# SUMMARY OF PRODUCT CHARACTERISTICS

## 1. NAME OF THE MEDICINAL PRODUCT

EFAMAT Gel 5%, 40 g

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

In each tube,
**Active substance:**
Etofenamate 2.00 g

**Excipient(s):**
Polyethylene glycol 1.20 g
For the full list of excipients, see section 6.1.

## 3. PHARMACEUTICAL FORM

Gel
Clear, semi-solid gel with characteristic odor.

## 4. CLINICAL PARTICULARS

### 4.1 Therapeutic indications

Externally supportive symptomatic treatment of pain that occurs in the following situations:
Painful conditions related to acute bruises, sprains and strains in the joints after blunt trauma such as sports injuries
Painful conditions of periarticular soft tissues (bursae, tendons, ligaments and joint capsule) in gonarthrosis

### 4.2 Posology and method of administration

**Frequency and duration of administration**
EFAMAT is applied 3 times a day. Depending on the width of the painful areas, a strip of approximately 10 cm in length (equivalent to approximately 3 g of gel and 150 mg of etofenamate) will be sufficient. For treatment of blunt trauma, the maximum daily dose is 9 g of gel, equivalent to 450 mg of etofenamate.
For treatment of blunt trauma (like sport injuries) usually 1-week treatment is sufficient. Therapeutic benefit of a longer use has not been verified.
For rheumatic disorders, 3-4 weeks of treatment is sufficient in most cases. If symptoms continue, a doctor should be consulted to determine whether further treatment is needed.

**Method of administration:**
It is for topical use.
EFAMAT is applied as a thin layer on the affected areas of the body and gently rubbed into the skin.
EFAMAT should be allowed to dry on the skin for a few minutes after application. It is not recommended to cover it with a bandage or dressing.

**Additional information on special populations**

**Renal/Hepatic Impairment:**
Dose adjustment is not required.

**Pediatric population:**
There is limited experience with use in children. EFAMAT is not recommended for use in children and adolescents.

**Geriatric population:**
Dose adjustment is not required.

**4.3 Contraindications**
EFAMAT is contraindicated in the followings:
- In individuals with hypersensitivity to etofenamate, to any substance contained in EFAMAT or to other non-steroidal anti-inflammatory agents.
- It should not be applied on eczema and mucous membranes on the skin or on open wounds, inflammation or infection on the skin.
- Third trimester of pregnancy.
- Children and adolescents, as clinical experience is not yet sufficient.

**4.4 Special warning and precautions for use**
Conditions in which EFAMAT should be used with certain precautions and only under close medical supervision:
- In patients suffering from asthma, chronic obstructive airway disease, hay fever or chronic swelling of the nasal mucosa (also-called nasal polyps), or in patients with chronic obstructive respiratory disease or chronic respiratory infections, especially those with hay fever-like clinical manifestations.
- Patients with hypersensitivity to other non-steroidal antiphlogistic/analgesic agents.
- These patients are at greater risk for EFAMAT than those with symptoms similar to asthma attacks (also called analgesic intolerance/analgesic asthma), local swelling of the skin and mucous membranes, or urticaria.
- In patients showing allergic reactions against other medical products like skin reactions, itching or urticaria.

EFAMAT should not come into contact with eyes. In case of any contact, the contact area should be washed immediately with plenty of water.

EFAMAT may cause damage and discoloration on polished furniture or plastic surfaces. Therefore, hands should be washed after applying the product or contact with the above substances should be avoided.

**4.5 Interaction with other medicinal products and other forms of interaction**
No interactions are known with topical use of etofenamate as recommended.

**4.6 Pregnancy and lactation**

***General Recommendation***
Pregnancy category: C/D (3rd trimester).

***Women of child-bearing potential/Birth control (Contraception)***
The use in women planning to become pregnant is not recommended. If EFAMAT is to be administered, an effective contraception method should be used.
There are no data on the use of EFAMAT in pregnant women. Animal studies are insufficient with respect to effects on pregnancy /and-or/ embryonal/fetal development/ and-or/ parturition/ and-or/ postnatal development. The potential risk for humans is unknown.

***Pregnancy***
There are no adequate data from the use of etofenamate in pregnant women. Since the impact of prostaglandin synthesis inhibition on human pregnancy has not yet been fully explored, Rheumon Gel should only be used in the first and second trimester of pregnancy after carefully weighing the risk/benefit ratio. The maximum daily dose must not be exceeded (see section 4.2).
Use of EFAMAT Gel is contraindicated in the third trimester of pregnancy.
During the last three months of pregnancy, the mechanism of action of these medicinal products may lead to suppression of labor activity, prolongation of pregnancy and to a prolonged birth process. Further, it may cause cardiovascular (with premature closure of ductus arteriosus and pulmonary hypertension) and renal (with oliguresis and oligoamnios) toxicity in the child, increased bleeding tendency in mother and child as well as an increased risk of edema formation in the mother.

***Breast-feeding***
Long-term use of EFAMAT in breastfeeding mothers should be avoided as small amounts of etofenamate may pass into breast milk. To avoid exposure to infants, this product should not be used in the breast area of the mother.

**4.7 Effects on ability to drive and use machines**
EFAMAT has no effect on driving and using machines.

**4.8 Undesirable effects**
The evaluation of undesirable effects is based on the following frequency information.
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); unknown (cannot be estimated from available data)
If EFAMAT is applied to large skin surface areas and for prolonged periods, it is possible to develop side effects that may affect specific organ systems or the whole body, as seen after systemic use of drugs containing etofenamate.

**Skin and subcutaneous tissue disorders**
Uncommon: Local skin reactions such as skin redness, itching, burning sensation, skin rash, sometimes blisters or urticaria
Very rare: Hypersensitivity skin reactions or local allergic reactions (contact dermatitis)

Reporting of suspected adverse reactions:
Reporting suspected adverse reactions after authorization 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.

**4.9 Overdose and treatment**
If EFAMAT is applied on the skin more than the recommended dose, the gel should be removed

and the skin should be washed with water.
There is no specific antidote.

## 5. PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Non-steroidal anti-inflammatory/analgesic drugs
ATC code: M02AA06

Etofenamate is a non-steroidal anti-inflammatory drug with analgesic properties that has been proven effective by inhibiting prostaglandin synthesis in well-known animal models of inflammation.

### 5.2 Pharmacokinetic properties

**General properties**

Absorption:
Following administration of 300 mg etofenamate in the form of EFAMAT to volunteers, peak plasma fenamate levels were achieved between 12 and 24 hours. Bioavailability of products containing etofenamate shows large inter- and intra-individual fluctuations, mainly due to the site of application, skin moisture and other factors. Following dermal application, relative bioavailability is within the limits of other etofenamate products (up to 20%).
Distribution:
It is 98-99% bound to plasma proteins.
Biotransformation:
Etofenamate is metabolized in the liver by hydroxylation, ether and ester separation. It can participate in enterohepatic circulation.
Elimination:
Etofenamate is excreted in the form of numerous metabolites (hydroxylation, ether and ester decomposition) and their conjugates, 35% via the kidneys and to a greater extent via bile and faeces.
Etofenamate passes into breast milk in low concentrations as flufenamic acid.

### 5.3 Preclinical safety data

When etofenamate is applied topically, the absorption must be borne in mind in the evaluation of the toxicological data.

Acute toxicity:
Investigations of the acute toxicity of etofenamate have been carried out with various forms of administration in rats, mice and rabbits. Oral administration route has been shown to be more toxic than intramuscular route. The appearance of intoxication is characterized by gastrointestinal disorders with diarrhea and weight loss. The first appearance of these symptoms usually occurs a few days after the administration of the active substance. Death occurs between the 2$^{nd}$ and 14$^{th}$ days of the application of the active substance. After sublethal doses, the animals recovered in a period of about 14 days. The post-mortem examination of the dead animals was associated with acid in the peritonitis and abdomen.

Subchronic and chronic toxicity:
Subchronic toxicity has been investigated in various animal species. One-year studies with oral

administration were carried out in rats (7, 27, 100 mg/kg/day) and primates (7, 26, 100 mg/kg/day). Rats given 100 mg/kg body weight developed gastrointestinal hemorrhages and ulcers with subsequent peritonitis and increased mortality. The high dose led to a reduction in body weight, thymus gland weight and hemoglobin in primates.

Mutagenicity and Carcinogenicity:
*In vitro* and *in vivo* investigations of gene and chromosome mutation induction produced negative results. The possibility of mutagenicity was excluded with sufficient confidence. Long-term studies involving oral administration to rats (7, 21, 63 mg/kg/day) and mice (15, 45, 140 mg/kg/day) provided no evidence of a tumorigenic potential of etofenamate.

Reproduction toxicology:
Etofenamate crosses the placental barrier.
There is no experience with administration to humans. In animal experiments, the embryotoxic dose was lower than the maternotoxic dose. In rats, there was an increased incidence of dilation of the renal pelvis from a dose of 21 mg/kg body administered orally and an increased incidence of 14 rib pairs from 7 mg/kg administered orally in pups whose mothers had been treated.

## 6. PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients
Cremophor EL (Polioxil 35 Castor-oil)
Polyethylene glycol 400 (PEG 400)
Carbopol 980
Isopropyl Alcohol
Sodium hydroxide
Deionized water

### 6.2 Incompatibilities
Not applicable.

### 6.3 Shelf life
36 months

### 6.4 Special precautions for storage
Store at room temperature below 25°C.

### 6.5 Nature and contents of container
40 g aluminum tube + HDPE cap, printed on the outside and coated with lacquer on the inside.

### 6.6 Special precautions for disposal and other handling
Any unused material should be disposed according to local disposal regulations.

## 7. MARKETING AUTHORIZATION HOLDER

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## 7. MARKETING AUTHORIZATION NUMBER

231/77

## 8. DATE OF FIRST AUTHORIZATION/RENEWAL OF THE AUTHORIZATION

Date of first authorization : 09.05.2011
Date of last renewal :

## 10. DATE OF REVISION OF THE TEXT