IRISH MEDICINES BOARD ACTS 1995 AND 2006

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

(S.I. No.540 of 2007)

PA0727/001/001
Case No: 2058294

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

Diomed Developments

Tatmore Place, **Gosmore**, **Hitchin**, **Hertfordshire SG4 7QR**, **England**

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

Ibuleve 5% 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 **31/03/2009** until **18/09/2010**.

Signed on behalf of the Irish Medicines Board this

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A person authorised in that behalf by the said Board.

Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Ibuleve 5% w/w Gel

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Ibuprofen 5.0% w/w.

For excipients, see 6.1.

3 PHARMACEUTICAL FORM

Gel
Non-greasy, fragrance-free, clear aqueous-alcoholic gel.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

For fast topical treatment of rheumatic and muscular pain, sprains, strains, sports injuries, and backache.

4.2 Posology and method of administration

Apply the gel to the affected areas, up to three times daily, or as directed by the physician. On each occasion apply only enough gel to thinly cover the affected area, and gently massage well into the skin, until completely absorbed. Do not use excessively.

Treatment should be reviewed after 14 days and should not normally continue for more than a few weeks, unless recommended to do so by a doctor.

The same dosage and dosage schedule applies to all age groups, although Ibuleve is not normally recommended for use on children under the age of 12 years, unless instructed by their doctor.

4.3 Contraindications

Not to be used in cases of sensitivity to any of the ingredients.
Not to be used on broken skin.
Not to be used in asthmatic patients known to be hypersensitive to aspirin or other non-steroidal anti-inflammatory agents.

4.4 Special warnings and precautions for use

Seek medical advice if symptoms worsen or persist.
Oral non-steroidal anti-inflammatory drugs (NSAID's), including ibuprofen, can sometimes be associated with renal impairment, aggravation of active peptic ulcers, and can induce allergic bronchial reactions in susceptible asthmatic patients. Although systemic absorption of topically applied ibuprofen is less than for oral dosage forms, these complications can occur in rare cases. For these reasons, waterproof protective dressings should not be used over the treated areas, and patients with an active peptic ulcer, a history of kidney problems or asthma should seek medical advice before using Ibuleve.

The excipient propylene glycol may on rare occasions cause skin irritation in sensitive people.
Keep away from the eyes and mucous membranes.
This product should not be used with occlusive dressings.

4.5 Interaction with other medicinal products and other forms of interaction

Non-steroidal anti-inflammatory drugs may interact with blood pressure lowering drugs, and may possibly enhance the effects of anticoagulants, although the chance of either of these occurring with a topically administered preparation is extremely remote. Concurrent aspirin or other NSAIDS may result in an increased incidence of adverse reactions. Experimental data suggest that oral ibuprofen may inhibit the effect of low dose aspirin on platelet aggregation when they are dosed concomitantly. However, the limitations of these data and the uncertainties regarding extrapolation of ex vivo data to the clinical situation imply that no firm conclusions can be made for regular ibuprofen use, and no clinically relevant effect is considered to be likely for occasional ibuprofen use (see section 5.1).

4.6 Pregnancy and lactation

Not to be used during pregnancy or lactation.

4.7 Effects on ability to drive and use machines

None known.

4.8 Undesirable effects

Occasionally mild skin rashes, itching or irritation may occur at the site of application.

Very rarely, susceptible patients may experience the following side effects with ibuprofen, but these are extremely uncommon when ibuprofen is administered topically. If they occur, treatment should be discontinued:-

Hypersensitivity: Hypersensitivity reactions have been reported following treatment with ibuprofen. These may consist of (a) non-specific allergic reactions and anaphylaxis, (b) respiratory tract reactivity comprising asthma, aggravated asthma, bronchospasm, or dyspnoea, or (c) assorted skin disorders, included rashes of various types, pruritus, urticaria, purpura, angioedema and, less commonly, bullous dermatoses (including epidermal necrolysis and erythema multiforme).

Renal: renal impairment can occur in patients with a history of kidney problems.

Gastrointestinal: side effects such as abdominal pain and dyspepsia have been reported.

4.9 Overdose

Not applicable. Any overdose with a topical preparation of ibuprofen is extremely unlikely.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Ibuleve is a topical preparation which has anti-inflammatory and analgesic properties. It contains the active ingredient, ibuprofen, which exerts its effects directly in inflamed tissues underlying the site of application, mainly by inhibiting prostaglandin biosynthesis.

Because it is formulated in an aqueous/alcoholic gel, Ibuleve also exerts a soothing and cooling effect when applied to the affected area.

Experimental data suggest that ibuprofen may inhibit the effect of low dose aspirin on platelet aggregation when they are dosed concomitantly. In one study, when a single dose of ibuprofen 400mg was taken within 8 h before or within 30 min after immediate release aspirin dosing (81mg), a decreased effect of ASA on the formation of thromboxane or platelet aggregation occurred. However, the limitations of these data and the uncertainties regarding extrapolation of ex vivo data to the clinical situation imply that no firm conclusions can be made for regular ibuprofen use, and no clinically relevant effect is considered to be likely for occasional ibuprofen use.

5.2 Pharmacokinetic properties

Specially formulated for external application, the active ingredient penetrates through the skin rapidly and extensively, achieving high, therapeutically relevant local concentrations in underlying soft tissues, joints and the synovial fluid, whilst producing plasma levels that are unlikely to be sufficient to cause any systemic side-effects, other than in rare individuals who are hypersensitive to ibuprofen.

Furthermore, there do not appear to be any appreciable differences between the oral and topical routes of administration regarding metabolism or excretion.

5.3 Preclinical safety data

Published information on subchronic toxicity studies confirms that topically applied ibuprofen is well tolerated both locally and by the gastro-intestinal tract. Any local erythema is only mild and no signs of mucosal lesions or ulcerogenic effects have been determined in the gastro-intestinal tract.
In the course of assessing mucosal tolerance, topical ibuprofen has been found to cause acute, but reversible, irritant reactions in the eyes and mucous membranes.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Industrial Methylated Spirit (IMS)
Carbomer
Propylene glycol
Diethylamine
Purified water

6.2 Incompatibilities

None known.

6.3 Shelf Life

30 g containers: - 36 months from the date of manufacture.

6.4 Special precautions for storage

Do not store above 25°C.

6.5 Nature and contents of container

1. Membrane sealed, epoxy resin coated, collapsible aluminium TUBE, fitted with a SCREWCAP (containing 30 g of product).

2. Membrane-sealed laminate TUBE, made of a HDPE/aluminium/Ethylene Acrylic Acid (EAA) copolymer, fitted with a CAP (containing 30 g of product).

3. Laminate TUBE made of a HDPE/aluminium/Ethylene Acrylic Acid (EAA) copolymer, fitted with an air-return-free 'Precitube' pump head and CAP (containing 30 g of product).

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

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Diomed Developments Limited
Tatmore Place
Gosmore
Hitchin
Hertfordshire SG4 7QR
United Kingdom

8 MARKETING AUTHORISATION NUMBER

PA 727/1/1

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 19 September 1995

Date of last renewal: 19 September 2005

10 DATE OF REVISION OF THE TEXT

March 2009