NUROFEN EXTRA STRENGTH 400MG TABLETS
PL 00327/0184

UKPAR

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PL 00327/0184

LAY SUMMARY

The MHRA granted Crookes Healthcare Ltd a Marketing Authorisation (licence) for the medicinal product Nurofen Extra Strength 400mg Tablets (PL 00327/0184). This medicine is available through pharmacies (P) for the relief of headaches, backache, period pain, dental pain, neuralgia, rheumatic pain, muscular pain, migraine, cold and flu symptoms, feverishness and pain of non-serious arthritic conditions.

Nurofen Extra Strength 400mg Tablets contain the active ingredient ibuprofen which is a non-steroidal anti-inflammatory drug (NSAID).

The product was a line extension of Nurofen 200mg Caplets and was considered to be bioequivalent from the data submitted.

No new or unexpected safety concerns arose from this application and it was therefore judged that the benefits of taking Nurofen Extra Strength 400mg Tablets outweigh the risks, hence a Marketing Authorisation has been granted.

NUROFEN EXTRA STRENGTH 400MG TABLETS
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SCIENTIFIC DISCUSSION

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INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the UK granted a Marketing Authorisation for the medicinal product Nurofen Extra Strength 400mg Tablets (PL 00327/0184) to Crookes Healthcare Ltd on 21 February 2007. The product is available through pharmacies.

The application was submitted as a line extension, according to Article 8.3 of Directive 2001/83/EC as amended, of the original product Nurofen 200mg Caplets.

The product contains the active ingredient ibuprofen and is indicated for the relief of migrane-headaches, backache, dental pain, neuralgia and period pains as well as rheumatic and muscular pains and pain of non-serious arthritic conditions. Nurofen Extra Strength 400mg Tablets relieve pain and reduce inflammation and temperature as well as relieving headaches and other types of pain; they also relieve cold and flu symptoms.

Ibuprofen is a propionic acid derivative NSAID. It prevents the synthesis of prostaglandin and inhibits platelet aggregation.

Nurofen Extra Strength 400mg Tablets are a direct two-fold scale-up of Nurofen 200mg Caplets and bioequivalence of the products has been inferred from the dissolution profile data and previous bioequivalence studies.

PHARMACEUTICAL ASSESSMENT

COMPOSITION

The product is formulated as a coated tablet containing the active ingredient ibuprofen at a strength of 400mg. The excipients present are croscarmellose sodium, sodium laurilsulfate, sodium citrate, stearic acid and colloidal anhydrous silica. Carmellose sodium, talc, spray-dried acacia, sucrose, titanium dioxide, macrogol 6000 and purified water are present in the coating. In addition, opacode S-1-9460 HV Brown and industrial methylated spirit are present in the printing ink.

The tablets are presented in aluminium-foil sealed PVC blisters or aluminium-foil sealed PVC/PVdC blisters in packs of 2, 3, 4, 5, 8, 10, 12, 15, 16, 18, 20, 24, 28, 32, or 48 tablets. Tablets are also available in HDPE bottles with child resistant caps in packs of 96 tablets.

DRUG SUBSTANCE

Ibuprofen

All aspects of the manufacture and control of ibuprofen are supported by an EDQM Certificate of Suitability. This certificate is accepted as confirmation of the suitability of ibuprofen for inclusion in this medicinal product.

Stability data have been generated which support a retest period of 3 years when stored in the proposed packaging.

DRUG PRODUCT

Other ingredients

All excipients used in the manufacture of the tablets are routinely tested for compliance with the current relevant international standard with the exception of the printing ink which complies with a satisfactory in-house specification.

Satisfactory certificates of analysis have been provided for all excipients.

None of the excipients used contain material of animal or human origin.

Dissolution profiles

Dissolution profiles for the drug product were found to be mathematically similar to Nurofen 200mg Caplets (Crookes Healthcare Ltd). The drug product has been shown to be linear over the therapeutic dose range.

Manufacture

A full description and a detailed flow-chart of the manufacturing method including in-process control steps has been provided.

In-process controls are satisfactory based on process validation data and controls on the finished product. Satisfactory process validation has been carried out.

Satisfactory batch formulae have been provided for the manufacture of the product along with an appropriate account of the manufacturing process. The manufacturing process has been validated and appropriate in-process controls are applied.

Finished product specification
The proposed finished product specification is acceptable and the analytical methods used have been suitably validated. Batch analysis data have demonstrated compliance with the proposed release specification.

Container Closure System
Satisfactory specifications and certificates of analysis have been provided for the packaging components. All primary product packaging complies with EU legislation regarding contact with food.

Stability
Finished product stability data support the proposed shelf-life of 24 months with storage conditions of 'Store in the original pack'. The aluminium-foil sealed PVC blisters have the additional storage condition 'Do not store above 30°C'.

Bioequivalence/bioavailability
Refer to the clinical assessment.

SPC, PIL and Labels
The SPC and labels are pharmaceutically acceptable.

The marketing authorisation holder has provided a commitment to update the marketing authorisation with a patient information leaflet in compliance with Article 59 of Council Directive 2001/83/EC and that the leaflet shall reflect the results of consultation with target patient groups, no later than 01 July 2008.

CONCLUSION
It is recommended that a Marketing Authorisation is granted for this application.

PRECLINICAL ASSESSMENT

No new preclinical data have been supplied with this application and none are required for an application of this type.

CLINICAL ASSESSMENT

INTRODUCTION AND BACKGROUND

This is a national abridged application for coated tablets containing 400mg ibuprofen.

The application is submitted under the provisions of Directive 2001/83/EC Article 8.3, as a line extension of Nurofen 200mg Caplets which are authorised in the UK. The formulation used in this product uses a novel melt extrusion technology to produce a tablet containing smaller proportion of excipients and therefore the tablets are smaller than the current marketed 400 mg tablet which will be more convenient for consumers who find swallowing tablets difficult.

Ibuprofen is one of the most widely used NSAIDs. The primary biological action of ibuprofen is the inhibition of cyclooxygenase (COX), which is responsible for the synthesis of prostaglandins and other mediators, leading to an anti-inflammatory, analgesic and antipyretic effect.

INDICATIONS

The proposed indications are:

> For the relief of migraine-headaches, backache, dental pain, neuralgia and period pains as well as rheumatic and muscular pains, and pain of non-serious arthritic conditions.
> Nurofen relieves pain and reduces inflammation and temperature as well as relieving headaches and other types of pain. It also relieves cold and flu symptoms.

These are considered satisfactory.

DOSE AND DOSE SCHEDULE

The proposed dose and dose schedule for this product to be used for the above indications ranges from 400mg to 1200mg daily for short term use only.

CLINICAL PHARMACOLOGY

Pharmacokinetics

Ibuprofen is rapidly absorbed from the gastrointestinal tract. Maximum plasma concentrations are reached 45 minutes after ingestion on an empty stomach. When taken with food, peak levels are observed 1 to 2 hours after administration. Elimination half-life is approximately 2 hours.

Ibuprofen is metabolised in the liver to two major inactive metabolites and these together with unchanged ibuprofen are excreted by the kidney either as such or as conjugates. Excretion by the kidney is both rapid and complete.

Ibuprofen is extensively bound to plasma proteins.

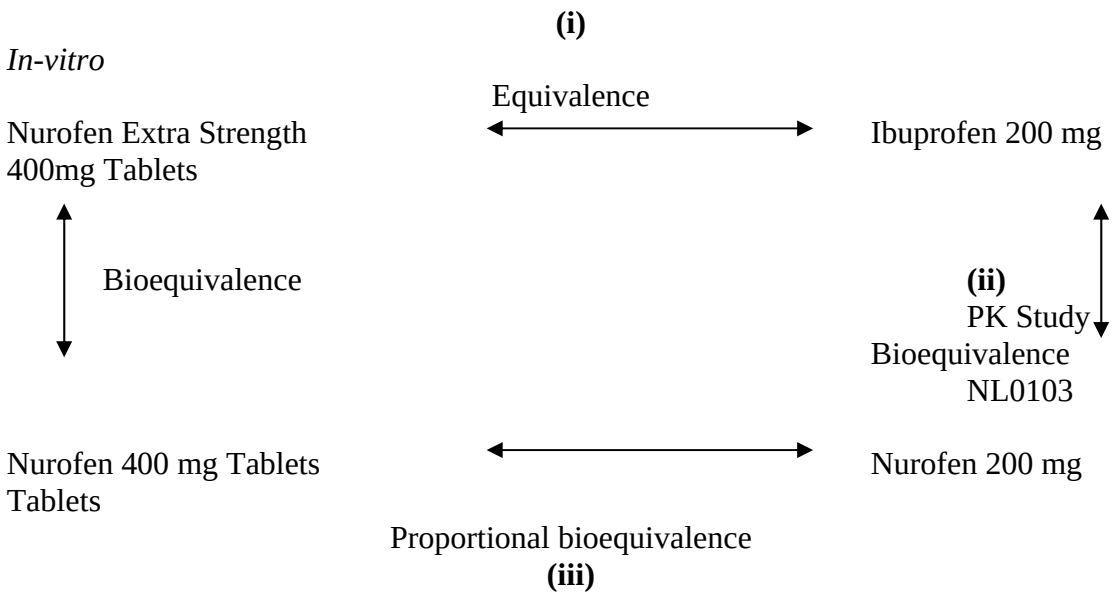
Pharmacodynamics
Ibuprofen is a propionic acid derivative, having analgesic, anti-inflammatory and antipyretic activity. The drug's therapeutic effects as a non-steroidal anti-inflammatory are thought to result from inhibitory activity on prostaglandin synthetase.

Bioequivalence
This application for Nurofen Extra Strength 400mg Tablets has been submitted as a line extension of the applicant's product, Nurofen 200mg Caplets. The 400mg tablet is a direct two-fold scale up of the 200mg tablet with the same active principles and the same pharmaceutical form.

The applicant has justified the lack of conducting a bioequivalence study since bioequivalence between the two formulations is implicit from the following:

i) Nurofen Extra Strength 400mg Tablets have a mathematically similar *in vitro* dissolution profile under identical conditions to that of Ibuprofen 200 mg Tablets. The formulation of Nurofen Extra Strength 400mg Tablets is a simple 2 x multiple of that of Nurofen 200 mg Caplets.
ii) A bioavailability study has shown that Nurofen 200 mg Caplets are bioequivalent to Nurofen 200 mg Tablets
iii) Nurofen 200 mg Tablets have previously been shown to be bioequivalent to Nurofen 400 mg Tablets, when the dose administered is taken into account. This was presented in the original marketing authorisation application for Nurofen 400 mg Tablets.

A diagrammatic summary is given below:



Conclusion
It follows that Ibuprofen 200 mg Tablets are bioequivalent to Nurofen 400 mg Tablets.

CLINICAL EFFICACY

No new efficacy data are presented in this application and none are required.

CLINICAL SAFETY

No formal safety data are presented in this application and none are required.

CLINICAL EXPERT REPORT

The clinical expert report has been written by an appropriately qualified medical doctor. It is an adequate summary of the clinical data provided in the dossier.

SPC, PIL and LABELS

The SPC, PIL and labels are acceptable.

CONCLUSIONS

The clinical efficacy and safety of ibuprofen is well known from its use in clinical practice. No new data were submitted and this is acceptable. A Marketing Authorisation should be granted for this application.

OVERALL CONCLUSION AND RISK BENEFIT ASSESSMENT

QUALITY

The important quality characteristics of Nurofen Extra Strength 400mg Tablets are well defined and controlled. The specifications and batch analytical results indicate consistency from batch to batch. There are no outstanding quality issues that would have a negative impact on the benefit/risk balance.

PRECLINICAL

No new preclinical data were submitted and none are required for applications of this type.

EFFICACY

Bioequivalence has been inferred between the applicant's Nurofen Extra Strength 400mg Tablets and Nurofen 200mg Caplets (Crookes Healthcare Ltd) from the dissolution profile data and previous bioequivalence studies.

No new or unexpected safety concerns arise from these applications.

RISK BENEFIT ASSESSMENT

The quality of the product is acceptable and no new preclinical or clinical safety concerns have been identified. The risk benefit is, therefore, considered to be positive.

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STEPS TAKEN FOR ASSESSMENT

1 The MHRA received the Marketing Authorisation application on 12 November 2003.

2 Following standard checks and communication with the applicant the MHRA considered the application valid on 09 January 2004.

3 Following assessment of the application the MHRA requested further information relating to the quality dossier on 26 August 2004, 20 December 2004 and 08 February 2005 and further information relating to the clinical dossier on 28 May 2004, 17 September 2004 and 22 September 2004.

4 The applicant responded to the MHRA's requests, providing further information on 15 October 2004, 02 February 2005 and 11 March 2005 relating to the quality section and on 19 October 2004 relating to the clinical section.

5 The application was determined on 21 February 2007.

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STEPS TAKEN AFTER AUTHORISATION – SUMMARY

Date submitted	Application type	Scope	Outcome
28 February 2007	Type II Medical Variation	Changes to section 4 of the SPC following opinion on non-selective NSAIDs adopted by CHMP in October 2006.	Granted 19 June 2007
01 August 2007	Type IB Pharmaceutical Variation	To replace the excipient calcium sulphate dehydrate with talk.	Granted 30 August 2007
01 August 2007	Type IB Pharmaceutical Variation	To replace the excipient carnauba wax powder with macrogol 6000.	Granted 30 August 2007

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Nurofen Extra Strength 400 mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Ibuprofen 400 mg.

For excipients, see 6.1

3 PHARMACEUTICAL FORM

Coated Tablet

A white to off-white, biconvex, round, sugar coated tablet printed with an identifying logo in red on one face.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For the relief of migraine-headaches, backache, dental pain, neuralgia and period pains as well as rheumatic and muscular pains, and pain of non-serious arthritic conditions.

Nurofen relieves pain and reduces inflammation and temperature as well as relieving headaches and other types of pain. It also relieves cold and flu symptoms.

4.2 Posology and method of administration

For oral administration and short-term use only.

Adults and children over 12 years: Initial dose one tablet

taken with water, then if necessary, one tablet every four hours. Do not exceed three tablets in any 24 hours. Not for use by children under 12 years of age without medical advice.

Elderly: No special dosage modifications are required.

The minimum effective dose should be used for the shortest time necessary to relieve symptoms. If the product is required for more than 10 days or if symptoms persist or worsen, the patient should consult a doctor.

Leave at least four hours between doses and do not take more than 1200 mg in any 24 hour period.

4.3 Contraindications

Hypersensitivity to ibuprofen or any of the constituents in the product.

Patients who have previously shown hypersensitivity reactions (eg asthma, rhinitis, angioedema or urticaria) in response to aspirin or other NSAIDs.

Active or previous peptic ulcer.

History of upper gastrointestinal bleeding or perforation, related to previous NSAID therapy.

Use with concomitant NSAIDS including cycloxygenase-2 specific inhibitors (see section 4.5 Interactions).

Severe hepatic failure, renal failure or heart failure (see section 4.4, Special Warnings and Precautions for Use).

Last trimester of pregnancy (see section 4.6 Pregnancy and Lactation).

Severe heart failure.

4.4 Special warnings and precautions for use

Caution (discussion with doctor or pharmacist) is required prior to starting treatment in patients with a history of hypertension and/or heart failure as fluid retention, hypertension and oedema have been reported in association with NSAID therapy.

Undesirable effects may be minimised by using the lowest effective dose for the shortest duration necessary to control symptoms (see GI and cardiovascular risks below).

Cardiovascular and cerebrovascular effects

Clinical trial and epidemiological data suggest that use of ibuprofen, particularly at high doses (2400mg daily) and in long-term treatment may be associated with a small increased risk of arterial thrombotic events (for example myocardial infarction or stroke). Overall, epidemiological studies do not suggest that low dose ibuprofen (e.g. ≤ 1200mg daily) is associated with an increased risk of myocardial infarction.

Bronchospasm may be precipitated in patients suffering from, or with a previous history of, bronchial asthma or allergic disease.

The elderly are at increased risk of serious consequences of adverse reactions.

Systemic lupus erythematosus and mixed connective tissue disease – increased risk of aseptic meningitis (see section 4.8 Undesirable Effects).

Chronic inflammatory intestinal disease (ulcerative colitis, Crohn's disease)- as these conditions may be exacerbated (see section 4.8 Undesirable effects).

Hypertension and/or cardiac impairment since renal function may deteriorate and/or fluid retention occur.

Renal impairment as renal function may further deteriorate (see section 4.3 Contraindications and section 4.8 Undesirable effects).

Hepatic dysfunction (see section 4.3 Contraindications and section 4.8 Undesirable effects).

There is limited evidence that drugs which inhibit cyclo-oxygenase/prostaglandins synthesis may cause impairment of female fertility by an effect on ovulation. This is 7reversible on withdrawal of treatment.

Gastrointestinal bleeding, ulceration or perforation, which can be fatal, has been reported with all NSAID's at anytime during treatment, with or without warning symptoms or a previous history of serious gastrointestinal events.

Patients with a history of gastrointestinal toxicity, particularly when elderly, should report any unusual abdominal symptoms (especially gastrointestinal bleeding) particularly in the initial stages of treatment.

Caution should be advised in patients receiving concomitant medications which could increase the risk of gastrotoxicity or bleeding, such as corticosteroids, or anticoagulants such as warfarin or anti-platelet agents such as aspirin (see section 4.5 Interactions).

Where gastrointestinal bleeding or ulceration occurs in patients receiving ibuprofen, the treatment should be withdrawn.

The label will include:

Read the enclosed leaflet before taking this product

Do not take if you have or have ever had a stomach ulcer, perforation or bleeding or are allergic to ibuprofen or any of the ingredients of the product, aspirin or other related painkillers are taking other NSAID painkillers, or aspirin with a daily dose above 75 mg are in the last 3 months of pregnancy

Speak to your doctor or pharmacist before taking this product if you have asthma, liver, heart, kidney or bowel problems are in the first 6 months of pregnancy

If symptoms persist or worsen consult your doctor.

Do not exceed the stated dose.

Keep out of the reach and sight of children.

4.5 Interaction with other medicinal products and other forms of interaction

Ibuprofen (like other NSAIDs) should not be used in combination with:

aspirin unless low-dose aspirin (not above 75 mg daily) has been advised by a doctor, as this may increase the risk of adverse reactions (see section 4.3 Contraindications).

Other NSAIDs. This may result in an increased incidence of adverse reactions (see section 4.3 Contraindications).

Ibuprofen should be used with caution in combination with:

Antihypertensives and diuretics: NSAIDs may diminish the effects of these drugs.

Anti-coagulants. NSAIDs may enhance the effects of anticoagulants such as warfarin (see section 4.4 Special warnings).

Corticosteriods may increase the risk of adverse reactions in the gastrointestinal tract (see section 4.4 Special warnings).

Lithium: there is evidence for potential increases in plasma levels of lithium.

Methotrexate. There is a potential for an increase in plasma levels methotrexate.

Zidovudine: There is evidence of an increased risk of haemarthroses and haematoma in HIV (+) haemophiliacs receiving concurrent treatment with zidovudine and ibuprofen.

4.6 Pregnancy and lactation

Whilst no teratogenic effects have been demonstrated in animal experiments, the use of Nurofen during pregnancy should, if possible, be avoided during the first 6 months of pregnancy.

During the 3rd trimester, ibuprofen is contraindicated as there is a risk of premature closure of the foetal ductus arteriosus with possible persistent pulmonary hypertension. The onset of labour may be delayed and duration of labour increased with an increased bleeding tendency in both mother and child (see section 4.3 Contraindications).

In limited studies, ibuprofen appears in the breast milk in very low concentration and is unlikely to affect the breast-fed infant adversely.

See section 4.4 regarding female fertility.

4.7 Effects on ability to drive and use machines

None expected at recommended doses and duration of therapy.

4.8 Undesirable effects

Oedema, hypertension, and cardiac failure, have been reported in association with NSAID treatment.

Clinical trial and epidemiological data suggest that use of ibuprofen (particularly at high doses 2400mg daily) and in long-term treatment may be associated with a small increased risk of arterial thrombotic events (for example myocardial infarction or stroke) (see section 4.4).

Hypersensitivity reactions have been reported and these may consist of non-specific allergic reactions and anaphylaxis respiratory tract reactivity e.g. asthma, aggravated asthma, bronchospasm, dyspnoea various skin reactions e.g. pruritus, urticaria, angioedema and more rarely exfoliative and bullous dermatoses (including epidermal necrolysis and erythema multiforme)

The list of the following adverse effects relates to those experienced with ibuprofen at OTC doses, for short-term use. In the treatment of chronic conditions, under long-term treatment, additional adverse effects may occur.

Hypersensitivity Reactions	Uncommon:	Hypersensitivity reactions with urticaria and pruritus.
	Very rare:	Severe hypersensitivity reactions. Symptoms could be: facial, tongue and larynx swelling, dyspnoea, tachycardia, hypotension, (anaphylaxis, angioedema or severe shock).
		Exacerbation of asthma and bronchospasm.
Gastrointestinal Disorders	Uncommon:	Abdominal pain, dyspepsia and nausea.
	Rare:	Diarrhoea, flatulence, constipation and vomiting.
	Very rare:	Peptic ulcer, perforation or gastrointestinal haemorrhage, sometimes fatal, particularly in the elderly (see section 4.4 Special warnings). Exacerbation of ulcerative colitis and Crohn's disease (see section 4.4 Special warnings).
Nervous System	Uncommon:	Headache.
Renal	Very rare:	Acute renal failure, papillary necrosis, especially in long-term use, associated with increased serum urea concentrations and oedema.
Hepatic	Very rare:	Liver disorders.
Haematological	Very rare:	Haematopoietic disorders (anaemia, leucopenia, thrombocytopenia, pancytopenia, agranulocytosis). First signs are: fever, sore throat, superficial mouth ulcers, flu-like symptoms, severe exhaustion, unexplained bleeding and bruising.
Skin	Uncommon:	Various skin rashes.
	Very rare:	Severe forms of skin reactions such as erythema multiforme and epidermal necrolysis can occur.

Immune System	In patients with existing auto-immune disorders (such as systemic lupus erythematosus, mixed connective tissue disease) during treatment with ibuprofen, single cases of symptoms of aseptic meningitis, such as stiff neck, headache, nausea, vomiting, fever or disorientation have been observed (see section 4.4 Special warnings).

4.9 Overdose

In children ingestion of more than 400 mg/kg may cause symptoms. In adults the dose response effect is less clear cut. The half-life in overdose is 1.5 - 3 hours.

Symptoms – Most patients who have ingested clinically important amounts of NSAIDs will develop no more than nausea, vomiting, epigastric pain, or, more rarely, diarrhoea. Tinnitus, headache and gastrointestinal bleeding are also possible. In more serious poisoning, toxicity is seen in the central nervous system, manifesting as drowsiness, occasionally excitation and disorientation or coma. Occasionally patients develop convulsions. In serious poisoning, metabolic acidosis may occur and the prothrombin time/INR may be prolonged, probably due to interference with the actions of circulating clotting factors. Acute renal failure and liver damage may occur. Exacerbation of asthma is possible in asthmatics.

Management – Management should be symptomatic and supportive and include the maintenance of a clear airway and monitoring of cardiac and vital signs until stable. Consider oral administration of activated charcoal if the patient presents within 1 hour of ingestion of a potentially toxic amount. If frequent or prolonged, convulsions should be treated with intravenous diazepam or lorazepam. Give bronchodilators for asthma.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Ibuprofen is a propionic acid derivative NSAID that has demonstrated its efficacy by inhibition of prostaglandin synthesis. In humans, ibuprofen reduces inflammatory pain, swellings and fever. Furthermore, ibuprofen reversibly inhibits platelet aggregation.

ATC Code: M01A E01

5.2 Pharmacokinetic properties

Ibuprofen is well absorbed from the gastrointestinal tract. Ibuprofen is extensively bound to plasma proteins.

Peak serum concentration occurs approximately 1-2 hours after administration.

Ibuprofen is metabolised in the liver to two major metabolites with primary excretion via the kidneys, either as such or as major conjugates, together with a negligible amount of unchanged ibuprofen. Excretion by the kidney is both rapid and complete.

Elimination half-life is approximately 2 hours.

No significant differences in pharmacokinetic profile are observed in the elderly.

5.3 Preclinical safety data

There are no preclinical safety data of relevance to the consumer.

6.1. List of excipients

Tablet Core
Croscarmellose Sodium
Sodium Laurilsulfate
Sodium Citrate
Stearic Acid
Colloidal Anhydrous Silica

Sugar Coat Ingredients
Carmellose Sodium
Talc
Acacia Spray Dried
Sucrose
Titanium Dioxide
Macrogol 6000
Purified Water

Tablet Printing Ink
Opacode S-1-9460 HV Brown (solids)[1]
Industrial Methylated Spirit
[1] Opacode S-1-8152 HV Brown contains the following residual materials after application:

Shellac USNF 28.877%
Iron oxide red (E172) 25.000%
Soya lecithin 1.000%
Simethicone 0.005%

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 months.

6.4 Special precautions for storage

PVC blister pack only – Do not store above 30°C.

Store in the original pack.

PVC/PVDC Blister: Store in the original pack.

HDPE bottle: Store in the original pack.

6.5 Nature and contents of container

The tablets will be packed in blisters consisting of:

Push through laminate consisting of opaque, white 250 micron PVC heat-sealed to 20 micron aluminium foil

Or

Push through laminate consisting of opaque, white 250 micron PVC with 40 gsm PVdC, heat-sealed to 20 micron aluminium foil.

The blisters are contained in a cardboard carton.

2, 3, 4, 5, 8, 10, 12, 15, 16, 18, 20, 24, 28, 32 or 48 tablets. Not all packs will be marketed.

Or

High density polyethylene bottle with a child resistant cap that is internally wadded with expanded polyethylene. 96 tablets. Not all packs will be marketed.

6.6 Special precautions for disposal

Not applicable.

7 MARKETING AUTHORISATION HOLDER

Crookes Healthcare Limited

1 Thane Road West

Nottingham NG2 3AA

8 MARKETING AUTHORISATION NUMBER(S)

PL 00327/0184

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

20/02/2007

10 DATE OF REVISION OF THE TEXT

30/08/2007

PATIENT INFORMATION LEAFLET

NUROFEN®
EXTRA STRENGTH
400 mg Tablets
IBUPROFEN 400 mg

PLEASE READ ALL OF THIS LEAFLET CAREFULLY BEFORE YOU START TO TAKE YOUR MEDICINE. Keep this leaflet. You may want to read it again.

WHAT IS IN NUROFEN EXTRA STRENGTH 400 MG TABLETS

Each tablet contains the active ingredient Ibuprofen Ph Eur 400 mg.
They also contain: Sucrose, Sodium Citrate, Calcium Sulphate Dihydrate, Croscarmellose Sodium, Stearic Acid, Titanium Dioxide, Colloidal Anhydrous Silica, Acacia, Carmellose Sodium, Sodium Laurylsulphate, Carnauba Wax, Brown Ink, (contains Shellac, Iron Oxide Red, Soya Lecithin, Simeticone). Nurofen Extra Strength 400 mg Tablets are available in packs of 12, 24 and 48 tablets.

Licence holder and manufacturer:
Crookes Healthcare Limited, Nottingham NG2 3AA
Product Licence No:PL 00327/0184

HOW DO NUROFEN EXTRA STRENGTH 400 MG TABLETS WORK?

Nurofen Extra Strength 400 mg Tablets contain ibuprofen which belongs to a group of medicines known as non-steroidal anti-inflammatory drugs (NSAIDs). NSAIDs provide relief by changing the body's response to pain, swelling and high temperature.

Nurofen Extra Strength 400 mg Tablets are for the fast and effective relief of **headaches, backache, period pain, dental pain, neuralgia, rheumatic pain, muscular pain, migraine, cold and flu symptoms, feverishness and pain of non serious arthritic conditions.**

BEFORE YOU TAKE NUROFEN EXTRA STRENGTH 400 MG TABLETS:

Do not take Nurofen Extra Strength 400 mg Tablets if you:
- have or have ever had a stomach ulcer, perforation or bleeding
- are allergic to ibuprofen, to any of the ingredients, or to aspirin or other painkillers
- suffer from severe liver, kidney or heart problems
- are taking other NSAIDs pain killers or aspirin with a daily dose above 75 mg
- are in the last 3 months of pregnancy
- are under 12 years of age.

Ask your doctor before taking Nurofen Extra Strength 400 mg Tablets if:
- you have asthma or have suffered from asthma
- you have kidney, heart or liver or bowel problems
- have Systemic Lupus Erythematosus (SLE) - a condition of the immune system affecting connective tissue resulting in joint pains, skin changes and disorder of other organs
- you are taking any regular medication, especially:
  - if you are on low dose aspirin (up to 75 mg daily)
  - medicines for high blood pressure and water tablets (diuretics)
  - medicines for thinning the blood (anti-coagulants)
  - corticosteroids
  - Methotrexate
  - Lithium (used to treat depression)
  - Zidovudine (an anti-viral drug)
- you are in the first 6 months of pregnancy or breast-feeding.
- Nurofen belongs to a group of medicines which may impair fertility in women. This is reversible on stopping the medicine. It is unlikely that Nurofen, used occasionally, will affect your chances of becoming pregnant. However, tell your doctor before taking this medicine if you have problems becoming pregnant.

HOW TO TAKE NUROFEN EXTRA STRENGTH 400 MG TABLETS:
Adults the elderly and children of 12 years and older:
Swallow 1 tablet with water, then if necessary take 1 tablet every 4 hours.
Do not exceed 3 tablets in 24 hours.
Not suitable for children under 12 years.

WHILST TAKING NUROFEN EXTRA STRENGTH 400 MG TABLETS:
If you take too many tablets by mistake, talk to your doctor or pharmacist as soon as possible.
If symptoms persist or worsen, or if new symptoms occur, talk to your doctor or pharmacist. This product is intended for short-term use only. You should take the lowest dose for the shortest time necessary to relieve your symptoms. You should not take Nurofen Extra Strength 400 mg Tablets for longer than 10 days unless your doctor tells you to.
Side effects: Nurofen Extra Strength 400 mg Tablets are generally well tolerated by the majority of people, however, elderly patients are at increased risk of developing problems associated with side effects.

Disorders of the stomach and bowel including abdominal discomfort or pain, nausea, dyspepsia, indigestion, heartburn, diarrhoea, flatulence (wind), constipation, stomach ulcer, vomiting containing either blood or brown grit (like coffee grounds), pass blood in your stools or pass black tarry stools, worsening of existing bowel diseases (ulcerative colitis or Crohn's disease).

Blood disorders resulting in unexplained or unusual bruising or bleeding, fever, sore throat, mouth ulcers, extreme pallor or weakness.

Allergic reactions including worsening of asthma, unexplained wheezing or shortness of breath, swelling of the face and tongue, collapse. In addition, there may be skin reaction (including hives and itching): these can sometimes be severe with blistering and peeling of skin.

If you develop any of the symptoms above, stop taking the tablets and contact your doctor immediately.
Liver disorders that may be indicated by yellowing of the skin and eyes and/or pale stools and dark urine.
Kidney disorders that may be indicated by passing less or more urine than normal, cloudy urine, blood in the urine, pain in the back and/or swelling (particularly of the legs).
Nervous system disorders indicated by severe headaches, neck stiffness, disorientation, and light hurting the eyes.

If you experience any of these, or have any other unusual symptoms or concerns, stop taking the product and see your doctor.

HOW SHOULD NUROFEN EXTRA STRENGTH 400 MG TABLETS BE STORED?
Do not use after the expiry date shown on the pack.
Do not store above 30°C.
Store in the original packaging.
Remember: Keep all medicines out of the reach and sight of children.

HOW CAN YOU OBTAIN MORE INFORMATION ABOUT NUROFEN EXTRA STRENGTH 400 MG TABLETS?
This leaflet gives you the most important patient information about Nurofen Extra Strength 400 mg Tablets. If you have any questions after you have read it, ask your doctor or pharmacist, who will give you further information.

Date of revision September 2005.

CROOKES
HEALTHCARE

Crookes Healthcare Ltd. Nottingham NG2 3AA.

NNKE7

LABELLING


NUROFEN
EXTRA STRENGTH
400 mg Tablets
NUROFEN®
EXTRA STRENGTH
400 mg Tablets
Ibuprofen 400 mg
Easy to swallow tablets
Effective relief
12 tablets
TARGETED RELIEF FOR PAIN
NUROFEN
EXTRA STRENGTH
400 mg Tablets
NUROFEN
EXTRA STRENGTH
400 mg Tablets
0 000000 000000
NEW V1
LOT:
EXP:
DOSAGE:
Adults, the elderly and children 12 years and older: Swallow 1 tablet with water, then if necessary take 1 tablet every 4 hours.
Do not exceed 3 tablets in 24 hours.
Not suitable for children under 12 years.
If symptoms persist or worsen, or if new symptoms occur, consult your doctor or pharmacist.
DO NOT TAKE IF YOU:
have or have ever had a stomach ulcer, or perforation or bleeding of the stomach
are allergic to any of the ingredients or to aspirin or to other painkillers
suffer from severe liver, kidney or heart problems
are taking other NSAID painkillers, or aspirin with a daily dose above 75mg
are in the last 3 months of pregnancy
are under 12 years old
Speak to your doctor or pharmacist before taking the tablets if you
have asthma, liver, kidney, heart or bowel problems
are in the first 6 months of pregnancy
WARNING: Do not exceed the stated dose.
P
for short term use only. If you need to take it for more than 10 days talk to your doctor.
Croda Healthcare Ltd., Nottingham NG2 3AA
PL 00327/0184
CROOKES HEALTHCARE
Each tablet contains: Ibuprofen Ph.Eur 400 mg.
Store in the original pack.
Do not store above 30°C.
KEEP ALL MEDICINES OUT OF THE REACH AND SIGHT OF CHILDREN
Read the enclosed leaflet carefully before use.
FAST, EFFECTIVE RELIEF FROM:
headaches
period pain
dental pain
migraine
pain non-serious
arthritis
backache
muscular pain
rheumatic pain
neuralgia
cold & flu symptoms
feverishness
NUROFEN works where it's needed - at the site of pain. It quickly relieves pain, reduces inflammation and lowers temperature.
NUROFEN
EXTRA STRENGTH
400 mg Tablets


NUROFEN
EXTRA STRENGTH
400 mg Tablets
NUROFEN®
EXTRA STRENGTH
400 mg Tablets
Ibuprofen 400 mg
Easy to swallow tablets
Effective relief
24 tablets
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NUROFEN
EXTRA STRENGTH
400 mg Tablets
NUROFEN
EXTRA STRENGTH
400 mg Tablets
0 000000 000000
FAST, EFFECTIVE RELIEF FROM:
• headaches • pain non-serious • rheumatic pain
• period pain • arthritis • neuralgia
• dental pain • backache • cold & flu symptoms
• migraine • muscular pain • feverishness
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P
KWNS8
LOT:
EXP:


NUROFEN
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400 mg Tablets
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EXTRA STRENGTH
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Ibuprofen 400 mg
Easy to swallow tablets
Effective relief
48 tablets
TARGETED RELIEF FOR PAIN
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400 mg Tablets
NUROFEN
EXTRA STRENGTH
400 mg Tablets
0 000000 000000
NKXK9
LOT:
EXP:
DOSAGE:
DO NOT TAKE IF YOU:
WARNING: Do not exceed the stated dose.
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