Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Easofen Rapid Relief Max Strength 400 mg soft capsules

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each soft capsule contains 400 mg ibuprofen.

Excipient(s) with known effect
Each soft capsule contains 72 mg sorbitol.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Soft capsule.

A transparent, oval shape, soft gelatine capsule (about 15.8 mm x 9.8 mm) containing clear colourless liquid.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Easofen is indicated in adults and adolescents weighing from 40 kg (12 years of age and above) for the short-term symptomatic treatment of mild to moderate pain such as headache, period pain, dental pain and fever and pain associated with the common cold.

4.2 Posology and method of administration

Posology

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

Adults and adolescents weighing from 40 kg (12 years of age and above)
Initial dose is 400 mg of ibuprofen (one capsule). Then, if necessary, additional dose of 400 mg can be taken with the interval of six hours between doses. A total dose of 1 200 mg ibuprofen (three capsules) should not be exceeded in any 24-hour period.

If in adults the product is required for more than 3 days in the case of fever and 4 days for treatment of pain, or if the symptoms worsen the patient is advised to consult a doctor.

Special patient groups

Elderly
No special dose adjustment is required. Because of the possible undesirable-effect profile (see section 4.4), the elderly should be monitored particularly carefully.

Renal insufficiency
No dose reduction is required in patients with mild to moderate impairment to renal function (patients with severe renal insufficiency, see section 4.3).

Hepatic insufficiency (see section 5.2)
No dose reduction is required in patients with mild to moderate impairment to hepatic function (patients with severe hepatic dysfunction, see section 4.3).

Paediatric population

Easofen is not intended for use in adolescents weighing less than 40 kg or children under 12 years of age.
If in adolescents this medicinal product is required for more than 3 days, or if symptoms worsen a doctor should be consulted.

Method of administration
Oral use.
Easofen should be taken with a glass of water.
The capsules should not be chewed.
It is recommended that patients with a sensitive stomach take Easofen with food.
If taken shortly after eating, the onset of action of Easofen may be delayed. If this happens, patients should not take more Easofen than recommended within section 4.2 or until the correct re-dosing interval has passed

Duration of treatment
For short-term use only.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- In patients with a history of hypersensitivity reactions (e.g. bronchospasm, asthma, rhinitis, angioedema or urticaria) associated with the intake of acetylsalicylic acid (ASA) or other non-steroidal anti-inflammatory drugs (NSAIDs).
- 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 ulceration or bleeding).
- Patients with severe hepatic failure, severe renal failure, or severe heart failure (NYHA Class IV). See also section 4.4.
- In patients with cerebrovascular or other active bleeding.
- In patients with unclarified blood-formation disturbances.
- In patients with severe dehydration (caused by vomiting, diarrhoea or insufficient fluid intake).
- During the 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 possible duration necessary to control symptoms (see gastrointestinal (GI) and cardiovascular risks below).

Caution is required in patients with certain conditions, which may be made worse:

- systemic lupus erythematosus and mixed connective tissue disease – increased risk of aseptic meningitis (see section 4.8)
- congenital disorder of porphyrin metabolism (e.g. acute intermittent porphyria)
- gastrointestinal disorders and chronic inflammatory intestinal disease (ulcerative colitis, Crohn's disease) (see section 4.8)
- hypertension and/or cardiac impairment (see section 4.3 and 4.8)
- renal impairment as renal function may deteriorate (see sections 4.3 and 4.8)
- hepatic dysfunction (see sections 4.3 and 4.8)
- directly after major surgery
- in patients who show allergic reactions to other substances, as they are also at a higher risk of hypersensitivity reactions when using ibuprofen
- in patients who suffer from hayfever, nasal polyps, chronic obstructive respiratory disorders, or have a history of allergic disease, as an increased risk exists for them of allergic reactions occurring. These may present as asthma attacks (so-called analgesics asthma), Quincke's oedema or urticaria

Gastrointestinal (GI) safety
The use with concomitant NSAID's, including cyclo-oxygenase-2 specific inhibitors, increases risk of adverse reactions (see section 4.5) and should be avoided.

Elderly
The elderly have an increased frequency of adverse reactions to NSAIDs especially gastrointestinal (GI) bleeding and perforation which may be fatal (see section 4.2).

Gastrointestinal (GI) bleeding, ulceration or perforation
Gastrointestinal (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.
When GI bleeding or ulceration occurs in patients receiving ibuprofen, the treatment should be withdrawn.

The risk of GI bleeding, ulceration or perforation is higher with increasing NSAID doses and 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 acetylsalicylic acid, or other drugs likely to increase gastrointestinal risk (see below and section 4.5).
Patients with a history of GI toxicity, particularly the 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 (SSRI's) or anti-platelet agents such as aspirin (see section 4.5).

NSAID's 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).

Severe cutaneous adverse reactions (SCARs)
Severe cutaneous adverse reactions (SCARs) including exfoliative dermatitis, erythema multiforme, Stevens-Johnson syndrome (SJS), Toxic Epidermal Necrolysis (TEN), Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS syndrome), and acute generalised exanthematous pustulosis (AGEP), which can be life-threatening or fatal, have been reported in association with the use of ibuprofen (see section 4.8). Most of these reactions occurred within the first month.If signs and symptoms suggestive of these reactions appear ibuprofen should be withdrawn immediately and an alternative treatment considered (as appropriate).
Exceptionally, *Varicella* can be at the origin of serious cutaneous and soft tissues 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 ibuprofen in case of *Varicella*.

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 data suggest that use of ibuprofen, particularly at high doses (2 400 mg daily) may be associated with a small increased risk of arterial thrombotic events (e.g. myocardial infarction or stroke). Overall, epidemiological studies do not suggest that low dose ibuprofen (e.g. ≤ 1 200 mg 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 (2 400 mg/day) should be avoided.
Careful consideration should also be exercised before initiating long-term treatment for patients with risk factors for cardiovascular events (e.g. hypertension, hyperlipidaemia, diabetes mellitus, smoking), particularly if high doses of ibuprofen (2 400 mg/day) are required.

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.

Other notes
Severe acute hypersensitivity reactions (for example anaphylactic shock) are observed very rarely. At the first signs of a hypersensitivity reaction after taking/administering ibuprofen therapy must be stopped. Medically required measures, in line with the symptoms, must be initiated by specialist personnel.

Ibuprofen, the active substance of Easofen Rapid Relief Max Strength may temporarily inhibit the blood-platelet function (thrombocyte aggregation). Therefore, it is recommended to monitor patients with coagulation disturbances carefully.

In prolonged administration of ibuprofen, regular checking of the liver values, the kidney function, as well as of the blood count, is required.

Prolonged use of any type of painkiller for headaches can make them worse. If this situation is experienced or suspected, medical advice should be obtained and treatment should be discontinued. The diagnosis of medication overuse headache (MOH) should be suspected in patients who have frequent or daily headaches despite (or because of) the regular use of headache medications.

The habitual intake of painkillers, particularly the combination of several painkillers, may lead to permanent renal damage with the risk of renal failure (analgesic nephropathy). This risk may be increased by salt loss and dehydration.

Through concomitant consumption of alcohol, active substance-related undesirable effects, particularly those that concern the gastrointestinal tract or the central nervous system, may be increased on use of NSAIDs.

There is a risk of renal impairment in dehydrated adolescents.

Masking of symptoms of underlying infections
Easofen Rapid Relief Max Strength 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 Easofen Rapid Relief Max Strength is administered for fever or pain relief in relation to infection, monitoring of infection is advised. In non-hospital settings, the patient should consult a doctor if symptoms persist or worsen.

Excipients
This medicinal product contains sorbitol. Patients with hereditary fructose intolerance (HFI) should not take/be given this medicinal product.

4.5 Interaction with other medicinal products and other forms of interaction

Acetylsalicylic acid (low dose)
Concomitant administration of ibuprofen and acetylsalicylic 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 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 clinical relevant effect is considered to be likely for occasional ibuprofen use (see section 5.1).

Other NSAIDs, including cyclooxygenase-2 selective inhibitors
The concomitant administration of several NSAIDs may increase the risk of gastrointestinal ulcers and bleeding due to a synergistic effect. The concomitant use of ibuprofen with other NSAIDs should therefore be avoided (see section 4.4).

Digoxin, phenytoin, lithium
The concomitant use of ibuprofen with digoxin, phenytoin or lithium preparations may increase serum levels of these medicinal products. A check of serum-lithium, serum-digoxin and serum-phenytoin levels is not as a rule required on correct use (maximum over 4 days).

Corticosteroids
Corticosteroids as these may increase the risk of adverse reactions, especially of the gastrointestinal tract (gastrointestinal ulceration or bleeding) (see section 4.3).

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

Anticoagulants
NSAIDs may enhance the effect of anti-coagulants, such as warfarin (see section 4.4).

Probenecid and sulfinpyrazone
Medicinal products that contain probenecid or sulfinpyrazone may delay the excretion of ibuprofen.

Diuretics, ACE inhibitors, beta-receptor-blocker and angiotensin-II antagonists

NSAIDs may reduce the effect of diuretics and other antihypertensive 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, beta-receptor-blocker 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. 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.

Potassium sparing diuretics
The concomitant administration of ibuprofen and potassium-sparing diuretics may lead to hyperkalaemia.

Methotrexate
The administration of ibuprofen within 24 hours before or after administration of methotrexate may lead to elevated concentrations of methotrexate and an increase in its toxic effect.

Cyclosporine
The risk of a kidney-damaging effect due to cyclosporine is increased through the concomitant administration of certain nonsteroidal anti-inflammatory drugs. This effect also cannot be ruled out for a combination of cyclosporine with ibuprofen.

Tacrolimus
The risk of nephrotoxicity is increased if the two medicinal products are administered concomitantly

Zidovudine
There is evidence of an increased risk of haemarthroses and haematoma in HIV (+) haemophiliacs receiving concurrent treatment with zidovudine and ibuprofen. Increased risk of haematological toxicity when NSAIDs are given with zidovudine.

Sulfonylureas
Clinical investigations have shown interactions between nonsteroidal anti-inflammatory drugs and antidiabetics (sulphonylureas). Although interactions between ibuprofen and sulphonylureas have not been described to date, a check of blood-glucose values is recommended as a precaution on concomitant intake.

Quinolone antibiotics
Animal data indicate that NSAID's can increase the risk of convulsions associated with quinolone antibiotics. Patients taking NSAID's and quinolones may have an increased risk of developing convulsions.

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

CYP2C9 inhibitors
Concomitant administration of ibuprofen with CYP2C9 inhibitors may increase the exposure to ibuprofen (CYP2C9 substrate). In a study with voriconazole and fluconazole (CYP2C9 inhibitors), an increased S(+)-ibuprofen exposure by approximately 80 to 100 % has been shown. Reduction of the ibuprofen dose should be considered when potent CYP2C9 inhibitors are administered concomitantly, particularly when high-dose ibuprofen is administered with either voriconazole and fluconazole.

4.6 Fertility, 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.

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 (premature constriction/closure of the ductus arteriosus and pulmonary hypertension);
- renal dysfunction (see above)
- 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 (see sections 4.3 and 5.3).

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

Fertility
There is some evidence that drugs which inhibit cyclooxygenase/prostaglandin synthesis may cause impairment of female fertility by an effect on ovulation. This is reversible on withdrawal of treatment.

4.7 Effects on ability to drive and use machines

Ibuprofen generally has no or negligible influence on the ability to drive and use machines. However, since at higher dose central nervous undesirable effects such as tiredness and dizziness may occur, the ability to react and the ability to take part actively in road traffic and to operate machines may be impaired in individual cases and these patients should avoid driving or using machinery. This applies to a greater extent in combination with alcohol.

4.8 Undesirable effects

The list of the following undesirable effects comprises all undesirable effects that have become known under treatment with ibuprofen, also those under high-dose long-term therapy in rheumatism patients. The stated frequencies, which extend beyond very rare reports, refer to the short-term use of daily doses up to a maximum of 1 200 mg ibuprofen for oral dosage forms and a maximum of 1 800 mg for suppositories.

With the following adverse drug reactions, it must be accounted for that they are predominantly dose-dependent and vary interindividually.

The most commonly observed adverse events are gastrointestinal in nature. Peptic ulcers, perforation or GI bleeding, sometimes fatal, particularly 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) have been reported following administration. Less frequently, gastritis has been observed. Particularly the risk of gastrointestinal bleeding occurring is dependent on the dose range and the duration of use.

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

Clinical studies suggest that use of ibuprofen, particularly at a high dose (2 400 mg/day) may be associated with a small increased risk of arterial thrombotic events (for example myocardial infarction or stroke) (see section 4.4).

Hypersensitivity reactions have been reported and these may consist of:
(a) non-specific allergic reactions and anaphylaxis
(b) respiratory tract reactivity, e.g. asthma, aggravated asthma, bronchospasm, dyspnoea
(c) various skin reactions, e.g. pruritus, urticaria, angioedema and more rarely exfoliative and bullous dermatoses (including epidermal necrolysis and erythema multiforme)

The patient is to be instructed to inform a doctor at once and to stop taking Easofen Rapid Relief Max Strength if they experience any of the above.

Please note that within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

Very common (≥1/10)
Common (≥1/100 to <1/10)
Uncommon (≥1/1 000 to <1/100)
Rare (≥1/10 000 to <1/1 000)
Very rare (<1/10 000)
Not known (cannot be estimated from the available data)

Infections and infestations
Very rare: Exacerbation of infection-related inflammations (e.g. development of necrotising fasciitis) coinciding with the use of nonsteroidal anti-inflammatory drugs has been described. This is possibly associated with the mechanism of action of the nonsteroidal anti-inflammatory drugs.

If signs of an infection occur or get worse during use of ibuprofen, the patient is therefore recommended to go to a doctor without delay. It is to be investigated whether there is an indication for an anti-infective/antibiotic therapy.

The symptoms of aseptic meningitis with neck stiffness, headache, nausea, vomiting, fever or consciousness clouding have been observed under ibuprofen. Patients with autoimmune disorders (SLE, mixed connective-tissue disease) appear to be predisposed.

Blood and lymphatic system disorders
Very rare: Disturbances to blood formation (anaemia, leukopenia, thrombocytopenia, pancytopenia, agranulocytosis). The first signs may be fever, sore throat, superficial wounds in the mouth, influenza-like complaints, severe lassitude, nosebleeds and skin bleeding. In such cases the patient should be advised to discontinue the medicine immediately, to avoid any self-medication with analgesics or antipyretics and to consult a physician.

The blood count should be checked regularly in long-term therapy

Immune system disorders
Uncommon: Hypersensitivity reactions with urticaria and pruritus, as well as asthma attacks (possibly with drop in blood pressure).
Very rare: Severe general hypersensitivity reactions. Symptoms could be: facial, tongue and laryngeal swelling, dyspnoea, tachycardia, hypotension, (anaphylaxis, angioedema or severe shock).
Exacerbation of asthma and bronchospasm.

Psychiatric disorders
Very rare: Psychotic reactions, depression.

Nervous system disorders
Uncommon: Central nervous disturbances such as headache, dizziness, sleeplessness, agitation, irritability or tiredness.

Eye disorders
Uncommon: Visual disturbances.

Ear and labyrinth disorders
Rare: Tinnitus, hearing impaired.

Cardiac disorders
Very rare: Palpitations, heart failure, myocardial infarction.
Not known: Kounis syndrome.

Vascular disorders
Very rare: Arterial hypertension, vasculitis.

Gastrointestinal disorders
Common: Gastrointestinal complaints such as dyspepsia, pyrosis, abdominal pain, nausea, vomiting, flatulence, diarrhoea, constipation and slight gastrointestinal blood losses that may cause anaemia in exceptional cases.

Uncommon: Gastrointestinal ulcers, potentially with bleeding and perforation. Ulcerative stomatitis, exacerbation of colitis and Crohn's disease (see section 4.4), gastritis.

Very rare: Oesophagitis, pancreatitis, formation of intestinal diaphragm-like strictures.
The patient is to be instructed to withdraw the medicinal product and to go to a doctor immediately if severe pain in the upper abdomen or melaena or haematemesis occurs.

Hepatobiliary disorders
Very rare: Hepatic dysfunction, hepatic damage, particularly in long-term therapy, hepatic failure, acute hepatitis.

Skin and subcutaneous tissue disorders
Uncommon: Various skin rashes.
Very rare: Severe cutaneous adverse reactions (SCARs) (including Erythema multiforme, exfoliative dermatitis, Stevens-Johnson syndrome, and toxic epidermal necrolysis), alopecia. In exceptional cases, severe skin infections and soft-tissue complications may occur during a varicella infection (see also "Infections and infestations").
Not known: Drug reaction with eosinophilia and systemic symptoms (DRESS syndrome), acute generalised exanthematous pustulosis (AGEP), photosensitivity reactions.

Renal and urinary disorders
Rare: Kidney-tissue damage (papillary necrosis) and elevated uric acid concentrations in the blood may also occur rarely. Elevated urea concentrations in the blood.

Very rare: Formation of oedemas, particularly in patients with arterial hypertension or renal insufficiency, nephrotic syndrome, interstitial nephritis that may be accompanied by acute renal insufficiency. Renal function should therefore be checked regularly.

Investigations
Rare: Decreased haemoglobin levels.

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
Website: www.hpra.ie

4.9 Overdose

In adolescents and adults, the dose response effect is not 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 dizziness, 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.

No special antidote is available.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antiinflammatory and antirheumatic products, Propionic acid derivative; ATC Code: M01A E01

Ibuprofen is a nonsteroidal anti-inflammatory drug (NSAID) that in the conventional animal experiment inflammation models has proven to be effective via prostaglandin-synthesis inhibition. In humans, ibuprofen reduces inflammatory-related pain, swellings and fever. Furthermore, ibuprofen reversibly inhibits ADP – and collagen – induced platelet aggregation.

Experimental data suggest that ibuprofen may competitively inhibit the effect of low dose acetylsalicylic acid on platelet aggregation when they are dosed concomitantly. Some pharmacodynamics studies show that when single doses of ibuprofen 400 mg were taken within 8 h before or within 30 min after immediate release acetylsalicylic acid dosing (81 mg), a decreased effect of acetylsalicylic 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 acetylsalicylic 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
On oral administration, ibuprofen is partly absorbed in the stomach and then completely in the small intestine.
Peak plasma levels following oral administration of a normal-release pharmaceutical form (tablet) are reached after 1 – 2 hours. Ibuprofen is absorbed rapidly from the gastrointestinal tract following oral administration. In a pharmacokinetic study (R07-1009), the time to peak plasma levels (median T_{max}) in fasted state, for normal release pharmaceutical form ibuprofen acid tablets was 90 min compared with 40 min for ibuprofen soft capsules. Ibuprofen is detected in the plasma for more than 8 hours after administration of ibuprofen.

Distribution
Plasma-protein binding is about 99 %.

Elimination
Following hepatic metabolism (hydroxylation, carboxylation, conjugation), the pharmacologically inactive metabolites are completely eliminated, mainly renally (90 %), but also with the bile. The elimination half-life in healthy individuals and those with liver and kidney diseases is 1.8 - 3.5 hours.

5.3 Preclinical safety data

The subchronic and chronic toxicity of ibuprofen in animal experiments was observed principally as lesions and ulcerations in the gastro-intestinal tract. *In vitro* and *in vivo* studies gave no clinically relevant evidence of a mutagenic potential of ibuprofen. In studies in rats and mice no evidence of carcinogenic effects of ibuprofen was found. Ibuprofen led to inhibition of ovulation in rabbits as well as disturbance of implantation in various animal species (rabbit, rat, mouse). Experimental studies have demonstrated that ibuprofen crosses the placenta, for maternally toxic doses, an increased incidence of malformations (e.g. ventricular septal defects) was observed. In animal studies, it has been observed that the use of NSAIDs, known to inhibit prostaglandin synthesis, may increase the incidence of dystocia and delayed parturition.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Capsule fill
Macrogol 600 (E1521)
Potassium hydroxide (E525)
Purified Water

Capsule shell
Gelatin (E441)
Sorbitol, Liquid Partially Dehydrated (E420)
Purified Water

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

This medicine does not require any special temperature storage conditions. Store in the original package in order to protect from moisture.

6.5 Nature and contents of container

Aluminium – White opaque PVC/PE/PVdC blister.
Each carton may contain 10 or 20 soft capsules in blister strips.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Clonmel Healthcare Ltd
Waterford Road
Clonmel, Co. Tipperary
E91 D768
Ireland

8 MARKETING AUTHORISATION NUMBER

PA0126/343/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 5th August 2022

10 DATE OF REVISION OF THE TEXT

October 2025