1 NAME OF THE MEDICINAL PRODUCT

Fastum gel.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Fastum Gel contains ketoprofen 2.5 % w/w.

3 PHARMACEUTICAL FORM

A colourless, almost transparent, non-greasy, non staining gel with an aromatic fragrance for topical application.

4 CLINICAL PARTICULARS

4.1. Therapeutic indications

Local treatment of painful disorders of the osteo-articular and muscular system of rheumatic or traumatic origin: contusions, distortions, muscle strains, stiff neck, lumbago.

4.2 Posology and method of administration

Fastum gel should be applied to the affected area one or two times daily. Maximum duration of use should not exceed 7 days. Fastum gel should be applied with gentle massage only.

Adults and elderly: **Tube or dispenser:** Apply 5-10cm of gel (100-200mg ketoprofen) with each application; for the pump dispenser push the pump 3-6 times.
Children under 12 years of age: Not recommended, as experience in children is limited.

4.3 Contraindications

- History of any photosensitivity reaction.
- Known hypersensitivity reactions, such as symptoms of asthma, allergic rhinitis or urticaria to ketoprofen, fenofibrate, tiaprofenic acid, acetylsalicylic acid, or to other NSAIDs.
- History of skin allergy to ketoprofen, tiaprofenic acid, fenofibrate or UV blocker or perfumes.
- Sun exposure, even in case of hazy sun, including UV light from solarium, during the treatment and 2 weeks after its discontinuation.
- Hypersensitivity to any of the excipients of the product.
- Ketoprofen gel should not be applied to open or infected wounds or lesions of the skin, such as occurs, for example, with eczema or acne, or near the eyes.
- Third trimester of pregnancy (see section 4.6).

4.4 Special warnings and precautions for use

- The gel should be used with caution in patients with reduced heart, liver or renal function: isolated cases of systemic adverse reactions affecting renal function have been reported.
- The topical use of large amounts of product may give rise to systemic effects such as hypersensitivity and asthma.
- The treatment should be interrupted if rash appears.
- The recommended length of treatment should not be exceeded due to the risk of developing contact dermatitis and photosensitivity reactions increases over time.
- Hands should be washed thoroughly after each application of the product.
- 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 avoid exposure of treated skin to direct sunlight including solarium (sunbeds), and to protect treated areas by wearing clothing during treatment with the product and for two weeks following its discontinuation to avoid the risk of photosensitisation.
- Do not use with occlusive dressings.
- The gel must not come into contact with mucous membranes.
- 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 use of topical products, especially if it is prolonged, may give rise to phenomena of sensitisation or local irritation.

Keep out of the reach and sight of children.

Paediatrics: The safety and efficacy of ketoprofen gel in children have not been established.

4.5 Interaction with other medicinal products and other forms of interaction

Interactions are unlikely as serum concentrations following topical administration are low. It is, however, advisable to monitor patients under treatment with coumarinic substances.

4.6 Pregnancy and lactation

Pregnancy

During the first and second trimester:
In mice and rats, there is no evidence of teratogenic or embryotoxicity. In the rabbit, slight embryotoxicity likely related to maternal toxicity has been reported.
As the safety of ketoprofen in pregnant women has not been evaluated, the use of ketoprofen during the first and second trimester of pregnancy should be avoided.

During the third trimester of pregnancy:

All 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 the mother and child may occur. Therefore, ketoprofen is contraindicated during the last trimester of pregnancy.

Lactation

No data are available on excretion of ketoprofen in human milk. Ketoprofen is not recommended in nursing mothers.

4.7 Effects on ability to drive and use machinery

Not 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 15 days 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.

The following CIOMS frequency rating is used: Very common (≥1/10); common (≥1/100 to <1/10); 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
Not known: Secondary impetigo

Blood and lymphatic system disorders
Not known: Eosinophilia

Immune system disorders
Not known: Anaphylactic reaction, angioedema, hypersensitivity

Eye disorders
Not known: Eyelid oedema

Vascular disorders
Not known: Vasculitis

Gastrointestinal disorders
Not known: Peptic ulcer, gastrointestinal bleeding, diarrhoea, lip oedema

Skin and subcutaneous tissue disorders
Uncommon: Rash (erythematous, generalised, maculo-papular, papular, pruritic, pustular, vesicular), eczema, pruritus, burning sensation, application site burn
Rare: Dermatitis (allergic, bullous, contact, exfoliative, vesicular), urticaria, blister, photosensitivity reaction, photosensitivity allergic reaction, skin exfoliation, skin oedema,

Renal and urinary disorders
Very rare: Acute renal failure, insufficiency aggravated

General disorders and administration site Conditions
Not known: Pyrexia

Injury, poisoning and procedural complications
Not known: Wound complication

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

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 symptomatic and supportive in accordance with overdosage of oral anti-inflammatories.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic category: non-steroid anti-inflammatory drug for topical use.

Ketoprofen is an inhibitor of both the cyclooxygenase and lipoxygenase pathways. Inhibition of prostaglandin synthesis provides for potent anti-inflammatory, analgesic and antipyretic effects. Lipoxygenase inhibitors appear to attenuate cell mediated inflammation and thus retard the progression of tissue destruction in inflamed joints. In addition, ketoprofen is a powerful inhibitor of bradykinin (a chemical mediator of pain and inflammation), it stabilises lysosomal membranes against osmotic damage and prevents the release of lysosomal enzymes that mediate tissue destruction in inflammatory reactions.

5.2 Pharmacokinetic properties

After oral administration of a single dose, maximum blood concentrations are achieved within 2 hours.
Ketoprofen plasma half-life ranges from 1 to 3 hours. Plasma protein binding is 60%-90%.
Elimination is mainly by urinary route and in glucuronated form; approximately 90% of the amount administered is excreted within 24 hours.
By cutaneous route, absorption is instead very low. In fact the percutaneous application of 50-150 mg of ketoprofen produces plasma levels of the active ingredient of 0.08-0.15 µg/mL approx. 5-8 hours after application.

Fastum gel allows the site specific topical delivery of ketoprofen with very low plasma concentrations of drug. Therapeutic levels in the affected tissues provide relief from pain and inflammation, yet will satisfactorily overcome the problem of significant systemic unwanted effects.

5.3 Preclinical safety data

In animal trials no embryopathic effects have been found, while there is no epidemiological evidence of the safety of ketoprofen in human pregnancy. In preclinical and clinical trials on Ketoprofen no serious adverse effects have been observed, although anecdotal cases of systemic adverse reactions have been described.

There are no preclinical data of relevance to the prescriber which are additional to that already included in other parts of the SPC.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Fastum Gel contains the following excipients: carbomer, ethanol, neroli essence, lavender oil, triethanolamine, purified water.

6.2 Incompatibilities Not applicable.

6.3 Shelf life

Tube: 60 months.
Dispenser: 48months

After first opening: 6 months within the approved shelf life

6.4 Special precautions for storage

Store below 25^{o}C.

6.5 Nature and contents of container

Soft aluminium tube, treated inside with non-toxic epoxy resin. The tubes are packed in cardboard together with a package insert. The following pack sizes are approved:
Aluminium Tube: 30g pack, Aluminium Tube 50g pack
Dispenser: rigid polypropylene dispenser containing 50g gel.

6.6 Special precautions for disposal

Not applicable.

7 MARKETING AUTHORISATION HOLDER AND MAUFACTURER

A Menarini Industrie Farmaceutiche Ruinite srl
Via Sette Santi, 3
50131 Florence
Italy

8 REGISTRATION NUMBER

126-32-30507-00

9 REGISTRATION HOLDER

Genmedix, 12 Beit Harishonim St. Emek Hefer 38777

10 DATE OF REVISION OF THE TEXT

22.10.2014

The format of this leaflet has been determined by the Ministry of Health and its content has been examined and approved in November 2014.