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.
Pharmacodynamics.
Diclosafe® Forte with diclofenac as active ingredient is a non-steroidal anti-inflammatory drug (NSAID) for external use.
Diclofenac is a NSAID that has a pronounced anti-rheumatic, analgesic, anti-inflammatory, and antipyretic effect. The main mechanism of therapeutic action of diclofenac is the inhibition of prostaglandins biosynthesis by cyclooxygenase 2 (COX-2).
In case of inflammation and pain 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 showed that in ankle sprains, diclofenac gel significantly reduced pain on movement compared to placebo-treated patients within three days of starting treatment, including a subset of patients with severe pain. In addition, treatment with this drug also significantly improved ankle function within three days of starting treatment.
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. the degree of systemic absorption of the drug, defined as the concentration of the active substance in the blood plasma, is equivalent to applying diclofenac diethylamine with a concentration of 1.16% 4 times a day.

The relative systemic bioavailability of diclofenac when using a gel with diclofenac on the 7th day is 4.5% compared to tablets of 50 mg (at the same dose of diclofenac sodium). Absorption does not depend on the use of moisture-permeable and vapor-permeable bandages.
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. Diclofenac binding to proteins is 99.7%, mainly to 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 mainly enters deeper inflamed tissues, such as joints, ligaments, where it continues to act and is determined in concentrations up to 20 times higher than in blood plasma.
Diclofenac is metabolized partly by glucuronidation and mainly by hydroxylation to form several phenolic derivatives, two of which are pharmacologically active, but to a much lesser extent than diclofenac.
Diclofenac and its metabolites are excreted predominantly in urine. The final half-life of diclofenac from blood plasma 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 renal failure, the accumulation of diclofenac and its metabolites in the body is not observed. In chronic hepatitis or non-decompensated cirrhosis, 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 or to other components of the drug.
- A history of bronchial asthma attacks, angioedema, urticaria, or acute rhinitis precipitated by the intake of acetylsalicylic acid or other NSAIDs.
- The third 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. However, possible interactions that are known for oral forms of diclofenac must be taken into account. The combined use of Diclosafe® Forte with other systemic NSAIDs and steroids may increase the frequency of side effects.

Special precautions.

Concomitant use of systemic NSAIDs should be cautioned.

The possibility of the development of systemic side effects (which occur with the use of systemic forms of diclofenac) should be considered when using the drug on larger areas of the skin or for a longer time than recommended.
Diclosafe® Forte gel is recommended to be applied only to intact, undamaged areas of the skin, preventing contact with damaged (wounded or infected) skin. It should not be allowed to come into contact with the eyes or mucous membranes. The drug should not be ingested.
Discontinue the treatment if a skin rash develops after applying the product.
Diclosafe® Forte gel can be used with non-occlusive bandages but should not be used with an airtight occlusive dressing.
There is some possibility of gastrointestinal bleeding with topical diclofenac in patients with peptic ulcer disease (present or history).
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.
Due to the possibility of photosensitivity, it is necessary to avoid exposure to direct sunlight.
It is necessary to advise the patient not to smoke and not to approach open flames, as this is a risk of serious burns. Fabric (clothing, bedding, dressing material) that has come into contact with the product can easily ignite and is a serious fire hazard. Washing clothes and bedding can reduce gel accumulation, but does not remove it completely.
Excipients
Diclosafe® Forte gel contains propylene glycol and butylhydroxytoluene. Propylene glycol may cause skin irritation. Butylhydroxytoluene can cause local skin reactions (e.g., contact dermatitis) or irritation of the eyes and mucous membranes.

Use during pregnancy or breastfeeding.
Pregnancy.
There are no clinical data on the use of Diclosafe® Forte during pregnancy. Even if the systemic exposure of diclofenac is lower compared to its oral administration, it is not known whether the systemic exposure of diclofenac achieved after topical application of Diclosafe® Forte could be harmful to the embryo/fetus.
During the first and second trimesters of pregnancy, Diclosafe® Forte should not be used unless clearly necessary. If used, the dose should be kept as low as possible and the duration of treatment as short as possible.
During the third trimester of pregnancy, systemic use of prostaglandin synthesis inhibitors, including diclofenac, may cause cardiopulmonary and renal toxicity in the fetus. In late pregnancy, prolonged bleeding may occur in both the mother and the child, and delayed labour may occur. Therefore, Diclosafe® is contraindicated during the third 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. Because of a lack of controlled studies in lactating 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 does not affect or has a minor effect on the ability to drive a car and work with other

mechanisms.

Administration and dosage.
The drug is intended for external use only.
Adults and children aged 14 years and above
Diclosafe® Forte gel should be applied 2 times a day (in the morning and in the evening), slightly rubbing into the skin at the place of pain localization. The amount of product 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). The analgesic effect lasts up to 12 hours.
After application, the hands should be washed unless they are the site being treated.
Duration of therapy depends on the nature of the disease and the treatment efficacy.
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.
It is necessary to seek medical advice if the symptoms of the disease do not diminish or increase after 7 days of treatment.
Elderly patients
The drug dose adjustment is not required.
If large areas of the body are covered with Diclosafe® Forte gel, systemic absorption of diclofenac will be greater and the risk of side-effects increased, especially if the therapy is used frequently.

Children.
There is not enough data on the efficacy and safety for children aged under 14 (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).
Treatment
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 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. Adverse reactions include mild, temporary skin reactions at the application site. In rare cases, allergic reactions may occur.

The category of frequency of adverse reactions is defined as follows: very common (≥1/10); common (≥1/100, <1/10); uncommon (≥1/1,000, <1/100); rare (≥1/10,000, <1/1000); very rare (<1/10,000); not known (cannot be estimated from available data).
Infections and invasions: very rare – pustular rash.
Immune system: very rare – hypersensitivity reactions (including urticaria), angioneurotic edema.
Respiratory system, chest and mediastinum: very rare – bronchial asthma.
Skin and subcutaneous tissue: common – rash, itching, eczema, erythema, dermatitis, including contact dermatitis, rare – bullous dermatitis; very rare – photosensitivity reactions; not known – desquamation, skin discoloration, burning sensation of the skin.
In case of adverse reactions, the treatment should be discontinued and a doctor should be consulted.
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. Medical and pharmaceutical workers, as well as patients or their legal representatives are asked to report any suspected adverse reactions and lack of effectiveness of the medicinal product through the Pharmacovigilance Automated Information System at: https://aisf.dec.gov.ua.

Shelf life.
3 years.

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

Package.
30 g, 50 g, 100 g in tube. 1 tube in a carton package.

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.