Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Voltarol 1% w/w Emulgel

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

The gel contains 1% w/w diclofenac sodium (as diethylammonium).

Excipients: Proplylene glycol

For full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Gel

Product imported from Austria and Germany:
White, pleasantly perfumed, homogenous, non-greasy emulsion in an aqueous 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

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

Undesirable effects may be minimised by using the lowest effective dose for the shortest duration necessary to control symptoms *(see section 4.4).*

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: Not recommended.

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

4.3 Contraindications

- Use in asthmatic patients hypersensitive to aspirin or other non-steroidal agents, including diclofenac. Use in patients hypersensitive to propylene glycol or isopropanol.
- Previous sensitivity to diclofenac or any of the excipients
- Patients with a history of hypersensitivity reactions (e.g. bronchospasm, rhinitis, urticaria) in response to Voltarol, aspirin or other non-steroidal anti-inflammatory drugs.
- History of gastrointestinal bleeding or perforation, related to previous NSAIDs therapy. Active, or history of recurrent peptic ulcer/haemorrhage (two or more distinct episodes of proven ulceration or bleeding).
- Severe heart failure

4.4 Special warnings and precautions for use

The use of Voltarol Emulgel may impair female fertility and is not recommended in women attempting to conceive. In women who have difficulties conceiving or who are undergoing investigation of infertility, withdrawal of Voltarol Emulgel should be considered.

The use of Voltarol Emulgel with concomitant NSAIDs including cyclooxygenase-2 selective inhibitors should be avoided.

Gastrointestinal bleeding, ulceration and perforation:GI bleeding, ulceration or perforation, which can be fatal, has been reported with all NSAIDs at anytime during treatment, with or without warning symptoms or a previous history of serious GI events.

The risk of GI bleeding, ulceration or perforation is higher with increasing NSAID doses, in patients with a history of ulcer, particularly if complicated with haemorrhage or perforation *(see section 4.3),* and in the elderly. These patients should commence treatment on the lowest dose available. Combination therapy with protective agents (e.g. misoprostol or proton pump inhibitors) should be considered for these patients, and also for patients requiring concomitant low dose aspirin, or other drugs likely to increase gastrointestinal risk *(see below and 4.5)*

Patients with a history of GI toxicity, particularly when elderly, should report any unusual abdominal symptoms (especially GI bleeding) particularly in the initial stages of treatment.

Caution should be advised in patients receiving concomitant medications which could increase the risk of ulceration or bleeding, such as oral corticosteroids, anticoagulants such as warfarin, selective serotonin-reuptake inhibitors or anti-platelet agents such as aspirin *(see section 4.5).*

When GI bleeding or ulceration occurs in patients receiving Voltarol Emulgel, the treatment should be withdrawn.

NSAIDs should be given with care to patienta with a history of gastrointestinal disease (ulcerative colitis, Crohn's disease) as their condition may be exacerbated *(see section 4.8 – undesirable effects).*

Caution is required in patients with a history of hypertension and/or heart failure as fluid retention and oedema have been reported in association with NSAID therapy

Serious skin reactions, some of them fatal, including exfoliative dermatitis, Stevens-Johnson syndrome, and toxic epidermal necrolysis, have been reported rarely in association with the use of NSAIDs *(see 4.8).* Patients appear to be at highest risk of these reactions early in the course of therapy, the onset of the reaction occurring in the majority of cases within the first month of treatment. Voltarol Emulgel should be discontinued at the first appearance of skin rash, mucoal lesions, or any other sign of hypersensitivity.

Undesirable effects may be minimised by using the minimum effective dose for the shortest duration necessary to control the symptoms *(see section 4.2, and GI and cardiovascular risks below)*

Cardiovascular and cerebrovascular effects

Appropriate monitoring and advice are required for patients with a history of hypertension and/or mild to moderate congestive heart failure as fluid retention and oedema have been reported in association with NSAID therapy.

Clinical trial and epidemiological data suggest that the use of diclofenac, particularly at high dose (150mg daily) and in long term treatment may be associated with a small increased risk of arterial thrombotic events (for example myocardial infarction or stroke).

Patients with uncontrolled hypertension, congestive heart failure, established ischaemic heart disease, peripheral aerterial disease, and/or cerebrovascular disease should not be treated with diclofensc after careful consideration. Similar consideration should be made before initiating longer-term treatment of patients with risk factors for cardiovascular events (e.g. hypertension, hyperlipidaemia, diabetes mellitus, and smoking).

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

Elderly: The elderly have an increased incidence of adverse reactions to NSAID's especially gastro-intestinal bleeding and perforation which may be fatal *(see section 4.2).*

Asthma has been rarely reported in patients using topical 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 not be used with occlusion.

4.5 Interaction with other medicinal products and other forms of interaction

To date, no drug interactions during treatment with Voltarol Emulgel have been reported but the theoretical risk of the interactions listed below occurring should be borne in mind.

Corticosteroids: increased risk of gastrointestinal ulceration or bleeding *(see section 4.4)*

Anti coagulants: NSAIDs may enhance the effects of anti-coagulants, such as warfarin *(see section 4.4)*

Anti-platelet agents and selective serotonin reuptake inhibitors (SSRIs):increased risk of gastrointestinal bleeding *(see section 4.4).*

The following interactions occur with <u>oral</u> forms of Voltarol:

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

<u>Antidiabetic agents</u>: 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.

<u>Ciclosporin</u>: 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.

<u>Methotrexate</u>: 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: Co-administration of Voltarol and other systemic NSAID's may increase the frequency of unwanted events. 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

Since no experience has been acquired with Voltarol Emulgel in pregnancy or lactation, it is not recommended for use in these circumstances.

Use of prostaglandin synthetase inhibitors may result in premature closure of the ductusarteriosus or uterine inertia, such drugs are therefore not recommended during the last trimester of pregnancy.

Following doses of 50mg gastro-resistant tablets every 8 hours, traces of active substance have been detected in breast milk, but in quantities so small that no undesirable effects on the infant are to be expected.

4.7 Effects on ability to drive and use machines

Patients who experience dizziness or other central nervous system disturbances, including visual disturbances, while taking NSAIDs should refrain from driving or operating machinery.

4.8 Undesirable effects

Gastro-intestinal : The most commonly observed adverse events are gastronintestinal in nature. Peptic ulcers, perforation or GI bleeding, sometimes fatal, particularly in the elderly, may occur *(see section 4.4)*. Nausea, vomiting, diarrhoea, flatulence, constipation, dyspepsia, abdominal pain, melaaena, haematemesis, ulcerative stomatitis, exacerbation of colitis and Crohn's disease *(see section 4.4 – Special warnings and precautions for use)* have been reported following administration. Less frequently, gastritis has been observed.

Bullous reactions including Stevens-Johnson syndrome and toxic epidermal necrolysis (very rare).

Voltarol Emulgel is usually well tolerated. Itching, reddening or smarting of the skin, or skin rash, may occasionally occur. Photosensitivity reactions have been observed in isolated cases.

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 been rarely reported in patients using topical NSAID preparations.

Oedema, hypertension, and cardiac failure, have been reported in association with NSAID treatment.

Clinical trial and epidemiological data suggests that use of diclofenac, particularly at high doses (150mg daily) and in long term treatment may be associated with a small increased risk of arterial thrombotic events (for example myocardial infarction or stroke) *(see section 4.4)*

4.9 Overdose

The low systemic absorption of topical diclofenac renders overdosage extremely unlikely. 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.

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, 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.

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 an aqueous-alcoholic 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 diclofenac 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

Carbomer
Diethylamine
Cetomacrogol
Caprylic/capric acid fatty alcohol ester
Isopropyl alcohol
Paraffin
Perfume
Propylene glycol
Purified water

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

The shelf-life expiry date of this product is the date shown on the container and outer package of the product on the market in the country of origin.

6.4 Special precautions for storage

Do not store above 25ºC.

6.5 Nature and contents of container

Aluminium tubes with protective inner coating, in a pack size of 40g and 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

PCO Manufacturing
Unit 10, Ashbourne Business Park
Rath
Ashbourne
Co. Meath
Ireland

8 PARALLEL PRODUCT AUTHORISATION NUMBER

PPA 0465/013/005

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 30 June 2006

10 DATE OF REVISION OF THE TEXT

April 2011