Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Diclac 1% w/w Gel

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 100g of Diclac 1% w/w Gel contains Diclofenac Sodium 1g.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Gel.

A slightly yellow emulsion, cutaneous gel with an alcoholic smell.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

-Post-traumatic inflammation 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

Therapy should be reviewed after 4 weeks.

4.2 Posology and method of administration

Topical.

Recommended Dosage Schedule:

Adults and children 14 years and over:

Diclofenac gel is applied locally to the skin 3 or 4 times daily and rubbed in gently. The amount needed depends on the size of the painful site. For example, 2 to 4 g Diclofenac gel (a quantity ranging from the size of a cherry to the size of a walnut) is sufficient to treat an area of about 400 to 800 cm^2. After application, the hands should be washed, unless they are the site being treated. The duration of treatment depends on the indication and the response obtained. It is recommended that treatment be reviewed after 2 weeks. These indications should not warrant treatment for more than 6 weeks.

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.

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).

Elderly
There is no evidence to suggest that elderly patients require different dosages or experience side effects different from those in younger patients.

4.3 Contraindications

Hypersensitivity to the active substance or any of the excipients.
Use in asthmatic patients hypersensitive to acetylsalicylic acid/aspirin or other non-steroidal agents, including diclofenac.
Patients with a history of hypersensitivity reactions (e.g., bronchospasm, urticaria or acute rhinitis precipitated by diclofenac, acetylsalicylic acid/aspirin or other non-steroidal anti-inflammatory agents).
Third trimester of pregnancy
The use in children and adolescents aged less than 14 years is contraindicated.

4.4 Special warnings and precautions for use

Undesirable effects may be reduced by using the minimum effective dose for the shortest possible duration.

If there is no improvement, or the condition is aggravated the doctor should be consulted.

Warnings
The likelihood of systemic side effects with topical diclofenac is small, compared with the frequency of side effects in patients using oral diclofenac. However, when Diclofenac gel is applied to relatively large areas of skin over a prolonged period of time, the possibility of systemic side effects cannot be excluded. These side effects 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.

Precautions
Diclofenac gel should be applied only to healthy and intact skin surfaces (those without open wounds or injuries). It should not be allowed to come into contact with the eyes or with mucous membranes.

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

Diclofenac gel can be used with non-occlusive bandages but should not be used with an airtight occlusive dressing.

Diclofenac gel should not be ingested.

Concomitant use of oral NSAID's should be cautioned as the incidence of untoward side effects, particularly systemic side effects, may ensue. (See also 'Interactions') Diclac Gel should not be co-administered with other products containing diclofenac.

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.

4.5 Interaction with other medicinal products and other forms of interaction

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

The following interactions occur with oral forms of diclofenac.
Lithium and digoxin:
Diclofenac Sodium may increase plasma concentrations of lithium and digoxin.

Anticoagulants:
Although clinical investigations do not appear to indicate that diclofenac has an influence on 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 high dose can reversibly inhibit platelet aggregation.

Antidiabetic agents:

Clinical studies have shown that Diclac 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 Diclofenac Sodium. This might be mediated through combined renal antiprostaglandin 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 NSAID.

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 Diclac with other systemic NSAIDs and steroids may increase the frequency of unwanted effects. Concomitant therapy with aspirin lowers the plasma levels of each, although no clinical significance is known.

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

There is no clinical data from the use of diclofenac during pregnancy.
The systemic concentration of diclofenac is lower after topical administration compared to oral formulations. Even if systemic exposure is lower compared with oral administration, it is not known if the systemic diclofenac exposure reached after topical administration can be harmful to an embryo/fetus. With reference to experience from treatment with NSAID's 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 used 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 synthetase 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, Diclac Gel is contraindicated during the third trimester of pregnancy (see Section 4.3).

Lactation

Like other NSAIDs diclofenac passes into breast milk in small amounts, However at therapeutic doses of Diclac 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 and if the expected benefit justifies the potential risk to the newborn. Under this circumstance, Diclac 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

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

4.8 Undesirable effects

Diclac Gel is usually well tolerated. Itching, reddening or smarting of the skin, or skin rash, may occasionally occur. Skin photosensitivity, desquamation, discoloration and bullous or vesicular eruptions have been reported in isolated cases. Patients should be warned against excessive exposure to sunlight in order to reduce the incidence of photosensitivity.

Systemic absorption of topically applied diclofenac is very low and the resulting diclofenac plasma levels are also very low compared with plasma levels following oral intake of diclofenac. The probability of systemic undesirable effects (such as e.g. gastrointestinal, hepatic or renal disturbances, bronchospasm) is thus very low following topical application compared with the frequency of undesirable effects associated with oral intake of diclofenac if diclofenac is used on a large area of skin and for a prolonged period, however, undesirable systemic effects may occur.

Adverse reactions are listed below, by system organ class and ranked under heading of frequency. Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness, the most frequent first, using the following convention: Frequencies are defined as: 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
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: 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 HPRA Pharmacovigilance, website: www.hpra.ie.

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 DICLAC 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

ATC codes: Topical products for joint and muscular pain
MO2AA15: Anti inflammatory preparations, non steroids for topical use.

Mechanism of action
Diclofenac, the active substance of Diclofenac gel, is an NSAID with pronounced anti-rheumatic, anti-inflammatory, analgesic and antipyretic properties.

Inhibition of prostaglandin biosynthesis by diclofenac has been demonstrated experimentally and is regarded as an important component of its mechanism of action.

Pharmacodynamic effects
In inflammation of traumatic or rheumatic origin, Diclofenac gel has been shown to relieve pain, reduce oedema, and shorten the time needed to regain normal function.

5.2 Pharmacokinetic properties

Absorption
The amount of diclofenac absorbed through the skin is proportional to the contact time and skin area covered with diclofenac gel, and depends on the total topical dose and the hydration of the skin. Absorption amounts to about 6% of the dose of diclofenac after topical application of 2.5 g diclofenac gel per 500 cm^2 skin, determined by reference to the total renal elimination compared with diclofenac tablets. Occlusion over a period of 10 hours leads to a three-fold increase in the amount of diclofenac absorbed.

Distribution
After topical administration of diclofenac gel to hand and knee joints diclofenac can be measured in plasma, synovial tissue and synovial fluid. Maximum plasma concentrations of diclofenac after topical administration of diclofenac gel are about 100 times lower than after oral administration of diclofenac tablets. 99.7% of diclofenac binds to serum proteins, chiefly to albumin (99.4%).
Diclofenac accumulates in the skin which acts as 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, where it 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 these phenolic metabolites are biologically active, however, to a much smaller extent than diclofenac.

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

Characteristics in patients

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

5.3 Preclinical safety data

Preclinical data from acute and repeated dose toxicity studies, as well as from genotoxicity, mutagenicity, and carcinogenicity studies with diclofenac revealed no specific hazard for humans at the intended therapeutic doses. There was no evidence that diclofenac had a teratogenic potential in mice, rats or rabbits. Diclofenac had no influence on the fertility of parent animals in rats. The prenatal, perinatal and postnatal development of the offspring was not affected.

Diclofenac gel was well tolerated in a variety of studies. There was no potential for phototoxicity and Diclofenac gel caused no skin sensitization.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

α-tocopherol (Copherol F 1300)
Carbomer (Carbopol 980 NF)
Decyl oleate
2-Octyldodecanol
Lecithin (phospholipon 80)*
Ammonia Solution 10%
Disodium edetate
Perfume oil Verte de Creme
Isopropyl alcohol
Purified water

(*used as a mixture of phospholipon 80/ isopropyl alcohol 75:25)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Do not store above 25°C. Keep the tube tightly closed.

6.5 Nature and contents of container

The primary container for Diclac 1% w/w Gel is an internally lacquered collapsible aluminium tube. The tube caps are made of polyethylene or polypropylene. Diclac 1% w/w Gel is available in 50g and 100g tubes.
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

Rowex Limited,

Newtown
Bantry
Co. Cork
Ireland

8 MARKETING AUTHORISATION NUMBER

PA0711/009/002

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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10 DATE OF REVISION OF THE TEXT

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