SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Diklofenak Mimer 23.2 mg/g gel

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 gram of {Product name} 23.2 mg/g gel contains 23.2 mg (2.32%) diclofenac diethylamine, which corresponds to 20 mg diclofenac sodium.

Excipients with known effect
{Product name} 23.2 mg/g gel contains 50 mg propylene glycol per gram gel.
{Product name} 23.2 mg/g gel contains 0.2 mg butylhydroxytoluene per gram gel.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Gel
Viscous white gel with characteristic smell.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

For symptomatic treatment of local pain of mild to moderate intensity in connection with muscles and joint injury, e.g., sporting injuries.

4.2 Posology and method of administration

Posology
For cutaneous use only. Patients should contact their doctor if symptoms persist or worsen 7 days after starting the treatment.

Adults and adolescents above the age of 14 years
{Product name} gel is applied on the painful or inflamed site twice a day and is rubbed gently into the skin. The amount of gel is depending on the size of the affected site to be treated: 2-4 g {Product name} gel (5-10 cm gel string) is enough to treat an area of 400-800 cm^2. The maximum daily dose is 8 g. After application, the hands should be wiped with a paper towel or wet wipe and thereafter washed, unless they are the site being treated. If too much gel is accidentally applied, the excess gel should be wiped with a paper towel. The paper towel or wet wipe should be discarded in the waste bin after use to prevent unused product reaching the aquatic environment. Before applying a bandage, the gel should be left to dry for a few minutes on the skin. The duration of treatment depends on the indication and the clinical response. The gel treatment should not exceed 14 days in muscle and joint injuries, unless recommended by a physician.

Children and adolescents below the age of 14 years:
Available data on efficacy and safety regarding treatment of children and adolescents below 14 years of age are insufficient (see also contraindications section 4.3).

Elderly:

The usual adult dosage may be used.

4.3 Contraindications

- Known hypersensitivity to diclofenac or to any of the excipients listed in section 6.1.
- Patients with a history of symptoms of asthma, angioedema, urticaria or acute rhinitis after using acetylsalicylic acid or other non-steroidal anti-inflammatory drugs (NSAID).
- Third trimester of pregnancy
- Should not be used by children and adolescents below the age of 14 years.

4.4 Special warnings and precautions for use

The risk of experiencing systemic adverse reactions (adverse reactions associated with the use of systemic forms of diclofenac) should be considered if {Product name} gel is used at a higher dose and over a longer period of time than recommended. The gel should therefore be used with caution in patients with impaired kidney, heart or liver function as well as in patients with active peptic ulcers in the stomach or duodenum (see also the product information of systemic forms of diclofenac).

{Product name} gel should not be applied to pathologically changed skin, e.g. eczema, acne, infected skin or open wounds. Contact with the eyes or mucous membranes must be avoided and the gel must not be taken orally.

Exposure to direct sunlight, also sunbeds, should be avoided during treatment and 2 weeks after treatment since the risk of photosensitivity reactions cannot be excluded.

{Product name} gel is not intended for use with occlusive bandages. Joint sprains can be supported by bandage, but the winding must not be so hard that the blood circulation is stopped.

{Product name} gel contains propylene glycol, which may cause skin irritation. The gel also contains butyl hydroxytoluene which may cause skin reactions (e.g., contact dermatitis) or irritation to the eyes and mucous membranes.

The recommended treatment duration should not be exceeded since the risk of development of contact dermatitis increases over time.

Discontinue the treatment if rash develops after applying the product.

4.5 Interaction with other medicinal products and other forms of interaction

Since systemic absorption of diclofenac from topical application is very low, interactions with other medical products are very unlikely.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are no clinical data from the use of {product name} during pregnancy. Even if systemic exposure is lower compared with oral administration, it is not known if the systemic {product name} exposure reached after topical administration can be harmful to an embryo/fetus. With reference to treatment with NSAIDs with systemic uptake, the following is recommended:
Inhibition of prostaglandin synthesis may adversely affect the pregnancy and/or the embryonic/fetal development. Data from epidemiological studies indicate an increased risk of miscarriage, as well as cardiac malformation and gastroschisis after use of a prostaglandin synthesis inhibitor in early pregnancy. The absolute risk for cardiovascular malformation increased from less than 1 %, up to approximately 1.5 %. The risk is believed to increase with higher dose and duration of treatment. In animals, administration of a prostaglandin synthesis inhibitor has been shown to result in increased pre- and post-implantation loss and embryo fetal death. In addition, increased incidences of various malformations, including cardiovascular malformations, have been reported in animals exposed to a

prostaglandin synthesis inhibitor during the organogenetic period. During the first and second trimester of pregnancy, {Product name} gel should not be given unless absolutely necessary. If diclofenac is used by a woman attempting to conceive, or during the first and second trimester of pregnancy, the dose should be as low as possible and the duration of treatment as short as possible.

During the third trimester of pregnancy, all prostaglandin synthesis inhibitors may expose the fetus to:
- cardiopulmonary toxicity (with premature closure of the ductus arteriosus and pulmonary hypertension);
- renal dysfunction, which may progress to renal failure and thus reduced amount of amnionic fluid;

During the third trimester of pregnancy, all prostaglandin synthesis inhibitors may expose the mother and the fetus, at the end of pregnancy, to:
- prolongation of bleeding time, due to an anti-aggregating effect on thrombocytes which may occur even at very low doses.
- inhibition of uterine contractions, which may result in delayed or prolonged labour.
Consequently, {Product name} is contraindicated during the third trimester of pregnancy.

Breastfeeding
Like other NSAIDs, diclofenac passes into breast milk in small amounts. The risk of affecting the child appears unlikely when therapeutic doses are administered to the mother. Due to the lack of controlled studies in lactating women, the product should only be used during lactation under advice from a physician. {Product name} must not be applied on the breasts of lactating women, 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

{Product name} has no influence on the ability to drive and use machines.

4.8 Undesirable effects

Adverse reactions are listed below, by system organ class and frequency. Frequencies are defined as: *Very common* (≥ 1/10) *Common* (≥ 1/100 to < 1/10); *Uncommon* (≥ 1/1,000 to < 1/100); *Rare* (≥ 1/10,000 to < 1/1,000); *Very rare* (< 1/10,000), *Not known*; cannot be estimated from available data. Adverse reactions that have been observed post marketing are reported on a voluntary basis in an unknown population, the frequency of these adverse reactions is not known but are probably rare or very rare.

Infections and infestations	*Very rare*	Pustular rash
Immune system disorders	*Very rare*	Angioedema, hypersensitivity (including urticaria)
Respiratory, thoracic and mediastinal disorders	*Very rare*	Asthma
Skin and subcutaneous tissue disorders	*Common*	Dermatitis (including contact dermatitis), rash, erythema, eczema, pruritus
	Rare	Dermatitis bullous
	Very rare	Photosensitivity reaction

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. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.*

4.9 Overdose

Due to the low systemic absorption of topical diclofenac, overdose is unlikely. However undesirable effects, similar to those observed following an overdose of diclofenac tablets, can be expected if gel is ingested (1 tube of 50 g contains the equivalent of 1000 mg diclofenac sodium.)
In the event of accidental ingestion, resulting in significant systemic adverse effects, general therapeutic measures normally adopted to treat poisoning with non-steroidal anti-inflammatory medicines should be used. Treatment should be continued if clinically justified or according to available national guidelines.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Anti-inflammatory preparations, non-steroids for topical use, ATC code: M02A A15

Mechanism of action and pharmacodynamic effects
Diclofenac is a non-steroidal anti-inflammatory drug (NSAID) with analgesic, anti-inflammatory and antipyretic properties. Inhibition of prostaglandin synthesis via cyclo-oxygenase 2 (COX-2) is the primary mechanism of action of diclofenac.

{Product name} gel is intended for topical application.
Diclofenac 23.2 mg/g gel relieves pain and shortens the time to return to normal function (measured according to Karlsson scoring scale).

In one ankle sprain study (VOPO-P-307), diclofenac 23.2 mg/g significantly decreased pain.
Two days after the start of treatment, patients treated with diclofenac 23.2 mg/g gel experienced a 32 mm reduction in Pain of Movement (POM), while POM in the placebo group had only been reduced by 18 mm ($p < 0.0001$). POM after four days, which was the primary endpoint, decreased by 49 mm on a 100 mm visual analogue scale (VAS) in patients using diclofenac 23.2 mg gel, compared to the 25.4 mm decrease observed in the placebo group. Diclofenac 23.2 mg/g gel showed statistically significantly better effect compared to placebo ($p < 0.0001$).

Additional evidence for the efficacy of diclofenac 23.2 mg/g is demonstrated by the fact that the median time to a 50 % reduction in POM was 4 days after starting treatment in the diclofenac 23.2 mg/g group, versus 8 days after starting treatment in the placebo group ($p < 0.0001$). Thus, treatment with diclofenac 23.2 mg/g gel is considered to accelerate healing by 4 days.

5.2 Pharmacokinetic properties

Absorption
The quantity of diclofenac absorbed systemically from diclofenac 23.3 mg/g gel 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 400 cm^2 of skin, the systemic absorption (AUC och Cmax) of diclofenac 23.2 mg/g gel (2 applications/day) was equivalent to diclofenac 11.6 mg/g gel (4 applications/day). The total daily dose was 80 mg diclofenac in both cases. The relative bioavailability of diclofenac (AUC ratio) for this medicine versus tablet was 4.5% on day 7 (for equivalent diclofenac sodium dose). Absorption was not modified by a moisture and vapour permeable bandage.
A study with diclofenac 11.6 mg/g gel has shown that 10 hours of occlusion resulted in a threefold increase in the absorption of diclofenac.

Distribution

Diclofenac concentrations have been measured from plasma, synovial tissue and synovial fluid after application of topical diclofenac 11.6 mg/g gel to hand and knee joints. Maximum plasma concentrations were approximately 100 times lower than after oral administration of the corresponding quantity of diclofenac. 99.7 % of diclofenac is bound to serum proteins, mainly albumin (99.4 %).

The concentration of diclofenac is higher in synovial fluid than in plasma. This preferential distribution depends on the degree of protein binding of diclofenac, the volume of distribution, the weakness of the moleculeacid properties and changes in the hemodynamics of inflamed tissue.

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 the phenolic metabolites are biologically active, however, to a much smaller extent than diclofenac.

Elimination
The total clearance of diclofenac from plasma is 263 ± 56 ml/min. 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 longer half-life but is virtually inactive. Approximately 60 % of the administered dose is excreted in the urine in the form of metabolites. Less than 1% is excreted as unchanged substance. The rest of the dose is eliminated as metabolites in the bile and faeces.

Specific patient populations
No accumulation of diclofenac and its metabolites is to be expected in patients suffering from renal impairment. In patients with chronic hepatitis or non-decompensated cirrhosis, the kinetics and metabolism of diclofenac are the same as in patients without liver disease.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential, toxicity to reproduction and development.
Diclofenac 23.3 mg/g gel was well tolerated in a number of studies. No risk of phototoxicity has been demonstrated, and diclofenac-containing gel caused no skin sensitisation.
Diclofenac has not shown any effect on fertility in male or female rats.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Butylhydroxytoluene
Carbomer
Cocoyl caprylocaprate
Diethylamine
Isopropyl alcohol
Liquid paraffin
Macrogol cetostearyl ether
Oleyl alcohol
Propylene glycol
Perfume
Purified water

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

This medical product does not require any special storage conditions.

6.5 Nature and contents of container

Aluminium tube with polypropene screwcap.

Pack sizes: Tubes with 30, 50, 60, 100, 120, 150 and 180 g.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7. MARKETING AUTHORISATION HOLDER

<[To be completed nationally]>

8. MARKETING AUTHORISATION NUMBER(S)

<[To be completed nationally]>

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

<Date of first authorisation: {DD month YYYY}>
<Date of latest renewal: {DD month YYYY}>

<[To be completed nationally]>

10. DATE OF REVISION OF THE TEXT

6-Dec-2024

<Detailed information on this medicinal product is available on the website of {name of Member State Agency (link)}>