NUROFEN MEDICATED PLASTER 200MG

Prescribing Information

1. NAME OF THE MEDICINAL PRODUCT

Nurofen medicated plaster 200mg

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each medicated plaster contains 200 mg of ibuprofen.

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Medicated plaster.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Nurofen Medicated Plaster 200mg is indicated for the short-term symptomatic treatment of local pain in acute muscular strains, or sprains in benign traumas close to the joint of the upper or lower limb in adults or adolescents aged 16 years and older.

4.2 Posology and method of administration

Posology

Adults or adolescents aged 16 years and over:

One dose is equal to one medicated plaster. The maximum dose for a single 24 hour period is one medicated plaster. The plaster can be applied at any time during the day or night, but should be removed and a new plaster re-applied at the same time on the following day.

The medicated plaster should be used for the shortest duration necessary to control symptoms. The treatment duration should not exceed 5 days. The therapeutic benefit of treatment longer than 5 days has not been established.

If there is no improvement, during the recommended duration of treatment or a worsening of symptoms, a healthcare professional should be consulted.

Elderly patients:

No special dose adjustment is necessary.

Paediatric population:

The safety and efficacy of Nurofen Medicated Plaster 200mg in children or adolescents under 16 years of age has not yet been established.

Method of administration

For cutaneous use and short-term use only.

The medicated plaster should be used whole and not be cut.

The medicated plaster should not be used together with an occlusive dressing.

It is recommended to carefully wash and dry the area to be treated before applying the medicated plaster.

Apply to intact skin only.

Tear or cut the sachet along the dotted line to remove a medicated plaster.

First remove the central portion of the release liner used to protect the adhesive surface and apply this surface to the painful area, once securely in place remove the remaining release liner at the edges of the plaster.
The medicated plaster is flexible and conformable, and if necessary can be applied on or near a joint and will allow for normal movement.
Avoid getting the medicated plaster wet.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- In patients who have previously shown hypersensitivity reactions (e.g. asthma, bronchospasm, rhinitis, angioedema or urticaria) in response to ibuprofen, acetylsalicylic acid or other non-steroiidal anti-inflammatory drugs (NSAIDs).
- Application on broken or damaged skin
- Third trimester of pregnancy.
- Use on the eyes, lips or the mucous membranes.

4.4 Special warnings and precautions for use

If symptoms persist for longer than 5 days or worsen, a healthcare professional should be consulted.
Undesirable effects can be reduced by reducing the duration of treatment.
Bronchospasm can occur in patients using ibuprofen who suffer or have previously suffered from bronchial asthma or allergies.
The treatment should be discontinued immediately if a skin rash develops after applying the medicated plaster.
Patients should be warned against exposure of the treated area to strong sources of natural and/or artificial light (e.g. tanning lamps) during treatment and for one day after removal of the medicated plaster, in order to reduce the risk of photosensitivity.
Although the systemic availability of topically applied ibuprofen is significantly less than for oral dosage forms, complications may occur in rare cases. For these reasons, patients with:
an impaired renal, cardiac or hepatic function; active or a history of peptic ulcer, intestinal inflammation or haemorrhagic diathesis should seek medical advice before using this medicinal product.
Non-steroidal anti-inflammatory drugs should be used with caution in elderly patients, as they are more likely to experience undesirable effects.

4.5 Interaction with other medicinal products and other forms of interaction

Non-steroidal anti-inflammatory drugs may interact with antihypertensives, and may possibly enhance the effects of anticoagulants, however if the medicated plaster is used correctly, the rate of systemic transfer is low, so that the interactions reported in association with oral ibuprofen are unlikely to occur. Concurrent aspirin or other NSAIDs may result in an increased incidence of adverse reactions.

4.6 Fertility, pregnancy and lactation

Pregnancy:
The systemic concentration of ibuprofen is lower after topical administration, compared to oral formulations. With reference to experience from treatment with systemically applied NSAIDs, 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 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.

During the first and second trimester of pregnancy, Nurofen Medicated Plaster 200mg should not be given unless clearly necessary. If Nurofen Medicated Plaster 200mg is used during the first and second trimester of pregnancy, the dose should be kept as low and duration of treatment as short as possible.

Rarely, taking NSAIDs after the 20th week of pregnancy may cause impaired renal function of the fetus, which may cause low levels of amniotic fluid (oligohydramnios).

The effects were observed after days to weeks of treatment. However, in rare cases, low levels of amniotic fluid were observed already after 48 hours of taking NSAIDs. In most cases, oligohydramnios passed with the treatment discontinuation.

Using NSAIDs after the 20th week of pregnancy should be limited. If it was decided that the benefit outweighs the risk for the fetus and the treatment with the medicine is essential after the 20th week of pregnancy, the lowest effective dose should be used for the shortest possible period.

Referring the patient to ultrasound scan should be considered, in order to estimate the amount of amniotic fluid when the treatment with therapeutic dosage of these medicines exceeding 5 days and stopping the treatment if low levels of amniotic fluid is detected.

During the third trimester of pregnancy, all prostaglandin synthesis inhibitors 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, ibuprofen is contraindicated during the third trimester of pregnancy.

Breast-feeding:
After systemic application, only small amounts of ibuprofen and its metabolites pass into the breast milk. As no harmful effects to infants are known to date, it is not usually necessary to interrupt breast-feeding during short-term treatment with this medicated plaster at the recommended dose.
However, as a precautionary measure, this medicated plaster should not be applied directly onto the breast area of women who are breast-feeding.

4.7 Effects on ability to drive and use machines
None known.

4.8 Undesirable effects
Systemic availability of topical ibuprofen is very low compared to orally administered NSAIDs. Adverse events, particularly those affecting the gastrointestinal tract, are less common with the use of topical ibuprofen.
The list of the following adverse events relates to those experienced with topical ibuprofen at OTC (dose maximum 500 mg per day), in short term use.
The following frequency conventions are used in the rating of undesirable effects: 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).
Within each frequency grouping, adverse events are presented in order of decreasing seriousness.

System Organ Class	Frequency	Adverse Events
Immune System Disorders	Not known	Hypersensitivity [1]
Gastrointestinal Disorders	Not known	Abdominal pain, dyspepsia
Renal and Urinary Disorders	Not known	Renal impairment [2]
General Disorders and Administration Site conditions	Not known	Application site reaction [3]
Skin and subcutaneous tissue disorders	Not known	Photosensitivity reactions

[1] Hypersensitivity reactions have been reported following treatment with oral ibuprofen. These may consist of (a) non-specific allergic reaction and anaphylaxis, (b) respiratory tract reactions comprising asthma, aggravated asthma, bronchospasm or dyspnoea, or (c) skin reactions, including rashes of various types, urticaria, purpura, angioedema and, more rarely, exfoliative and bullous dermatoses (including toxic epidermal necrolysis, Stevens-Johnson Syndrome and erythema multiforme), and pruritus.
[2] Renal impairment may occur following the use of topical ibuprofen, particularly in those with pre-existing renal dysfunction.
[3] The most common undesirable effects are application site reactions.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product.
Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form: https://sideeffects.health.gov.il

4.9 Overdose
Accidental overdose with a medicated plaster is unlikely. However, possible signs of overdose may include nausea, vomiting, abdominal pain or more rarely, diarrhoea. Tinnitus, headache and gastrointestinal bleeding is also possible. The half-life of ibuprofen in ibuprofen overdose is 1.5-3 hours. In the event of overdose, management should be symptomatic and medical advice should be sought.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

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

ATC code: M02AA13

Ibuprofen is a propionic acid derivative NSAID that exerts it's efficacy through the inhibition of prostaglandin synthesis. In humans ibuprofen reduces inflammatory pain, swellings and fever. Ibuprofen also reversibly inhibits platelet aggregation.

In the form of a medicated plaster, which locally delivers ibuprofen continuously at the site of pain over the 24 hours of application, it has topical anti-inflammatory and analgesic activity.

Pooled data from two clinical efficacy and safety studies in adults with acute soft tissue injuries showed that when applied once every 24h, the medicated plaster provided long lasting relief, with a statistically significant decrease in pain on movement compared with a placebo plaster from 2hrs post first dose and every subsequent time point over 5 days.

Analysis of tenderness at the injured site also showed a significant difference compared with placebo at 24 and 120 hours following use.

In a confirmatory efficacy and safety study ‘excellent’ or ‘good’ ratings of treatment efficacy for the medicated plaster were given by 70.3% of patients and 70.3% of healthcare professionals at 24 hours, and 92.2% of patients and 89.1% of healthcare professionals after 5 days. ‘excellent’ or ‘good’ ratings for local tolerability were given by 100% of patients and healthcare professionals after 24 hours, and 98.4% of patients and healthcare professionals following 5 consecutive days’ use. Subjective ratings were significantly better than for placebo ($p<0.0001$).

Data from clinical studies indicate that the rates of detachment or loss of adhesion of the medicated plaster over 24 hours are low.

5.2 Pharmacokinetic properties

This medicated plaster provides a topical formulation of ibuprofen designed to provide a sustained transfer of ibuprofen through the skin directly to the local site of the pain and inflammation.
In a human pharmacokinetic study, 28 subjects had the medicated plaster applied once daily for 5 consecutive days over a 7 day observation period. Plasma concentrations of ibuprofen rose rapidly reaching a mean concentration of 0.49 (95% CI: 0.39-0.58) µg/ml 24hr after application of the first patch. On day 5 of treatment, the mean C_{max} was 0.51 (95% CI: 0.44-0.60) µg/ml, and the mean AUC_{0-24} was 9.59 (95% CI: 8.33-11.0) µghr/ml. The mean C_{max} and systemic bioavailability are low compared to oral ibuprofen and consistent with literature reviews for topical NSAIDs. The typical C_{max} for a 200-400mg counterpart oral dose of ibuprofen is in the order of 20-50 µg/ml. The low C_{max} and low AUC for the medicated plaster indicate that if used concomitantly with systemic ibuprofen, the contribution of the medicated plaster to systemic ibuprofen exposure would be negligible.
The PK profile demonstrated that of ibuprofen does not accumulate on repeated application and that there is rapid attenuation to baseline within 24 hours after discontinuation.

5.3 Preclinical safety data

After systemic application, the subchronic and chronic toxicity of ibuprofen in animal experiments showed up mainly in form of lesions and ulcerations in the gastro-intestinal tract. In vitro and in vivo studies gave no clinically relevant evidence of a mutagenic potential of ibuprofen. In studies in rats and mice no evidence of carcinogenic effects of orally applied ibuprofen was found.
Systemically applied ibuprofen inhibited ovulation in rabbits and led to implantation disorders in various animal species (rabbit, rat, mouse). Experimental studies in rat and rabbit have shown that ibuprofen crosses the placenta. Following administration of maternotoxic doses, an increased incidence of malformations (ventricular septal defects) occurred in the progeny of rats.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Adhesive layer
Liquid paraffin
Hydrogenated rosin glycerol ester
Styrene-Isoprene-Styrene Block Copolymer
Polyisobutylene
Macrogol 20000
Macrogol 400
Levo-menthol
Backing layer
Woven Polyethylene terephthalate (PET)
Release liner
Silicone coated Polyethylene Terephthalate (PET)

6.2 Incompatibilities

Not applicable.

6.3 Shelf-life

2 years (2 patches per sachet)
The expiry date of the product is indicated on the packaging materials.
Shelf life after first opening of the sachet: 6 months.

6.4 Special precautions for storage

Do not store above 25ºC (2 patches per sachet).
Store in the original package in order to protect from light.

6.5 Nature and contents of container

Each sachet is made of composite PET/LDPE/aluminium/LDPE film.
Each sachet contains 2 medicated plasters.

6.6 Special precautions for disposal

Any unused medicinal product or waste material should be disposed of according to local requirements. Do not flush used plasters down the toilet.

7. MANUFACTURER

Reckitt Benckiser Healthcare International Limited,
Nottingham, United Kingdom

8. REGISTRATION HOLDER

Reckitt Benckiser (Near East) Ltd.,
6 Hanagar St., Hod-Hasharon

9. REGISTERATION NUMBER

172-40-35676-00

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