Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Ibuprofen Chanelle Medical 400 mg capsules, soft

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each soft capsule contains 400 mg of ibuprofen (equivalent to 684 mg ibuprofen lysine)

Excipients with known effect
Each 400mg soft capsule contains 171mg of Sorbitol
Ibuprofen Chanelle Medical contains soya oil.
Ibuprofen Chanelle Medical contains azoderivative Allura red (E129).

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Opaque red, oblong capsule with "400" printed in white ink.
Each capsule is approximately 25.7 to 27.7 mm long.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

For the short-term symptomatic treatment of mild to moderate pain and/or fever.

Ibuprofen Chanelle Medical 400 mg is for use in adults and adolescents from 40 kg body weight (12 years old)

4.2 Posology and method of administration

Posology
For oral use and short-term use only. Capsules should not be chewed.
Undesirable effects may be minimised by using the lowest effective dose for the shortest duration necessary to control the symptoms (see section 4.4)

Adults and adolescents
Adults and adolescents ≥ 40 kg (12 years and older):
Initial dose 400 mg ibuprofen. If necessary additional doses of 1 capsule (400 mg ibuprofen) can be taken. The respective dosing interval should be chosen in line with the observed symptoms and the maximum recommended daily dose. It should not be below 6 hours. A total dose of 1200 mg ibuprofen should not be exceeded in any 24-hour period.

Body weight	Single dose in number of capsules	Maximum daily dose in number of capsules
≥40kg Adolescents, adults and the elderly	1 capsule (equivalent to 400 mg ibuprofen)	3 capsules (equivalent to 1200 mg ibuprofen)

In adolescents between 12 and 17 years:
If in adolescents this medicinal product is required for more than 3 days, or if symptoms persist or worsen a doctor should be consulted.

In adults:
If in adults this product is required for more than 3 days in the case of fever or for more than 4 days for pain treatment, or if the symptoms persist or worsen the patient is advised to consult a doctor.
It is recommended that patients with sensitive stomachs take Ibuprofen Chanelle Medical with food.
If taken shortly after eating, the onset of action of Ibuprofen Chanelle Medical may be delayed. If this happens do not take more Ibuprofen Chanelle Medical than recommended within section 4.2 (posology) or until the correct re-dosing interval has passed.

Pediatric Populations

Paediatric population:
Ibuprofen Chanelle Medical is contraindicated in adolescents less than 40 kg or below 12 years of age.
For use in the paediatric population, see also section 4.3.

Elderly population:
No special dose adjustment is required. Because of the possible undesirable-effect profile (see section 4.4), it is recommended to monitor the elderly particularly carefully.

Renal impairment:
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 impairment (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).

Method of administration
The capsules should be taken orally with water.

4.3 Contraindications

Children less than 40 kg or below 12 years of age.

- Hypersensitivity to ibuprofen or any of the excipients listed in Section 6.1.
- Patients who have previously shown hypersensitivity reactions (e.g. bronchospasm, asthma, rhinitis, angioedema or urticaria) associated with the intake of acetylsalicylic acid (ASA), ibuprofen 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.
- 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).
- The last trimester of pregnancy (see section 4.6).
- Ibuprofen Chanelle Medical contains lecithin (soybean). Lecithin may contain peanut protein. Patients allergic to peanut or soya, should not use this medicinal product.

4.4 Special warnings and precautions for use

Undesirable effects may be minimised by using the lowest effective dose for the shortest duration necessary to control symptoms (see GI and cardiovascular risks below).

The elderly have an increased frequency of adverse reactions to NSAIDs especially gastrointestinal bleeding and perforation, which may be fatal.

Respiratory:
Bronchospasm may be precipitated in patients suffering from, or with a 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 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).

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 (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/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.

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 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 aspirin (see section 4.5).

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

Dermatological:

Severe skin reactions
Serious skin reactions, some of them fatal, including exfoliative dermatitis, Stevens-Johnson syndrome, and toxic epidermal necrolysis (Lyell's syndrome), have been reported very rarely in association with the use of NSAIDs (see section 4.8). Patients appear to be at highest risk for these reactions early in the course of therapy: the onset of the reaction occurring in the majority of cases within the first month of treatment. Acute generalised exanthematous pustulosis (AGEP) has been reported in relation to ibuprofen-containing products. Ibuprofen 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 tissues infectious complications. To date, the contributing role of NSAIDs in the worsening of these infections cannot be ruled out. Thus, it may be advisable to avoid use of Ibruprofen Chanelle Medical in case of varicella.

Other notes:
Caution is required in patients:
- with congenital disorder of porphyrin metabolism (e.g. acute intermittent porphyria)
- immediately after major surgery
- with dehydration
- who have had hypersensitivity or allergic reactions to other substances, as they could be at an increased risk of hypersensitivity reactions with <Invented name>
- who suffer from hayfever, nasal polyps or chronic obstructive respiratory disorders, as for them an increased risk of allergic reactions exists. These may present as asthma attacks (so-called analgesic asthma), Quincke's oedema or urticaria.

Severe acute hypersensitivity reactions (for example anaphylactic shock) are observed very rarely. At the first signs of hypersensitivity reaction after taking Ibruprofen Chanelle Medical 200 mg, therapy must be stopped. Medically required measures, in line with the symptoms, must be initiated by competent persons.

Ibuprofen, the active substance of Ibruprofen Chanelle Medical may temporarily inhibit the blood-platelet function (thrombocyte aggregation). Therefore, it is recommended to monitor patients with coagulation disturbances carefully.

In prolonged administration of Ibruprofen Chanelle Medical regular control of liver function tests, 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.

In general, habitual intake of painkillers, particularly a combination of several analgesic 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 loss of salt and dehydration.

Concomitant use of NSAIDs and alcohol may increase the occurrence of undesirable effects associated with the medicinal product, particularly those that concern the gastrointestinal tract or the central nervous system.

NSAIDs may mask symptoms of infection and fever.

Paediatric population
200 mg strength:
There is a risk of renal impairment in dehydrated children and adolescents.

Warning on excipients
Ibruprofen Chanelle Medical contains lecithin (soybean). Lecithin may contain peanut protein. Patients allergic to peanut or soya, should not use this medicinal product.

Ibruprofen Chanelle Medical 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 interactions

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 aspirin (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)

Corticosteroids: as these may increase the risk of gastrointestinal ulceration or bleeding (see section 4.4)

Antihypertensives (ACE inhibitor, betareceptor-blockers and Angiotensin II Antagonists) 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, betareceptor-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. 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).

Antiplatelet agents and selective serotonin reuptake inhibitors (SSRIs): increased risk of gastrointestinal bleeding (see section 4.4).

Digoxin, phenytoin, lithium: The concomitant use of <Product name> with digoxin, phenytoin or lithium preparations may increase serum levels of these active substances. A check of serum-lithium, serum-digoxin and serum-phenytoin levels is not as a rule required on correct use (maximum over 3 or 4 days).

Methotrexate: The use of Ibuprofen Chanelle Medical within 24 hours before or after use of methotrexate may lead to elevated concentrations of methotrexate and an increase in its toxic effect.

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

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.

Sulfonylureas: Clinical investigations have shown interactions between nonsteroidal anti-inflammatory drugs and antidiabetics (sulphonylureas). Rare cases of hypoglycemia were reported in patients with concomitant use of sulfonylurea and ibuprofen. A check of blood-glucose values is recommended as a precaution on concomitant intake.

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.

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

Herbal extracts: Ginkgo biloba may potentiate the risk of bleeding with NSAIDs.

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.

During the first and second trimester of pregnancy, Ibuprofen Chanelle Medical should not be given unless clearly necessary. If Ibuprofen Chanelle Medical is used by a woman attempting to conceive 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 Chanelle Medical is contraindicated during the third trimester of pregnancy.
- Lactation/Breastfeeding:
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.

Breast-feeding:
Only small amounts of ibuprofen and its decomposition products pass into the breast milk. As no harmful effects to infants are known to date, it is usually not necessary to interrupt breast feeding during short-term use of Ibuprofen Chanelle Medical at the recommended doses.

4.7 Effects on ability to drive and use machines

For short-term use and at recommended dosage, Ibuprofen Chanelle Medical has no or negligible influence on the ability to drive and use machines. Patients who experience dizziness, drowsiness, vertigo or visual disturbances while they are taking ibuprofen, 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 the 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 1200 mg ibuprofen for oral dosage forms and a maximum of 1800 mg for suppositories.

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

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 which is dependent on the dosage range and duration of treatment. 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.

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

Clinical studies suggest that use of ibuprofen, particularly at high dose (2400 mg daily), may be associated with a small increased risk of arterial thrombotic events (for example myocardial infarction or stroke) (see section 4.4).

Exacerbation of infection-related inflammations (e.g. development of necrotising fasciitis) coinciding with the use of NSAIDS has been described. This is possibly associated with the mechanism of action of the NSAIDS.

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 antimicrobial/antibiotic therapy.

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

The patient is to be instructed to inform a doctor at once and no longer to take ibuprofen if one of the symptoms of hypersensitivity reactions occurs, which can happen even on first use, the immediate assistance of a doctor is required.

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.

Adverse events which have been associated with Ibuprofen are given below, listed by system organ class and frequency. Frequencies are defined as:

<Very common ([3]1/10)>
<Common ([3]1/100 to <1/10)>
<Uncommon ([3]1/1,000 to <1/100)>
<Rare ([3]1/10,000 to <1/1,000)>
<Very rare (<1/10,000)>
<not known (cannot be estimated from the available data)>

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

Infections and infestations	Very rare	Exacerbation of infection-related inflammations (e.g. development of necrotising fasciitis), in exceptional cases, severe skin infections and soft-tissue complications may occur during a varicella infection.
Blood and Lymphatic System Disorders	Very rare	Haematopoietic disorders (anaemia, leukopenia, thrombocytopenia, pancytopenia, agranuloctosis). The first signs may be fever, sore throat, superficial mouth ulcers, flu-like symptoms, severe exhaustion, nose and skin bleeding and bruising. In such cases, the patient should be advised to discontinue this medicinal product, to avoid any self-medication with analgesics or antipyretics and to consult a physician.
Immune System Disorders		Hypersensitivity reactions consisting of [1]
	Uncommon	Urticaria and pruritus
	Very rare	Severe general hypersensitivity reactions. They may present as face oedema, tongue and laryngeal swelling, dyspnoea, tachycardia, hypotension (anaphylaxis, angioedema or severe shock). Exacerbation of asthma
	Not Known	Respiratory tract reactivity comprising asthma, bronchospasm or dyspnoea
Psychiatric disorders	Very rare	Psychotic reactions, depression.

Nervous System Disorders	Uncommon	Central nervous disturbances such as headache, dizziness, sleeplessness, agitation, irritability or tiredness.
	Very rare	Aseptic meningitis. [2]
Eye disorders	Uncommon	Visual disturbances.
Ear and labyrinth disorders	Rare	Tinnitus, Hearing Impaired.
Cardiac Disorders	Very rare	Cardiac failure, palpitations and oedema myocardial infarction.
Vascular disorders	Very rare	Arterial hypertension, vasculitis.
Gastrointestinal Disorders	Common	Gastro-intestinal complaints such as abdominal pain, nausea and dyspepsia. Diarrhoea, flatulence, constipation, heartburn, vomiting and slight gastro-intestinal 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.
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 forms of skin reactions such as bullous reactions including Stevens-Johnson syndrome, erythema multiforme and toxic epidermal necrolysis (Lyell's syndrome), alopecia.
	Not Known	Drug reaction with eosinophilia and systemic symptoms (DRESS syndrome). Acute generalised exanthematous pustulosis (AGEP)
Renal and Urinary Disorders	Rare	Kidney-tissue damage (papillary necrosis) and elevated urea concentrations in the blood may also occur rarely; elevated uric acid concentrations in the blood, 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.
Investigations	Rare	Decreased haemoglobin levels.

Description of Selected Adverse Reactions

[1]Hypersensitivity reactions have been reported following treatment with ibuprofen. These may consist of (a) non-specific allergic reaction and anaphylaxis, (b) respiratory tract activity comprising asthma, aggravated asthma, bronchospasm or dyspnoea, or (c) assorted skin disorders, including rashes of various types, pruritus, urticaria, purpura, angioedema and, more rarely, exfoliative and bullous dermatoses (including toxic epidermal necrolysis, Stevens-Johnson Syndrome 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 immune 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 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 are unlikely at doses below 100 mg/kg.

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

Management – A specific antidote does not exist. 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. The local Poisons centre should be contacted for medical advice.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC Code: M01AE01 Pharmacotherapeutic group: Anti-inflammatory and anti-rheumatic products, non-steroids; propionic acid derivative. Ibuprofen lysine is the lysine salt of ibuprofen. Ibuprofen is a propionic acid derivative NSAID that has demonstrated its efficacy by inhibition of prostaglandin synthesis. In humans, ibuprofen reduces inflammatory pain, swellings and fever. Furthermore, ibuprofen reversibly inhibits 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 400mg were taken within 8h before or within 30 min after immediate release (acetylsalicylic acid) dosing (81mg), 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).

Each capsule contains 684mg of ibuprofen lysine. Following oral administration, ibuprofen lysine dissociates to ibuprofen acid and lysine. Lysine has no recognised pharmacological activity. The pharmacological properties of ibuprofen lysine, therefore, are the same as those of ibuprofen acid.

5.2 Pharmacokinetic properties

Most pharmacokinetic data obtained following the administration of ibuprofen acid also apply to ibuprofen lysine.

Absorption
On oral application, ibuprofen is partly absorbed in the stomach and then completely in the small intestine. Peak plasma concentrations occur 1 - 2 hours after administration of ibuprofen acid in solid oral immediate-release formulation. Following the administration of Ibuprofen Chanelle Medical ibuprofen is more rapidly absorbed from the gastrointestinal tract with peak serum concentration occurring 45 minutes (Tmax median of both enantiomere) after administration in the fasting state (with reference to BE study CPA 498-17 in 2017/2018).

Distribution
Plasma-protein binding about 99 %.

Biotransformation
Ibuprofen is metabolised in the liver (hydroxylation, carboxylation).

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

Elderly
No significant differences in pharmacokinetic profile are observed in the elderly.

Breast-feeding
In limited studies, ibuprofen appears in the breast milk in very low concentrations.

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.

Ibuprofen poses a risk to the aquatic environment (see section 6.6).

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Capsule Content
Medium Chain Triglycerides (MCT)
Lecithin (soybean)

Purified Water
Sorbitol Liquid partially dehydrated (E420)
Titanium dioxide in sorbitol liquid; 1:2 w/w (E171)
FD&C red #40; Allura red (E129)

Capsule Shell
Gelatin (Bloom 150)

Printing Ink
Purified water
Titanium dioxide (E171)
Propylene glycol (E1520)
Isopropyl alcohol
HPMC 2910/Hypromellose

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 months

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

Transparent PVC/PE/PVDC-AU blister packed in cardboard boxes.

Ibuprofen Chanelle Medical 400 mg is packaged in blister packages of 8, 10, 12, 16, 20 and 24 capsules.

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.
This medicinal product poses a risk to the environment (see section 5.3).

7 MARKETING AUTHORISATION HOLDER

Chanelle Medical
Dublin Road
Loughrea
Co. Galway
Ireland

8 MARKETING AUTHORISATION NUMBER

PA0688/053/002

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 6th December 2019

10 DATE OF REVISION OF THE TEXT