SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

NIMELID 1% Gel

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1 of gel contains:

Active Substance:

Nimesulide..... 10 mg

Excipients:

Methylparaben..... 1.75 mg
Ethyl paraben..... 0.45 mg
Propylparaben..... 0.35 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Gel.
White in colour, with a characteristic odour (alcohol), and a homogeneous appearance.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

NIMELID is indicated for the treatment of the following conditions:

- Pain, inflammation, and swelling caused by accidents or sports injuries such as sprains, contusions, and strains;
- Localised forms of soft tissue rheumatism such as tendovaginitis, bursitis, shoulder-hand syndrome, and peri-arthropathy;
- Localised rheumatic diseases (e.g., osteoarthritis of the peripheral joints and vertebral column).

4.2 Posology and method of administration

Dosage/frequency and duration of administration:

Unless otherwise recommended by the doctor, it should be applied to the affected area 2 or 3 times a day. However, the dose may be adjusted depending on the size of the affected area and the response. The treatment duration is 7-15 days.

Method of administration:

NIMELID is intended for external use only. Do not bandage or occlude the area. Do not rub vigorously.

Additional information on specific populations:

Renal/Hepatic impairment:
NIMELID should be used with caution in patients with severe renal and hepatic impairment.

Paediatric population:
Dosage recommendations and indications for use in children (under 12 years of age) have not been established. Therefore, it should not be used in children.

Geriatric population:
There are no special considerations for use.

4.3 Contraindications

NIMELID should not be used in patients with known hypersensitivity to nimesulide.

NIMELID should not be used in patients who are sensitive to aspirin and other nonsteroidal anti-inflammatory drugs that inhibit prostaglandin synthesis and induce allergic reactions such as bronchospasm, rhinitis, angioedema, nasal polyps or urticaria.

It should not be used on skin surfaces with local infection, damage, or abrasion. It should not be used concomitantly with other topical preparations.

It should not be used in children under 12 years of age.

4.4 Special warnings and precautions for use

If local irritation develops, NIMELID should be discontinued and appropriate treatment administered as necessary. An occlusive dressing should not be applied to the area where NIMELID is applied. It should not be applied to the eyes, mucous membranes (genital, nasal, oral), open skin lesions, dermatoses, or infected skin areas. In case of accidental contact, wash immediately with water. Do not ingest. Wash hands after application. If irritation, redness or itching develops at the application site, discontinue use and consult a doctor. Use in children under 12 years of age is not recommended (see Section 4.3).

Undesirable effects can be minimised by using the minimum effective dose for the shortest possible duration.

It should be used with caution in patients with gastrointestinal bleeding, active or possible peptic ulcer, severe renal or hepatic impairment, severe coagulation disorders, or severe/uncontrolled heart disease.

Special precautions should be taken when used in the treatment of patients with hypersensitivity to other NSAIDs. The possibility of developing sensitivity during treatment should not be overlooked.

When NIMELID is used concomitantly with other topical NSAIDs during treatment, a burning sensation and, exceptionally, photodermatosis may occur.

To reduce the risk of photosensitivity, patients should avoid direct exposure to sunlight.

If symptoms persist or worsen, a doctor should be consulted.

Methylparaben, ethylparaben, and propylparaben, which are contained in NIMELID, may cause allergic reactions (possibly delayed).

4.5 Interaction with other medicinal products and other forms of interaction
No clinically significant interactions have been reported with topical application.

Additional information for specific populations:
No interaction studies have been conducted in special populations.

Paediatric population:
No interaction studies have been conducted in children.

4.6 Fertility, pregnancy and lactation
General recommendation
Pregnancy Category C.

Women of childbearing potential/Birth control (Contraception)
Studies in animals have shown reproductive toxicity (see Section 5.3). The potential risk to humans is unknown.

The benefit/risk ratio of treatment with NIMELID should be assessed by the physician and it should not be used during pregnancy unless necessary.

There is insufficient data on the effects of nimesulide on reproductive capacity in women of childbearing potential.

Pregnancy
The use of NIMELID during pregnancy is not recommended. Nimesulide should not be used, particularly during the third trimester of pregnancy, due to the risk of premature closure of the arterial duct and uterine atony.

There is insufficient data on the use of NIMELID in pregnant women.

Animal studies have shown reproductive toxicity (see Section 5.3). The potential risk to humans is unknown.

Lactation
As there are no studies on the transfer of nimesulide into breast milk and its possible effects on the breastfed child, its use during lactation is not recommended.

Reproductive ability/Fertility
There are no data on the effects of nimesulide on reproductive ability and fertility in humans.

Studies in animals have shown that nimesulide causes adverse effects that may affect fertility (see Section 5.3).

4.7 Effects on the ability to drive and use machines
There is no effect on the ability to drive or operate machinery.

4.8 Undesirable effects
Side effects associated with local application have been reported rarely. In clinical studies, the most common side effects were local reactions at the application site, such as mild or moderate local irritation, erythema, skin rash, scaling, and itching. There is a possibility of staining clothing.

The frequency of side effects is categorised as follows:
Very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000), not known (cannot be estimated from the available data).

Skin and subcutaneous tissue disorders
Uncommon : Pruritus, erythema.
Not known : Scaling, itching, skin rash, mild or moderate local irritation.

When nimesulide is applied topically, the likelihood of systemic side effects is much lower than the frequency of side effects seen with oral nimesulide treatment. However, the possibility of systemic side effects occurring cannot be disregarded when NIMELID is applied to larger areas or for longer periods than necessary.

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
No cases of overdose have been reported with topical application.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Topical Non-Steroidal Anti-Inflammatory Preparations
ATC code: M02AA26
Nimesulide is a non-steroidal anti-inflammatory drug (NSAID). The sulfonanilide group, which has functional content, distinguishes nimesulide from other NSAIDs containing carboxyl and enol groups. Nimesulide has antipyretic, analgesic and anti-inflammatory properties.

5.2 Pharmacokinetic properties

General properties

Absorption:
When applied topically, nimesulide is continuously and gradually released from the skin into the muscle or synovial fluid, and equilibrium is rapidly established between the skin, muscle, and synovial fluid.

In a clinical study with nimesulide, the product was applied three times daily for 4–7 days by patients undergoing arthroscopy for osteoarthritis. Nimesulide concentrations in synovial fluid and plasma were calculated 1–2 hours after the last application.

Nimesulide levels were found to be 22.1±10.5 ng/ml in synovial fluid and 11.8±3 ng/ml in plasma.

Distribution:
The fact that nimesulide was found at significant levels in plasma from 30 minutes to 8 hours after topical application indicates that the drug is slowly released into the systemic circulation. Eight hours after topical application, plasma concentrations of nimesulide ranged from 14 to 57.5 ng/ml.

Biotransformation:
It is metabolised in the liver. The metabolite is likely to be the active 4-hydroxy nimesulide.

Elimination:
Approximately 51-63% is excreted via the kidneys. Less than 0.1% of the drug is excreted unchanged in the urine. Approximately 18-36% is excreted in the faeces.

The elimination half-life ($t_{1/2}$, β) is calculated to be approximately 10 hours on average.

5.3 Preclinical safety data

In a primary dermal irritation study conducted on rabbits with nimesulide and placebo, the potential irritant and corrosive effects of applications to intact and damaged skin were investigated, and no "primary skin irritant" properties were detected in any of the tested products.

Safety, pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential, and reproductive toxicity studies conducted with systemic administration of nimesulide did not reveal any particular hazard to humans.

In repeated dose toxicity studies, nimesulide caused gastrointestinal, renal, and hepatic toxicity.

In reproductive toxicity studies conducted on rabbits, nimesulide (at non-toxic dose levels) caused embryotoxic and teratogenic effects (skeletal malformations, enlargement of cerebral ventricles). However, these effects were not observed in studies conducted on rats.

Studies conducted on rats have found that nimesulide causes increased mortality in newborn pups and produces adverse effects that affect fertility.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Ethanol
Carbomer 980
Paraffin (liquid)
Triethanolamine
Methyl paraben
Ethyl paraben
Propylparaben
Disodium EDTA
Deionised water

6.2 Incompatibilities

No known incompatibilities exist.

6.3 Shelf life

36 months

6.4 Special precautions for storage

It should be stored at a room temperature below 25°C and in its original packaging.

6.5 Nature and contents of container

Box containing HDPE screw-top laminated tubes
Each tube contains 20 g or 30 g of gel.
Not all packaging formats may be available for sale.

6.6 Special precautions for disposal and other handling

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

7. MARKETING AUTHORISATION HOLDER

Deva Holding A.S.
Halkalı Merkez Mah. Basın Ekspres Cad.
No:1 34303 Küçükçekmece - ISTANBUL/TÜRKİYE
Tel: 0212 692 92 92
Fax: 0212 697 00 24
Email: deva@devaholding.com.tr

8. MARKETING AUTHORISATION NUMBER(S)

28.01.2009 – 218/4

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorization : 28.01.2029
Date of last renewal :

10. DATE OF REVISION OF THE TEXT

31 January 2014