

## SUMMARY OF PRODUCT CHARACTERISTICS

### 1. NAME OF THE MEDICINAL PRODUCT

SANTAFENAMAT gel

### 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

#### Active substance:

1 g gel contains 50 mg of etofenamate.

#### Excipients:

For a full list of excipients, see section 6.1.

### 3. PHARMACEUTICAL FORM

Gel.

Colorless or slightly yellow, transparent gel.

### 4. CLINICAL PARTICULARS

#### 4.1 Therapeutic indications

External supportive symptomatic treatment of pain in the following conditions:

- Painful conditions due to acute contusion, sprains and strains of joints following blunt trauma such as those caused by sport injuries
- Painful conditions of periarticular soft tissues (bursa, tendons, ligaments and joint capsule) in gonarthrosis.

#### 4.2 Posology and method of administration

##### Posology / frequency and duration of administration:

SANTAFENAMAT is applied 3 times daily. Depending on the size of the painful site, applying about a 10 cm strip (equivalent to about 3 g of gel and 150 mg of etofenamate) will be sufficient. In blunt trauma maximum daily dose is 9 g of gel, equivalent to 450 mg of etofenamate.

In blunt trauma (e.g. sports injuries) 1 week of treatment is usually sufficient. The therapeutic benefit of a longer-term use has not been verified.

For rheumatic diseases, 3-4 weeks of treatment is sufficient in most cases. If symptoms persist, the patient is advised to consult a doctor to determine if further treatment is required.

##### Method of administration:

For topical application.

SANTAFENAMAT is applied in a thin layer to the affected areas of the body and massaged gently into the skin. After application of SANTAFENAMAT it should be allowed to dry on the skin for a few minutes. It is not recommended to cover it with a bandage or dressing.

##### Additional information on special populations:

##### Renal/hepatic impairment:

No dosage adjustment is necessary.

**Pediatric population:**

Experience with the use on children is limited. SANTAFENAMAT is not recommended for use in children and adolescents.

**Geriatric population:**

No dosage adjustment is necessary.

**4.3 Contraindications**

SANTAFENAMAT is contraindicated in the following situations.

- In patients with hypersensitivity to etofenamate, to any of the ingredients contained in SANTAFENAMAT, or to other non-steroidal anti-inflammatory drugs.
- It should not be applied on eczema on skin and mucous membranes or open wounds, inflammation or infection on the skin.
- Last trimester of pregnancy.
- In children, due to insufficient clinical experience.

**4.4 Special warnings and precautions for use**

Conditions for using SANTAFENAMAT when certain precautions are taken and only under medical supervision:

- In patients with asthma, chronic obstructive airways disease, hay fever or chronic swelling of nasal mucosa (also called nasal polyps), or in particular in patients with chronic obstructive airways disease or chronic respiratory tract infection with hay fever-like clinical manifestations.  
In patients with hypersensitivity to other non-steroidal antiphlogistic/analgesic agents.
- These patients have a higher risk for SANTAFENAMAT comparison with the patients who suffer from symptoms like asthma attack (analgesic intolerance/analgesic asthma), local swelling of the skin or mucous membranes, or urticaria.
- Patients with hypersensitivity to other substances, manifested by skin reactions, itching or hives.

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

SANTAFENAMAT can lead to damage and discoloration on polished furniture or plastic surfaces. Therefore, hands should be washed after applying the product or contact with the above material should be avoided.

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

No interaction is known in the topical use of etofenamate as recommended.

**4.6 Pregnancy and lactation****General advice**

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

**Women of childbearing potential / Birth control (Contraception)**

It is not recommended for use in women who plan to become pregnant. If SANTAFENAMAT is to be used, an effective birth control method should be applied.

There is no data concerning use of etofenamate in pregnant women. Studies in animals are inadequate

in terms of effects on the pregnancy and/or embryo/fetal development and/or peri- and/or postnatal development. The potential risk for humans is unknown.

### **Pregnancy**

Since the effect of inhibition of prostaglandin synthesis on human pregnancy cannot be entirely ruled out, SANTAFENAMAT should be used carefully during the first and second trimesters of pregnancy only in situations where the benefits outweigh the risks. Maximum daily dose should not be exceeded (see section 4.2).

SANTAFENAMAT use is contraindicated in the last trimester of pregnancy.

During the last trimester of pregnancy, these medicinal products' mechanism of action may lead to suppression of birth activity, prolongation of pregnancy and labor and may cause cardiovascular (premature closure of ductus arteriosus and pulmonary hypertension) and renal (oliguria and oligoamnios) toxicity, increased bleeding tendency in the mother and child, and increased and an increased risk of edema in the mother.

### **Lactation**

Since etofenamate may pass into breast milk in small amounts, long-term use of SANTAFENAMAT in nursing mothers should be avoided. To avoid exposure of babies, this products should not be applied to the breast area of nursing mothers.

## **4.7 Effects on ability to drive and use machines**

SANTAFENAMAT has no effects on ability to drive and use machines.

## **4.8 Undesirable effects**

The assessment of undesirable effects is based of the following frequencies:

Very common ( $\geq 1/10$ ); common ( $\geq 1/100$  to  $< 1/10$ ); uncommon ( $\geq 1/1.000$  to  $< 1/100$ ); rare ( $\geq 1/10.000$  to  $< 1/1000$ ); very rare ( $< 1/10.000$ ); not known (cannot be estimated from the available data).

If SANTAFENAMAT is applied on a large area of skin and for a prolonged period, development of side effects that may affect specific organ systems or the entire body is likely, as seen after systemic use of drugs containing etofenamate.

### **Skin and subcutaneous tissue disorders:**

Uncommon: Redness of the skin, itching, burning sensation, skin rash, and sometimes local skin reactions like blisters or urticaria

Rare: Hypersensitivity skin reactions or local allergic reactions (contact dermatitis)

## **4.9 Overdose and management**

If SANTAFENAMAT 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 PARTICULARS**

### **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, demonstrated to be

effective by inhibiting prostaglandin synthesis in well-known animal models of inflammation.

## **5.2 Pharmacokinetic properties**

### Absorption:

Following application of 300 mg of etofenamate in gel form, maximum plasma levels of flufenamic acid are reached after approximately 12-24 hours. Largely interindividual and intraindividual variations occur in bioavailability of etofenamate containing product primarily due to application site, skin moisture and other factors. Its relative bioavailability following application on the skin is within the limits of other etofenamate preparations (up to 20%).

### Distribution:

Etofenamate binds to proteins at a rate of 98-99%.

### Biotransformation:

Etofenamate is metabolized in the liver by hydroxylation, cleavage of ether and ester. It enters into enterohepatic circulation.

### Elimination:

Etofenamate is eliminated as many metabolites (hydroxylation, cleavage of ether or ester groups) and their conjugates via the kidneys at a rate of 35%, and at a higher rate through the bile in the feces.

Etofenamate is excreted in breast milk as flufenamic acid in low concentrations.

## **5.3 Preclinical safety data**

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

### Acute toxicity:

Etofenamate acute toxicity studies were carried out with different application methods in rats, mice, guinea pigs and rabbits. Oral administration route was shown to be more toxic than the intramuscular route. The appearance of intoxication is characterized by diarrhea and weight loss associated with gastrointestinal disorders. The first appearance of these symptoms is usually a few days after administration of the active substance. Death occurs between the 2nd and 14th days of administration of the active substance. After sublethal doses, animals have recovered in about a 14 day period. Post-mortem examination of animals has been associated with peritonitis and abdominal acid.

### Subchronic and chronic toxicity:

Subchronic toxicity has been investigated in several animal species. One-year studies by oral administration were carried out in rats (7, 27, 100 mg/kg/day), and primates (7, 26, 100 mg/kg/day). In rats given 100 mg/kg body weight peritonitis developed following gastrointestinal bleeding and ulcers and mortality was increased.

High doses resulted in an increase in body weight, an increase in thymus gland weight and a decrease in hemoglobin in primates.

### Mutagenicity and carcinogenicity:

In vitro and in vivo induced gene and chromosomal mutation studies yielded negative results. The likelihood of being mutagenic 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) did not provide evidence of any tumorigenic potential for etofenamate.

### Reproductive toxicity:

Etofenamate crosses the placental barrier.

There is no experience in administration in humans. In animal studies, embryotoxic dose was lower than maternal toxic dose. In rats, there was an increased incidence of dilated renal pelvis at orally administered 21 mg/kg dose, and an increased incidence of 14 pairs of ribs in the litters of dams treated orally at 7 mg/kg dose.

## **6. PHARMACEUTICAL PARTICULARS**

### **6.1 List of excipients**

Eucalyptus essential oil  
Pine essential oil  
Polyethylene glycol 400  
Emulgin M8  
Carbomer  
Triethanolamine  
Isopropyl alcohol  
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, in the original package.

### **6.5 Nature and contents of container**

Presented in a metal tube with plastic screw cap, containing 40 g of gel packed in a boxes.

### **6.6 Disposal of waste materials derived from the medicinal product and other special precautions**

There are no special requirements.

Any unused medicinal product or waste material should be disposed of in accordance with the “Regulations on Control of Medical Waste” and “Regulations on Control of Package and Package Waste”.

## **7. MARKETING AUTHORIZATION HOLDER**

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Okmeydani, Boruciçegi Sok. No: 16  
34382 Sisli - ISTANBUL  
0212 220 64 00  
0212 222 57 59

## **8. MARKETING AUTHORIZATION NUMBER(S)**

173/42

**9. DATE OF FIRST AUTHORIZATION/RENEWAL OF THE AUTHORIZATION**

Date of first authorization: 19.04.1995

Date of renewal of authorization: 19.04.2010

**10. DATE OF REVISION OF THE TEXT**

