combined renal anti-prostaglandin effects of both the NSAID and ciclosporin.

Methotrexate: Cases of serious toxicity have been reported when methotrexate and NSAIDs are given within 24 hours of each other. This interaction is mediated through accumulation of methotrexate resulting from impairment of renal excretion in the presence of the non-steroidal anti-inflammatory drugs.

Quinolone antimicrobials: Convulsions may occur due to an interaction between quinolones and NSAIDs. This may occur in patients with or without a previous history of epilepsy or convulsions. Therefore, caution should be exercised when considering the use of a quinolone in patients who are already receiving an NSAID.

Other NSAIDs and steroids: Co-administration of Voltarol with other systemic NSAIDs and steroids may increase the frequency of unwanted effects. Concomitant therapy with aspirin lowers the plasma levels of each, although the clinical significance is unknown.

Diuretics: Various NSAIDs are liable to inhibit the activity of diuretics. Concomitant treatment with potassium-sparing diuretics may be associated with increased serum potassium levels, hence serum potassium should be monitored.

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 1.16% 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 1.16% 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.

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. Itching, reddening or smarting of the skin, or skin rash, commonly occurs. Photosensitivity reactions have very rarely been observed.

Systemic absorption of Voltarol Emulgel is low compared with plasma levels obtained following oral forms of Voltarol. However, where Voltarol Emulgel is applied to a relatively large area of skin and over a prolonged period, the possibility of systemic side effects cannot be completely excluded.

Asthma has very rarely been reported in patients using topical NSAID preparations.

4.9 Overdose

The low systemic absorption of topical diclofenac renders overdosage very unlikely. However, undesirable effects, similar to those observed following an overdose of diclofenac tablets, can be expected if topical diclofenac is inadvertently 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. Gastric decontamination and the use of activated charcoal should be considered, especially within a short time of ingestion.

Management of overdosage with NSAIDs essentially consists of supportive and symptomatic measures. There is no typical clinical picture resulting from Voltarol overdosage. Supportive and symptomatic treatment should be given for complications such as hypotension, renal failure, convulsions, gastrointestinal 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.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group:
Non-steroidal anti-inflammatory drug (NSAID).

Mode of action:
Voltarol Emulgel is an anti-inflammatory and analgesic preparation designed for external application. Due to aqueous-alcohol base it exerts a soothing and cooling effect.

5.2 Pharmacokinetic properties

When Voltarol Emulgel is applied locally, the active substance is absorbed through the skin. In healthy volunteers approximately 6% of the dose applied is absorbed when determined by urinary excretion of diclofenac and its hydroxylated metabolites. Findings in patients confirm that diclofenac penetrates inflamed areas following local application of Voltarol Emulgel.

After topical administration of Voltarol Emulgel to hand and knee joints diclofenac can be measured in plasma, synovial tissue and synovial fluid. Maximum plasma concentrations of dicofenac are about 100 times lower than after oral administration of Voltarol.

5.3 Preclinical safety data

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

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Diethylamine
Carbopol 934P
Macrogol cetostearyl ether
Cocoyl caprylocoprate
Isopropanol
Liquid paraffin
Perfume cream 45
Propylene glycol
Deionised water

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

The shelf life expiry date of this product shall be the date shown on the tube and outer package of the product on the market in the country of origin.

6.4 Special precautions for storage

Do not store above 30^{o}C.

6.5 Nature and contents of container

An overlabelled aluminium laminated tube consists of low density polyethylene / aluminium / high density polyethylene (internal layer) fitted with a high density polyethylene shoulder and closed by a moulded seal. The tube is closed with a polypropylene white screw cap, incorporating a moulded feature used to insert, twist and remove the seal before first use.

Available in pack of 100g.

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 PARALLEL PRODUCT AUTHORISATION HOLDER

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8 PARALLEL PRODUCT AUTHORISATION NUMBER

PPA1328/204/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 8th February 2013

10 DATE OF REVISION OF THE TEXT