Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Motusol Max 2 % w/w gel

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

1 g of gel contains diclofenac as 23.2 mg diclofenac diethylamine corresponding to 20 mg diclofenac sodium.

Excipient(s) with known effect
1 g of gel contains 54 mg propylene glycol (E1520), 0.2 mg butylhydroxytoluene (E321) and 1 mg fragrance (contains 0.15 mg benzyl alcohol per g gel,, citral, citronellol, coumarin, eugenol, farnesol, geraniol, d-limonene, and linalool).

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Gel

White to almost white, homogeneous gel

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For adults and adolescents aged 14 years and over
For local symptomatic treatment of pain in acute strains, sprains or contusions following blunt trauma

For adolescents aged 14 years and over the medicinal product is intended for short term treatment.

4.2 Posology and method of administration

Posology
Adults and adolescents aged 14 years and over
Motusol Max 2 % w/w Gel is used 2 times a day (preferably morning and evening).
Depending on the size of the affected site to be treated, a cherry to walnut sized quantity is required, corresponding to 1 -4 g of gel (23.2 - 92.8 mg diclofenac diethylamine corresponding to 20-80 mg diclofenac sodium). This is sufficient to treat an area of 400 – 800 cm^2.

The maximum daily dose is 8 g of gel corresponding to 185.6 mg diclofenac diethylamine (corresponding to 160 mg diclofenac sodium).

The duration of use depends on the symptoms and the underlying disease. Motusol Max 2 % w/w Gel should not be used longer than 1 week without medical advice.

If symptoms worsen or do not improve after 3 -5 days, a doctor should be consulted.

Special patient groups

Elderly
No special dose adjustment is required. Because of the potential undesirable effect profile, elderly people should be carefully monitored.

Patients with renal impairment
No dose reduction is required in patients with renal impairment.

Patients with hepatic impairment

No dose reduction is required in patients with hepatic impairment.

Paediatric population
Children and adolescents under 14 years
There are insufficient data on efficacy and safety in children and adolescents under 14 years of age (see section 4.3)..

Adolescents 14 years and over
In adolescents aged 14 years and over, if this medicinal product is required for more than 7 days for pain relief or if the symptoms worsen the patient/parents of the adolescent is/are advised to consult a doctor.

Method of administration
For cutaneous use.

The gel is applied to the affected parts of the body thinly and gently rubbed into the skin. Afterwards, the hands should be wiped with a paper towel and then washed, unless the hands are the area to be treated.

If too much gel is accidentally applied, the excess gel should be wiped with a paper towel.

The paper towel should be disposed in the household waste 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.

4.3 Contraindications

- hypersensitivity to the active substance or to any of the excipients listed in section 6.1
- patients with a history of hypersensitivity reactions, such as asthma, bronchospasmus, urticaria, acute rhinitis in response to acetylsalicylic acid or non-steroidal anti-inflammatory drugs (NSAIDs).
- on open injuries, inflammations or infections of the skin as well as on eczema or mucous membranes;
- in the last trimester of pregnancy (see section 4.6);
- in children and adolescents under 14 years of age.

4.4 Special warnings and precautions for use

The possibility of systemic undesirable effects from application of topical diclofenac cannot be excluded if the preparation is used on large areas of skin and over a prolonged period. The gel should therefore be used with caution by patients with reduced renal function, reduced heart function or reduced liver function as well as patients with active peptic ulcers in the stomach or duodenum (see product information on systemic forms of diclofenac).

Motusol Max 2 % w/w Gel must only be applied to intact, not diseased or injured skin. Eyes and mucous membranes must not come into contact with the medicinal product and it must not be taken orally.

Topical diclofenac may be used with a non-occlusive bandage but not with an airtight occlusive dressing (see section 5.2).

In acute conditions that are associated with severe redness, swelling, or overheating of joints, in prolonged joint pain or severe back pain that radiates into the legs and/or is associated with neurological deficiencies (e.g. numbness, tingling) a physician should be consulted.

If symptoms worsen or do not improve after 3 - 5 days, a doctor should be consulted.

Patients suffering from asthma, hay fever, swelling of nasal mucous membranes (so-called nasal polyps) or chronic obstructive pulmonary disease, chronic respiratory infections (particularly associated with hay fever-like symptoms), and patients with hypersensitivity to painkillers and anti-rheumatic medicinal products of all kinds are rather at risk to asthma attacks (so called analgesic intolerance/analgesic asthma), to local skin or mucous membrane swelling (so-called Quincke edema) or to urticaria than other patients when treated with Motusol Max 2 % w/w Gel.

In these patients, Motusol Max 2 % w/w Gel may only be used under certain precautions (emergency preparedness) and direct medical supervision. The same applies for patients who are also allergic to other substances e.g. with skin reactions, itching or urticaria.

If a skin rash occurs during the treatment with Motusol Max 2 % w/w Gel, the treatment should be stopped.

During treatment photosensitivity can occur with the appearance of skin reactions after exposition to sunlight.

Preventive measures should be taken so that children do not contact the skin areas to which the gel has been applied.

This medicinal product contains butylhydroxytoluene which may cause local skin reactions (e.g. contact dermatitis) or irritation to the eyes and mucous membranes.

This medicinal product contains 54 mg propylene glycol per g gel.

This medicinal product contains fragrance with benzyl alcohol (0.15 mg/g gel), citral, citronellol, coumarin, eugenol, farnesol, geraniol, d-limonene and linalool which may cause allergic reactions.
In addition, benzyl alcohol may cause mild local irritation.

4.5 Interaction with other medicinal products and other forms of interaction

Since the systemic absorption of diclofenac is very low with topical application, interactions are very unlikely in use as intended.

4.6 Fertility, pregnancy and lactation

The systemic concentration of diclofenac is lower after topical administration, compared to oral formulations. With reference to experience from treatment with NSAIDs with systemic uptake, the following is recommended:

Pregnancy
Inhibition of prostaglandin synthesis may adversely affect the pregnancy and/or the embryo/fetal development. Data from epidemiological studies suggest an increased risk of miscarriage and of cardiac malformation and gastroschisis after use of a prostaglandin synthesis inhibitor in early pregnancy. The absolute risk for cardiovascular malformation was increased from less than 1%, up to approximately 1.5 %. The risk is believed to increase with dose and duration of therapy. In animals, administration of a prostaglandin synthesis inhibitor has been shown to result in increased pre-and post-implantation loss and embryo-fetal lethality. In addition, increased incidences of various malformations, including cardiovascular, have been reported in animals given a prostaglandin synthesis inhibitor during the organogenetic period.

During the first and second trimester of pregnancy, diclofenac should not be used unless clearly necessary. If diclofenac is 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.

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 with oligo hydroamniosis;
- the mother and the neonate, at the end of pregnancy, to:
- 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 third trimester of pregnancy.

Breast-feeding
Diclofenac passes into breast milk in small amounts. However, at therapeutic doses of Motusol Max 2 % w/w Gel no effects on the breast-fed child are anticipated. Because of a lack of controlled studies in breast-feeding women, the medicinal product should only be used during breast-feeding under advice from a healthcare professional. Under this circumstance, Motusol Max 2 % w/w Gel should not be applied on the breasts of breast-feeding mothers, 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

The topical use of diclofenac has no or negligible 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* (³1/10); *Common* (³1/100 to <1/10); *Uncommon* (³1/1,000 to <1/100); *Rare* (³1/10,000 to <1/1,000); *Very rare* (< 1/10,000), *Not known* (cannot be estimated from the available data).

System organ class database	Adverse reactions and frequency
Infections and infestations	*Very rare*: Rash pustular
Immune system disorders	*Very rare*: Hypersensitivity (including urticaria), angioedema
Respiratory, thoracic and mediastinal disorders	*Very rare*: Asthma
Gastrointestinal disorders	*Very rare*: Gastrointestinal complaints
Skin and subcutaneous tissue disorders	*Common*: Dermatitis (including contact dermatitis), skin rash, erythema, eczema, pruritus *Uncommon*: Scaling, dehydration of the skin, oedema *Rare*: Dermatitis bullous *Very rare*: Photosensitivity reaction *Not known*: Burning sensation at the application site, dry skin

When the gel is applied on large areas of skin and over a prolonged period, the possibility of systemic undesirable-effects (e.g. renal, hepatic or gastrointestinal undesirable effects, systemic hypersensitivity reactions), as they occur possibly after systemic administration of diclofenac-containing medicinal products, cannot be excluded.

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 HPRA Pharmacovigilance Website: www.hpra.ie.

4.9 Overdose

Due to the low systemic absorption of diclofenac in limited topical use an overdose is unlikely.

Undesirable effects similar to those observed following an overdose of systemic diclofenac can occur if topical diclofenac is inadvertently ingested (1 tube of 100 g contains the equivalent of 2,320 diclofenac diethylamine corresponding to 2,000 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 medicinal products should be used. Gastric lavage and the use of activated charcoal should be considered, especially within a short time of ingestion.

A specific antidote does not exist.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Topical products for joint and muscular pain; Anti-inflammatory preparations, non-steroids for topical use.

ATC code: M02AA15

Mechanism of action
Diclofenac is a potent non-steroidal anti-inflammatory drug. It develops its therapeutic efficacy mainly via inhibition of prostaglandin synthesis by cyclooxygenase 2 (COX-2). Diclofenac has proven to be effective via the prostaglandin synthesis inhibition in the conventional animal-experiment inflammation models. In humans, diclofenac reduces inflammatory-related pain, swellings and fever. Furthermore, diclofenac inhibits reversibly the ADP and the collagen-induced thrombocyte aggregation.

In a clinical study on patients 23.2 mg of diclofenac diethylamine salt/g gel reduced clinically relevant and statistically significantly the pain (on movement) three days after start of treatment compared with the placebo group. In addition, the gel significantly improved functioning of the foot joint within the first three days of treatment.

5.2 Pharmacokinetic properties

Absorption
The quantity of diclofenac absorbed through the skin is proportional to the duration of the skin contact and the size of the treated area and depends on both the total dose applied and the degree of skin hydration. After local application of Motusol Max 2 % w/w Gel to hand and knee joints, the active substance is absorbed through the skin and detectable in the plasma as well as the tissue in varying quantities – depending on the diffusion range – beneath the application site. Absorption amounts to about 6 % of the applied dose of diclofenac after topical application of 2.5 g diclofenac gel on 500 cm^2 skin, determined by measuring total renal elimination of diclofenac and its hydroxylated metabolites, compared with the oral administration of diclofenac sodium. Due to a depot-effect in the skin, there is a delayed and prolonged release of active substance into the underlying tissue and the plasma. Under occlusive conditions (10 hours), percutaneous absorption of diclofenac in adults can be increased three-fold (serum concentration).

Distribution
99.7 % of diclofenac is bound to serum proteins, mainly albumin (99.4 %). Plasma levels after application of diclofenac gel are not sufficient to explain the observed therapeutic efficacy; this is more likely due to the presence of significantly higher active substance concentrations beneath the application site. Due to its properties (such as short plasma half-life, low pKa value, small distribution volume and high protein binding), diclofenac has an affinity to inflamed tissue.
Diclofenac preferentially distributes and persists in inflamed tissues, it is found there in concentrations up to 20 times higher than in plasma.

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 systemic 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. Diclofenac and its metabolites are excreted mainly in the urine.

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

5.3 Preclinical safety data

Based on conventional studies on safety pharmacology, genotoxicty and carcinogenic potential, the pre-clinical data do not reveal any specific hazards for humans apart from those already described in other sections of the SPC. In the animal studies the chronic toxicity of diclofenac following systemic application mainly manifested as gastrointestinal lesions and ulcers. In a 2-year toxicity study, a dose-dependent increase in the incidence of thrombosis of the heart was observed in diclofenac-treated rats.

In animal studies on reproductive toxicity, systemically administered diclofenac caused inhibition of ovulation in rabbits and impairment of implantation and early embryonic development in rats. Gestation and duration of parturition were prolonged by diclofenac. The embryotoxic potential of diclofenac was investigated in three animal species (rat, mouse, rabbit). Fetal death and growth retardation occurred at materno-toxic dose levels. Based on the available non-clinical data, diclofenac is regarded as being non-teratogenic. Doses below the maternotoxic threshold had no impact on the postnatal development of the offspring

Diclofenac poses a risk to the aquatic environment (see section 6.6).

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Carbomer
Cocoyl caprylocaprate
Macrogol cetostearyl ether
Paraffin, liquid
Diethylamine
Isopropyl alcohol
Propylene glycol (E1520)
Oleic acid (E570)
Butylhydroxytoluene (E321)
Fragrance (contains benzyl alcohol, citral, citronellol, coumarin, eugenol, farnesol, geraniol, d-limonene and linalool)
Purified water

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

18 months

6.4 Special precautions for storage

Do not store above 25°C.
Store in the original package in order to protect from light.

6.5 Nature and contents of container

The gel is packed in aluminium laminated tubes, closed with PE seal and PP screw caps in pack sizes: 30 g, 50 g, 60 g, 100 g, 150 g, 180 g per tube.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

This medicinal product poses a risk to the environment (see section 5.3).

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

7 MARKETING AUTHORISATION HOLDER

Teva B.V.
Swensweg 5
2031GA Haarlem
Netherlands

8 MARKETING AUTHORISATION NUMBER

PA1986/093/002

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 25th August 2020
Date of last renewal: 10th June 2025

10 DATE OF REVISION OF THE TEXT