SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT
Ibuprofen 200mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Ibuprofen 200mg
For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM
Tablets.
White, capsule-shaped, sugar-coated tablets with no markings

4 CLINICAL PARTICULARS

4.1 Therapeutic indications
Rheumatic or muscular pain, pain of non-serious arthritic conditions, backache, neuralgia, migraine, headache, dental pain, dysmenorrhoea (period pain), feverishness, symptoms of colds and influenza

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

Adults, the elderly and children over 12 years:
The minimum effective dose should be used for the shortest time necessary to relieve symptoms.
Swallow 200mg – 400mg (1-2 tablets), preferably with water, up to three times a day, as required. Leave at least four hours between doses and do not take more than 1200mg (6 tablets) in any 24 hour period.

If in adults this medicinal product is required for more than 10 days, or if symptoms worsen the patient should consult a doctor.

If in children and adolescents between 12 and 18 years this medicinal product is required for more than 3 days, of if symptoms worsen a doctor should be consulted.

Not to be given to children under 12 years.

Undesirable effects may be minimised by using the lowest effective dose for the shortest duration necessary to control symptoms (see section 4.4).

4.3 Contraindications

Hypersensitivity to ibuprofen or any of the excipients listed in section 6.1.

Patients who have previously shown hypersensitivity reactions (e.g. asthma, rhinitis, or urticaria) in response to aspirin or other non-steroidal anti-inflammatory drugs.

Active or history of recurrent peptic ulcer/haemorrhage (two or more distinct episodes of proven ulceration or bleeding).

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

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

Last trimester of pregnancy (see section 4.6 Fertility, pregnancy and lactation).

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 200mg Tablets with concomitant NSAIDs including cyclooxengenase-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).
There is a risk of renal impairment in dehydrated children aged between 12 and 18 years.

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 studies suggest that use of ibuprofen, particularly at a high dose (2400 mg/day) 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. ≤ 1200 mg/day) is associated with an increased risk of arterial thrombotic events.

Patients with uncontrolled hypertension, congestive heart failure (NYHA II-III), established ischaemic heart disease, peripheral arterial disease, and/or cerebrovascular disease should only be treated with ibuprofen after careful consideration and high doses (2400 mg/day) should be avoided.
Careful consideration should also be exercised before initiating long-term treatment of patients with risk factors for cardiovascular events (e.g. hypertension, hyperlipidaemia, diabetes mellitus, smoking), particularly if high doses of ibuprofen (2400 mg/day) are required.

**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 200mg Caplets should be discontinued at the first appearance of skin rash mucosal lesions, or any other sign of hypersensitivity.
**Information about some of the ingredients in this medicine:**

Contains sucrose: Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

Contains Lactose: Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

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

**Do not take if you:**
- have ever had a stomach ulcer, perforation or bleeding
- are allergic to ibuprofen (or anything else in this medicine), 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:**
- have asthma, diabetes, high cholesterol, high blood pressure, had a stroke, liver, heart, kidney or bowel problems
- are a smoker

Do not take more medicine than the label tells you to. Keep out of the sight and reach of children.

If symptoms do not get better or get worse or if you get new symptoms, talk to your doctor.

**4.5 Interaction with other medicinal products and other forms of interaction**

**Ibuprofen should not be used in combination with:**

*Acetylsalicylic acid (Aspirin)*

Concomitant administration of ibuprofen and acetylsalicylic acid (aspirin) is not generally recommended, unless low-dose aspirin (not above 75mg daily) has been advised by a doctor because of the potential of increased adverse effects.

Experimental data suggest that ibuprofen may competitively inhibit the effect of low dose aspirin on platelet aggregation when they are dosed concomitantly. Although there are uncertainties regarding extrapolation of these data to the clinical situation,
the possibility that regular, long-term use of ibuprofen may reduce the cardioprotective effect of low-dose aspirin cannot be excluded. No clinically relevant effect is considered to be likely for occasional ibuprofen use (see section 5.1).

*Other NSAIDs including cyclooxygenase-2 selective inhibitors:* Avoid concomitant use of two or more NSAIDs as this 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 anti-coagulants, such as warfarin (see section 4.4 Special Warnings and Precautions for Use).

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

*Corticosteroids:* Increased risk of gastrointestinal ulceration or bleeding (see section 4.4 Special Warnings and Precautions for Use).

*Anti-platelet agents and selective serotonin reuptake inhibitors (SSRIs):* Increased risk of gastrointestinal bleeding.

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

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

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

*Cyclosporin:* Increased risk of nephrotoxicity

*Mifepristone:* NSAIDs should not be used for 8-12 days after mifepristone. Administration of NSAID’s can reduce the effect of mifepristone.

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

*Zidovudine:* Increased risk of haematological activity 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 NSAID’s can increase the risk of convulsions associated with quinolone antibiotics. Patients taking NSAIDs and quinolones may have an increase risk of developing convulsions.

4.6 **Fertility, pregnancy and lactation**

**Pregnancy:**

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

During the 3\textsuperscript{rd} trimester, 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).

**Lactation/Breastfeeding:**

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

**Fertility:**

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**

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 long-term treatment, additional adverse effects may occur.

The adverse effects have been listed in order of decreasing frequency, using the following convention:

- Very Common ($\geq 1/10$)
- Common ($\geq 1/100$ to $<1/10$)
- Uncommon ($\geq 1/1,000$ to $<1/100$)
- Rare ($\geq 1/10,000$ to $<1/1,000$)
- Very Rare ($<1/10,000$)
- Not Known (cannot be estimated from the available data)

**Blood and Lymphatic System Disorders:**
**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.

**Immune System Disorders:**

**Uncommon:** Hypersensitivity reactions with urticaria and pruritus.

**Very Rare:** Severe hypersensitivity reactions. Symptoms could include: facial, tongue and laryngeal swelling, dyspnoea, tachycardia, hypotension (anaphylaxis, angioedema or severe shock).

**Not Known:** Non-specific allergic reactions. Respiratory tract reactivity (e.g. asthma, aggravated asthma and bronchospasm). Various skin reactions including exfoliative and bullous dermatoses (including epidermal necrolysis and erythema multiforme).

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 and Precautions for Use).

**Nervous System Disorders:**

**Uncommon:** Headache.

**Very Rare:** Aseptic Meningitis – single cases have been reported very rarely.

**Cardiac Disorders:**

**Not Known:** 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).

**Gastrointestinal Disorders:**

The most commonly observed side effects of ibuprofen are gastrointestinal in nature.

**Uncommon:** Abdominal pain, nausea and dyspepsia.

**Rare:** Diarrhoea, flatulence, constipation and vomiting.

**Very Rare:** Peptic ulcer, perforation or gastrointestinal haemorrhage, melaena, haematemesis, sometimes fatal, particularly in the elderly, ulcerative stomatitis, gastritis.

**Not Known:** Exacerbation of ulcerative colitis and Crohn’s disease (see section 4.4 Special Warnings and Precautions for Use).

**Hepatobiliary Disorders:**
Very Rare: Liver disorders.

Skin and Subcutaneous Tissue Disorders:
Uncommon: Various skin rashes.
Very Rare: Severe forms of skin reactions such as bullous reactions, including Stevens Johnson syndrome, erythema multiforme and toxic epidermal necrolysis can occur.

Renal and Urinary Disorders:
Very Rare: Acute renal failure, papillary necrosis, especially in long-term use, associated with increased serum urea and oedema.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard.

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 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, non-steroids, propionic acid derivatives.

*ATC code:* M01A E01

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.

Experimental data suggest that ibuprofen may competitively inhibit the effect of low dose aspirin on platelet aggregation when they are dosed concomitantly. Some pharmacodynamic studies show that when single doses of ibuprofen 400mg were taken within 8 h before or within 30 min after immediate release aspirin dosing (81mg), a decreased effect of aspirin on the formation of thromboxane or platelet aggregation occurred. Although there are uncertainties regarding extrapolation of these data to the clinical situation, the possibility that regular, long-term use of ibuprofen may reduce the cardioprotective effect of low-dose aspirin cannot be excluded. No clinically relevant effect is considered to be likely for occasional ibuprofen use.

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, high peak levels are observed after 1 to 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

There are no preclinical data of relevance to the prescriber, which are additional to those already included in other sections of the SmPC.
6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients
Lactose monohydrate
Maize Starch
Hydroxy Propyl Methyl Cellulose
Sodium Starch Glycolate
Colloidal Anhydrous Silica
Magnesium Stearate
Sucrose
Talc
Titanium Dioxide (E171)

6.2 Incompatibilities
Not applicable.

6.3 Shelf life
3 years

6.4 Special precautions for storage
Do not store above 25°C.

6.5 Nature and contents of container
Al/PVC blister packs 20 µm aluminium foil, 250 µm PVC enclosed in an outer carton containing 24, 48 or 96 tablets.

Al/PVC/PVDC blister strips containing 24, 48 or 96 tablets.
6.6 Special precautions for disposal
Not applicable.

7 MARKETING AUTHORISATION HOLDER
Galpharm Healthcare Limited
Wrafton
Braunton
Devon
EX33 2DL
United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)
PL 16028/0161

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORIZATION
13/03/2017

10 DATE OF REVISION OF THE TEXT
13/03/2017