Professional information for DICOREN GEL

SCHEDULING STATUS

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1. NAME OF THE MEDICINE

DICOREN GEL, 10 mg/g

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each gram gel contains 10 mg diclofenac sodium.

Excipients with known effect:

Each gram contains 200 mg propylene glycol.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Gel.

A colourless, transparent gel.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Symptomatic relief of localised traumatic inflammation and pain.

4.2 Posology and method of administration

Posology

Adults and children 12 years and older:

Depending on the size of the painful site to be treated, apply 2 g to 4 g DICOREN GEL three to

four times daily to the affected parts and rub in gently.

The duration of treatment will be determined by the indication and the response obtained.

It is recommended that treatment be reviewed after 2 weeks.

Patients should consult their doctor if the condition does not improve or worsens within 7 days of starting treatment.

Paediatric population

The safety and efficacy of DICOREN GEL in children under the age of 12 years have not been established.

Method of administration

For cutaneous use only.

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

4.3 Contraindications

- Hypersensitivity to diclofenac sodium, acetylsalicylic acid or other nonsteroidal anti-inflammatory medicines. Hypersensitivity to any other ingredient of the gel.
- Patients with or without chronic asthma in whom attacks of asthma, urticaria or acute rhinitis are precipitated by aspirin or other nonsteroidal anti-inflammatory medicines.
- Concomitant use of other products containing diclofenac.
- Concomitant use of oral NSAIDs.
- DICOREN GEL should not be used by patients with porphyria.
- During the last trimester of pregnancy.
- Heart failure.
- History of gastrointestinal bleeding or perforation (PUBs) related to previous NSAIDs.
- Active or history of recurrent ulcer/haemorrhage/perforations.
- Patients with renal impairment.

4.4 Special warnings and precautions for use

The possibility of systemic adverse events from topical application of DICOREN GEL cannot be excluded if it is used on large areas of skin and over a prolonged period (see section 4.8).

Serious skin reactions, some of them fatal, have been reported, including exfoliative dermatitis, Stevens-Johnson syndrome and toxic epidermal necrolysis, associated with the administration of nonsteroidal anti-inflammatory medicines (see section 4.8.). The risk of occurrence of these reactions is higher at the beginning of the treatment and in most cases these reactions manifested during the first month of treatment. Caution is required with concomitant use of oral nonsteroidal anti-inflammatory medicines, as the incidence of untoward effects, particularly systemic side effects, may increase.

DICOREN GEL should be discontinued at the first signs of rash, mucosal injuries or other hypersensitivity manifestations.

DICOREN GEL 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.

The area treated with DICOREN GEL should not be exposed to sunlight.

DICOREN GEL can be used with non-occlusive bandages but should not be used with an airtight occlusive dressing.

DICOREN GEL contains propylene glycol, which may cause skin irritation.

4.5 Interaction with other medicines and other forms of interaction

Diuretics, angiotensin-converting enzyme inhibitors (ACEI) and angiotensin II antagonists (AIIA):

Nonsteroidal anti-inflammatory medicines may decrease the effectiveness of diuretics and other antihypertensive medicines. In some patients with impaired renal function (e.g. dehydrated patients or elderly patients with impaired renal function) the co-administration of an ACEI or AIIA and cyclooxygenase inhibitor may result in the progression of renal function deterioration, including the

possibility of acute renal insufficiency, which is usually reversible. The occurrence of these interactions should be considered in patients applying DICOREN GEL in combination with an ACEI or AIIA, particularly if on large areas of the skin and for prolonged periods. Consequently, this combination should be used with caution, especially in elderly patients. Patients should be properly hydrated and the need to monitor the renal function after the beginning of the concomitant treatment and periodically thereafter should be considered.

Since systemic absorption of diclofenac sodium as in DICOREN GEL is very low, such interactions are very unlikely.

Lithium and digoxin:

Diclofenac may increase plasma concentrations of lithium and digoxin.

Anticoagulants:

Although clinical investigations do not appear to indicate that DICOREN GEL 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 nonsteroidal anti-inflammatory medicines, diclofenac in a high dose can reversibly inhibit platelet aggregation.

Antidiabetic medicines:

Clinical studies have shown that DICOREN GEL can be given together with oral antidiabetic medicines 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 medicines.

Ciclosporin:

Cases of nephrotoxicity have been reported in patients receiving concomitant cyclosporin and NSAIDs, including diclofenac. This might be mediated through combined renal antiprostaglandin effects of both the NSAID and cyclosporin.

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 DICOREN GEL 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.

Mifepristone:

NSAIDs should not be used for 8-12 days after mifepristone administration as NSAIDs can reduce the effects of mifepristone.

Anti-hypertensives:

Concomitant use of NSAIDs with antihypertensive medicines (i.e. beta-blockers, angiotensin converting enzyme (ACE) inhibitors, diuretics) may cause a decrease in their antihypertensive effect via inhibition of vasodilatory prostaglandin synthesis.

4.6 Fertility, pregnancy and lactation

Fertility:

Treatment with DICOREN GEL is unlikely to have an adverse effect on fertility because the systemic exposure to diclofenac after application of DICOREN GEL is low.

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/foetal 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-foetal 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 oligohydramnios;
- 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.

Regular use of nonsteroidal anti-inflammatory medicines during the third trimester of pregnancy, may result in premature closure of the foetal ductus arteriosus in utero, and possibly, in persistent pulmonary hypertension of the new-born. The onset of labour may be delayed, and its duration increased.

Lactation:

Diclofenac passes into breast milk in small amounts. However, at therapeutic doses of DICOREN 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 health care provider. Under this circumstance, DICOREN 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

Cutaneous application of DICOREN GEL has no or negligible influence on the ability to drive a vehicle and use machines.

4.8 Undesirable effects

Although less likely with the topical administration, some side effects normally associated with systemically administered diclofenac sodium, as in DICOREN GEL, may also occur. The prolonged use of DICOREN GEL in

a relatively extensive area can cause systemic side effects such as nausea, vomiting, diarrhoea or epigastric pain.

Tabulated summary of adverse reactions

Infections and infestations	
Less frequent:	Pustular rash.
Immune system disorders	
Less frequent:	Hypersensitivity (including urticaria), anaphylactoid reactions (including shock and hypotension)*, angioedema (including face oedema)*, bullous reactions*, including toxic epidermal necrolysis* and Steven-Johnson*. syndrome*.
Respiratory, thoracic and mediastinal disorders	
Less frequent:	Asthma (including dyspnoea), pneumonitis*.
Skin and subcutaneous tissue disorders	
Frequent:	Rash and skin reactions*, eczema, erythema, dermatitis (including contact dermatitis), pruritus.
Less frequent:	Bullous dermatitis, photosensitivity reaction.
Frequency unknown:	Burning sensation at the application site, dry skin.
Blood and lymphatic system disorders	
Less frequent:	Leucopenia*, thrombocytopenia*, aplastic anaemia*, haemolytic anaemia*, agranulocytosis*.
Psychiatric disorders	
Less frequent:	Disorientation*, insomnia*, irritability*, depression*, nightmares*, psychotic reactions*.
Nervous system disorders	
Frequent:	Headache*, dizziness*, nervousness*.
Less frequent:	Tiredness*, disturbances of sensation (including paraesthesia)*, memory disturbance*, convulsions*,

	anxiety*, tremor*, aseptic meningitis*, somnolence*, taste disturbances*, cerebrovascular accident*.
Eye disorders	
Less frequent:	Disturbances in vision (diplopia, blurred vision)*.
Ear and labyrinth disorders	
Frequent:	Vertigo*.
Less frequent:	Impaired hearing, tinnitus*.
Cardiac disorders	
Less frequent:	Palpitation*, chest pain*, congestive heart failure*, oedema*, myocardial infarction*.
Vascular disorders	
Less frequent:	Vasculitis, hypertension*.
Gastrointestinal disorders	
Frequent:	Epigastric pain*, nausea*, vomiting*, diarrhoea*, abdominal cramps*, dyspepsia*, flatulence*, eructation*, anorexia*, local irritation*, abdominal pain*.
Less frequent:	Gastrointestinal bleeding*, haematemesis*, melaena*, bloody diarrhoea*, peptic ulcer with or without bleeding* or perforation*, lower gut disorders such as non-specific haemorrhagic colitis*, exacerbation of ulcerative colitis* or Crohn's proctocolitis*, glossitis*, aphthous stomatitis*, oesophageal lesions*, diaphragm-like intestinal strictures*.
Hepatobiliary disorders	
Frequent:	Elevated transaminase levels (ALT, AST)*.
Less frequent:	Hepatitis with or without jaundice*, fulminant hepatitis*, liver disorder*, hepatic necrosis*, hepatic

	failure*.
Renal and urinary disorders	
Less frequent:	Acute renal failure*, urinary abnormalities such as haematuria*, proteinuria*, interstitial nephritis*, nephritic syndrome*, papillary necrosis*.

** Reported for systemically absorbed diclofenac.*

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of DICOREN GEL is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are asked to report any suspected adverse reactions to the South African Health Products Regulatory Authority (SAHPRA) via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on the SAHPRA website.

4.9 Overdose

Signs and symptoms

The low systemic absorption of DICOREN GEL renders overdose very unlikely. However, undesirable effects, similar to those observed following an overdose of diclofenac sodium tablets, can be expected if DICOREN GEL is inadvertently ingested.

Treatment

In the event of accidental ingestion resulting in significant systemic adverse effects, general therapeutic measures normally adopted to treat poisoning with nonsteroidal anti-inflammatory medicines should be used. The use of activated charcoal should be considered, especially within a short time (within one hour) of ingestion.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Category and class: A 3.1 Antirheumatics (anti-inflammatory agents)

Pharmacotherapeutic group: Topical products for joint and muscular pain, anti-inflammatory preparations, non-steroids for topical use. **ATC code:** M02AA15.

Diclofenac sodium is a phenylacetic acid derivative. It leads to the inhibition of cyclooxygenase activity, which then leads to the inhibition of the synthesis of prostaglandin and other mediators of inflammation. Diclofenac sodium acts as an anti-inflammatory and analgesic medicine.

5.2 Pharmacokinetic properties

Absorption

After topical application, diclofenac sodium is well-absorbed into the subcutaneous layers of the skin. The maximum level of diclofenac sodium after a 7,5 g dose of the 1 % concentration was, on average, approximately 3,9 ng/mL. After several days of treatment, the concentration on skin and soft tissues of patients with arthrosis reached values 30 to 40 times higher than the ones from plasma. Absorption of diclofenac sodium (1 % concentration) applied on healthy skin reached 6 % to 7 % in healthy individuals.

Distribution

The diclofenac sodium concentration was measured in plasma and tissue and synovial fluid after topical administration on the hands and knee joints. Maximum plasma concentration was about 100 times lower than after oral administration. Diclofenac sodium binds 99,7 % to plasma proteins, mainly albumin (99,5 %).

Biotransformation

Biotransformation of diclofenac involves partly glucuronidation of the intact molecule, and mainly single and multiple hydroxylations, most of which are converted to glucuronide conjugates (hydroxyl-gluconates). The main metabolite is 4-hydroxy-diclofenac (30 % – 40 %). All the

metabolites are biologically active, but to a much lesser extent than diclofenac sodium.

Elimination

Diclofenac sodium and its metabolites are excreted mainly in the urine. Total clearance of diclofenac sodium from plasma is 263 ± 56 mL/min. The terminal plasma half-life is 1 – 2 hours. Its metabolites have similar plasma half-lives of 1 – 3 hours. Approximately 60 % of the dose administered is eliminated in the urine in the form of metabolites, only 1 % in the form of diclofenac sodium. The remaining is eliminated as metabolites by bile and in faeces.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Carbopol 940

Isopropyl alcohol

l-menthol powder

Propylene glycol (E1520)

Purified water

Triethanolamine.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months.

Store at or below 30 °C.

6.4 Special precautions for storage

DICOREN GEL does not require any special storage conditions.

6.5 Nature and contents of container

Aluminium tube with sealed membrane over the opening, closed with a white HDPE piercer cap, packed in an outer cardboard carton.

Pack sizes: 20 g and 45 g.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

LeBasi Pharmaceuticals (Pty) Ltd

San Domenico Building, Unit 6, Ground Floor

10 Church Street

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7551

8. REGISTRATION NUMBER

57/3.1/0327

9. DATE OF FIRST AUTHORISATION

12 August 2025

10. DATE OF REVISION OF THE TEXT