Ibuprofen 10% w/w gel
Nurofen Maximum Strength 10 % Gel

PL 10972/0089

UKPAR

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On 27th July 2012, the MHRA granted Marketing Authorisation (licence) for the medicinal product Ibuprofen 10% w/w gel, Nurofen Maximum Strength 10 % Gel (PL 10972/0089). This is a pharmacy medicine (P).

Nurofen Maximum Strength 10% Gel contains ibuprofen and belongs to a group of medicines called non-steroids anti-inflammatory drugs (NSAID’s). These medicines, used on the skin, reduce pain and inflammation.

Nurofen Maximum Strength 10% Gel is used to treat a number of painful conditions affecting the joints and muscles, such as backache, rheumatic and muscular pain, sprains, strains and sports injuries. It is also used for the relief of pain caused by non-serious arthritic conditions and nerve pain (neuralgia).

No new or unexpected safety concerns arose from this application and it was, therefore, judged that the benefits of taking Ibuprofen 10% w/w gel, Nurofen Maximum Strength 10 % Gel outweigh the risks; hence Marketing Authorisation has been granted.
Ibuprofen 10% w/w gel
Nurofen Maximum Strength 10 % Gel

PL 10972/0089

SCIENTIFIC DISCUSSION

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INTRODUCTION

The Medicines and Healthcare Products Regulatory Agency (MHRA) granted marketing authorisation (licence) for the medicinal product Ibuprofen 10% w/w gel, Nurofen Maximum Strength 10 % Gel (PL 10972/0089) to Goldshield Group Limited on the 27th July 2012. This medicine is used for the relief of pain and inflammation associated with backache, rheumatic and muscular pain, strains, sprains, neuralgia, sports injuries and for the relief of pain of non-serious arthritic conditions.

This application was submitted as abridged application according to Article 10c of Directive 2001/83/EC as amended, cross-referring to Fenbid Forte 10% gel (PL 10972/0082), held by Goldshield Group Limited, which was granted marketing authorisation on 5th January 1999.

No new data were submitted nor were they necessary for this simple application, as the data are identical to those of the previously granted cross-reference product. As the cross-reference product was granted prior to the introduction of current legislation, no Public Assessment Report (PAR) was generated.

A pharmacovigilance system has been provided with this application and is satisfactory. A suitable justification for non-submission of the Risk Management Plan has been provided.

No environmental risk assessment (ERA) has been undertaken, as this is not considered necessary. This product is essentially similar and the therapeutic indications and posology of the finished product are the same as those already licensed products. The applicant’s justification for absence of ERA is satisfactory.
PHARMACEUTICAL ASSESSMENT

LICENCE NO: PL 10972/0089  
PROPRIETARY NAME: Ibuprofen 10% w/w gel, Nurofen Maximum Strength 10 % Gel  
COMPANY NAME: Goldshields Group Limited  
E.C. ARTICLE: Article 10c of Directive 2001/83/EC  
LEGAL STATUS: P

1 INTRODUCTION  
This is an informed consent application for Ibuprofen 10% w/w gel, Nurofen Maximum Strength 10 % Gel, submitted under Article 10c of Directive 2001/83/EC as amended. This product is cross-referring to Fenbid Forte 10% gel (PL 10972/0082), approved on 5th January 1999 to the marketing authorisation holder, Goldshield Group Limited. The current application is considered valid.

2 MARKETING AUTHORISATION APPLICATION (MAA)  
2.1 Name(s)  
The proposed names of the product are Ibuprofen 10% w/w gel, Nurofen Maximum Strength 10 % Gel. The product has been named in line with current requirements.

2.2 Strength, pharmaceutical form, route of administration, container and pack sizes  
The product is a gel for topical use and contains the active ingredient ibuprofen.

The product is packed in collapsible aluminium tubes with internal protective lacquer with HDPE screw caps. Pack sizes of 30g and 50g.

The packaging and pack sizes are the same as those for the reference product.

The proposed shelf life is 36 months with a storage conditions “Do not store above 25ºC” and “Keep the tube in the outer carton in order to protect from light”. The shelf-life and storage conditions are identical to those for the reference product and are satisfactory.

2.3 Legal status  
This product is supplied through Pharmacy (P).

2.4 Marketing authorisation holder/Contact Persons/Company  
The proposed Marketing Authorisation holder is Goldshield Group Limited, (trading as Goldshield Pharmaceuticals), NLA Tower, 12-16 Addiscombe Road, Croydon, Surrey CR0 0XT, UK

2.5 Manufacturers  
The proposed manufacturing sites are consistent with those registered for the reference products and evidence of Good Manufacturing Practice (GMP) compliance has been provided.
2.6 Qualitative and quantitative composition
The proposed composition is consistent with the details registered for the referenced product.

2.7 Manufacturing process
The proposed manufacturing process is consistent with the details registered for the referenced product and the maximum full scale batch size is stated.

2.8 Finished product/shelf-life specifications
The proposed finished product and shelf-life specification are in line with the details registered for the referenced product.

2.9 Drug substance specificatio
The proposed drug substance specification conforms to the current European Pharmacopoeia monograph for ibuprofen and is in-line with those for the referenced product.

2.10 TSE Compliance
No materials of human or animal origin have been used in the manufacture of this product. This is consistent with the reference product.

2.11 Bioequivalence
No bioequivalence data are required to support this informed consent application, as the proposed product is manufactured to the same formula utilising the same process as the reference product Fenbid Forte 10% gel (PL 10972/0082).

3 EXPERT REPORT
The applicant has included detailed expert reports of the application. Signed declarations and copies of the experts’ CVs are enclosed for the quality, non-clinical and clinical experts. All are considered to have sufficient experience for their responsibilities.

4 PRODUCT NAME & APPEARANCE
See 2.1 for details of the proposed product names. The appearance of the product is identical to those of the reference products.

5 SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)
The proposed SmPC is consistent with the details registered for the reference products.

6 PATIENT INFORMATION LEAFLET (PIL)/LABELLING
User testing of the package leaflet has been accepted, based on a bridging report provided by the applicant making reference to the user-testing of the PIL for Ibuprofen Tablets. The products are from the same therapeutic class and have similar indications. A critical analysis demonstrated that the key messages for safe and effective use for both leaflets were similar. The justification on the rationale for bridging is accepted.
The applicant has committed to submitting the mock-ups with the name Ibuprofen 10% w/w gel to the relevant regulatory authorities before marketing.

7. CONCLUSIONS
The data submitted with the application are acceptable. The grant of marketing authorisation is recommended.
NON-CLINICAL ASSESSMENT

No new non-clinical data have been supplied with this application and none are required for applications of this type.
CLINICAL ASSESSMENT

No new clinical data have been supplied with this application and none are required for applications of this type.
OVERALL CONCLUSION AND RISK BENEFIT ASSESSMENT

QUALITY
The data for this application are consistent with those previously assessed for the cross reference product and, as such, have been judged to be satisfactory.

NON-CLINICAL
No new non-clinical data were submitted and none are required for applications of this type.

EFFICACY
This application is identical to the previously granted application for Fenbid Forte 10% gel (PL 10972/0082), granted to Goldshield Group Limited on 5th January 1999.

Pharmaceutical, non-clinical and clinical expert statements have been provided, together with CVs showing the experts are appropriately qualified. The experts confirm that the product is identical in composition, manufacture and pharmaceutical characteristics to the respective reference products and that there are no toxicological or clinical issues.

No new or unexpected safety concerns arise from this application.

The SmPCs, PIL and labelling are satisfactory and consistent with those for the reference product.

RISK BENEFIT ASSESSMENT
The quality of the product is acceptable and no new non-clinical or clinical safety concerns have been identified. The applicant’s products are identical to the reference products. Extensive clinical experience with ibuprofen is considered to have demonstrated the therapeutic values of the compounds. The risk benefit is, therefore, considered to be positive.
STEPS TAKEN FOR ASSESSMENT

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<tr>
<td>1</td>
<td>The MHRA received the marketing authorisation application on 14\textsuperscript{th} November 2011</td>
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<td>2</td>
<td>Following standard checks and communication with the applicant the MHRA considered the application is valid on 3\textsuperscript{rd} January 2012</td>
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<td>3</td>
<td>Following assessment of the application the MHRA requested further information on 8\textsuperscript{th} March 2012</td>
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<td>4</td>
<td>The applicant responded to the MHRA’s request, providing further information on 30\textsuperscript{th} March 2012</td>
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<td>The application was determined on 27\textsuperscript{th} July 2012</td>
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SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT
   Ibuprofen 10% w/w gel
   Nurofen Maximum Strength 10 % Gel

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
   Ibuprofen 10% w/w
   “For the full list of excipients, see section 6.1”

3 PHARMACEUTICAL FORM
   Gel for topical application
   Clear or slightly opalescent, colourless or almost colourless gel with Isopropanol odour.

4 CLINICAL PARTICULARS
   4.1 Therapeutic indications
      For the relief of pain and inflammation associated with backache, rheumatic and muscular
      pain, strains, sprains, neuralgia and sports injuries. For the relief of pain of non-serious
      arthritic conditions.

   4.2 Posology and method of administration
      Method of administration
      For topical application to the skin.

      Dosage
      Adults, the elderly and children over 14 years: Squeeze 50 to 125 mg (2 to 5 cm) of the gel
      from the tube and lightly rub into the affected area until absorbed.

      The dose should not be repeated more frequently than every four hours and no more than 4
      times in any 24 hour period.

      Wash hands after each application. Do not exceed the stated dose. Review treatment after 2
      weeks, especially if the symptoms worsen or persist.

      Children under 14 years: Do not use on children 14 years of age, except on the advice of a
      doctor.

   4.3 Contraindications
      Hypersensitivity to any of the constituents. Hypersensitivity to aspirin, or other non-steroidal
      anti-inflammatory drugs, asthma, rhinitis or urticaria.
      Not to be used on broken or damaged skin.

   4.4 Special warnings and precautions for use
      Apply with gentle massage only. Avoid contact with eyes, mucous membranes and inflamed
      or broken skin.
      Discontinue if rash develops.
      Hands should be washed immediately after use.
      Not for use with occlusive dressings.
      The label will state:
      Do not exceed stated dose
      Keep out of reach of children
      For external use only.

      If symptoms persist consult your doctor or pharmacist
      Do not use if you are allergic to Ibuprofen or any of the ingredients, aspirin, or any other
      painkillers.
Consult your doctor or pharmacist before use if:
-you are taking aspirin or any other pain relieving medication
-you are pregnant
Not recommended for children under 14 years

Oral NSAIDs, 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 the systemic absorption of topically applied ibuprofen is less than for oral dosage forms, these complications can occur in rare cases. For these reasons, patients with an active peptic ulcer, a history of kidney problems or asthma should seek medical advice before using Ibuprofen gel as should patients already taking other painkillers.

Patients should seek medical advice if symptoms worsen or persist.

Patients should be advised against excessive exposure to sunlight of area treated in order to avoid possibility of photosensitivity.

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.

4.6 Pregnancy and lactation
Not to be used during pregnancy or lactation.

Pregnancy:
Although no teratogenic effects have been demonstrated, ibuprofen should be avoided during pregnancy. The onset of labour may be delayed and the duration of labour increased.

Lactation:
Ibuprofen appears in breast milk in very low concentrations but is unlikely to affect breast fed infants adversely.

4.7 Effects on ability to drive and use machines
None known

4.8 Undesirable effects
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 reaction and anaphylaxis (b) respiratory tract reactivity comprising of asthma, aggravated asthma, bronchospasm or dyspnoea, or (c) assorted skin disorders, including rashes of various types, pruritis, urticaria, purpura, angioedema and less commonly, bullous dermatoses (including epidermal necrolysis and erythema multiforme).

Gastro-intestinal: Side effects such as abdominal pain and dyspepsia have been reported.

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

4.9 Overdose
Overdosage with a topical presentation of Fenbid Forte Gel is unlikely. Symptoms of severe ibuprofen overdosage (eg following accidental oral ingestion) include headache, vomiting, drowsiness and hypotension. Correction of severe electrolyte abnormalities should be considered.
5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties
ATC code: M02A A13, Antiinflammatory preparations, non-steroids for topical use. The gel is for topical application. It contains the active ingredient, ibuprofen, a phenylpropionic acid derivative which exerts its anti-inflammatory and analgesic effects directly in inflamed tissues underlying the site of application, mainly by inhibiting prostaglandin biosynthesis. Because it is formulated in an aqueous/ alcoholic gel, the preparation also exerts a soothing and cooling effect when applied to the affected area.

5.2 Pharmacokinetic properties
Specially formulated for external application, the active ingredient penetrates through the skin rapidly and extensively (approximately 22% of a finite dose within 48 hours), 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
There are no preclinical data of relevance to the prescriber, which are additional to those already included in other sections of the SmPC.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients
Hydroxyethyl cellulose E1525
Sodium Hydroxide E524
Benzyl alcohol E1519
Isopropyl alcohol
Purified water

6.2 Incompatibilities
None known

6.3 Shelf life
36 months.

6.4 Special precautions for storage
Do not store above 25°C.
Keep the tube in the outer carton in order to protect from light.

6.5 Nature and contents of container
Collapsible aluminium tubes with internal protective lacquer with HDPE screw caps.
P: 30g, 50g
“Not all pack sizes may be marketed”

6.6 Special precautions for disposal
No special instructions.

7 MARKETING AUTHORISATION HOLDER
GOLDSHIELD GROUP LIMITED
(TRADEING AS GOLDSHIELD PHARMACEUTICALS)
NLA TOWER
12-16 ADDISCOMBE ROAD
CROYDON
SURREY CR0 0XT, UK

8 MARKETING AUTHORISATION NUMBER(S)
PL 10972/0089
9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
27/07/2012

10 DATE OF REVISION OF THE TEXT
27/07/2012
PATIENT INFORMATION LEAFLET

Read all of this leaflet carefully before you start taking this medicine. Keep this leaflet. You may need to read it again. If you have any further questions, ask your doctor or pharmacist. This medicine is for you, do not pass it on to others. It may harm them, even if their symptoms are the same as yours. If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:
1. What is Nurofen Maximum Strength 10% Gel and what it is used for
2. Before you use Nurofen Maximum Strength 10% Gel
3. How to use Nurofen Maximum Strength 10% Gel
4. Possible side effects
5. How to store Nurofen Maximum Strength 10% Gel
6. Further information

1. What is Nurofen Maximum Strength 10% Gel and what it is used for
Nurofen Maximum Strength 10% Gel contains ibuprofen and belongs to a group of medicines called non-steroidal anti-inflammatory drugs (NSAIDs). These medicines, used on the skin, reduce pain and inflammation.
Nurofen Maximum Strength 10% Gel is used to treat a number of painful conditions affecting the joints and muscles, such as backache, rheumatic and muscular pain, sprains, strains and sports injuries. It is also used for the relief of pain caused by non-serious arthritic conditions and nerve pain (neuralgia).

2. Before you use Nurofen Maximum Strength 10% Gel
DO NOT use Nurofen Maximum Strength 10% Gel:
- If you are allergic to ibuprofen, aspirin or similar medicines (e.g. NSAIDs) or any of the other ingredients in this gel (listed at the end of this leaflet).
- If you are asthmatic, or suffer from rhinitis (allergic runny nose) or urticaria (hives)
- On broken, damaged, infected or diseased skin

Take special care with Nurofen Maximum Strength 10% Gel
- Protect treated areas from direct sunlight to avoid any sensitivity reaction, e.g. a rash
- If you have had an ulcer or some other problem affecting your stomach or intestines in the past
- If you have asthma or wheezing attacks (or if you have had asthma in the past)
- If you have any kidney problems
- If you develop a rash after using the gel also using it any further
- If you suffer from bronchial asthma or any allergic disease
If any of the above apply to you, only use this product on advice from your doctor or pharmacist.
Nurofen Maximum Strength 10% Gel is FOR EXTERNAL USE ONLY

Can you take Nurofen Maximum Strength 10% Gel with other medicines?
The effect of this medicine may affect or be affected by taking the following medicines at the same time:
- Medicines to lower your blood pressure (e.g. atenolol)
- Medicines used to thin the blood (e.g. warfarin)
- Aspirin or other NSAIDS, used for pain and inflammation
Tell your doctor or pharmacist if you are taking, or have recently taken any of the above or any other medicines - even those not prescribed.

Pregnancy and breast feeding
You should not use Nurofen Maximum Strength 10% Gel if you are pregnant or breast-feeding.
Ask your doctor or pharmacist for advice before taking any medicine.

Driving and using machines
Nurofen Maximum Strength 10% Gel should not affect the ability to drive or use machines.
3. How to use Nurofen Maximum Strength 10% Gel

Nurofen Maximum Strength 10% Gel is designed for topical (on the skin) application only. Never take the gel by mouth.

Always use Nurofen Maximum Strength 10% Gel exactly as this leaflet tells you. You should check with your doctor or pharmacist if you are not sure.

Check the seal is intact before first use (invert cap to break seal). If the seal is not intact, do not use the gel.

Adults: Squeeze 2 to 5 cm of gel (i.e. 50g to 125mg of ibuprofen) from the tube on affected skin area. Massage until absorbed. This dose should not be repeated more frequently than every four hours and no more than four times a day in any 24 hour period.

Nurofen Maximum Strength 10% Gel should only be used on healthy, unbroken skin. Do not use it on or near cuts or graze or under dressings such as plasters. Also do not use it on the genital area.

Do not let any gel come in contact with your eyes. If it does, rinse your eyes with cold water and consult your doctor. Hands should be washed after applying Nurofen Maximum Strength 10% Gel, unless they are the site of treatment.

If the condition does not improve after two weeks of use, or becomes worse at any time, speak to your doctor or pharmacist.

Children: Nurofen Maximum Strength 10% Gel is not recommended for use in children under 14 years.

If you accidentally swallow any Nurofen Maximum Strength 10 % Gel, rinse out your mouth thoroughly and contact your doctor or nearest hospital, as soon as possible. If swallowed, the gel may cause an upset stomach.

If you forget to use Nurofen Maximum Strength 10% Gel:

If you miss a dose, just carry on with the next dose as normal. Do not apply a double dose.

4. Possible side effects

Like all medicines Nurofen Maximum Strength 10% Gel can cause side effects, although not everybody gets them.

All medicines can cause allergic reactions although serious allergic reactions are rare. Any sudden wheeziness, difficulty in breathing, swelling of the eyelids, face or lips or itching (especially affecting your whole body) should be reported to a doctor immediately.

Side effects include:

- Itching or reddening of the skin
- A burning feeling
- Scree or weeping spots
- Abdominal pains (pains in your stomach) or other abnormal stomach symptoms
- Kidney problems (particularly in people who have a history of kidney disease)

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

5. How to store Nurofen Maximum Strength 10% Gel

Keep out of the reach and sight of children. Do not use Nurofen Maximum Strength 10% Gel after the expiry date which is stated on the carton. Store in a cool, dry place, below 25°C. Keep the tube tightly closed.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. Further information

What Nurofen Maximum Strength 10% Gel contains

The active substance is ibuprofen. The other ingredients are hydroxyethyl cellulose, sodium hydrosulphate, benzyl alcohol, isopropyl alcohol, purified water.

What Nurofen Maximum Strength 10% Gel looks like and contents of the pack

Nurofen Maximum Strength 10% Gel is a transparent gel supplied in aluminium tubes containing 50g or 85g of gel (available in pharmacy). Not all pack sizes are marketed.

Marketing Authorisation Holder:
Goldshield Group Limited trading as Goldshield Pharmaceuticals, NLA Tower, 12 – 16 Addiscombe Road, Croydon, Surrey CR0 0XT, UK

Manufacturer
Farmaservi Manufacturing S.L. Carretera De Irún KM 26,200 28700, SAN Sebastian De Los Reyes, Madrid, Spain.

Distributor: Reckitt Benckiser Healthcare (UK) Ltd, SL1 4AQ.

This leaflet was last revised in March 2012.
How to use this Gel

Read the leaflet carefully. Before first use, check that the seal is not broken then pierce it with the point in the end of the cap.

Adults, the elderly and children over 14 years:
Squeeze 2-5 cm of gel (equivalent to 50-125 mg of Ibuprofen) onto the affected area then replace the cap. Gently rub the gel in until it is absorbed. Wash your hands after use.
- Do not cover the treated area with plaster or dressing.
- Do not reapply more gel within 4 hours.
- Do not apply more than 4 times in 24 hours.
- Do not use on broken or inflamed skin, on the lips or near the eyes.
- Talk to your doctor if your symptoms worsen or if there is no improvement after 14 days.

DO NOT USE:
- If you are allergic to any of the ingredients, aspirin or any other non-steroidal anti-inflammatory drugs (NSAIDs).
- If you are under 14 years old, except on the advice of a doctor

Consult your doctor before use if you are asthmatic, have active peptic ulcer, kidney problem, are taking any medical treatment or are pregnant.

DO NOT EXCEED THE STATED DOSE

FOR EXTERNAL USE ONLY.

Store below 25°C

KEEP OUT OF THE REACH AND SIGHT OF CHILDREN

Active Ingredient: Ibuprofen 10% w/w. Also contains: Purified water, Isopropyl alcohol, Hydroxyethylcellulose, Benzyl alcohol, Sodium hydroxide.

Licence Holder: Goldshield Group Limited trading as Goldshield Pharmaceuticals, CRO DXT, UK.

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