SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Ibuprofen 200 mg Tablets
Ibucalm 200 mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains: - Ibuprofen 200 mg

For full excipients, see Section 6.1.

3 PHARMACEUTICAL FORM

Coated tablet

A pink biconvex round film coated tablet

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, symptoms of colds and influenza.

4.2 Posology and method of administration

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

For oral administration and short-term use only.

Adults, the elderly and children over 12 years:

The lowest effective dose should be used for the shortest duration 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 or two tablets to be taken three times a day as required. These tablets should be taken with water. Leave at least four hours between doses and do not take more than 1200 mg (6 tablets) in any 24-hour period.

Not to be given to children under 12 years of age.

4.3 Contraindications

Hypersensitivity to Ibuprofen or any of the excipients 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 history of recurrent peptic ulcer / haemorrhage (two or more distinct episodes of proven ulceration or bleeding).

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

Severe hepatic failure, renal failure or heart failure NYHA class IV (See section 4.4)

Last trimester of pregnancy (See Section 4.6).

4.4 Special warnings and precautions for use

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).

The elderly are at an increased risk of the serious consequences of adverse reactions to NSAIDs especially gastrointestinal bleeding and perforation which may be fatal.

There is a risk of renal impairment in dehydrated children and adolescents.

Caution is required in patients with certain conditions:

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 with concomitant NSAIDs including cyclo-oxygenase-2 selective inhibitors should be avoided (see section 4.5).

SLE as well as mixed connective tissue disease:

Systemic lupus erythematosus and mixed connective tissue disease due to increased risk of aseptic meningitis (see section 4.8).

Renal:

Renal impairment as renal function may further deteriorate (see section 4.3 and 4.8)

Renal tubular acidosis and hypokalaemia may occur following acute overdose and in patients taking ibuprofen products over long periods at high doses (typically greater than 4 weeks), including doses exceeding the recommended daily dose.

Hepatic:

Hepatic dysfunction (see section 4.3 and 4.8)

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 renal function may deteriorate and fluid retention, hypertension and oedema have been reported in association with NSAID therapy (see section 4.5).

Clinical trial and epidemiological data suggest that use of ibuprofen, particularly at high doses (2400 mg 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. ≤ 1200 mg daily) is associated with an increased risk of myocardial infarction.

Cases of Kounis syndrome have been reported in patients treated with Ibuprofen. Kounis syndrome has been defined as cardiovascular symptoms secondary to an allergic or hypersensitive reaction associated with constriction of coronary arteries and potentially leading to 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 upon 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).

GI bleeding, ulceration or perforation, which can be fatal, has been reported with all NSAIDs at any time during treatment, with or without warning symptoms or a previous history of serious GI events including ulcerative colitis, Crohn's Disease.

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), 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 corticosteroids, or anticoagulants such as warfarin, selective serotonin uptake inhibitors or anti-platelet agents such as aspirin (See Section 4.5 Interactions).

When GI bleeding or ulceration occurs in patients receiving Ibuprofen, the treatment should be withdrawn immediately.

Dermatological:

Severe skin reactions:

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). 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. Acute generalised exanthematous pustulosis (AGEP) has been reported in relation to ibuprofen-containing products.

Ibuprofen 200 mg Tablets/ Ibucalm 200 mg Tablets should be discontinued, at the first appearance of signs and symptoms of severe skin reactions, such as skin rash, mucosal lesions, or any other sign of hypersensitivity.

Masking of symptoms of underlying infections

Ibuprofen can mask symptoms of infection, which may lead to delayed initiation of appropriate treatment and thereby worsening the outcome of the infection. This has been observed in bacterial community acquired `pneumonia and bacterial complications to varicella. When Ibuprofen is administered for fever or pain relief in relation to infection, monitoring of infection is advised. In nonhospital settings, the patient should consult doctor if symptoms persist or worsen.

This medicine contains less than 1 mmol sodium (23mg) per 200 mg tablet, that is to say essentially 'sodium-free'.

The label will include:

Read the enclosed leaflet before taking this product. Do not take if you

- Have (or have had two or more episodes of) 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 NSAID painkillers, or aspirin with a daily dose above 75 mg.
- Are in the last 3 months of pregnancy.

Speak to a pharmacist or your doctor before taking this product if you:

- Have or have had asthma, diabetes, high cholesterol, high blood pressure, a stroke, liver, heart, kidney, or bowel problem
- Are a smoker
- Are pregnant

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 daily) has been advised by a doctor, as this may increase the risk of adverse reactions (See Section 4.4).

Experimental data suggest that ibuprofen may inhibit the effect of low dose aspirin on platelet aggregation when they are dosed concomitantly. However, the limitations of data and the uncertainties regarding extrapolation of ex-vivo data to the clinical situation imply that no firm conclusions can be made for regular ibuprofen use, and 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 4.4)

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).

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

Corticosteroids: Corticosteroids may increase the risk of adverse reactions especially of the gastrointestinal tract (see section 4.4)

Anti-platelet agents and selective serotonin reuptake inhibitors (SSRIs): increased risk of gastrointestinal bleeding (see section 4.4)

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. Ciclosporin: Increased risk of nephrotoxicity.

Mifepristone: NSAIDs should not be used for 8-12 days after Mifepristone administration as NSAIDs can reduce the effect of Mifepristone.

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 Fertility, pregnancy and lactation

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

From the 20th week of pregnancy onward, Ibuprofen use may cause oligohydramnios resulting from foetal renal dysfunction. This may occur shortly after treatment initiation and is usually reversible upon discontinuation. In addition, there have been reports of ductus arteriosus constriction following treatment in the second trimester, most of which resolved after treatment cessation. Therefore, during the first and second trimester of pregnancy, Ibuprofen should not be given unless clearly necessary. If Ibuprofen is used by a woman attempting to conceive, or during the first and second trimester of pregnancy, the dose should be kept as low and duration of treatment as short as possible. Antenatal monitoring for oligohydramnios and ductus arteriosus constriction should be considered after exposure to ibuprofen for several days from gestational week 20 onward. Ibuprofen should be discontinued if oligohydramnios or ductus arteriosus constriction are found.

During the third trimester of pregnancy, all prostaglandin synthesis inhibitors may expose the foetus to:

- cardiopulmonary toxicity (with premature **constriction**/closure of the ductus

arteriosus and pulmonary hypertension);

- renal dysfunction (**see above**);

the mother and the neonate, at the end of pregnancy, to:

- possible prolongation of bleeding time, an anti-aggregating effect which may occur even at very low doses;
- inhibition of uterine contractions resulting in delayed or prolonged labour.

Consequently, ibuprofen is contraindicated during the third trimester of pregnancy (see sections 4.3 and 5.3).

In limited studies, Ibuprofen appears in breast milk in a 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

Hypersensitivity reactions have been reported and these may consist of: -

- Non-specific allergic reaction and anaphylaxis,
- Respiratory tract reactivity, e.g., asthma, aggravated asthma, bronchospasm, dyspnoea or
- Various skin reactions, e.g., pruritis, urticaria, angioedema and, more rarely, exfoliative and bullous dermatoses (including epidermal necrolysis and 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 long-term treatment, additional adverse effects may occur.

Infections and infestations:

Very rare: Aseptic meningitis

Immune system reactions:

Uncommon: hypersensitivity reactions with urticaria and pruritus.

Very rare: Exacerbation of asthma and bronchospasm.

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.

Severe hypersensitivity reactions:

Symptoms could be facial, tongue and larynx swelling, dyspnoea, tachycardia, hypotension (anaphylaxis, angioedema or severe shock).

Psychiatric disorders:

Very rare: Nervousness.

Gastrointestinal disorders:

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

Uncommon: Abdominal pain, abdominal distension, 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 (see section 4.4) Mouth ulceration.

Exacerbation of ulcerative colitis and Crohn's disease (See Section 4.4)

Nervous system:

Uncommon: Headache

Eye disorders:

Very rare: Visual disturbance

Ear and labyrinth disorders:

Very rare: Tinnitus and vertigo

Renal and urinary disorders:

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

Not known: Ureteric colic, dysuria, Renal tubular acidosis*

Hepatobiliary disorders:

Very rare: Liver disorders, especially in long-term treatment, hepatitis and jaundice.

Haematological disorders:

Very rare: Haematopoietic disorders (anaemia, leucopenia, thrombocytopenia, pancytopenia, granulocytosis). First signs are: fever, sore throat, superficial mouth ulcers, flu-like symptoms, severe exhaustion, unexplained bleeding and bruising.

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.

Not known

Acute generalised exanthematous pustulosis (AGEP)

Drug reaction with eosinophilia and systemic symptoms (DRESS syndrome)

Cardiovascular disorders:

Very rare: Cardiac failure.

Clinical trial and epidemiological data suggest that use of ibuprofen (particularly at high doses 240 mg 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)

Vascular disorders:

Very rare: Hypertension

Cardiac disorders:

Not Known: Kounis syndrome

Respiratory, thoracic and mediastinal disorders:

Very rare: Asthma, bronchospasm, dyspnoea and wheezing.

General disorders:

Very rare: Oedema, peripheral oedema.

Investigations:

Very rare: Decreased haematocrit and haemoglobin levels.

Metabolism and Nutrition Disorders:

Not known: Decreased Appetite, Hypokalaemia*

Description of Selected Adverse Reactions:

*Renal tubular acidosis and hypokalaemia have been reported in the post-marketing setting typically following prolonged use of the ibuprofen component at higher than recommended doses.

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 or search for MHRA Yellow Card in the Google Play or Apple App Store.

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 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 vertigo, headache, respiratory depression, dyspnoea, 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.

Prolonged use at higher than recommended doses or overdose may result in severe hypokalaemia and renal tubular acidosis. Symptoms may include reduced level of consciousness and generalised weakness (see section 4.4 and section 4.8).

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 antirheumatic, non-steroids.

ATC code: M01AE01

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

Experimental data suggest that ibuprofen may inhibit the effect of low dose aspirin on platelet aggregation when they are dosed concomitantly. In one study, when a single dose of ibuprofen 400 mg was taken within 8 hours before or 30 minutes after immediate release aspirin dosing (81mg), a decreased effect of aspirin on the formation of thromboxane or platelet aggregation occurred. However, the limitations of these data and the uncertainties regarding extrapolation of ex vivo data to the clinical situation imply that no firm conclusions can be made for regular ibuprofen use, and 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, 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 breast milk in very low concentrations.

5.3 Preclinical safety data

There are no clinically relevant preclinical safety data.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Colloidal Anhydrous Silica

Povidone

Croscarmellose Sodium

Microcrystalline Cellulose

Potato Starch

Alginic Acid

Magnesium Stearate

Sodium Lauryl Sulphate

Sodium Starch Glycollate

Opadry Pink 04M34628 (Titanium dioxide E171, Carmine E120, Hypromellose E464, Glycerol)

6.2 Incompatibilities

None Known

6.3 Shelf life

2 years

6.4 Special precautions for storage

Do not store above 25ºC. Store in the original package (blisters) to protect from moisture.

6.5 Nature and contents of container

Blister packs of Aluminium foil/UPVC containing 12 or 16 tablets.

6.6 Special precautions for disposal

None

7 MARKETING AUTHORISATION HOLDER

ASPAR Pharmaceuticals Ltd
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Acrewood Way,
St Albans,
AL4 0JY,
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8 MARKETING AUTHORISATION NUMBER(S)

PL 08977 / 0068

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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