Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Advil 200 mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains Ibuprofen 200 mg.

Excipients: Also contains sucrose, methyl parahydroxybenzoate (E 218) + propylparahydroxybenzoate (E 216)

For a full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Coated tablet (tablet)
A pinkish brown, sugar coated tablet with 'Advil' printed in black on one side.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Short term management of pain and fever conditions such as:

- Acute pain from dysmenorrhoea.
- Dental pain.
- Muscular pain.
- Headaches.
- Colds and flu symptoms.
- Backache.

4.2 Posology and method of administration

Adults, the elderly and young persons over the age of 12:

If this medicinal product is required for more than 3 days, or if symptoms worsen, a doctor should be consulted. Undesirable effects may be minimised by using the lowest effective dose for the shortest duration necessary to control symptoms (See Section 4.4).

1 to 2 tablets every 4-6 hours.
Do not exceed 6 tablets in 24 hours.
Do not give to children under 12.

Elderly:
Non –steroidal anti-inflammatory drugs (NSAIDs) should be used with particular caution in elderly patients who are prone to adverse events. The lowest dose compatible with adequate safe clinical control should be employed. See also Section 4.4.

4.3 Contraindications

- Use in patients allergic to any of the ingredients.
- Use in patients hypersensitive to aspirin (acetylsalicyclic acid) or with bronchospasm, asthma, rhinitis or urticaria associated with non-steroidal anti-inflammatory drugs.
- History of gastrointestinal bleeding or perforation, related to previous NSAIDs therapy.
- Active or history of recurrent peptic ulcer/haemorrhage (two or more distinct episodes of proven ulcerations or bleeding)
- Use in children under 12 years.
- Patients with severe heart failure (NYHA Class IV).

- Do not use in the last 3 months of pregnancy.

4.4 Special warnings and precautions for use

- The use of Advil 200mg tablets with concomitant NSAIDs including cyclooxygenase-2 selective inhibitors should be avoided.
- Undesirable effects may be minimized by using the minimum effective dose for the shortest duration necessary to control symptoms.
- Elderly: The elderly have an increased frequency of adverse reactions to NSAIDs especially gastrointestinal bleeding and perforation which may be fatal (see section 4.2)
- Gastrointestinal bleeding, ulceration and perforation: 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 GU 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. Combination therapy with protective agents (e.g. misoprostol or proton pump inhibitors) should be considered for these patients and also for patients requiring concomitant low dose aspirin (acetylsalicyclic acid) or other drugs likely to increase gastrointestinal risk (see below and 4.5)
- 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 anti-platelet agents such as aspirin (acetylsalicyclic acid) (see section 4.5).
- When GI bleeding or ulceration occurs in patients receiving Advil 200mg tablets, the treatment should be withdrawn.

- NSAIDs should be given with care to patients with a history of gastrointestinal disease (ulcerative colitis, Crohn's disease) as their condition may be exacerbated (see sections 4.8 – undesirable effects).
- Should not be taken with other analgesics
- At the outset of treatment, monitoring of the urine volume and renal function is necessary in cardiac insufficiency, cirrhotic and nephrotic patients, in patients taking a diuretic and in those with chronic renal insufficiency. The use of NSAIDs should preferably be avoided in patients with pre-existing renal disease or volume depletion
- There is a risk of renal impairment in dehydrated adolescents or young persons, between the age of 12 and 18 years.
- Patients who are pregnant, elderly or suffering from asthma or renal, or hepatic insufficiency should consult their doctor

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 and oedema have been reported in association with NSAID therapy. Undesirable effects may be minimised using the lowest effective dose for the shortest duration necessary to control symptoms (see GI cardiovascular risks below)

Cardiovascular and cerebrovascular effects:

Clinical studies suggest that use of ibuprofen particularly at a high dose (2400mg/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. £ 1200mg daily) 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.

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 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.Advil 200mg tablets should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity.

Exceptionally, varicella can be at the origin of serious cutaneous and soft tissue infectious complications. To date, the contributing role of NSAIDs in the worsening of these infections cannot be ruled out. Thus, it is advisable to avoid use of Advil 200mg tablets in case of varicella.

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.

4.5 Interaction with other medicinal products and other forms of interactions

It is considered unsafe to take NSAID's in combination with warfarin or heparin unless under direct medical supervision.

Ibuprofen should be avoided in combination with:
Aspirin (Acetylsalicylic acid):
Concomitant administration of ibuprofen and aspirin (acetylsalicyclic acid) is not generally recommended because of the potential of increased adverse effects.

Experimental data suggest that ibuprofen may competitively inhibit the effect of low dose aspirin (acetylsalicyclic 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 aspirin (acetylsalicyclic acid) cannot be excluded. No clinically relevant effect is considered to be likely for occasional ibuprofen use (see section 5.1).

Care should be taken in patients treated with any of the following drugs as interactions have been reported:

Anti-hypertensives: Reduced anti-hypertensive effect.

Diuretics: Reduced diuretic effect. Diuretics can increase the risk of nephrotoxicity of NSAIDs.

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

Lithium: Decreased elimination of lithium.

Methotrexate: Decreased elimination of methotrexate.

Cyclosporin: Increased risk of nephrotoxicity with NSAIDs.

Other NSAID's: Avoid concomitant use of two or more NSAIDs.

Corticosteroids: Increased risk of gastrointestinal bleeding and ulceration (see section 4.4).

Aminoglycosides: Reduction in renal function in susceptible individuals decreased elimination of aminoglycoside and increased plasma concentrations.

Probenecid: Reduction in metabolism and elimination of NSAID and metabolites.

Oral hypoglycaemic agents: Inhibition of metabolism of sulfonylurea drugs, prolonged half-life and increased risk of hypoglycaemia.

Anti-coagulants: NSAIDs may enhance the effects of anticoagulants (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).

4.6 Fertility, pregnancy and lactation

Although no teratogenic effect has been reported in the literature, it is recommended, as for all NSAIDs, not to administer ibuprofen during the first trimester.

The onset of labour may be delayed and the duration of labour may be increased, so ibuprofen should not be used towards the end of the third trimester.

Ibuprofen appears in breast milk in very low concentrations and is unlikely to affect the breast-fed infant adversely.

4.7 Effects on ability to drive and use machines

None known.

4.8 Undesirable effects

Gastrointestinal: The most common observed adverse events are gastrointestinal in nature. Peptic ulcers, perforation or GI bleeding, sometimes fatal in the elderly, may occur (see section 4.4). Nausea, vomiting, diarrhoea, flatulence, constipation, dyspepsia, abdominal pain, melaena, haematemesis, ulcerative stomatitis, exacerbation of colitis and Crohn's disease (see section 4.4 – Special warnings and precautions for use) have been reported following administration. Less frequently, gastritis has been observed.

Skin: Rashes, pruritus, fluid build up in the tissue below the skin and in the mucous membranes which appear as spots or lumps, blood blisters and occasionally flaking of the skin.

Haematological: Most frequently the blood does not clot as well which may result in easy bruising or bleeding and occasionally anaemia. Thrombocytopenia, occasionally agranulocytosis and aplastic anaemia have also been reported.

Kidney: Blood in the urine, kidney damage and kidney failures have been reported.

Breathing: Wheezing and breathing difficulties may be triggered in patients suffering from or with previous history of bronchial asthma or allergic disease.

Liver: Abnormal liver function tests, jaundice, inflammation of the liver and occasional liver failure.

In addition, fluid retention and weight gain, headache, ringing in the ear, dizziness and vertigo, visual disturbances, depression, confusion, hallucinations and generalised allergic reactions including sudden collapse have been reported.

Bullous reactions including Stevens-Johnson syndrome and toxic epidermal necrolysis (very rare).

Drug reaction with eosinophilia and systemic symptoms (DRESS syndrome).Acute generalised exanthematous pustulosis (AGEP) Frequency is unknown.

Clinical studies suggest that the 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) (see section 4.4).

Oedema, hypertension and cardiac failure have been reported in association with NSAID treatment.

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 HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; e-mail: medsafety@hpra.ie.

4.9 Overdose

Symptoms include headache, vomiting, drowsiness and hypotension. Hyperkalaemia may develop.

In the event of overdose, gastric lavage is recommended. It is also advisable to monitor renal function and blood pressure following overdose.

In serious poisoning metabolic acidosis may occur.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Ibuprofen is a non-steroidal anti-inflammatory agent of the propionic acid group. It has analgesic, antipyretic and anti-inflammatory properties.

Experimental data suggest that ibuprofen may competitively inhibit the effect of low dose aspirin (acetylsalicyclic acid) 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 (acetylsalicyclic acid) dosing (81mg), a decreased effect of aspirin (acetylsalicyclic acid) 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 (acetylsalicyclic acid) cannot be excluded No clinically relevant effect is considered to be likely for occasional ibuprofen use (see section 4.5).

5.2 Pharmacokinetic properties

- Absorption:

Ibuprofen is 99% protein bound and it has an elimination half-life of about two hours.

- Distribution:

The short plasma half-life does not lead to accumulation phenomena. Ibuprofen appears in breast milk in low concentrations and is unlikely to affect the breast-fed infant adversely.

- Metabolism:

Ibuprofen does not have any enzyme-inducing effect. It is 90% metabolised in the liver to 2-Hydroxyibuprofen and 2-Carboxyibuprofen.

- Excretion:

The metabolites are excreted in the urine along with approximately 9% of unchanged drug.

Elderly:
Age has no significant effect on the kinetics of ibuprofen.

5.3 Preclinical safety data

As a well-established and widely used ingredient, the preclinical safety of ibuprofen is well documented.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Maize starch
Pregelatinised starch
Colloidal anhydrous silica
Stearic acid
Corn starch grade 826
Croscarmellose sodium
Sodium laurilsulfate
Microcrystalline cellulose
Carnauba wax
Sucrose

Opalux Brown AS-R-9030-A
Sucrose
Titanium dioxide (E171)
Red iron oxide (E172)
Povidone (E1201)
Sodium benzoate (E211)
Methyl parahydroxybenzoate (E218)
Propyl parahydroxybenzoate (E216)

Opagloss Regular GS-2-0310
Pharmaceutical shellac
Povidone
Acetylated monoglyceride

Opacode Black –S-1-8152HV
Shellac
Black iron oxide (E172)
Soya lecithin MC thin
Antifoam DC 1510

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

A PVC, PE, PVDC, paper/aluminium foil blister pack containing 2, 4, 10 or 20 tablets.
Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

No special requirements

7 MARKETING AUTHORISATION HOLDER

Pfizer Healthcare Ireland
9 Riverwalk
National Digital Park

Citywest Business Campus
Dublin 24
Ireland

8 MARKETING AUTHORISATION NUMBER

PA0822/163/002

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