APPROVED
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INSTRUCTION
for medical use

DICLOSAFE® FORTE

Composition:
active substance: diclofenac diethylamine;
1 g of gel contains 23.2 mg of diclofenac diethylamine, equivalent to diclofenac sodium 20 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.
Diclosafe® Forte 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.
Thanks to the water-alcohol basis, the diclofenac gel also exhibits local anesthetic and cooling effect.
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 topical application to the skin area of 400 cm^2, the degree of systemic absorption of diclofenac gel, which is defined as the concentration of active substance in blood plasma, is equivalent to diclofenac application 4 times a day at a concentration of 1.16%. Relative systemic bioavailability of diclofenac in the use of diclofenac gel on day 7 is 4.5% compared to tablets (at the same dose of diclofenac sodium). Absorption does not depend on the use of a waterproof and vapor permeable bandage.
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. 99.7% of diclofenac binds to plasma proteins, preferably albumin (99.4%).
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 partly by glucuronization, and 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 1–2 hours. Four metabolites, including two active ones, also have a short half-life of 1–3 hours. One of the metabolites, 3'-hydroxy-4'-methoxydiclofenac, has a longer half-life, but is almost inactive.
In the renal failure, the accumulation of diclofenac and its metabolites is not observed in the body. In chronic hepatitis or non-decompensated cirrhosis of the liver, the kinetics and metabolism of diclofenac do not change.

Clinical characteristics.

Indication.

Treatment of pain, inflammation and edema at:
- soft tissue damage: injuries to the tendons, ligaments, muscles, and joints (for example, due to dislocation, stretching, clogging) and back pain (sports injuries);
- localized forms of rheumatism of soft tissues: tendonitis (including "tennis elbow"), bursitis, shoulder syndrome and periarthropathy.

Symptomatic treatment of osteoarthritis of small and medium joints, located superficially, such as joints of the fingers or knee joints.

Contraindication.

- Hypersensitivity to diclofenac, acetylsalicylic acid, other NSAIDs, 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;
- concomitant use with other diclofenac agents;
- concomitant use with other NSAIDs;
- the last trimester of pregnancy.

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*. Co-administration of Diclosafe® Forte with steroids may increase the incidence of side effects. Concomitant use of Diclosafe® Forte with other systemic NSAIDs is contraindicated (see "Contraindications" section).

* 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.
Diclosafe® Forte 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® Forte 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 in patients with peptic ulcer (present or in the past), there is some probability of gastrointestinal bleeding.
As with other drugs that inhibit prostaglandin synthetase, diclofenac and other NSAIDs can lead to bronchospasm, if used in patients with or with history of bronchial asthma.
Diclosafe® Forte 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® Forte gel does not provide any effect on breastfeeding. Due to the lack of controlled studies in breastfeeding women, within this period Diclosafe® Forte 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.

The drug has no or little influence on the ability to drive and use machines.

Administration and dosage.
Adults and children aged 14 years and above: Diclosafe® Forte gel should be used twice a day (morning and evening), slightly rubbing into the skin at the painful area. 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 longer than 14 days, unless otherwise recommended by your doctor.
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® Forte 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® Forte gel (it should be noted that 1 tube of 30 g contains an equivalent of 0.6 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).
If side effects occur, stop treatment and seek medical advice.
* Information on adverse reactions associated with systemic administration of diclofenac is available in relevant sources.

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.