APPROVED
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INSTRUCTION
for medical use

DICLOSAFE®

Composition:
active substance: diclofenac diethylamine;
1 g of gel contains 11.6 mg of diclofenac diethylamine, equivalent to diclofenac sodium 10 mg;
excipients: propylene glycol, isopropyl alcohol, carbomer, diethylamine, cocoyl caprylocaprate, oleyl alcohol, polyethylene glycol cetostearyl ether, light mineral oil, butylhydroxytoluene (E 321), purified water.

Pharmaceutical form. Emulsion gel for external use.
Basic physical and chemical properties: white to off-white soft homogeneous gel.

Pharmacotherapeutic group. Agents for topical use for joint and muscular pain. Non-steroidal anti-inflammatory agents for topical use. Diclofenac.
ATC Code M02A A15.

Pharmacological properties.
Pharmacodynamics.
Diclosafe® with diclofenac as active ingredient is a non-steroidal anti-inflammatory drug (NSAID) for external use.
Diclofenac is a non-steroidal anti-inflammatory agent that has a pronounced anti-rheumatic, analgesic, anti-inflammatory, and antipyretic effect. The main mechanism of action is the inhibition of prostaglandins biosynthesis.
In case of inflammation caused by trauma or rheumatic diseases, the diclofenac gel reduces pain, swelling of tissues and shortens the period of renewal of damaged joints, ligaments, tendons and muscles. Clinical data has proven that diclofenac gel reduces acute pain in 1 hour after initial application. The drug reduces pain on movement by 75% within 2 days. 94% of patients had a positive response to diclofenac gel after 2 days of treatment, compared with 8% of patients who had a positive response to placebo. Overcoming of pain and functional impairment was achieved after 4 days of treatment with diclofenac gel. Thanks to the water-alcohol basis, the diclofenac gel also exhibits local anesthetic and cooling effect.
Pharmacokinetics.
The amount 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. After a local application of 2.5 g of diclofenac gel on the skin area of 500 cm^2, the degree of diclofenac absorption is approximately 6%. Application of occlusion bandage for 10 hours leads to the 3-fold increase in the diclofenac absorption.

After applying diclofenac gel on the skin of hand and knee joints, diclofenac is detected in plasma (where its maximum concentration is approximately 100 times less than after oral administration of the same amount of diclofenac), in the synovial membrane and in synovial fluid. The protein binding of diclofenac is 99.7%.
Diclofenac accumulates in the skin, which serves as a reservoir, where the gradual release of the substance in adjacent tissues occurs. From there, diclofenac predominantly enters deeper inflamed tissues, joints, where it continues its action and is determined in concentrations up to 20 times higher than those in plasma.
Diclofenac is metabolized mainly through hydroxylation which results in the formation of several phenolic metabolites. Two of these phenolic metabolites are biologically active, but much less than diclofenac.
Diclofenac and its metabolites are excreted predominantly in urine. The total systemic plasma clearance of diclofenac is 263 ± 56 ml/min, and the terminal half-life is on average 1–3 hours.
In renal or hepatic insufficiency, metabolism and elimination of diclofenac do not change.

Clinical characteristics.

Indication.

Topical treatment for pain and inflammation of joints, muscles, ligaments and tendons of rheumatic or traumatic origin.

Contraindication.

- Hypersensitivity to diclofenac or to other components of the drug;
- a history of bronchial asthma attacks, urticaria, or acute rhinitis caused by the intake of acetylsalicylic acid or other NSAIDs;
- the last trimester of pregnancy;
- children's age under 14 years.

Interaction with other drugs and other types of interactions.

Since the systemic absorption of diclofenac after topical application of the drug is very low, the probability of interactions is very low. Currently there are no data on the interaction of diclofenac in the case of its topical application. Information on known interactions related to the systemic application of diclofenac is contained in the relevant sources.

Special precautions.

The likelihood of systemic side effects occurring following the topical application of diclofenac is small compared to oral diclofenac; but it is not excluded in the use of the drug in relatively large areas of the skin for a long time.
Caution should be exercised when co-administering diclofenac with oral NSAID, as the incidence of undesirable, especially systemic, side effects may increase (see "Interaction with other drugs and other types of interactions" section).
Diclosafe® gel should not be used concurrently with other diclofenac drugs.
Diclosafe® gel is recommended to apply only on intact, undamaged skin areas, preventing contact with inflamed, wounded or infected skin. Avoid contact with eyes and mucous membranes. The drug should not be swallowed.
In the event of any skin rash, the drug should be stopped.
Diclosafe® gel should not be used under an airtight occlusive bandage, but its use is permitted under a non-occlusive bandage. In the case of ligaments tension, the affected area can be banded.
When topical diclofenac is used, there is some probability of gastrointestinal bleeding in patients who have had it in the past.

Diclosafe® gel contains propylene glycol and butylhydroxytoluene. Propylene glycol may cause skin irritation. Butylhydroxytoluene can cause local skin reactions (eg, contact dermatitis) or irritation of the eyes and mucous membranes.

Use during pregnancy or breastfeeding.
Pregnancy.
Following topical use of diclofenac, its systemic concentration is lower compared with oral administration. Given the experience with systemic NSAIDs, it is recommended to take into account the following.
Inhibition of prostaglandin synthesis may adversely affect the course of pregnancy and/or the development of the embryo/fetus. Data from epidemiological studies indicate an increased risk of miscarriages and/or the risk of developing heart failure and gastroschisis after the use of a prostaglandin synthesis inhibitor in early pregnancy. The absolute risk of cardiovascular disease has been increased from less than 1% to about 1.5%. It is believed that the risk increases with the dose and duration of treatment. It has been shown that administration of prostaglandin synthesis inhibitor in animals results in an increase in pre- and postimplantation loss and embryo/fetus mortality.
In addition, increased incidences of various malformations, including cardiovascular, have been reported in animals given a prostaglandin synthesis inhibitor during organogenetic period. During the 1st and 2nd trimester of pregnancy, diclofenac should not be used unless it is necessary. If diclofenac is used by a woman attempting to conceive, or during the 1st or 2nd trimesters of pregnancy, the dose should be kept as low and duration of treatment as short as possible.
During the 3rd 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 oligohydroamniosis.
The use of prostaglandin synthesis inhibitors at the end of pregnancy can affect the mother and the neonate as follows:
- 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 3rd trimester of pregnancy (see "Contraindications" section).
Breastfeeding.
Like other NSAIDs, diclofenac passes into breast milk in small amounts. However, the use of therapeutic doses of Diclosafe® gel does not provide any effect on breastfeeding. Due to the lack of controlled studies in breastfeeding women, within this period Diclosafe® gel should only be used by medical prescription. During lactation, the drug should not be applied to the mammary glands or large skin areas; and it should not be used for a long time (see "Special precautions" and "Administration and dosage" sections).
Fertility.
Data on the effects of diclofenac on human fertility when used externally are not available.

Effects on ability to drive and use machines.
No effect.

Administration and dosage.

Adults and children aged 14 years and above: Diclosafe® gel should be used 3–4 times a day, slightly rubbing into the skin. The amount of medicine used depends on the size of the area affected by pain (thus, 2–4 g, about the size of a cherry and a walnut respectively, is sufficient to cover an area of 400–800 cm^2).
After applying the product, it is necessary to wash hands, except when this is the area to be treated.
Duration of therapy depends on the nature of the disease and the treatment effectiveness.
The drug should not be used for more than 14 consecutive days in damages or rheumatism of soft tissues and for longer than 21 days in case of joints pain of arthritic origin, unless otherwise recommended by the physician.
You should seek medical advice if the symptoms of the disease do not diminish or increase after 7 days of treatment.
Elderly patients: do not need adjustment of drug dose.
If you apply Diclosafe® gel to large body areas, systemic absorption of diclofenac is greater and the risk of side effects increases, especially if the therapy is used frequently.

Children.
Since there is not enough data on the efficacy and safety of diclofenac gel for children aged under 14, the drug is contraindicated for use in children under the age of 14 years (see "Contraindications" section). When using the product for children above 14 years of age longer than 7 days or if the symptoms of the disease increase, you should seek medical advice.

Overdose
Symptoms.
Overdose is unlikely due to the low diclofenac absorption in the systemic bloodstream at the topical application. At the same time, the development of systemic adverse reactions can be observed in the case of accidental ingestion of Diclosafe® gel (it should be noted that 1 tube of 30 g contains an equivalent of 0.3 g of diclofenac sodium). In case of accidental drug ingestion and the occurrence of significant systemic adverse reactions, general therapeutic measures used in the treatment of NSAID poisoning should be taken. Gastric lavage and activated charcoal are recommended, especially when swallowing has occurred recently.
Treatment.
Treatment of NSAID overdose consists in the use of supportive and symptomatic therapy. There is no typical clinical picture caused by overdose of diclofenac gel. Supportive and symptomatic treatment is indicated with such complications as arterial hypotension, renal failure, seizures, gastrointestinal disorders and respiratory depression. It is unlikely that forced diuresis, hemodialysis or hemoperfusion are useful for NSAID removal because active substances of these drugs are highly bound to plasma proteins and undergo an intensive metabolism.

Adverse reactions.
Diclofenac gel is usually well tolerated. Undesirable reactions include mild, temporary skin reactions at the site of application. In rare cases, allergic reactions may occur.
Infections and invasions: pustular rash.
Immune system: hypersensitivity reactions (including urticaria), angioneurotic edema.
Respiratory system, chest and mediastinum: bronchial asthma.
Skin and subcutaneous tissue: rash, itching, eczema, erythema, dermatitis, including contact dermatitis, bullous dermatitis, photosensitivity reactions, burning sensation of the skin.
Topical diclofenac can not exclude the possibility of adverse reactions, which are usually associated with its systemic use (see "Special precautions" section).

Shelf life.
2 years.

Storage conditions.
Store at the temperature below 25°C in original package.
Keep out of reach of children.

Package.
30 g in tube. 1 tube in a cardboard box.

Condition of supply.
Without prescription.

Manufacturer.
KUSUM HEALTHCARE PVT LTD.

Location of manufacturer and its address of business activity.
SP-289 (A), RIICO Industrial area, Chopanki, Bhiwadi, Dist. Alwar (Rajasthan), India.

Date of last revision.