

IRISH MEDICINES BOARD ACTS 1995 AND 2006

MEDICINAL PRODUCTS(CONTROL OF PLACING ON THE MARKET)REGULATIONS,2007

(S.I. No.540 of 2007)

PA0915/001/003

Case No: 2070812

The Irish Medicines Board in exercise of the powers conferred on it by the above mentioned Regulations hereby grants to

Helsinn Birex Therapeutics Ltd

Damastown, Mulhuddart, Dublin 15, Ireland

an authorisation, subject to the provisions of the said Regulations, in respect of the product

Mesulid 3 %w/w Gel

The particulars of which are set out in Part I and Part II of the attached Schedule. The authorisation is also subject to the general conditions as may be specified in the said Regulations as listed on the reverse of this document.

This authorisation, unless previously revoked, shall continue in force from **10/12/2009**.

Signed on behalf of the Irish Medicines Board this

A person authorised in that behalf by the said Board.

Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Mesulid 3% w/w Gel

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Mesulid 3% w/w gel contains 3% w/w nimesulide (1 g of gel contains 30 mg of nimesulide).

Excipients:

Methyl parahydroxybenzoate 0.80% w/w

Propyl parahydroxybenzoate 0.02% w/w

For a full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Gel.

Opalescent, pale yellow gel.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Symptomatic relief of pain associated with sprains and acute traumatic tendinitis.

4.2 Posology and method of administration

Adults:

Nimesulide 3% w/w gel (usually 3 g, corresponding to a line 6-7 cm long) should be applied in a thin layer to the affected area 2-3 times daily and massaged until it is completely absorbed.

Duration of treatment: 7 – 15 days.

Children under 12 years:

Nimesulide 3% w/w gel has not been studied in children. Therefore, safety and efficacy have not been established and the product should not be used in children (see section 4.3).

4.3 Contraindications

Known hypersensitivity to nimesulide or to any other excipients in the gel.

Use in patients in whom aspirin, or other medicinal products inhibiting prostaglandin synthesis, induced allergic reactions such as rhinitis, urticaria or bronchospasm.

Use on broken or denuded skin or in the presence of local infection.

Simultaneous use with other topical creams.

Use in children under 12 years.

4.4 Special warnings and precautions for use

Nimesulide 3% w/w gel should not be applied to skin wounds or open injuries.

Nimesulide 3% w/w gel should not be allowed to come into contact with the eyes or mucous membranes; in case of

accidental contact, wash immediately with water.
The product should never be taken by mouth. Hands should be washed after applying the product.
Nimesulide 3% w/w gel should not be used with occlusive dressings.
Nimesulide 3% w/w gel is not recommended for use in children under 12 years (see section 4.3).
Undesirable effects may be reduced by using the minimum effective dose for the shortest possible duration.

Patients with gastro-intestinal bleeding, active or suspected peptic ulcer, severe renal or hepatic dysfunction, severe coagulation disorders or severe/non controlled heart failure should be treated with caution.
Since Nimesulide 3% w/w gel has not been studied in hypersensitive subjects, particular caution should be used when treating patients with known hypersensitivity to other NSAIDs. The possibility of developing hypersensitivity in the course of therapy cannot be excluded.
Since with other topical NSAIDs burning sensation and exceptionally photodermatitis can occur, care should be taken during treatment with Nimesulide 3% w/w gel.
To reduce the risk of photosensitivity, patients should be warned against exposure to direct and solarium sunlight.

If symptoms persist or the condition is aggravated medical advice should be sought.

This product contains parahydroxybenzoates. These substances may cause allergic reactions (possibly delayed).

4.5 Interaction with other medicinal products and other forms of interaction

No interactions of Nimesulide 3% w/w gel with other medicinal products are known or to be expected via the topical route.

4.6 Pregnancy and lactation

There are no data relevant to the topical use of Nimesulide 3% w/w gel in pregnant women or during breastfeeding. Therefore, Nimesulide 3% w/w gel should not be used during pregnancy or lactation unless clearly necessary.

4.7 Effects on ability to drive and use machines

No studies on the effect of Nimesulide 3% w/w gel on the ability to drive and use machines have been performed.

4.8 Undesirable effects

The following side effects listings is based on reports from clinical studies, in a limited number of patients, where mild local reactions have been reported. The reporting rates are classified as: very common (>1/10); common (>1/100, <1/10), uncommon (>1/1,000, <1/100); rare (>1/10,000, <1/1,000); very rare (<1/10,000), including isolated cases.

Skin and subcutaneous tissue disorders (see also section 4.4)	Common	Itching Erythema
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4.9 Overdose

Intoxication with nimesulide as a result of topical application of Nimesulide 3% w/w gel is not to be expected since the highest plasma levels of nimesulide following application of Nimesulide gel are far below those found following systemic administration.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: ATC code: M02AA.
Non-steroidal anti-inflammatory drug (NSAID) for topical use.

Nimesulide is an inhibitor of the prostaglandin synthesis enzyme cyclo-oxygenase.

Cyclo-oxygenase produces prostaglandins, some of them being implicated in the development and maintenance of inflammation.

5.2 Pharmacokinetic properties

When Nimesulide 3% w/w gel is applied topically, plasma concentrations of nimesulide are very low in comparison with those achieved following oral intake. After a single application of 200mg of nimesulide, in the gel form, the highest plasma level of 9.77 ng/ml was noted after 24 hours. No trace of the main metabolite 4-hydroxy-nimesulide, was detected. At steady-state (day 8) peak plasma concentrations were higher (37.25 ± 13.25 ng/ml) but almost 100 times lower than those measured following repeated oral administration.

5.3 Preclinical safety data

The local tolerance and the irritation and sensitisation potential of Nimesulide 3% w/w gel have been tested in several recognised animal models. The results of these studies indicate that Nimesulide 3% w/w gel is well tolerated.

Preclinical data for systemically administered nimesulide reveal no special hazards for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity and carcinogenic potential. In repeated dose toxicity studies, nimesulide showed gastrointestinal, renal and hepatic toxicity. In reproductive toxicity studies, embryotoxic and teratogenic effects (skeletal malformations, dilatation of cerebral ventricles) were observed in rabbits, but not in rats, at maternally non-toxic dose levels. In rats, increased mortality of offspring was observed in the early postnatal period and nimesulide showed adverse effects on fertility.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Purified water
Diethylene glycol monoethyl ether
Caprylcaproyl macrogol glycerides
Carbomers
Disodium edetate
Triethanolamine
Methyl-parahydroxybenzoate (E218)
Propyl-parahydroxybenzoate (E216)

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

2 years

6.4 Special precautions for storage

Do not store above 30°C

6.5 Nature and contents of container

15g, 30g, 50g and 100g aluminium tubes lined with lacquer made of an epoxyphenolic resin and closed with a polypropylene cap.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

Wash hands after use.

7 MARKETING AUTHORISATION HOLDER

Helsinn Birex Therapeutics Ltd.
Damastown
Mulhuddart
Dublin 15

8 MARKETING AUTHORISATION NUMBER

PA 0915/001/003

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of First Authorisation: 20 March 2000
Date of last Renewal: 10 December 2009

10 DATE OF REVISION OF THE TEXT

March 2010