IBUPROFEN 400MG TABLETS
PL 20395/0080
UKPAR

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The MHRA granted Relonchem Limited a Marketing Authorisation (licence) for the medicinal product Ibuprofen 400mg Tablets (PL 20395/0080) on 05 January 2011. This is a pharmacy (P) medicine used for the treatment of rheumatic or muscular pain, pain of non-serious arthritic conditions (characterized by pain and stiffness in your body), back pain, neuralgia (painful disorder of the nerves), headache including migraine, toothache, period pain, feverishness, and symptoms of colds and influenza.

Ibuprofen belongs to the group of medicines called non-steroidal anti-inflammatory drugs (NSAIDS). These drugs are painkillers and reduce inflammation.

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

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INTRODUCTION

The UK granted a Marketing Authorisation for the medicinal product Ibuprofen 400mg tablets (PL 20395/0080) to Relonchem Limited on 05 December 2010. The product is available as a pharmacy (P) medicine and is indicated for the treatment of rheumatic or muscular pain, pain of non-serious arthritic conditions, backache, neuralgia, migraine, headache, dental pain, dysmenorrhoea, feverishness and symptoms of colds and influenza.

The application was submitted as a simple abridged application according to Article 10c of Directive 2001/83/EC, as amended, cross-referring to Ibuprofen Tablets 400mg (PL 19348/0004), which is currently authorised to LPC Medical (UK) Limited after a change in authorisation holder on 08 July 2002. The reference product was originally granted to OBG Pharmaceutical on 07 April 1998.

Ibuprofen belongs to the class of medicines known as non-steroidal anti-inflammatory drugs (NSAIDs). These are effective in relieving pain that occurs in association with relatively common complaints such as influenza, soft tissue injuries and inflammatory conditions affecting joints and tendons. NSAIDs exert analgesic, antipyretic and anti-inflammatory effects, without affecting the underlying pathology to any extent. The anti-inflammatory action of ibuprofen is thought to be due to the peripheral inhibition of prostaglandin synthesis, whilst the analgesic effect results from central and peripheral actions of the S-form.

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.
PHARMACEUTICAL ASSESSMENT

LICENCE NO: PL 20395/0080
PROPRIETARY NAME: Ibuprofen 400mg Tablets
ACTIVE(S): Ibuprofen
COMPANY NAME: Relonchem Ltd
E.C. ARTICLE: Article 10c of Directive 2001/83/EC
LEGAL STATUS: P

1. INTRODUCTION
This is a simple, piggyback application for Ibuprofen 400mg tablets, submitted under Article 10c of Directive 2001/83/EC, as amended. The proposed Marketing Authorisation Holder is Relonchem Limited, 27 Old Gloucester Street, London, WC1 3XX, United Kingdom.

The application cross-refers to Ibuprofen Tablets 400mg (PL 19348/0004), which is currently authorised to LPC Medical (UK) Limited after a change in authorisation holder on 08 July 2002. The reference product was originally granted to OBG Pharmaceutical on 07 April 1998. The current application is considered valid.

2. MARKETING AUTHORISATION APPLICATION FORM
2.1 Name(s)
The proposed name of the product is Ibuprofen 400mg Tablets. The product has been named in line with current requirements.

2.2 Strength, pharmaceutical form, route of administration, container and pack sizes
Each tablet contains 400mg ibuprofen. The tablets are packaged in either:
1. white polvinylchloride/aluminium blisters, in pack sizes of 12, 21, 24, 28, 48, 56, 84, 96 and 100 tablets.
2. polypropylene containers with a low-density polyethylene tamper-evident lid, in pack sizes of 21, 100, 250, 500 and 1000 tablets.
3. polyethylene (free from additives) bags in pack sizes of 5,000 and 10,000 tablets for bulk supply

The proposed shelf-life (3 years for the blister pack and 2 years for the tablet container) and storage conditions (“Do not store above 25ºC. Store in original container/outer carton”) are consistent with the details registered for the cross-reference product.

2.3 Legal status
On approval, the product will be available as a pharmacy medicine (P).

2.4 Marketing Authorisation Holder/Contact Persons/Company
Relonchem Limited, 27 Old Gloucester Street, London, WC1 3XX, United Kingdom.

The Qualified Person (QP) responsible for pharmacovigilance is stated and his CV is included.
2.5 Manufacturers
The proposed manufacturing sites are consistent with those registered for the cross-reference product 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 cross-reference product.

2.7 Manufacturing process
The proposed manufacturing process is consistent with the details registered for the cross-reference product and the maximum batch size is stated.

2.8 Finished product/shelf-life specification
The proposed finished product specification is in line with the details registered for the cross-reference product.

2.9 Drug substance specification
The proposed drug substance specification is consistent with the details registered for the cross-reference product.

2.10 TSE Compliance
None of the excipients contain materials of animal or human origin. This is consistent with the cross-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 and utilising the same process as the reference product Ibuprofen Tablets 400mg (PL 19348/0004).

3. EXPERT REPORTS
The applicant cross-refers to the data for Ibuprofen Tablets 400mg (PL 19348/0004), to which it claims identiciality. This is acceptable.

4. PRODUCT NAME & APPEARANCE
See 2.1 for details of the proposed product name. The appearance of the product is identical to the cross-reference product.

5. SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)
The proposed Summary of Product Characteristics is consistent with the details registered for the cross-reference product.

6. PATIENT INFORMATION LEAFLET (PIL) AND LABELLING
PIL
The patient information leaflet has been prepared in-line with the details registered for the cross-reference product.

LPC Medical (UK) Limited has previously submitted results of consultations with target patient groups (“user testing”), in accordance with Article 59 of Council Directive
2001/83/EC, for the reference product Ibuprofen Tablets 400mg (PL 19348/0004). The results indicate that the leaflet is well-structured and organised, easy to understand, and written in a comprehensive manner. The test shows that the patients/users are able to act upon the information that it contains.

As the leaflet for Ibuprofen Tablets 400mg (PL 19348/0004) and this product are considered the same, no further user testing of the leaflet for this product is necessary.

**Carton and blister**
The proposed artwork is consistent with the artwork registered for the cross-reference product and complies with statutory requirements. In line with current legislation, the applicant has also included the name of the product in Braille on the outer packaging and has included sufficient space for a standard UK pharmacy dispensing label.

7. **CONCLUSION**
The data submitted with the application are acceptable. The grant of a Marketing Authorisation is recommended.
NON CLINICAL ASSESSMENT

As this is an abridged simple application, no new non-clinical data have been supplied and none are required.

The Marketing Authorisation Holder has provided adequate justification for not submitting an Environment Risk Assessment (ERA). As the application is for an identical version of an already authorised product, it is not expected that environmental exposure will increase following approval of the marketing authorisation for the proposed product.

The grant of a Marketing Authorisation is recommended.
CLINICAL ASSESSMENT

As this is an abridged simple application, no new clinical data have been supplied and none are required.

The Marketing Authorisation Holder has provided details of a suitable pharmacovigilance system that fulfils the requirements and provides adequate evidence that they have the services of a qualified person responsible for pharmacovigilance, and have the necessary means for the notification of any adverse reaction suspected of occurring either in the Community or in a third country.

The Marketing Authorisation Holder has not submitted a Risk Management Plan (RMP). As the application is for an identical version of an already authorised reference product, for which safety concerns requiring additional risk minimisation have not been identified, a risk minimisation system is not considered necessary. The reference product has been in use for many years and the safety profile of the active ingredient is well-established.

The grant of a Marketing Authorisation is recommended.
OVERALL CONCLUSION AND BENEFIT/RISK 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 an application of this type.

EFFICACY
This application is identical to a previously granted application for Ibuprofen Tablets 400mg (PL 19348/0004). No new or unexpected safety concerns arise from this application.

PRODUCT LITERATURE
The SmPC, PIL and labelling are satisfactory and consistent with that for the cross-reference product.

BENEFIT/RISK ASSESSMENT
The quality of the product is acceptable, and no new non-clinical or clinical safety concerns have been identified. The applicant’s product is identical to the cross-reference product. Extensive clinical experience with ibuprofen is considered to have demonstrated the therapeutic value of the compound. The benefit/risk is, therefore, considered to be positive.
IBUPROFEN 400MG TABLETS
PL 20395/0080

STEPS TAKEN FOR ASSESSMENT

1 The MHRA received the marketing authorisation application on 14 June 2010.
2 Following standard checks and communication with the applicant the MHRA considered the application valid on 19 August 2010.
3 Following assessment of the application the MHRA requested further information relating to the dossier on 20 August 2010, 05 October 2010 and 12 October 2010.
4 The applicant responded to the MHRA’s request, providing further information on 25 August, 07 October 2010 and 23 November 2010.
5 The application was determined on 05 January 2011.
SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT
Ibuprofen 400mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Ibuprofen 400mg
For excipients, see 6.1

3 PHARMACEUTICAL FORM
Film coated tablet (tablet) / Pink biconvex film coated tablets marked with ‘‘RC’’ on one side and ‘’400’’ on the other.

4 CLINICAL PARTICULARS
4.1 Therapeutic indications
Rheumatic or muscular pain, pain of non-serious arthritic conditions, backache, neuralgia, migraine, headache, dental pain, dysmenorrhoea, feverishness and symptoms of colds and influenza.

4.2 Posology and method of administration
For oral administration and short term use only.

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

Adults, the elderly and children over 12 years: One tablet with water up to three times a day, as required. Take with or after food. Leave at least 4 hours between doses and do not take more than three tablets in any 24 hour period.

Children: Not to be administered to children under 12 years

4.3 Contraindications
Hypersensitivity to Ibuprofen or any of the constituents in the product.

Previous hypersensitivity reactions (e.g. asthma, rhinitis, angioedema or urticaria) in response to aspirin or other non-steroidal anti-inflammatory drugs.

Active or previous peptic ulcer.

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

Use with concomitant NSAIDs including cyclo-oxygenase-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).

Bleeding disorders.

Severe heart failure.

4.4 Special warnings and precautions for use
Undesirable effects may be minimized by using the lowest effective dose for the shortest duration necessary to control symptoms (see GI and cardiovascular risks below).

The elderly have an increased frequency of adverse reactions to NSAID’s especially gastrointestinal bleeding and perforation which may be fatal.
Respiratory:
Bronchospasm may be precipitated in patients suffering from or with a previous history of bronchial asthma or allergic disease.

Other NSAIDs:
The use of Ibuprofen 400mg Tablets with concomitant NSAIDs including cyclooxygenase-2-selective inhibitors should be avoided.

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

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

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

Cardiovascular and cerebrovascular effects:
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.

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.

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

Gastrointestinal:
NSAIDs should be given with care to patients with a history of gastrointestinal disease (ulcerative colitis, Crohn’s disease) – as these conditions may be exacerbated (see section 4.8 Undesirable effects).

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

The risk of GI bleeding, ulceration or perforation is higher with increasing NSAID doses, in patients with a history of ulcer, particularly if complicated with haemorrhage or perforation (see section 4.3 Contraindications) and in the elderly. These patients should commence treatment on the lowest dose available.

Patients with a history of GI toxicity, particularly when elderly, should report any unusual abdominal symptoms (especially GI 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 oral corticosteroids, or anticoagulants such as warfarin, selective serotonin reuptake inhibitors, or anti-platelet agents such as aspirin (see section 4.5 Interactions).

Where GI bleeding or ulceration occurs in patients receiving ibuprofen, the treatment should be withdrawn.
**Dermatological:**
Serious skin reactions, some of them fatal, including exfoliative dermatitis, Stevens-Johnson syndrome and toxic epidermal necrolysis, have been reported very rarely in association with the use of NSAIDs (see section 4.8 Undesirable Effects). Patients appear to be at highest risk for these reactions early in the course of therapy: the onset of the reaction occurring in the majority of cases within the first month of treatment. Ibuprofen 400mg Tablets should be discontinued at the first appearance of skin rash mucosal lesions, or any other sign of hypersensitivity.

*The label will include:*
Please read the enclosed leaflet carefully before use.

**Do not take if you:**
- have or have had a stomach ulcer, perforation or bleeding of the stomach
- are allergic to ibuprofen or any other ingredient of the product, aspirin or other related painkillers
- are taking other NSAID painkillers, or aspirin with a daily dose above 75mg

If you are pregnant do not take this product and ask your doctor for advice

**Talk to a pharmacist or your doctor before taking this product if you:**
- are elderly
- have or have had asthma, diabetes, high cholesterol, high blood pressure, a stroke, heart, liver, kidney, stomach or bowel problems
- are a smoker

Do not exceed the stated dose. Keep all medicines out of the reach and sight of children. If symptoms persist or worsen, consult your doctor.

**4.5 Interaction with other medicinal products and other forms of interaction**
Ibuprofen should not be used in combination with:

*Aspirin:* Unless low-dose aspirin (not above 75 mg) has been advised by a doctor, as this may increase the risk of adverse effects (see section 4.3 Contraindications)

*Other NSAIDS:* As these may increase the risk of adverse effects (see section 4.3 Contraindications)

Ibuprofen should be used with caution in combination with:

*Anticoagulants:* NSAIDs may enhance the effects of anticoagulants, such as warfarin (See section 4.4 Special warnings and precautions)

*Antihypertensives and diuretics:* NSAIDs may diminish the effect of these drugs. Diuretics can increase the risk of nephrotoxicity of NSAIDs.

*Aminoglycosides:* Increased renal toxicity has been reported in patients receiving concomitant ibuprofen and aminoglycoside therapy.

*Cardiac Glycosides:* NSAIDs may exacerbate heart failure, reduce GFR and increase plasma cardiac glycoside concentration.

*Ciclosporin:* Increased risk of nephrotoxicity.

*Corticosteroids:* 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.

Mifepristone: NSAIDs shouldn’t be used for 8-12 days after mifepristone administration as NSAIDs can reduce the effect of mifepristone.

*Methotrexate:* There is potential for an increase in plasma methotrexate.
**Phenytoin Sodium:** Phenytoin concentration and toxicity have been increased by Ibuprofen.

**Tacrolimus:** Possible increased risk of nephrotoxicity when NSAIDs are given with tacrolimus.

**Zidovudine:** Increased risk of haematological toxicity when NSAIDs are given with zidovudine. There is evidence of an increased risk of haemarthroses and haematoma in HIV(+) haemophiliacs receiving concurrent treatment with zidovudine and ibuprofen.

**Quinolone antibiotics:** Animal data indicate that NSAIDs can increase the risk of convulsions associated with quinolone antibiotics. Patients taking NSAIDs and quinolones may have an increased risk of developing convulsions.

**4.6 Pregnancy and lactation**

Whilst no teratogenic effects have been demonstrated in animal experiments, the use of Ibuprofen 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 the duration 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.

See section 4.4 regarding female fertility.

**4.7 Effects on ability to drive and use machines**

None at the recommended doses and duration of therapy.

**4.8 Undesirable effects**

Hypersensitivity reactions have been reported and these may consist of:

a) Non-specific allergic reactions and anaphylaxis
b) Respiratory tract reactivity, e.g. asthma, aggravated asthma, bronchospasm, dyspnoea
c) Various skin reactions, e.g. pruritus, urticaria, angiodema and more rarely exfoliative and bullous dermatoses (including epidermal necrolysis, erythema multiforme).

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

**Gastrointestinal**

The most commonly-observed adverse events are gastrointestinal in nature.

Uncommon: abdominal pain, nausea and dyspepsia.

Rare: diarrhoea, flatulence, constipation and vomiting.

Very rare: peptic ulcer, perforation or gastrointestinal haemorrhage, sometimes fatal, particularly in the elderly. Exacerbation of ulcerative colitis and Crohn’s disease (see section 4.4).

**Nervous/Psychiatric disorders**

Uncommon: headache, dizziness, nervousness, depression, drowsiness and insomnia.

Very rare: Aseptic meningitis – single cases have been reported very rarely.

**Renal**

Very rare: acute renal failure, interstitial nephritis, nephrotic syndrome, papillary necrosis, especially in long term use, associated with increased serum urea and oedema. Haematuria.

Fluid retention may rarely precipitate congestive heart failure in elderly patients.

**Hepatic**

Very rare: liver disorders, abnormalities of liver function tests.
**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 (see Immune system)

Very rare: severe forms of skin reaction such as erythema multiforme and epidermal necrolysis can occur.

**Hypersensitivity reactions**

Uncommon: hypersensitivity reactions with urticaria and pruritis.

Very rare: severe hypersensitivity reactions. Symptoms could be: facial, tongue and laryngeal swelling, dyspnoea, tachycardia, hypotension (anaphylaxis, angioedema or severe shock).

Exacerbation of asthma and bronchospasm.

**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).

**Other**

Rare: vertigo, tinnitus.


In the treatment of chronic conditions, under long term use, additional adverse effects may occur.

**Cardiovascular and cerebrovascular:**

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).

**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
Pharmacotherapeutic group: Anti-inflammatory and anti-rheumatic products, nonsteroids, propionic acid derivatives. ATC code: MO1AE

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

5.2 Pharmacokinetic properties
Ibuprofen is rapidly absorbed following administration and is rapidly distributed throughout the whole body. The excretion is rapid and complete via the kidneys.

Maximum plasma concentrations are reached 45 minutes after ingestion if taken on an empty stomach. When taken with food, peak levels are observed after 1-2 hours. These times may vary with different dosage forms.

The half-life of ibuprofen is about 2 hours.

In limited studies, ibuprofen appears in the breast milk in very low concentrations.

5.3 Preclinical safety data
Ibuprofen has been used in general medicine over a long period exceeding 20 years.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients
Cores:
- Pregelatinised starch
- Maize starch
- Colloidal anhydrous silica
- Magnesium stearate

Coating:
- Hypromellose
- Macrogol 6000
- Erythrosine lake E127
- Titanium dioxide E171
- Docusate Sodium

6.2 Incompatibilities
None known

6.3 Shelf life
3 years (Blister)
2 years (container)

6.4 Special precautions for storage
Do not store above 25°C. Store in original container/outer carton.

6.5 Nature and contents of container
Tablet containers:
Pack sizes: 21, 100, 250, 500 and 1000 tablets
Packaging composition: Polypropylene container with a low density polyethylene tamper evident lid

Blisters Packs:
Pack sizes: 12, 21, 24, 28, 48, 56, 84, 96 and 100
Packaging composition: White rigid PVC and 20um aluminium foil.
Bags:
Pack sizes: 5,000 and 10,000 tablets for bulk supply
Packaging composition: Polyethylene free from additives
6.6 Special precautions for disposal
N/A

7 MARKETING AUTHORIZATION HOLDER
Relonchem Limited
27, Old Gloucester Street
London
WC1 3XX

8 MARKETING AUTHORIZATION NUMBER(S)
PL 20395/0080

9 DATE OF FIRST AUTHORIZATION/RENEWAL OF THE AUTHORIZATION
05/01/2011

10 DATE OF REVISION OF THE TEXT
08/02/2011
PATIENT INFORMATION LEAFLET

IBUPROFEN 400mg TABLETS
Ibuprofen

PACKAGE LEAFLET: INFORMATION FOR THE USER

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 has been prescribed 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 effect not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:
1. What Ibuprofen Tablets are and what they are used for
2. Before you take Ibuprofen Tablets
3. How to take Ibuprofen Tablets
4. Possible side effects
5. How to store Ibuprofen Tablets
6. Further information

1. WHAT IBUPROFEN TABLETS ARE AND WHAT THEY ARE USED FOR

The name of your medicine is Ibuprofen 400mg Tablets. They contain the active ingredient called ibuprofen.

Ibuprofen belongs to the group of medicines called non-steroidal anti-inflammatory drugs (NSAIDs). These drugs are painkillers and reduce inflammation.

Ibuprofen 400mg Tablets are used for:
• Rheumatic or muscular pain
• Pain of non-serious arthritic conditions (characterized by pain and stiffness in your body)
• Back pain
• Neuralgia (painful disorder of the nerves)
• Headache including migraine
• Toothache
• Period pain
• Feverishness
• Symptoms of cold & influenza

2. BEFORE YOU TAKE IBUPROFEN TABLETS

Do not take Ibuprofen Tablets if you:
• are allergic (hypersensitive) to ibuprofen or any of the other ingredients of Ibuprofen Tablets. See section 6.
• are allergic to Aspirin or other NSAIDs, like cyclooxygenase-2 specific inhibitor.
• suffer from asthma, especially if you also have frequent stuffy or runny nose or swelling of the inside of the nose.
• have swelling of the hands, arms, feet, ankles, or lower legs.
• develop hives (red and sometimes itchy bumps) on your skin after taking this medicine. Aspirin or any other NSAIDs.
• suffer from severe liver, kidney or heart disease.
• if you currently have an active ulcer or a history of recurrent peptic ulcers (more than five in your stomach or duodenum).
• have ever had bleeding in your digestive tract.
• get blurred or poorer vision, blind spots, or changes in colour vision
• if you are in the last three months of pregnancy.

Take special care with Ibuprofen Tablets if you:
• have a previous history of bronchial asthma or allergic disease
• suffer from high blood pressure
• have ever had Crohn’s disease (inflammation of the digestive system) or ulcerative colitis (disease that causes ulcers in the lining of the rectum and colon)
• have or ever had lupus (a condition in which the body attacks many of its own tissues and organs, often including the skin, joints, blood, and kidneys)
• are having surgery, including dental surgery
• are taking more than 75mg Aspirin daily
• Medicines such as Ibuprofen Tablets may be associated with a small increased risk of heart attack (“myocardial infarction”) or stroke. Any risk is more likely with high doses and prolonged treatment. Do not exceed the recommended dose or duration of treatment. If you have heart problems, previous stroke or think that you might be at risk of these conditions (for example if you have high blood pressure, diabetes or high cholesterol or are a smoker), you should discuss your treatment with your doctor or pharmacist.

Taking other medicines
You should tell your doctor if you are taking or have taken any of the following medicines as they may interact with Ibuprofen Tablets.

Examples of medicines that can affect Ibuprofen Tablets are:
• any other anti-inflammatory painkillers
• Aspirin
• antibiotics (e.g. tetracyclines, Quinolones)
• medicines for high blood pressure
• diuretics (water tablets)
• ß-blockers (cardioselective)
• Lithium to stabilise, normalise or even out mood swings
• Methotrexate to treat cancer and auto immune diseases
• Ciclosporin to dampen down the body’s immune reactions
• Mifepristone used to induce abortion in first two months of pregnancy
• Corticosteroids
• Warfarin, to prevent blood clots
• Ciprofloxacin - antibiotics called quinolones
• Tacrolimus to prevent rejection of liver transplants
• Phenytoin to treat epilepsy
• Zidovudine to treat human immunodeficiency virus (HIV) infection

Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without prescription.

Pregnancy and breastfeeding
Ibuprofen belongs to a group of medicines which may impair fertility in women. This effect is reversible on stopping the medicine. It is unlikely that Ibuprofen, used occasionally, will affect your chances of becoming pregnant, however, if you tell your doctor before taking this medicine if you have problems becoming pregnant. Do not take this medicinal product if you are in the last three months of pregnancy.

Consult your doctor if you are pregnant, you plan to become pregnant, or you are breastfeeding. If you become pregnant while taking Ibuprofen, call your doctor. Ask your doctor or pharmacist for advice before taking any medicine.

3. HOW TO TAKE IBUPROFEN TABLETS

Always take Ibuprofen Tablets exactly as your doctor or pharmacist has told you. You should check with your doctor or pharmacist if you are not sure. Swallow the tablets with water during or after meals.

The usual dose is:
• Adults, the elderly and children over 12 years: The starting dose is 1 tablet 3 times a day, as required. Leave at least four hours between doses and do not take more than three tablets in
any 24 hour period. The risk of side effects is greater in the elderly, so your doctor will give you the lowest dose possible, and take special care of you.

Children below 12 years: Not recommended.

Ibuprofen Tablets are for short term use only. Take the lowest dose for the shortest time necessary to relieve your symptoms. Do not take ibuprofen for longer than 10 days.

Ibuprofen may be associated with a small increased risk of heart attack ("myocardial infarction") or stroke. Any risk is more likely with high doses and prolonged treatment. Do not exceed the recommended dose or duration of treatment.

If you take more Ibuprofen Tablets than you should
If you or someone you know accidentally takes a lot more than the stated dose (an overdose), you should contact a doctor immediately or go to the nearest A&E department.

If you forget to take Ibuprofen Tablets
If you forget to take a dose, take it as soon as you remember unless it is almost time for your next dose. Do not take a double dose to make up for a forgotten tablet.

4. POSSIBLE SIDE EFFECTS

Like all medicines, Ibuprofen Tablets can cause side effects, although not everybody gets them.

If any of the following happens, STOP TAKING Ibuprofen Tablets and tell your doctor immediately or go to the nearest hospital emergency department:
- Rare allergic (hypersensitive) reactions such as difficulty of breathing, wheezing or dizziness
- Skin reactions including palling of skin, rash, itching, hives, blisters, blood spots, swelling of the skin with wheals and, less often, blistering skin diseases which may appear like a burn, or as a red-purple rash, or a scaly skin
- Asthma attacks (condition that affects the airways of the lungs causing breathing difficulties) or worsening of asthma
- Sensitivity to light
- Stomach ulcers, bleeding, or holes in the stomach or intestine, High blood pressure, Fluid retention (particularly in the elderly), vomiting a substance that is bloody or looks like coffee grounds, blood in the stool, or black and tarry stools. The risk may be higher for people who are older in age.
- Pass blood in your faeces (bowels motions)
- Pass black tarry stools
- Vomit blood or any dark particles that look like coffee grounds

STOP TAKING the medicine if you experience: indigestion or heartburn, abdominal pain (pains in stomach) or other abnormal stomach symptoms.

- Common (occurring in less than 1 in 10 patients)
  - Nausea, Vomiting
  - Gastro-intestinal:
  - Indigestion, Gas or Bloating, Constipation, Pain in abdomen or Upset stomach
- Uncommon (occurring in less than 1 in 100 patients)
  - Effects on kidney: Inflammation of kidney tissue, kidney disorder causing them to leak large amounts of protein from the blood into the urine, kidney failure, appearance of blood in the urine.
- Effects on Liver: Abnormal liver function tests, swelling of the liver that makes it stop working well (hepatitis) and yellowing of skin and the whites of your eyes (jaundice)
- Effects on Nervous system and special senses:
- Visual problems
- Inflammation of eye nerve
- Headache
- Feeling of burning, itching, prickling or tingling in the skin
- Aseptic Inflammation of the lining of the brain (With symptoms such as stiff neck, headache, nausea, vomiting, fever or disorientation) especially in patients with diseases like lupus erythematosus (a condition in which immune system attacks healthy cells and tissues of many parts of the body), mixed connective tissue disease (overlap disease)
- Nervousness, Depression, Confusion, Hallucinations
- Ringing in the ears
- Light-headedness (loss of balance)
- Feeling of general discomfort or uneasiness
- Sleeplessness
- Excessive Tiredness
- Drowsiness
- Effects on blood:
- Low platelet count
- Effective blood cell counts
- Failure of the bone marrow to produce sufficient blood cells for the circulation (Aplastic anaemia)
- Abnormal breakdown of red blood cells

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 IBUPROFEN TABLETS

Keep out of the reach and sight of children.

Do not store the tablets above 25°C. Keep them in the original pack.

Do not take these tablets after the expiry date shown on the pack.

The expiry date refers to the last day of that month.

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

6. FURTHER INFORMATION

What Ibuprofen Tablets contain:

The active substance is Ibuprofen. The other ingredients are Pregelatinised Starch, Methacrylates, Colloidal Aqueous Silica, Magnesium Stearate, Hydroxypropyl Methylcellulose, Erythrosine (E 127), Titanium Dioxide (E 171) and Docusate Sodium.

What Ibuprofen Tablets look like and contents of the pack:

Ibuprofen 400mg Tablets are pink, biconvex, film-coated tablets with “i 400” on one side and “RC” on the other and packed in tablet containers of 21, 100, 250, 500, 1000 and blister packs of 12, 21, 24, 28, 48, 56, 94, 96, 100.

Marketing Authorisation Holder and Manufacturer:

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27 Old Treasurer Street
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PL 20395/0080

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MHRA PAR – Ibuprofen 400mg Tablets (PL 20395/0080) - 20 -
LABELLING

For the relief of rheumatic or muscular pain, pain of non-serious arthritic conditions, headache, neuralgia, migraine, headache, dental pain, period pain, feverishness and symptoms of cold and influenza.

Each film-coated tablet contains 400mg Ibuprofen. Also contains Erythrosine (E127) and Titanium Dioxide (E171).

DOSE:
Adults: the elderly and children over 12 years: 1 tablet with water up to three times a day, as required.
Take with or after food. Leave at least 4 hours between doses and do not take more than 3 tablets in any 24 hour period.
If symptoms persist or worsen, consult your doctor.
Not to be administered to children under 12 years.
Do not exceed the stated dose.
- Read the package leaflet before use.
- Do not store above 25°C.
- Store in the original package.

KEEP OUT OF THE REACH AND SIGHT OF CHILDREN
Ibuprofen 400 mg Tablets

For the relief of rheumatic or muscular pain, pain of non-serious arthritic conditions, headache, menstrual, migraine, backache, dental pain, period pain. Swellings and symptoms of colds and influenza.

Directions:
- Adults: Take 1 tablet every 4–6 hours as required up to a maximum of 4 tablets per day.
- Elderly and children: Take 1 tablet every 6–8 hours as required up to a maximum of 2 tablets per day.
- Do not exceed the recommended dosage.
- If symptoms persist for more than 5 days, consult your doctor.
- Not for administration to children under 13 years.
- Keep out of reach and sight of children.

KEEP OUT OF THE REACH AND SIGHT OF CHILDREN
Marketing Authorisation Holder: Relonchem Limited, PL 20395/0080
27 Old Gloucester Street, London WC1X 3QZ, UK.

Manufactured by: Relonchem Limited, PL 20395/0080
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