Applicant: **Teva Pharmaceuticals (Pty) Ltd**
Product Name: FENACRATE 30 g / 50 g / 60 g / 100 g / 120 g / 150 g
Dosage form & strength: Each 1 g of gel contains 11,6 mg diclofenac diethylamine equivalent to 10 mg diclofenac sodium
Registration Numbers: 56/3.1/0373; 56/3.1/0374; 56/3.1/0375; 56/3.1/0376; 56/3.1/0377; 56/3.1/0378

PROFESSIONAL INFORMATION:

SCHEDULING STATUS:

S0 FENACRATE 30 g, 50 g

S1 FENACRATE 60 g, 100 g, 120 g, 150 g

1. NAME OF THE MEDICINE:

FENACRATE 30 g

FENACRATE 50 g

FENACRATE 60 g

FENACRATE 100 g

FENACRATE 120 g

FENACRATE 150 g

2. QUALITATIVE AND QUANTITATIVE COMPOSITION:

1 g contains 11,6 mg diclofenac diethylamine equivalent to 10 mg diclofenac sodium.

Excipient(s) with known effect:

1 g of gel contains 50 mg/g propylene glycol (E1520) and 1 mg fragrance contains 0,15 mg/g benzyl alcohol, citral, citronellol, coumarin, eugenol, farsenol, geranoil, d-limonene and linalool (see **section 4.4**).

For the full list of excipients, see **section 6.1**.

3. PHARMACEUTICAL FORM:

Gel (emulsion-based gel for topical administration).

White to almost white, homogeneous, cream like gel.

4. CLINICAL PARTICULARS:

4.1 Therapeutic indications:

For the symptomatic relief of localized traumatic inflammation and pain.

4.2 Posology and method of administration:

Posology:

Depending on the size of the painful site to be treated, apply 2 to 4 g FENACRATE gel 3 to 4 times daily to the affected parts and rub in gently.

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

Patients should consult their doctor if the condition does not improve or worsens within 7 days of starting treatment.

The duration of treatment depends on the indication and the response obtained. It is recommended that treatment be reviewed after 2 weeks.

Paediatric population:

The safety and efficacy in children 12 years and under have not been established.

Method of administration:

For cutaneous use only.

4.3 Contraindications:

- hypersensitivity to diclofenac, acetylsalicylic, other non-steroidal anti-inflammatory drugs or to any of the excipients listed in **section 6.1**

- patients with a history of hypersensitivity reactions, such as asthma, urticaria, acute rhinitis or angioedema in response to acetylsalicylic acid or non-steroidal anti-inflammatory drugs (NSAIDS)
- in the third trimester of pregnancy (see **section 4.6**)
- in patients with porphyria.

4.4 Special warnings and precautions for use:

The possibility of systemic undesirable effects those associated with the use of systemic forms of diclofenac from application of topical FENACRATE cannot be excluded if the preparation is used on large areas of skin and over a prolonged period (see Professional Information on systemic forms of diclofenac, e.g oral or injection). Concomitant use of systemic NSAIDs should be cautioned since the possibility of an increase in incidence of untoward effects, particularly systemic side effects, cannot be ruled out.

FENACRATE can precipitate bronchospasm if administered to patients suffering from or with a previous history of bronchial asthma.

Serious skin reactions, some of fatal, including exfoliative dermatitis, Stevens-Johnson syndrome, and toxic epidermal necrolysis have been reported. FENACRATE should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity.

FENACRATE must only be applied to intact, not diseased or injured skin. FENACRATE must not come into contact with eyes and mucous membranes and should not be ingested.
Discontinue FENACRATE treatment if a skin rash develops after application.

Occlusion can lead to an increase in the amount of diclofenac absorbed and may thus cause an increase in side effects. FENACRATE topical gel may be used with a non-occlusive bandage but not with an airtight occlusive dressing (see **section 5.2**).

Some possibility of gastro-intestinal bleeding in those with a significant history of this condition has been reported in isolated cases.

Patients should be warned against excessive exposure to sunlight in order to reduce the incidence of photosensitivity.

Instruct patients not to smoke or go near naked flames - risk of severe burns. Fabric (clothing, bedding, dressings etc) that has been in contact with FENACRATE burns more easily and is a serious fire hazard. Washing clothing and bedding may reduce product build-up but not totally remove it.

FENACRATE contains fragrance with benzyl alcohol (0,15 mg/g), citral, citronellol, coumarin, eugenol, farnesol, geraniol, d-limonene and linalool which may cause allergic reactions. In addition, benzyl alcohol may cause mild local irritation.

4.5 Interaction with other medicines and other forms of interaction:

Since the systemic absorption of diclofenac is very low with topical application, interactions are very unlikely in use as intended.

The bioavailability of FENACRATE is reduced by acetylsalicylic acid, and that of acetylsalicylic acid by FENACRATE, when the two medicines are administered together.

When given concomitantly with lithium, non-steroidal anti-rheumatic medicines raise the concentration of lithium in the blood.

4.6 Fertility, pregnancy and lactation:

The safety of FENACRATE in pregnancy and lactation has not been established.

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/foetal 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-foetal lethality. In addition, increased incidences of various malformations, including cardiovascular, have been reported in animals given a prostaglandin synthesis inhibitor during the organogenetic period.

If FENACRATE 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, FENACRATE may expose

- the foetus to:
    - cardiopulmonary toxicity (with premature closure of the ductus arteriosus and pulmonary hypertension)
    - renal dysfunction, which may progress to renal failure with oligo hydroamniosis
- 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, FENACRATE is contraindicated during the third trimester of pregnancy.

Breastfeeding:

Diclofenac passes into breast milk in small amounts. However, at therapeutic doses of FENACRATE no effects on the breast-fed child are anticipated. Because of a lack of controlled studies in breast-feeding women, FENACRATE should only be used during breastfeeding under advice from a healthcare professional. Under this circumstance, FENACRATE should not be applied on the breasts of breastfeeding mothers, nor elsewhere on large areas of skin or for a prolonged period of time (see **section 4.4**).

***Fertility*:**

There are no data available on the use of topical formulations of diclofenac such as FENACRATE and its effects on fertility in humans.

The cutaneous application of FENACRATE has no or negligible influence on the ability to drive and use machines.

4.7 Effects on ability to drive and use machines:

The cutaneous application of FENACRATE has no or negligible influence on the ability to drive and use machines

4.8 Undesirable effects:

System Organ Class	**Adverse reaction and frequency**
Infections and infestations:	*Less frequent*: Rash pustular.
Immune system disorders:	*Less frequent:* Hypersensitivity (including urticaria), angioedema.
Respiratory, thoracic and mediastinal disorders:	*Less frequent*: Asthma.

Skin and subcutaneous tissue disorders:	*Frequent*: Dermatitis (including contact dermatitis), rash, erythema, eczema, pruritus. *Less frequent*: Desquamation, skin discolouration, dermatitis bullous, photosensitivity reaction.

Reporting of suspected adverse reactions:

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare providers are asked to report any suspected adverse reactions to SAHPRA via the **Adverse drug reaction and quality problem reporting form** found online under SAHPRA's publications: https://www.sahpra.org.za/document/adverse-drug-reactions-and-quality-problem-reporting-form/

4.9 Overdose:

Signs and symptoms:

The low systemic absorption of FENACRATE renders overdose very unlikely. However, undesirable effects, similar to those observed following an overdose of diclofenac tablets, can be expected if FENACRATE is inadvertently ingested (e.g. 1 tube of 100 g contains the equivalent of 1000 mg of diclofenac sodium).

Treatment:

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

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 drugs should be used. The use of activated charcoal should be considered, especially within a short time (within one hour) of ingestion of a toxic dose.

5. PHARMACOLOGICAL PROPERTIES:

5.1 Pharmacodynamic properties:

A.3.1 Antirheumatics (anti-inflammatory agents)

Pharmacotherapeutic group: Topical products for joint and muscular pain; anti-inflammatory preparations, non-steroids for topical use.

ATC code: M02AA15

Mechanism of action:

FENACRATE is an anti-inflammatory and analgesic preparation designed for topical application. In inflammation and pain of traumatic origin, relieves pain and decreases swelling.

When applied locally, the active substance penetrates the skin and the underlying tissue, and combats both acute and chronic inflammatory reactions.

Due to an aqueous-alcoholic base the gel exerts a soothing and cooling effect.

5.2 Pharmacokinetic properties:

Absorption:

When FENACRATE is applied locally, the active substance is absorbed through the skin. The amount of diclofenac absorbed through the skin is relative to the contact time and the area covered with FENACRATE. 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 the gel. Protein binding: 99,7 %.

Distribution:

From the skin and underlying tissue, diclofenac preferentially distributes and persists in deep inflamed tissues (such as the joint), rather than in the bloodstream.

After topical administration of FENACRATE to hand and knee joints diclofenac can be measured in plasma, synovial tissue and synovial fluid. Maximum plasma concentrations of diclofenac are about 100 times lower than after oral administration of diclofenac.

Elimination:

The mean terminal elimination half-life of the unchanged drug is 1 to 2 hours.

Excretion:

Diclofenac and its metabolites are excreted mainly in the urine.

6. PHARMACEUTICAL PARTICULARS:

6.1 List of excipients:

Carbomer

Cocoyl Caprylocaprate

Macrogol cetostearyl ether

Paraffin, Liquid

Diethylamine

Isopropyl alcohol

Propylene glycol (E1520)

Fragrance (contains citronellol, geraniol, benzyl alcohol, linalool, limonene, citral, farnesol, coumarin, eugenol)

Purified water

6.2 Incompatibilities:

Not applicable.

6.3 Shelf life:

2 years.

6.4 Special precautions for storage:

Store at or below 25 °C.

Store in the original tube in order to protect from light.

6.5 Nature and contents of container:

The gel is packed in aluminium laminated tubes, closed with PE seal and PP screw caps, in pack sizes: 30 g, 50 g, 60 g, 100 g, 120 g, 150 g per tube.

Each tube is packed in an outer carton.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling:

This medicinal product poses a risk to the environment (see **section 5.3**).

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION:

Teva Pharmaceuticals (Pty) Ltd.

Applicant: **Teva Pharmaceuticals (Pty) Ltd**
Product Name: FENACRATE 30 g / 50 g / 60 g / 100 g / 120 g / 150 g
Dosage form & strength: Each 1 g of gel contains 11,6 mg diclofenac diethylamine equivalent to 10 mg diclofenac sodium
Registration Numbers: 56/3.1/0373; 56/3.1/0374; 56/3.1/0375; 56/3.1/0376; 56/3.1/0377; 56/3.1/0378

Maxwell Office Park

Magwa Crescent West

Waterfall City

Midrand

Gauteng

South Africa

2090

8. REGISTRATION NUMBER(S):

FENACRATE 30 g: 56/3.1/0373

FENACRATE 50 g: 56/3.1/0374

FENACRATE 60 g: 56/3.1/0375

FENACRATE 100 g: 56/3.1/0376

FENACRATE 120 g: 56/3.1/0377

FENACRATE 150 g: 56/3.1/0378

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION:

20 June 2023

10. DATE OF REVISION OF THE TEXT:

13 November 2023