SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

DIKLORON 5% Gel

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1 g gel contains:
Active Substance:
Diclofenac sodium……50 mg

Excipient(s) with known effects:
Propylene glycol ……93 mg
Methylparaben…….2 mg
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Gel.
A transparent homogeneous colorless or slightly yellow gel with slight alcohol odor.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

DIKLORON is effective for the local treatment of following diseases as an analgesic and anti-inflammatory drug:

- Rheumatic diseases e.g. osteoarthritis, periarthritis, tendinitis, tenosynovitis and bursitis.
- Trauma of the soft tissues e.g. due to strains and sprains.
- Musculoskeletal system diseases characterized by pain, inflammation, muscle tightness.

4.2 Posology and method of administration

Posology/Frequency and duration of administration
Adults and adolescents aged 14 years and older:
DIKLORON is applied over the affected area 3 or 4 times daily and rubbed gently into the skin. The amount needed depends on the size of the painful area. For example, 0.4-0.8 grams of DIKLORON is sufficient to treat an area of approximately 400-800 cm^2.

DIKLORON can also be used in aid of other pharmaceutical forms of DIKLORON.

Frequency and duration of administration
The duration of treatment depends on the indication and clinical response. It should not to be used for more than 14 days for soft tissue injuries or soft tissue rheumatism unless recommended by a doctor, or 21 days for arthritis pain.

It should not be used for more than 7 days without a doctor's assessment.

At the end of the 3rd day, if it does not contribute to improvement, the patient should be requested to inform the doctor.

Method of administration
DIKLORON should be applied over the affected area and rubbed gently into the skin. After administration, the hands should be washed (unless it is used to treat arthrosis of finger joints).

The treated area should be allowed to dry for a few minutes before dressing.

Additional information on special populations
Renal/Hepatic impairment
For patients with renal and hepatic impairment, see Section 4.4.

Pediatric population
Since there is insufficient data on the use of diclofenac in DIKLORON in children under 14 years of age, it is not recommended for use in this patient group.

Geriatric population
The usual adult dosage of DIKLORON may be used in the elderly.

4.3 Contraindications

DIKLORON is contraindicated in patients with known hypersensitivity to diclofenac or any of the other ingredients (see section 6.1).

DIKLORON is also contraindicated in patients in whom attacks of asthma, urticaria, or acute rhinitis are precipitated by other NSAIDs drugs like acetylsalicylic acid or ibuprofen.

It is contraindicated in 3rd trimester of pregnancy.

Administration to the breast area is contraindicated in nursing mothers.

4.4 Special warnings and precautions for use

DIKLORON should only be applied on undamaged and healthy skin (not on open wounds). It should not come into contact with eyes and mucous membranes.

Patients should be warned against excessive exposure to sunlight in order to reduce the incidence of photosensitivity.

If rashes develop, treatment should be stopped.

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

Concomitant use of oral NSAIDs should be cautioned as the incidence of systemic side effects, may increase.

Isolated cases of systemic reactions resulting in deterioration of renal function have been reported with topically administered NSAIDs.

When DIKLORON 5% gel is applied to a relatively large skin surface (e.g. more than 600 cm^2 of body surface) and for a long period of time (e.g. more than 4 weeks), the possibility of undesirable effects associated with DIKLORON 5% gel administration (e.g. hypersensitivity, asthma and renal adverse effect potential) cannot be excluded.

Since isolated cases have been reported with topical diclofenac, DIKLORON 5% gel should be used with extreme caution in patients with peptic ulcer, hepatic or renal insufficiency or bleeding tendency or inflammatory bowel disease.

Bronchospasm may occur in patients with bronchial asthma or allergic disease.

NSAIDs should be used with caution in elderly patients, as these patients are more prone to side effects.

DIKLORON Gel may cause skin irritation because it contains propylene glycol.

DIKLORON contains methylparaben, which may cause (possibly delayed) allergic reactions.

4.5 Interaction with other medicinal products and other forms of interaction

Since systemic absorption of diclofenac is very low following topical application of the gel, no interaction is expected (see section 4.8).

Concomitant use with acetylsalicylic acid and other NSAIDs may increase the incidence of adverse effects (see section 4.4).

4.6 Fertility, pregnancy and lactation

General recommendation
Pregnancy category is B/D (3rd trimester)

Women of child-bearing potential/Birth Control (Contraception)
DIKLORON is not recommended for use in women planning to become pregnant.

Pregnancy
DIKLORON is not recommended for use during pregnancy. Especially during the 3rd trimester of pregnancy, diclofenac is contraindicated due to the possibility of inhibition of normal development of the uterus and/or premature closure of the ductus arteriosus.

DIKLORON %5 Gel should not be given during the first and second trimester of pregnancy, unless clearly necessary. If diclofenac %5 Gel is need to be 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.

The following may be observed in the fetus exposed to prostaglandin synthesis inhibitors during the third trimester of pregnancy:
- cardiopulmonary toxicity (with premature closure of the ductus arteriosus and pulmonary hypertension);
- renal dysfunction, which may progress to renal failure with oligo-hydroamniosis;

In late pregnancy, the following may be observed in the mother and newborn baby:
- 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 labor.

- Therefore, diclofenac is contraindicated during the third trimester of pregnancy.

Breast-feeding/Lactation
It is not known whether topical diclofenac is excreted in human milk. Therefore; DIKLORON is not recommended for use during breast-feeding. If there are compelling reasons for using it, DIKLORON should not be applied to the breasts or to large areas of skin nor should it be used for a prolonged period (see section 4.4).

Reproductive ability / Fertility
Diclofenac had no influence on the fertility in preclinical trials (see section 5.3).

4.7 Effects on ability to drive and use machines

DIKLORON has no influence on the ability to drive and use machines.

4.8 Undesirable effects

The frequencies are defined as follows:
Very common (≥1/10); common (≥1/100, <1/10); uncommon (≥1/1,000, <1/100); rare (≥1/10,000, <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 system disorders
Rare: Asthma

Skin and subcutaneous tissue disorders
Common: Rash, eczema, erythema, dermatitis (including dermatitis contact), pruritus
Rare: Dermatitis bullous
Very rare: Photosensitivity reaction
Unknown: Dry skin, burning sensation at the administration site

The incidence of systemic side effects when diclofenac is applied topically is less than the incidence of side effects seen in oral diclofenac treatment. However, when DIKLORON is applied to very large skin areas and for a long time, the possibility of systemic side effects cannot be ruled out. When such application is considered, the summary of product characteristics of the oral forms of DIKLORON should be consulted.

Reporting of suspected adverse reactions:
Reporting suspected adverse reactions after authorization 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 the national reporting system.

4.9 Overdose and treatment

Since the systemic absorption of diclofenac with topical application is very low, overdose is not expected.

The side effects expected as a result of accidental ingestion of DIKLORON (a 50 g tube is equivalent to 2500 mg diclofenac sodium) are similar to the undesirable effects observed with an overdose of diclofenac tablets. In the event of accidental ingestion (e.g. in children), resulting in significant systemic adverse effects, general therapeutic measures normally adopted to treat poisoning with nonsteroidal anti-inflammatory medicines (NSAIDs) should be used. Gastric decontamination and the use of activated charcoal should be considered, especially within a short time of ingestion.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Non-steroidal anti-inflammatory preparations for topical use
ATC code: M02AA15

DIKLORON is an anti-inflammatory and analgesic preparation designed for external application. The colorless or slightly yellow, non-oily gel is easily absorbed through the skin. Due to an aqueous-alcoholic base the gel exerts a soothing and cooling effect.

Mechanism of action:
The inhibitory effect of diclofenac on prostaglandin biosynthesis is considered to be an important part of its mechanism of action.

In inflammation and pain of traumatic or rheumatic origin, diclofenac has been shown to relieve pain, decrease swelling, and shorten the time to return to normal function.

5.2 Pharmacokinetic properties

General properties
Absorption:
The amount of diclofenac absorbed through the skin is proportional to the contact time and skin area covered with DIKLORON, and depends on the total topical dose and the hydration of the skin.

After topical application of 0.5 g of diclofenac to an area of 500 cm^2, approximately 6 % of the diclofenac dose is absorbed. Occlusion over a period of 10 hours leads to a 3-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 DIKLORON are about 20 times lower than after oral administration of diclofenac tablets.

99.7% of diclofenac is bound to serum proteins, mainly to albumin (99.4%).

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 ± standard deviation). The terminal plasma half-life is 1-2 hours. Four of the metabolites, including the two active ones, also have short plasma half-lives of 1-3 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.

No teratogenic effect was observed in mice, rats and rabbits. Diclofenac had no influence on the fertility of parent animals in rats. It has no effect on the prenatal or postnatal development of the offspring.

No evidence that topical diclofenac causes phototoxicity has been identified in various studies.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Propylene glycol
Ethanol (96%)
Hydroxyethyl cellulose
Methyl paraben
Purified water

6.2 Incompatibilities

There are no known incompatibilities.

6.3 Shelf life

24 months.

6.4 Special precautions for storage

Store at room temperature below 25°C.

6.5 Nature and contents of container

The primary packaging material for our product is a lacquered aluminium tube closed with a twist-off, white HDPE cap. 50 grams tubes are packed in cardboard boxes. 1 tube in a box is supplied with instructions for use.

6.6 Special precautions for disposal and other handling

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORIZATION HOLDER

DEVA Holding A.Ş.
Halkalı Merkez Mah. Basın Ekspres Cad. No:1
34303 Küçükçekmece - ISTANBUL/TÜRKİYE
Phone: 0212 692 92 92
Fax: 0212 697 00 24
E-mail: deva@devaholding.com.tr

8. MARKETING AUTHORIZATION NUMBER

2024/203

9. DATE OF FIRST AUTHORIZATION/RENEWAL OF THE AUTHORIZATION

Date of first authorization : 28.06.2024
Date of last renewal :

10. DATE OF REVISION OF THE TEXT