EVANS BAROQUE LIMITED

SUMMARY OF PRODUCT CHARACTERISTICS

(SmPC) ALGAFEN 200MG

1. NAME OF THE MEDICINAL PRODUCT

{(Algafen Tablets) Ibuprofen 200mg Tablet}

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

[Ibuprofen 200mg: e.g.:
Each film-coated tablet contains:
Ibuprofen 200mg]

{For a full list of excipients, see section 6.1}

3. PHARMACEUTICAL FORM

Brown coloured round shaped, standard biconvex film coated tablet with 'eb' on one side and the other side plain. Packaging: 1 X 10, 1 X 10 X 10, 10 x 10 and 2 x 10 tablets

4. Clinical particulars

4.1 Therapeutic indications

{Algafen 200, Ibuprofen 200mg, tablet} is indicated in <adults> <children over 12years>
In adults and children over 12years: For short term treatment of fever and pain of mild to moderate intensity, including dysmenorrhea. Long term symptomatic treatment of pain and inflammation in chronic inflammatory rheumatic diseases

4.2 Posology and method ofadministration

Posology

Pediatric population

<The <safety> <and> <efficacy> of {Algafen 200} in children aged {below 12years} has not <yet> been established.>

Posology and method of administration:

Short term symptomatic treatment of fever and pain of mild to moderate intensity:
Children and Adolescents between 12 and 18 years:
Take 1 or 2 Tablets with water, up to three times a day as required.
Adults: Take 2 Tablets with water, up to three times a day as required.

Leave at least four hours between doses.
Do not take more than 6 Tablets in any 24 hour period.

Not for use by children under 12 years of age.

If you have severe liver and kidney disease or are elderly your doctor will tell you the correct dose to take which will be the lowest dose possible.

If you forget to take Algafen tablets
Do not use a double dose to make up for a forgotten dose.
If you have any further questions on the use of this product, ask your doctor or pharmacist

{Algafen 200, Ibuprofen 200mg, tablet} is contraindicated in children aged {below 12years} <(see Section 4.3).

Method of administration

Route of Administration: Oral

Take Algafen tablets with food and drink

Algafen tablets could be used together with food and drinks. Take your Algafen tablets with or after food, with plenty of fluid. Algafen tablets should be swallowed whole and not chewed, broken, crushed or sucked on to avoid oral discomfort and throat irritation.

4.3 Contraindications

Not for use by children under 12 years of age.
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 heart failure (NYHA Class IV), renal failure or hepatic failure (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 section 4.2 GI and cardiovascular risks below).

The elderly have an increased frequency of adverse reactions to NSAIDs especially gastrointestinal

bleeding and perforation which may be fatal.

Severe skin reactions:

Serious skin reactions, some of them fatal, including exfoliative dermatitis, Stevens- Johnson syndrome, and toxic epidermal necrolysis have been reported rarely in association with the use of NSAIDSs (see section 4.8). Patients appear to be at highest risk of 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 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.

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 cyclooxygenase-2 selective inhibitors should be avoided (see section 4.5).

SLE and mixed connective tissue disease: Systemic lupus erythematosus as well as those with mixed connective tissue disease–increased risk of aseptic meningitis (see section 4.8).

Renal: Renal impairment as renal function may further deteriorate (see sections 4.3 and 4.8). There is a risk of renal impairment in dehydrated children and adolescents.

Hepatic: Hepatic dysfunction (see sections 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 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 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 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), 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 ulceration or bleeding, such as oral corticosteroids, anticoagulants such as warfarin, selective serotonin-reuptake inhibitors or antiplatelet agents such as aspirin (see section 4.5).
When 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). 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 should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity.

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

4.5 Interaction with other medicinal products and other forms of interaction

Ibuprofen (like other NSAIDs) should be avoided in combination with:
Aspirin (Acetylsalicylic Acid):
Concomitant administration of ibuprofen and acetylsalicylic acid is not generally recommended because of the potential of increased adverse effects unless low-dose aspirin (not above 75mg daily) has been advised by a doctor, (see section 4.4).
Experimental data suggest that ibuprofen may competitively inhibit the effect of low dose acetylsalicylic acid 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 acetylsalicylic acid 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 reactions (see section 4.4).

Ibuprofen should be used with caution in combination with:
Corticosteroids: as these may increase the risk of gastrointestinal ulceration or bleeding (see section 4.4).
Antihypertensives and diuretics: Since NSAIDs may diminish the effects of these drugs. In some patients with compromised renal function (e.g. dehydrated patients or elderly patients with compromised renal function) the co-administration of an ACE inhibitor or Angiotensin II antagonist and agents that inhibit cyclo- oxygenase may result in further deterioration of renal function, including possible acute renal failure, which is usually reversible. These interactions should be considered in patients taking a coxib concomitantly with ACE inhibitors or angiotensin II antagonists. Therefore, the combination should be administered with caution, especially in the elderly. Patients should be adequately hydrated and consideration should be given to monitoring of renal function after initiation of concomitant therapy, and periodically thereafter.
Diuretics can increase the risk of nephrotoxicity of NSAIDs. Anticoagulants: NSAIDS may enhance the effects of anti-coagulants, such as warfarin (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 cardiac glycoside levels.
Lithium: There is evidence for potential increases in plasma levels of lithium.
Methotrexate: There is evidence for the potential 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 Pregnancy and Lactation

Pregnancy
Inhibition of prostaglandin synthesis may adversely affect the pregnancy and/or the embryo/foetal

development. Data from epidemiological studies suggest an increased risk of miscarriage and of cardiac malformation and gastroschisis after use of a prostaglandin synthesis inhibitor in early pregnancy. The absolute risk for cardiovascular malformation was increased from less than 1%, up to approximately 1.5%. The risk is believed to increase with dose and duration of therapy. In animals, administration of a prostaglandin synthesis inhibitor has been shown to result in increased pre- and post-implantation loss and embryofoetal lethality. In addition, increased incidences of various malformations, including cardiovascular, have been reported in animals given a prostaglandin synthesis inhibitor during the organogenetic period. 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.

During the third trimester of pregnancy, all prostaglandin synthesis inhibitors may expose the foetus to:
- cardiopulmonary toxicity (with premature closure of the ductus arteriosus and pulmonary hypertension);
- renal dysfunction, which may progress to renal failure with oligohydroamniosis;
the mother and the neonate, at the end of the 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.

Lactation/Breastfeeding
In limited studies, ibuprofen appears in breast milk in very low concentration and is unlikely to affect the breast-fed infant adversely. See section 4.4 regarding female fertility.

4.7 Effects on ability to drive and use machines

{Algafen 200, Ibuprofen 200mg, tablets} may impair reactions in some people. This should be taken into consideration on occasions when high alertness is required. Undesirable effects such as dizziness, drowsiness, fatigue and visual disturbances are possible after taking NSAIDs. If affected, patients should not drive or operate machinery

4.8 Undesirable effects

ADVERSE REACTIONS

Please note that Algafen tablets can prolong bleeding time.

There have been reports of high blood pressure and heart failure as well as worsening of ulcers in the large intestine and Crohn's disease (inflammatory bowel disease) in treatment with pain-relieving medicines (NSAIDs).

Exceptional serious infections of the skin in case of varicella. Exacerbation of infection-related inflammations (e.g. development of necrotising fasciitis) coinciding with the use of NSAIDs has been

described.

Medicines like Algafen tablets may entail a slightly increased risk of heart attack or stroke.

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

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 Pharmacodynamics properties

Pharmacotherapeutic group: {Anti-inflammatory and anti-rheumatic product, non-steroid, propionic acid derivative {Non-steroidal Anti-inflammatory Drugs; NSAIDs}, ATC code:{ M01A E01}

Mechanism of action

Ibuprofen works by non-selectively inhibiting the enzyme called cyclooxygenase (COX), which is required for the synthesis of prostaglandins via the arachidonic acid pathway. COX converts arachidonic acid to prostaglandin H2 (PGH2) in the body. PGH2, in turn, is converted by other enzymes to several other prostaglandins (which are mediators of pain, inflammation, and fever) and to thromboxane A2 (which stimulates platelet aggregation, leading to the formation of blood clots).

Ibuprofen is a nonselective COX inhibitor, in that it inhibits two isoforms of cyclooxygenase, COX-1 and COX-2. The inhibition of COX by ibuprofen therefore lowers the level of prostaglandins made by the body. The prostaglandins that are formed from PGH2 are important mediators of sensations such as pain and processes such as fever and inflammation, pain, fever and swelling. The antipyretic effects may arise as a result of action on the hypothalamus leading to vasodilation, an increased peripheral blood flow and subsequent heat dissipation.

Pharmacodynamic effects

Ibuprofen works by blocking the production of prostaglandins, substances that the body releases in response to illness and injury. Prostaglandins cause pain and swelling, or inflammation. They are released in the brain, and they can also cause fever. Ibuprofen's painkilling effects begin soon after taking a dose>

Clinical efficacy and safety

Clinical Pharmacology of Ibuprofen

Ibuprofen is supplied as tablets with a potency of 200 to 800 mg. The usual dose is 400 to 800 mg three times a day. It is almost insoluble in water having pKa of 5.3. It is well absorbed orally; peak serum concentrations are attained in 1 to 2 hours after oral administration. It is rapidly bio-transformed with a serum half life of 1.8 to 2 hours. The drug is completely eliminated in 24 hours after the last dose and eliminated through metabolism. The drug is more than 99% protein bound, extensively metabolized in the liver and little is excreted unchanged.

Although highly bound to plasma proteins (90-99%), displacement interactions are not clinically significant, hence the dose of oral anti-cogulants and oral hypoglycemic needs not be altered.1 More than 90% of an ingested dose is excreted in the urine as metabolites or their conjugates, the major metabolites are hydroxylated and carboxylated compounds.

Old age has no significant effects on the elimination of ibuprofen. Renal impairment also has no effect on the kinetics of the drugs, rapid elimination still occur as a consequence of metabolism. The administration of ibuprofen tablets either under fasting conditions or immediately before meals yield quiet similar serum concentrations-time profile. When it is administered immediately after a meal, there is a reduction in the rate of absorption but no appreciable decrease in the extent of absorption.>

Paediatric population

Not for use by children under 12 years of age.

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 elimination half-life of Ibuprofen is about 2 hours.
In limited studies Ibuprofen appears in the breast milk in very low concentrations

BIOAVAILABILTY/BIOEQUIVALENCE
Ibuprofen is rapidly absorbed from the gastrointestinal tract with a bioavailability of 80-90%. Peak serum concentrations occur one to two hours after administration. If administered with food, peak serum concentrations are lower and achieved more slowly than when taken on an empty stomach Food does not affect markedly total bioavailability.
Excretion by the kidney is both rapid and complete. The elimination half-life is approximately 2 hours. The excretion of ibuprofen is virtually complete 24 hours after the last dose.>

5.3 Preclinical safety data

CLINICAL DATA
Clinical Pharmacology of Ibuprofen

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inflammations (e.g. development of necrotising fasciitis) coinciding with the use of NSAIDs has been described.

Medicines like Algafen tablets may entail a slightly increased risk of heart attack or stroke.

TERATOGENICITY:

Pregnancy, breast-feeding and fertility

If you are pregnant or breast feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

Pregnancy

Pregnant women should not use Algafen tablets during the three final months of the pregnancy. Use of Algafen tablets should be avoided by women who are planning a pregnancy or are pregnant. Treatment at any time in pregnancy should only take place as directed by a doctor.

Breast-feeding

Algafen tablets passes into breast milk. The use of Algafen tablets is therefore not recommended while breast-feeding. However, consult a doctor if using Algafen tablets more than occasionally while breast-feeding is required.

Fertility

The use of Algafen tablets may affect fertility. The use of Algafen tablets is not recommended while attempting to conceive or during investigation of infertility.

TOXICOLOGICAL DATA
During varicella it is advisable to avoid use of this drug.

Serious skin reactions have been reported in very rare cases when using a NSAID. Stop taking Algafen tablets and contact a doctor if you develop a rash or mucous membrane lesions. The severe rashes may include blisters on the skin, especially on the legs, arms, hands and feet which can also involve the face and lips (erythema multiforme, Stevens-Johnson´s syndrome). This can get even more severe, where the blisters get larger and spread out and parts of the skin may slough off (toxic epidermal necrolysis). There may also be severe infection with destruction (necrosis) of skin, subcutaneous tissue and muscle.

Algafen tablets may cause a reduction in the number of white blood cells and your resistance to infection may be decreased. If you experience an infection with symptoms such as fever and serious deterioration of your general condition, or fever with local infection symptoms such as sore throat/pharynx/mouth or urinary problems you should see your doctor immediately. A blood test will be taken to check possible reduction of white blood cells (agranulocytosis). It is important to inform

your doctor about your medicine.

Children and adolescents

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

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

[List all excipients **except solvents removed during processing**.]

[**NAME AND FUNCTION OF EACH INGREDIENT**

Raw Material	**Function**
Ibuprofen	Active
Microcrystalline Cellulose Granules 200 CPS 5	Diluent/Binder
Croscarmellose Sodium	Disintegrant
Magnesium Stearate	Lubricant
Colloidal Anhydrous Silica	Glidant
Purified Talc	Lubricant
Colorcoat FC4W-H	Colourant

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years

6.4 Special precautions for storage

How to store Algafen tablets

Store below 30°C, away from light, Keep all medicines out of the reach of children

6.5 Nature and contents of container <and special equipment for use, administration or implantation>

Each film-coated tablet contains:

Ibuprofen 200mg in ALU/PVC blisters of 1 X 10, 1 X 10 X 10, 10 x 10 and 2 x 10 tablets

6.6 Special precautions for disposal <and other handling>

No special requirements. Any unused product or waste material should be disposed of in accordance with local requirements.

7. <APPLICANT/MANUFACTURER>

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