SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT
Ibusan 400mg capsules, soft

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Each capsule, soft contains ibuprofen 400 mg.

Excipient(s) with known effect: sorbitol (E420).
For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM
Capsule, soft
Transparent, pink/red colour (carmine red) oval capsule (approximately 15 x 10 mm)

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Ibusan 400mg capsules are indicated for symptomatic relief of headaches, migraine, dental pain, backache, dysmenorrhoea, muscular pain, neuralgia, non-serious arthritic conditions, rheumatic pain, feverishness, colds and influenza.

Ibusan 400mg capsules are recommended for adults and adolescents over 12 years (from 40 kg bodyweight).

Due to the amount of active substance in one capsule, Ibusan 200mg capsules are recommended for adults and children over 6 years (from 20 kg bodyweight).

4.2 Posology and method of administration

Posology
For oral administration and short-term use only.
Adults and adolescents over 12 years (from 40 kg bodyweight):
The lowest effective dose should be used for the shortest duration necessary to relieve symptoms.
Adults should consult a doctor if symptoms persist or worsen, or if the product is required for more than 10 days.
If in adolescents (12 years of age and above) this medicinal product is required for more than 3 days, or if symptoms worsen a doctor should be consulted.

The recommended dose ranges from 200 mg to 400 mg of ibuprofen, up to three times a day as required.

The interval between two doses should be at least 4 hours.

The dose of 1200 mg should not be exceeded in any 24 hour period.

Children over 6 years (≤ 39 kg bodyweight)
For children aged 6 to 12 years a product containing 200 mg of ibuprofen is recommended.

Ibusan 200 mg should only to be used for children with at least 20 kg bodyweight.
The maximum total daily dose of ibuprofen is 20-30 mg per kg of body weight, divided into 3 to 4 single doses with dosing intervals of 6 to 8 hours. The maximum recommended daily dose should not be exceeded. A total dose of 30 mg/kg ibuprofen should not be exceeded in any 24-hour period. For Ibusan 200 mg in children the following dosing instruction applies:

<table>
<thead>
<tr>
<th>Body weight</th>
<th>Single dose in number of capsules</th>
<th>Maximum daily dose in number of capsules</th>
</tr>
</thead>
<tbody>
<tr>
<td>Children 20 kg – 29 kg</td>
<td>1 capsule of Ibusan 200 mg (ibuprofen 200 mg)</td>
<td>3 (equivalent up to 600 mg ibuprofen)</td>
</tr>
<tr>
<td>Children 30 kg – 39 kg</td>
<td>1 capsule of Ibusan 200 mg (ibuprofen 200 mg)</td>
<td>4 (equivalent up to 800 mg ibuprofen)</td>
</tr>
</tbody>
</table>

If in children aged from 6 years this medicinal product is required for more than 3 days, or if symptoms worsen, a doctor should be consulted.

Children under 6 years (<20 kg bodyweight)
Ibusan 200 mg and Ibusan 400 mg are not suitable for children under 6 years (< 20 kg bodyweight), due to the amount of active substance in one capsule.

Elderly
In elderly patients the dosage is the same as in adults, but increased caution is necessary (see section 4.4).

Hepatic or renal impairment
No dose reduction is required in patients with mild to moderate impairment of renal or hepatic function, however increased caution is necessary (see section 4.4).

Method of administration
Capsules should be swallowed whole with a sufficient amount of liquid.
The capsule may be taken with or without food. If taken with food or shortly after eating, the onset of action may be delayed. However taking it with food improves tolerability of the product and reduces probability of gastrointestinal problems.

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

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1
- 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)
- 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
- Disorders of haemocoagulation and haemopoiesis
- Patients with severe hepatic failure, severe renal failure or severe heart failure (NYHA Class IV) (see also section 4.4).
- During the last trimester of pregnancy as there is a risk of premature closure of the foetal ductus arteriosus with possible persistent pulmonary hypertension. The onset of labour may be delayed and the duration increased with an increased bleeding tendency in both mother and child (see section 4.6).

Ibusan 400 mg is not suitable for children under 12 years (< 40 kg bodyweight), due to the amount of active substance in one capsule.

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).

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

Elderly
The elderly have an increased frequency of adverse reactions to NSAIDs especially gastrointestinal bleeding and perforation which may be fatal (see section 4.8).

Respiratory
Bronchospasm may be precipitated in patients suffering from, or with a history of, bronchial asthma or allergic disease. Caution is required in patients who suffer from hay fever, nasal polyps or chronic obstructive respiratory disorders as an increased risk of allergic reactions exists for them.

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 and 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). Monitoring of renal function is recommended in patients at risk, i.e. patients with cardiac and renal impairment, treated with diuretics or during dehydration of any etiology.

In general terms, the habitual intake of painkillers, particularly the combination of several pain-relieving active substances, may lead to permanent renal damage with the risk of renal failure (analgesic nephropathy). This risk may be increased under physical strain associated with the loss of salt and dehydration. Therefore, it should be avoided.

Hepatic
Hepatic dysfunction (see sections 4.3 and 4.8). Control of blood count and routine monitoring of kidney and liver function is advisable with prolonged administration. It is suitable to discontinue the therapy with ibuprofen when deterioration of the liver function occurs in connection with its administration. After discontinuation of the treatment the health state usually normalizes. Occasional monitoring of glycemia is also suitable.

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. ≤1200mg/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 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. In women who have difficulties conceiving or who are undergoing investigation of infertility, withdrawal of ibuprofen should be considered.

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 ulcers, 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 active substances 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 or anti-platelet agents such as acetylsalicylic acid (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 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. Ibuprofen should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity.

**Other notes**

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.

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 with use of NSAIDs.

Ibuprofen may mask the symptoms of an infection (fever, pain and swelling).

**Excipients**

Ibusan 400mg contains sorbitol. Patients with rare hereditary problems of fructose intolerance should not take this medicine.

Ibusan 400 mg contains 32 mg potassium per capsule.
4.5 Interaction with other medicinal products and other forms of interaction

Use with concomitant NSAIDs, including cyclooxygenase-2 specific inhibitors – increased risk of adverse reactions

Ibuprofen (like other NSAIDs) should not be used in combination with:

- *Acetylsalicylic acid*: 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 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:

- *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, beta-receptor-blockers or angiotensin-II antagonists and agents that inhibit cyclooxygenase 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. Diuretics can increase the risk of nephrotoxicity of NSAIDs.

- *Potassium sparing diuretics*: The concomitant administration of ibuprofen and potassium-sparing diuretics may lead to hyperkalaemia (a check of serum potassium is recommended).

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

- *Antiplatelet agents and selective serotonin reuptake inhibitors (SSRIs)*: These can increase the 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 increase in plasma levels of lithium.

- *Methotrexate*: There is evidence for the potential increase in plasma levels of methotrexate and an increase in its toxic effect, in particular the haematological toxic effects.

- *Baclofen*: there are clinical data indicating that NSAIDs may increase plasma level of this drug.

- *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 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.
• **Sulphonylurea derivatives**: 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 with concomitant intake.
• **Sulfinpyrazone, probenecid**: Medicinal products that contain probenecid or sulfinpyrazone may delay the excretion of ibuprofen.
• **Aminoglycosides**: since ibuprofen may decrease the clearance of aminoglycosides, their co-administration may increase the risk of nephrotoxicity and ototoxicity.
• **Pemetrexed**: since the concomitant administration may increase the toxic effects of pemetrexed.

### 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 gastrochisis 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 embryo-foetal 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 oligo-
hydroamnios
• the mother and the neonate, at the end of the pregnancy, to:
  - a possible prolongation of bleeding time, an anti-aggregating effect which
  may occur even at very low doses.
  - an inhibition of uterine contractions resulting in delayed or prolonged labour.
Consequently, ibuprofen is contraindicated during the third trimester of pregnancy
(see section 4.3).

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 (see section 4.4).

4.7 Effects on ability to drive and use machines
None expected at recommended dose and duration of therapy.

4.8 Undesirable effects

The following table summarises adverse drug reactions of ibuprofen divided into
groups according to MedDRA terminology together with their frequency: 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):

The list of the following adverse effects relates to those experienced with ibuprofen at
OTC doses, for short-term use. In the treatment of chronic conditions, under long-
term treatment, additional adverse effects may occur.

The adverse events observed most often are gastrointestinal in nature. Adverse events
are mostly dose-dependent, in particular the risk of occurrence of gastrointestinal
bleeding is dependent on the dosage range and duration of treatment.

<table>
<thead>
<tr>
<th>MedDRA system organ class</th>
<th>Frequency</th>
<th>Undesirable effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood and lymphatic system disorders</td>
<td>Very rare</td>
<td>Haematopoietic disorders (anaemia, leucopenia, thrombocytopenia, pancytopenia, agranulocytosis). First signs are: fever, sore throat, superficial mouth ulcers, flu-like symptoms, severe exhaustion, unexplained bleeding and bruising</td>
</tr>
<tr>
<td>Immune system disorders</td>
<td></td>
<td>Hypersensitivity reactions consisting of:</td>
</tr>
<tr>
<td></td>
<td>Uncommon</td>
<td>Urticaria, pruritus</td>
</tr>
<tr>
<td>Category</td>
<td>Frequency</td>
<td>Description</td>
</tr>
<tr>
<td>----------------------------------</td>
<td>------------</td>
<td>---------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Nervous system disorders</td>
<td>Uncommon</td>
<td>Headache</td>
</tr>
<tr>
<td></td>
<td>Very rare</td>
<td>Aseptic meningitis²</td>
</tr>
<tr>
<td>Ear and labyrinth disorders</td>
<td>Not known</td>
<td>Hearing impairment</td>
</tr>
<tr>
<td>Cardiac disorders</td>
<td>Not known</td>
<td>Cardiac failure and oedema</td>
</tr>
<tr>
<td>Vascular disorders</td>
<td>Not known</td>
<td>Hypertension</td>
</tr>
<tr>
<td>Gastrointestinal disorders</td>
<td>Uncommon</td>
<td>Abdominal pain, dyspepsia and nausea</td>
</tr>
<tr>
<td></td>
<td>Rare</td>
<td>Diarrhoea, flatulence, constipation and vomiting</td>
</tr>
<tr>
<td></td>
<td>Very rare</td>
<td>Peptic ulcer, perforation or gastrointestinal haemorrhage, melaena, haematemesis, sometimes fatal, particularly in the elderly (see section 4.4) Ulcerative stomatitis gastritis Exacerbation of ulcerative colitis and Crohn's disease (see section 4.4)</td>
</tr>
<tr>
<td></td>
<td>Not known</td>
<td>Exacerbation of ulcerative colitis and Crohn's disease (see section 4.4)</td>
</tr>
<tr>
<td>Hepatobiliary disorders</td>
<td>Very rare</td>
<td>Liver disorders</td>
</tr>
<tr>
<td>Skin and subcutaneous tissue disorders</td>
<td>Uncommon</td>
<td>Various skin rashes</td>
</tr>
<tr>
<td></td>
<td>Very rare</td>
<td>Severe forms of skin reactions such as bullous reactions, including Stevens-Johnson Syndrome, erythema multiforme and toxic epidermal necrolysis can occur</td>
</tr>
<tr>
<td>Renal and urinary disorders</td>
<td>Very rare</td>
<td>Acute renal failure, papillary necrosis, especially in long-term use, associated with increased serum urea and oedema</td>
</tr>
<tr>
<td></td>
<td>Not known</td>
<td>Renal insufficiency</td>
</tr>
<tr>
<td>Investigations</td>
<td>Very rare</td>
<td>Decreased haemoglobin level</td>
</tr>
</tbody>
</table>

Clinical studies suggest that use of ibuprofen (particularly at a high dose of 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).

¹ 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) assorted skin disorders, including rashes of various types e.g. pruritus, urticaria, purpura, angioedema and more rarely exfoliative and bullous dermatoses (including epidermal necrolysis and erythema multiforme)

2 The pathogenic mechanism of drug-induced aseptic meningitis is not fully understood. However, the available data on NSAID-related aseptic meningitis points to a hypersensitivity reaction (due to a temporal relationship with drug intake, and disappearance of symptoms after drug discontinuation). Of note, single cases of symptoms of aseptic meningitis (such as stiff neck, headache, nausea, vomiting, fever or disorientation) have been observed during treatment with ibuprofen, in patients with existing auto-immune disorders (such as systemic lupus erythematosus, mixed connective tissue disease).

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

4.9 Overdose
In children ingestion of more than 400 mg/kg may cause symptoms. In adults the dose response effect is less clear cut. The half-life in overdose is 1.5 to 3 hours.

Symptoms
Most patients who have ingested clinically important amounts of NSAIDs will develop no more than nausea, vomiting, epigastric pain, or more rarely diarrhoea. Tinnitus, headache and gastrointestinal bleeding are also possible. In more serious poisoning, toxicity is seen in the central nervous system, manifesting as drowsiness, occasionally excitation and disorientation or coma. Occasionally patients develop convulsions. In serious poisoning metabolic acidosis may occur and the prothrombin time/INR may be prolonged, probably due to interference with the actions of circulating clotting factors. Acute renal failure and liver damage may occur. Exacerbation of asthma is possible in asthmatics.

Management
Management should be symptomatic and supportive and include the maintenance of a clear airway and monitoring of cardiac and vital signs until stable. Consider oral administration of activated charcoal if the patient presents within 1 hour of ingestion of a potentially toxic amount. If frequent or prolonged, convulsions should be treated with intravenous diazepam or lorazepam. Give bronchodilators for asthma.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties
Pharmacotherapeutic group: Propionic acid derivatives
ATC Code: M01AE01

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

Clinical evidence demonstrates that when 400mg of ibuprofen is taken the pain relieving effects can last for up to 8 hours.

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 400mg were taken within 8 hours before or within 30 minutes 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

Ibuprofen is well absorbed from the gastrointestinal tract. Ibuprofen is extensively bound to plasma proteins.

Ibusan 400mg contains ibuprofen dissolved in a hydrophilic solvent inside a gelatine shell. On ingestion, the gelatine shell disintegrates in the gastric juice releasing the solubilised ibuprofen immediately for absorption. The median peak plasma concentration is achieved in approximately 30 minutes after administration when taken on an empty stomach.

The median peak plasma concentration for ibuprofen tablets is achieved approximately 1-2 hours after administration. A direct comparison of ibuprofen in the form of liquid capsule with ibuprofen in the form of tablet showed that the median peak plasma concentration was achieved more than twice as fast for the liquid capsule (32.5 min) compared to the tablets (90 min). When taken with food, peak plasma levels may be delayed.

Ibuprofen is metabolised in the liver to two major metabolites with primary excretion via the kidneys, either as such or as major conjugates, together with a negligible amount of unchanged ibuprofen. Excretion by the kidney is both rapid and complete. Elimination half-life is approximately 2 hours.

No significant differences in pharmacokinetic profile are observed in the elderly. In limited studies, ibuprofen appears in the breast milk in very low concentrations.
5.3 **Preclinical safety data**
No relevant information, additional to that contained elsewhere in the SPC.

6 **PHARMACEUTICAL PARTICULARS**

6.1 **List of excipients**
Macrogol 600
Potassium hydroxide 85% (E525)
Gelatine
Water purified
Sorbitol liquid, partially dehydrated (E420)
Carmine red 43% (E120)

6.2 **Incompatibilities**
Not applicable.

6.3 **Shelf life**
2 years

6.4 **Special precautions for storage**
Store below 25°C, store in the original package in order to protect from moisture.

6.5 **Nature and contents of container**
PVC/PVdC/Aluminium foil blister, paper folding box

Package size:
Ibusoft 200 mg: 12, 24 capsule, soft
Ibusoft 400 mg: 10, 12, 20 capsule, soft

Not all pack sizes may be marketed.
6.6 Special precautions for disposal
Any unused product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER
Winthrop Pharmaceuticals UK Limited
One Onslow Street
Guildford
Surrey
GU1 4YS
UK

Trading as: Zentiva, One Onslow Street, Guildford, Surrey, GU1 4YS, UK.

8 MARKETING AUTHORISATION NUMBER(S)
PL 17780/0663

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
30/09/2014

10 DATE OF REVISION OF THE TEXT
20/06/2016