SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Tiloket 2.5% Gel

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Tiloket gel contains ketoprofen 2.5% w/w

For the full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Gel
Homogeneous transparent gel with an odour of lavender and alcohol

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Ketoprofen is a non–steroidal anti-inflammatory drug. It has anti-inflammatory and analgesic actions.
Symptomatic relief of acute painful musculoskeletal conditions caused by trauma, such as soft tissue injuries, including sports injuries, sprains, strains, contusions and musculo-tendonitis swelling, backache and rheumatic pain.

Pain of non-serious arthritis

4.2 Posology and method of administration

Posology
Adults
To be applied two to four times daily to the skin in the painful or inflamed region for up to 7 days. Apply gently but massage well to ensure gel penetration. The usual recommendation dose is 15g per day (7.5grams correspond to approximately 14cm of gel)

Elderly
There are no specific dosage recommendations for the elderly

Paediatric population
Children under 15 years: Not recommended, as safety in children has not been established.

Method of administration
Local route.

4.3 Contraindications

Tiloket Gel must not be used in patients with:

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1
- Known hypersensitivity reactions, such as symptoms of asthma, allergic rhinitis or urticaria to fenofibrate, tiaprofenic acid, acetylsalicylic acid or to other Non-Steroidal Anti-Inflammatory drugs (NSAID).
- History of photosensitivity reaction
- History of skin allergy reactions to ketoprofen, tiaprofenic acid, fenofibrate or UV blockers or perfumes
- Sun exposure, even in case of hazy sun, including UV light from solarium, during treatment and for 2 weeks after its discontinuation (see section 4.4).
- Exudative dermatoses, on pathological skin changes such as eczema or acne; or in infected skin lesions, open wounds, broken skin and sores.
- Tiloket gel should not be applied to mucous membranes, anal or genital areas, eyes or used with occlusive dressings.
- Third trimester of pregnancy.

4.4 Special warnings and precautions for use

For topical use only.

- Although systemic effects are minimal, the gel should be used with caution in patients with reduced heart, liver or renal function: isolated cases of systemic adverse reactions consisting of renal affections have been reported.
- The topical use of large amounts of product may give rise to systemic effects such as hypersensitivity and asthma.
- Hands should be washed thoroughly after each application of the gel.
- Treatment should be discontinued immediately upon development of any skin reaction including cutaneous reactions after co-application of octocrylene-containing products.

- It is recommended to protect treated areas by wearing clothing during all the application of the gel and two weeks following its discontinuation to avoid the risk of photosensitisation.
- Do not apply Tiloket Gel beneath occlusive dressings.
- The gel must not come in contact with mucous membrane or the eyes.
- Keep the gel away from naked flames. Do not incinerate.
- Should a skin rash occur after gel application, treatment must be stopped.
- The recommended length of treatment should not be exceeded (see section 4.2) due to the risk of developing contact dermatitis and photosensitivity reactions which increases over time.
- Patients with asthma combined with chronic rhinitis, chronic sinusitis, and/or nasal polyposis have a higher risk of allergy to aspirin and/or NSAIDs than the rest of the population.
- The safety and efficacy of ketoprofen gel in children have not been established.
- Areas of skin treated with Tiloket Gel should not be exposed to direct sunlight, or solarium ultraviolet light, either during treatment or for two weeks following treatment discontinuation, in order to avoid, phototoxicity reactions and photoallergy.
- The use of topical products, especially if it is prolonged, may give rise to phenomena of sensitisation or local irritation.
- Keep out of the sight and reach of children.

4.5 Interaction with other medicinal products and other forms of interaction

Interactions are unlikely, as serum concentrations following topical application are low.

It is, however, advisable to monitor patients under treatment with coumarinic substances

Serious interactions have been recorded after the use of high dose methotrexate with non-steroidal anti-inflammatory agents, including ketoprofen, when administered by the systemic route.

4.6 Pregnancy and lactation

Pregnancy

There are no clinical data from the use of topical forms of ketoprofen during pregnancy. Even if systemic exposure is lower compared with oral administration, it is not known if the systemic ketoprofen exposure reached after topical administration can be harmful to an embryo/foetus. During the first and second trimester of pregnancy, Tiloket gel should not be used unless

clearly necessary. If used, the dose should be kept as low and duration of treatment as short as possible.

During the third trimester of pregnancy, systemic use of prostaglandin synthetase inhibitors including ketoprofen may induce cardiopulmonary and renal toxicity in the foetus. At the end of the pregnancy prolonged bleeding time in both mother and child may occur, and labour can be delayed. Therefore, Tiloket gel is contraindicated during the last trimester of pregnancy (see section 4.3).

Breast-feeding
Trace amounts of ketoprofen are excreted in breast milk; therefore, Tiloket gel should not be used during breast feeding.

4.7 Effects on ability to drive and use machines

None known.

4.8 Undesirable effects

The most common adverse reactions are photosensitive reactions (phototoxic and photosensitivity allergic reactions), the majority of which occurs after an incorrect use of the product (exposure of the skin to sunlight or solarium before 15days from the last application, see sections 4.3 and 4.4). There have been reports of localised skin reactions due to photosensitivity, including erythema, pruritus and burning sensations, which might spread beyond the area of application. Cases of more severe reactions such as bullous or phlyctenular eczema which may spread or become generalized have occurred rarely.

Other systemic effects of anti-inflammatory drugs: hypersensitivity, gastrointestinal and renal disorders (these depend on the transdermic spreading of the active ingredient, hence on the amount of gel applied, on the surface involved, on the degree of intactness of the skin, on the duration of the treatment and on the use of occlusive bandages).

The below mentioned adverse reactions have been collected in the post-marketing experience.

System Organ Class	Uncommon (≥1/1000 to <1/100)	Rare (≥1/10 000 to <1/1000)	Very rare (<1/10 000)	Not known (cannot be estimated from the available data).
Infections and infestations				Secondary impetigo
Blood and lymphatic system disorders				Eosinophilia
Immune System disorder				Anaphylactic reaction, angioedema, hypersensitivity

Eye disorders				Eyelid oedema
Vascular disorders				Vasculitis
Gastrointestinal disorders				Peptic ulcer, gastrointestinal bleeding, diarrhoea, lip oedema
Skin and subcutaneous tissue disorders	Rash (erythematous, generalised, maculo-papular, papular, pruritic, pustular, vesicular), eczema, pruritus, burning sensations application site burn.	Dermatitis (allergic, bullous, contact, exfoliative, vesicular), urticaria, blister, photosensitivity reaction, allergic reaction, skin exfoliation, skin oedema.		
Renal and urinary disorders			Acute renal failure, insufficiency aggravated	
General disorder and administration site condition				Pyrexia
Injury, poisoning and procedural complications				Wound complication

Elderly patients are particularly susceptible to the adverse effects of non-steroidal anti-inflammatory drugs

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 Yellow Card Scheme at: www.mhra.gov.uk/yellowcard

4.9 Overdose

Overdose is unlikely to be caused by topical administration. If accidentally ingested, the gel may cause systemic adverse effects depending on the amount ingested. However, if they occur, treatment should be supportive and symptomatic in accordance with over dosage of oral anti-inflammatories.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Ketoprofen is a non-steroidal anti-inflammatory of the propionics group, derivative of aryl-carboxylic acid.

It has anti-inflammatory and analgesic properties.
ATC code: M01AE

5.2 Pharmacokinetic properties

Plasma and tissue levels of ketoprofen have been measured in 24 patients undergoing knee surgery. After repeated percutaneous administration of Tiloket gel the plasma levels were about 60 fold less (9 - 39 ng/g) than those obtained after a single oral dose of ketoprofen (490 - 3300 ng/g). Tissue levels at the area of application were within the same concentration range for the gel as for the oral treatment, although the gel was associated with a considerably higher inter-individual variability.

The bioavailability of ketoprofen after topical administration has been estimated to be approximately 5% of the level obtained after an orally administered dose, based on urinary excretion data.

The protein binding in plasma is approximately 99%. Ketoprofen is excreted through the kidneys mainly as glucuronide conjugate

Applied locally in the form of a gel, ketoprofen is absorbed very gradually and is not accumulated in the body. The systemic passage of the gel compared to that of the oral formulations of ketoprofen is around 5 per cent, which enables a local effect to be obtained without systemic incidence.

5.3. Preclinical Safety Data

The main acute side effect seen during the safety studies after oral, sc and ip routes is the ulcerogenic potential. The target organs for chronic toxicity are the gastrointestinal tract, the kidney and, to a lesser degree the liver. Due to the low systemic passage of ketoprofen from the gel such safety data are not relevant for local administration. Studies on the local tolerance have shown that ketoprofen is well tolerated.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Carbomer
Triethanolamine
Lavender essential oil
Ethanol
Purified water

6.2. Incompatibilities

Do not mix with other medicinal products.

6.3 Shelf life

30 months.

Once opened, use within one month.

6.4. Special precautions for storage

Do not store above 25°C.

6.5 Nature and contents of container

Varnished aluminium tube - polyethylene screw cap. 50g and 100g

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

No special requirements for disposal
Any unused medicinal product or waste material should be disposed of in accordance with local requirements

7 MARKETING AUTHORISATION HOLDER

Tillomed Laboratories Ltd
220 Butterfield
Great Marlings
Luton, LU2 8DL
United Kingdom

8. MARKETING AUTHORISATION NUMBER

PL 11311/0127

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 09/10/2000
Date of latest renewal: 02/03/2009

10 DATE OF REVISION OF THE TEXT

26/05/2023