IBUPROFEN 200MG COATED TABLETS

PL 22958/0002

UKPAR

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IBUPROFEN 200MG COATED TABLETS

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LAY SUMMARY

The MHRA granted East Midlands Pharma Limited a Marketing Authorisation (licence) for the medicinal product Ibuprofen 200mg Coated Tablets (PL 22958/0002) on 31st May 2006. This medicine is used for the relief of rheumatic or muscular pain, backache, neuralgia, migraine, headache, dental pain, period pain, feverishness and the symptoms of colds and influenza. This medicinal product is available over the counter.

Ibuprofen tablets contain the active ingredient ibuprofen, which is a painkiller, reduces temperature and has anti-inflammatory properties.

This application is a Change of Ownership Application from Natural Health Options Health Products (Pl 18284/0003) which was a duplicate of a previously granted application, which has since been cancelled, for Sussex Ibuprofen Tablets BP 200mg (PL 05544/0092). This product was itself identical to the previously licensed product, Ibuprofen Tablets BP 200 mg (PL 05544/0065).

No new or unexpected safety concerns arose from this simple application and it was, therefore, judged that the benefits of taking Ibuprofen 200mg Coated Tablets outweigh the risks, hence a Marketing Authorisation has been granted.

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SCIENTIFIC DISCUSSION

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INTRODUCTION

The UK granted a marketing authorisation for the medicinal product Ibuprofen 200mg Coated Tablets (PL 22958/0002) to East midlands Pharma Ltd on 31st May 2006. This medicinal product is available as GSL.

The application was submitted according to article 10.1(a)(i) of Directive 2001/83/EC, cross-referring to Sussex Ibuprofen tablets BP 200mg (PL 05544/0092), which was granted a marketing authorisation on 2nd July 1997 and was subsequently cancelled. The referenced marketing authorisation was itself identical to Ibuprofen Tablets BP 200 mg (PL 05544/0065) granted on 25/10/1984.

No new data was submitted nor was it necessary for this simple application, as the data is identical to that 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 was generated for it.

The product contains the active ingredient ibuprofen which is an analgesic, antipyretic and has anti-inflammatory properties. Ibuprofen tablets are indicated for the relief of rheumatic or muscular pain, backache, neuralgia, migraine, headache, dental pain, dysmenorrhoea, feverishness, symptoms of colds and influenza.

PHARMACEUTICAL ASSESSMENT

INTRODUCTION

This is an abridged application made under Article 10.1(a)(i) of EC Directive 2001/83 and is considered to be an identical product to that of PL 05544/0092 (Sussex Ibuprofen tablets BP 200mg). The licence was held by Sussex Pharmaceuticals Ltd, granted 2nd July 1997. The licence has since been cancelled.

EXPERT REPORTS

Satisfactory statements provided.

PRODUCT LITERATURE

1. SUMMARY OF PRODUCT CHARACTERISTICS (SPC)

The SPC supplied is satisfactory and consistent with the cross-reference product.

2. LABELLING

The label supplied is satisfactory and consistent with the cross-reference product.

3. PATIENT INFORMATION LEAFLET (PIL)

The PIL supplied is satisfactory and consistent with the cross-reference product.

4. MARKETING AUTHORISATION APPLICATION (MAA)

The MAA form is satisfactory and consistent with the cross-reference product.

RECOMMENDATION

Grant of a Marketing Authorisation is acceptable.

PRECLINICAL ASSESSMENT

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

CLINICAL ASSESSMENT

As this is a duplicate application for PL 05544/0092, no new clinical data have been supplied and none are required.

OVERALL CONCLUSION AND RISK BENEFIT ASSESSMENT

QUALITY

The data for this application is consistent with that previously assessed for the cross-reference product and as such has been judged to be satisfactory.

PRECLINICAL

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

EFFICACY

Ibuprofen is a well known drug and has been used as an analgesic, antipyretic and anti-inflammatory for many years. This application is identical to the previously approved marketing authorisation for Sussex Ibuprofen tablets BP 200mg (PL 05544/0092).

No new or unexpected safety concerns arise from this application.

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

RISK BENEFIT ASSESSMENT

The quality of the product is acceptable and no new preclinical or clinical safety concerns have been identified. Extensive clinical experience with ibuprofen is considered to have demonstrated the therapeutic value of the compound. 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 for PL 18284/0003 on 04/02/2004.
2	Following standard checks and communication with the applicant the MHRA considered the application valid on 17/02/2004.
3	Following assessment of the application the MHRA requested further information on 04/11/2004, 05/07/2005, 07/12/2005 and 20/01/2006.
4	The applicant responded to the MHRA's requests, providing further information on 06/06//2005, and 30/01/2006.
5	The application subsequently went through a Change of Ownership and was granted on 31/05/2006.

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STEPS TAKEN AFTER ASSESSMENT

Date submitted	Application type	Scope	Outcome

IBUPROFEN 200MG COATED TABLETS

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SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Ibuprofen 200mg Coated Tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 200mg Ibuprofen
Also contains lactose monohydrate and sucrose as excipients.

For full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Coated tablet
White shiny sugar coated round tablets.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

Adults, elderly and children over 12 years:
Rheumatic or muscular pain, backache, neuralgia, migraine, headache, dental pain, dysmenorrhoea, feverishness, symptoms of colds and influenza.

4.2. Posology and method of administration

For oral administration and short-term use only.

Adults, elderly and children over 12 years:
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, the patient should consult a doctor.

Take one or two tablets with water to start with, repeat up to three times a day as required.
Leave at least 4 hours between doses and do not take more than six tablets 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 (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 NSAID 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).

4.4. Special warnings and precautions for use

Bronchospasm may be precipitated in patients suffering from or with a previous history of bronchial asthma or allergic disease.
Undesirable effects may be minimised by using the minimum effective dose for the shortest possible duration.
The elderly are at increased risk of the 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 as 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 some 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.
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.
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 corticosteroids or anticoagulants such as warfarin 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.
Patients with rare hereditary problems of galactose intolerance, fructose intolerance, the Lapp lactase deficiency, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

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
- Are allergic to ibuprofen or any other ingredients of the product, aspirin or other related painkillers.
- Are taking other NSIAD painkillers, or aspirin with a daily dose above 75mg
- Are in the last 3 months of pregnancy

Speak to your pharmacist or doctor 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.
Not to be given to children under 12 years of age.
Keep all medicines out of the reach of children.

4.5. Interactions with other medicinal products and other forms of interaction

Ibuprofen should not be used in combination with:
Aspirin: Unless low-dose aspirin (not above 75mg daily) has been advised by a doctor, as this may increase the risk of adverse reactions (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).
Antihypertensives and diuretics: NSAIDs may diminish the effects of anti-hypertensives or diuretics.
Corticosteroids: may increase the risk of adverse reactions in the gastrointestinal tract.
Lithium: There is evidence for potential increases in plasma levels of lithium.
Methotrexate; There is a potential for an increase in plasma 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 studies, ibuprofen should, if possible, be avoided during the first 6 months of pregnancy.
During the 3rd trimester, ibuprofen in 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 may be increased with an increased bleeding tendency in both mother and child (see section 4.3 Contraindications).

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

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, angiodema and, less commonly, bullous dermatoses (including epidermal necrolysis and erythema multiforme).

The following list of adverse reactions 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 laryngeal swelling, dyspnoea, tachycardia, hypotension, (anaphylaxis, angioedema or severe shock).

Exacerbation of asthma or bronchospasm.

Gastrointestinal:

Uncommon: abdominal pain, nausea and dyspepsia.

Rare: 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 system:

Uncommon: headache.

Renal:

Very rare: acute renal failure, papillary necrosis, especially in long-term use, associated with increase serum urea 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).

4.9. Overdose

In children ingestion of more than 400mg/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 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 one hour of ingestion of a potentially toxic amount. If frequent of prolonged, convulsions should be treated with intravenous diazepam or lorazepam. Give bronchodilators for asthma.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

ATC Code M01A E01, Non-steroidal anti inflammatory.

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.

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 to 2 hours. 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

None stated

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Lactose Monohydrate
Microcrystalline Cellulose

Sodium Starch Glycolate (Type A)
Colloidal Anhydrous Silica
Magnesium Stearate
Sucrose
Talc
Starch
Titanium Dioxide (E171)

6.2. Incompatibilities

None stated

6.3. Shelf life

5years

6.4. Special precautions for storage

Do not store above 25ºC. Store in the original package.

6.5. Nature and contents of container

Ibuprofen Tablets are available in blister packs of 6, 12, and 16 tablets.

Blister Pack Specification:
- PVC (white, rigid, opaque): 250 microns
- Aluminium foil (hard tempered): 20 microns
- Primer (nitrocellulose): 1.5 - 2.5 gsm
- Heat seal lacquer: 6.5 - 8.5 gsm

6.6. Instruction for use and handling

None.

7. MARKETING AUTHORISATION HOLDER

East Midlands Pharma Ltd
16 Rancliffe Road
Keyworth
Nottingham NG12 5HY
UK

8. MARKETING AUTHORISATION NUMBER

PL 22958/0002

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

10. DATE OF REVISION OF THE TEXT

IBUPROFEN 200MG COATED TABLETS

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PRODUCT INFORMATION LEAFLET

PATIENT INFORMATION LEAFLET
IBUPROFEN 200mg COATED TABLETS

Read all of this leaflet carefully because it contains important information for you.
This medicine is available without a prescription, for you to treat a mild illness without a doctor's help. Nevertheless you still need to use Ibuprofen 200mg Coated Tablets carefully to get the best results from it.

- Keep this leaflet. You may need to read it again
- Ask your pharmacist if you need more information or advice
- You must see a doctor if your symptoms worsen or do not improve.

In this leaflet:

1. What Ibuprofen 200mg Coated Tablets are and what they are used for

Each tablet contains 200mg of the active ingredient ibuprofen.
Ibuprofen is one of a group of medicines called non-steroidal anti-inflammatory drugs or NSAIDs, which work by changing the body's response to pain, swelling and high temperature.
These tablets are used to provide relief of headache, muscular pain, rheumatic pain, backache, neuralgia, migraine, period pain, dental pain, feverishness and the symptoms of colds and flu.

2. Before you take Ibuprofen 200mg Coated Tablets

Do not take these tablets if:

- You are allergic to Ibuprofen, aspirin or any other painkillers or to any of the other ingredients contained in the tablets.
  An allergic reaction may be recognised as a rash, itching, swollen face or lips, or shortness of breath.
- You are or have been suffering from a stomach or duodenal ulcer or other stomach disorders.
- You have a history of stomach disorders related to previous NSAID therapy.
- You are taking aspirin at doses above 75mg daily, or any other non-steroidal anti-inflammatory drugs (NSAIDs). If you are on low dose aspirin (up to 75mg daily) tell your doctor or pharmacist before taking this medicine.
- You suffer from severe liver, kidney or heart problems.
- You are in the last 3 months of pregnancy.

Before you take these tablets tell your doctor or pharmacist if:

- You suffer from asthma or hives.
- You are pregnant or breast-feeding.
- You have liver, kidney, raised blood pressure or heart problems.
- You have a history of stomach or abdominal problems.
- You have chronic intestinal disease (e.g. ulcerative colitis, Crohn's disease)
- If you are taking any other course of treatment.

If you are elderly you may be more prone to side effects, so you should take just enough to make you feel better.

Pregnancy and breast feeding
Ibuprofen must not be taken in the last 3 months of pregnancy and should be avoided during the first 6 months.
Ibuprofen 200mg Coated Tablets belongs to a group of medicines that 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, but tell your doctor before taking this medicine if you have problems becoming pregnant.
Ibuprofen appears in breast milk in very small amounts and so is unlikely to affect the breast fed infant.

Important information about some of the ingredients of this medicine.
These tablets contain lactose monohydrate and sucrose. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicine.

Taking other medicines.
Tell your doctor or pharmacist if you are taking any of the following medicines:

- Aspirin (low-dose, not above 75mg daily)
- Diuretics (water tablets)
- Medicines to treat high blood pressure (antihypertensives)
- Medicines used to thin the blood such as warfarin
- Lithium (used to treat depression or mania)
- Corticosteroids
- Methotrexate (used to treat some cancers including leukaemia)
- Zidovudine (used to treat patients with HIV).

Tell your doctor or pharmacist if you are taking any other medicines, including those you have bought yourself.

3. How to take your tablets.

Adults, the elderly and children over 12 years old.

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 Ibuprofen 200gm Coated Tablets for longer than 10 days. If symptoms persist or worsen consult your doctor, who may instruct you to continue taking the medicine.

- Swallow one or two tablets with water to start with, with or after food, followed by one or two tablets every 4 hours if necessary up to 3 times a day.
- Do not take more than six tablets in any 24-hour period.

Do not give to children under 12 years of age.

DO NOT EXCEED THE STATED DOSE. Consult your doctor immediately if you have taken too many tablets.

If you have missed a dose, do not double–up on a dose to make up for the one you have missed.

4. Possible side effects.

Like all medicines Ibuprofen 200mg Coated Tablets can have side effects.
In most cases, taking ibuprofen tablets does not cause any problems.

As with any medicine, a few people develop an allergic reaction.
If you experience any of the following:

- Unexplained wheezing, shortness of breath
- Swelling of the lips, face or neck
- Skin rash or itching

Tell your doctor immediately or go to the casualty department of the nearest hospital.

Side effects which may occur include:

- A worsening of a previous asthmatic condition.
- Nausea (feeling sick), digestive problems, heartburn, abdominal pain or headache. These are uncommon side effects.
- Rarely: Flatulence, constipation and vomiting
- Very rarely: peptic ulcer, bleeding in the stomach, particularly in the elderly. Worsening of conditions such as ulcerative colitis and Crohn's disease.
- Very rarely kidney or liver problems
- Blood disorders, the first signs of which may be fever, sore throat, mouth ulcers, flu-like symptoms, severe exhaustion, unexplained bleeding and bruising. These are very rare.
- Skin disorders including various rashes and very rarely peeling skin or raised wheals.
- Symptoms of aseptic meningitis (stiff neck, headache, nausea, vomiting, fever or disorientation) have been observed in patients with auto-immune disease (such as systemic lupus erythematosus or mixed connective tissue disease).

If you experience these or any other unusual symptoms contact your doctor or pharmacist straight away.

If you suffer from any of the following at any time during treatment STOP TAKING the medicine and seek immediate medical help:

- Pass blood in your faeces (stools/motions)
- Pass black tarry stools
- Vomit blood or dark particles that look like coffee grounds

STOP TAKING ibuprofen and tell your doctor if you experience:

- Indigestion or heartburn
- Abdominal pain (pains in your stomach) or other abdominal stomach symptoms.

5. Storing your medicine.

Do not store above 25°C. Store in the original package to protect from moisture
KEEP OUT OF THE REACH AND SIGHT OF CHILDREN

Do not use after the expiry date shown on the package.

6. Further information.

What does each tablet contain?

Each tablet contains the active ingredient Ibuprofen 200 mg.
The tablets also contain: lactose monohydrate, microcrystalline cellulose, sodium starch glycollate, colloidal anhydrous silica, magnesium stearate, sucrose, talc and titanium dioxide (E171).

What is in the pack?

This product contains white round sugar coated tablets and is available in packs of 6, 12 and 16 tablets (not all packs may be marketed).

Who supplies Ibuprofen 200mg Coated Tablets?

Ibuprofen 200mg Coated Tablets are manufactured by Sussex Pharmaceutical Ltd, East Grinstead, West Sussex. RH19 2HL for the Marketing Authorisation holder, East Midlands Pharma Ltd, Keyworth, Nottingham NG12 5HY

PL 22958/0002 Leaflet revised: January 2006

IBUPROFEN 200MG COATED TABLETS

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