SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE FINISHED PHARMACEUTICALPRODUCT

Remethan 1% gel

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Remethan gel contains 1% w/w diclofenac diethylamine.

1 g gel contains diclofenac diethylamine equivalent to 10 mg diclofenac sodium.

Excipient(s) with known effect
20 g gel contain 1 g of propylene glycol.
50g gel contain 2.5 g of propylene glycol.
100 g gel contain 5 g of propylene glycol.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Gel.

White, soft, homogeneous cream like gel.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

For the local symptomatic relief of pain and inflammation in:

• trauma of the tendons, ligaments, muscles and joints, e.g. due to sprains, strains and bruises
• localised forms of soft tissue rheumatism

For the relief of pain of non-serious arthritic conditions.

4.2. Posology and method of administration

Posology

Adultsand children 14 years and over: Remethan Gel should be rubbed gently into the skin**.** Depending on the size of the affected site to be treated 2-4g (a circular shaped mass approximately 2.0-2.5cm in diameter) should be applied 3 - 4 times a daily**.**The maximum daily dose is 16g. Therefore the maximum weekly dose is 112g.

For arthritis pain it may be necessary to apply the gel for up to 7 days (to allow its effect to build up on the joint) before an improvement in pain is noticed. The gel can be used for up to 14 days under pharmacy supervision.

After application, the hands should be washed unless they are the site being treated.

If symptoms do not improve by day 7, or if they worsen within the first 7 days, a consultation with a doctor is recommended. Consultation with a doctor is recommended if more than two major joints in the body are affected. Do not use for more than 14 days unless recommended by a doctor.

Use in the elderly: The usual adult dosage may be used.

Children and adolescents: There are insufficient data on efficacy and safety available for the children and adolescents below 14 years of age (see also contraindications section 4.3). In children aged 14 years and over, if this 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 external use only.

4.3. Contraindications

Remethan gel is contra-indicated in

- patients with or without chronic asthma in whom attacks of asthma, urticaria or acute rhinitis are precipitated by aspirin or other non-steroidal anti-inflammatory agents (NSAIDs)
- hypersensitivity to diclofenac, acetylsalicylic acid or other non-steroidal anti-inflammatory drugsor any of the excipients..
- third trimester of pregnancy.
- concomitant use of other products containing diclofenac.
- concomitant use of oral NSAIDS.
- the use in children and adolescents aged less than 14 years is contraindicated.

4.4. Special warnings and precautions for use

The possibility of systemic adverse events from application of diclofenac gel cannot be excluded if the preparation is used on large areas of skin and over a prolonged period (see the product information on systemic forms of diclofenac).

Diclofenac gel should be applied only to intact, non-diseased skin and not to skin wounds or open injuries. It should not be allowed to come into contact with the eyes or mucous membranes, and should not be ingested.

Discontinue the treatment if a skin rash develops after applying the product.

Patients with a history of, or active, peptic ulceration. Some possibility of gastro-intestinal bleeding in those with a significant history of this condition has been reported in isolated cases.

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.

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

Diclofenac gel contains propylene glycol
Propylene glycol may cause mild localised skin irritation in some people.

4.5. Interaction with other medicinal products and other forms of interaction

Since systemic absorption of diclofenac from topical application is very low,such interactions are very unlikely.

No drug interactions during treatment with diclofenac gel have been reported, but the following have been observed with oral forms of diclofenac or other NSAIDs.

Lithium and digoxin: diclofenac may increase plasma concentrations of lithium and digoxin.

Anticoagulants: Although clinical investigations do not appear to indicate that diclofenac has an influence on the effect of anticoagulants, there are isolated reports of an increased risk of haemorrhage with the combined use of diclofenac and anticoagulant therapy. Therefore, to be certain that no change in anticoagulant dosage is required, close monitoring of such patients is required. As with other non-steroidal anti-inflammatory agents, diclofenac in a high dose can reversibly inhibit platelet aggregation.

Antidiabetic agents: Clinical studies have shown that diclofenac can be given together with oral antidiabetic agents without influencing their clinical effect. However there have been isolated reports of hypoglycaemic and hyperglycaemic effects which have required adjustment to the dosage of hypoglycaemic agents.

Ciclosporin: Cases of nephrotoxicity have been reported in patients receiving concomitant cyclosporin and NSAIDs, including diclofenac. This might be mediated through combined renal antiprostaglandin effects of both the NSAID and cyclosporin.

Methotrexate: Cases of serious toxicity have been reported when methotrexate and NSAIDs are given within 24 hours of each other. This interaction is mediated through accumulation of methotrexate resulting from impairment of renal excretion in the presence of the NSAID.

Quinolone antimicrobials: Convulsions may occur due to an interaction between quinolones and NSAIDs. This may occur in patients with or without a previous history of epilepsy or convulsions. Therefore, caution should be exercised when considering the use of a quinolone in patients who are already receiving an NSAID.

Other NSAIDs and steroids: Co-administration of diclofenac with other systemic NSAIDs and steroids may increase the frequency of unwanted effects. Concomitant therapy with aspirin lowers the plasma levels of each, although no clinical significance is known.

Diuretics: Various NSAIDs are liable to inhibit the activity of diuretics. Concomitant treatment with potassium-sparing diuretics may be associated with increased serum potassium levels, hence serum potassium should be monitored.

Mifepristone: NSAIDs should not be used for 8-12 days after mifepristone administration as NSAIDs can reduce the effects of mifepristone.

Anti-hypertensives: Concomitant use of NSAIDs with antihypertensive drugs (i.e. beta-blockers, angiotensin converting enzyme (ACE) inhibitors, diuretics) may cause a decrease in their antihypertensive effect via inhibition of vasodilatory prostaglandin synthesis.

4.6. Fertility, pregnancy and lactation

Pregnancy

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:

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 given 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 oligohydroamniosis;

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.

Lactation
Like other NSAIDs, diclofenac passes into breast milk in small amounts. However, at therapeutic doses of diclofenac no effects on the suckling child are anticipated. Because of a lack of controlled studies in lactating women, the product should only be used during lactation under advice from a healthcare professional. Under this circumstance, diclofenac should not be applied on the breasts of nursing 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

Cutaneous application of diclofenac has no or negligible influence on the ability to drive and use machines.

4.8. Undesirable effects

Local:
Diclofenac gel is usually well tolerated.Local irritation, erythema, pruritus or dermatitis may occasionally occur. Skin photosensitivity, desquamation, discolouration and bullous or vesicular eruptions have been reported in isolated cases. Patients should be warned against excessive exposure to sunlight in order to reduce the incidence of photosensitivity.

General:
Systemic absorption of diclofenac gel is low compared with plasma levels obtained following oral forms of diclofenac. However, where diclofenac gel is applied to a relatively large area and over a prolonged period, the possibility of systemic side effects cannot be completely excluded.

Asthma has been rarely reported in patients using topical NSAID preparations.

Adverse reactions (Table 1) are ranked under heading of frequency, the most frequent first, using the following convention: 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.

Table 1

Immune system disorder	
Very rare:	Hypersensitivity (including urticaria),angioneurotic oedema.
Infections and infestations	
Very rare:	Rash pustular.
Respiratory, thoracic and mediastinal disorders	
Very rare:	Asthma.
Skin and subcutaneous tissue disorders	
Common:	Rash, eczema, erythema, dermatitis (including dermatitis contact), pruritus
Rare:	Dermatitis bullous

Very rare:	Photosensitivity reaction

General: Systemic absorption of diclofenac Gel is low compared with plasma levels obtained following administration of oral forms of diclofenac and the likelihood of systemic side-effects occurring with topical diclofenac is small compared with the frequency of side-effects associated with oral diclofenac. However, where diclofenac Gel is applied to a relatively large area of skin and over a prolonged period, the possibility of systemic side-effects cannot be completely excluded. If such usage is envisaged, the data sheet on diclofenac oral dosage forms should be consulted.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product isimportant. It allows continued monitoring of the benefit/risk balance of the medicinalproduct. Healthcare professionals are asked to report any suspected adverse reactionsvia the national reporting system.

4.9. Overdose

Signs and symptoms
The low systemic absorption of topical diclofenacrenders overdose very unlikely. However, undesirable effects, similar to those observed following an overdose of diclofenac tablets, can be expected if diclofenac gel is inadvertently ingested (1 tube of 100g contains the equivalent of 1000mg of 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. Gastric decontamination and the use of activated charcoal should be considered, especially within a short time of ingestion.

Treatment
Management of overdosage with NSAIDs essentially consists of supportive and symptomatic measures. There is no typical clinical picture resulting from diclofenac overdosage. Supportive and symptomatic treatment should be given for complications such as hypotension, renal failure, convulsions, gastro-intestinal irritation, and respiratory depression; specific therapies such as forced diuresis, dialysis or haemoperfusion are probably of no help in eliminating NSAIDs due to their high rate of protein binding and extensive metabolism.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: Topical products for joint and muscular pain, ATC code: M02AA15

Diclofenac gel is an anti-inflammatory and analgesic preparation designed for external application. Due to an aqueous-alcoholic base the gel exerts a soothing and cooling effect.

5.2. Pharmacokinetic properties

When diclofenacgel is applied locally, the active substance is absorbed through the skin. In healthy volunteers approximately 6% of the dose applied is absorbed, as determined by urinary excretion of diclofenac and its hydroxylated metabolites. Findings in patients confirm that diclofenac penetrates inflamed areas following local application of diclofenac gel.

Synovial fluid and tissue levels of diclofenac are higher than those detected in plasma.

5.3. Preclinical safety data

None known.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Triethanolamine
Carbomer
Cetomacrogol 1000
Cetiol LC
Isopropyl Alcohol
Liquid Paraffin
Propylene Glycol
Perfume
Purified Water

6.2. Incompatibilities

Not applicable.

6.3. Shelf life

3 years.

6.4. Special precautions for storage

Store below 25°C. Replace cap tightly after use.

6.5. Nature and contents of container

Aluminium tube.Pack-sizes of 20g, 50g and 100g.

Not all pack sizes maybe marketed.

6.6. Special precautions of disposal and other handling

No special requirements.

7. MARKETING AUTHORISATION HOLDER

Remedica Ltd
Aharnon Str.,
Limassol Industrial Estate,
3056 Limassol, Cyprus

8. MARKETING AUTHORISATION NUMBER(S)

06749/REN/2018

9. DATE OF FIRST AUTHORISATION/ RENEWAL OF THE AUTHORISATION

Date of latest renewal: 16-12-2019

10. DATE OF REVISION OF THE TEXT

05/07/2023