1.5 Product Information: IBUREN TABLETS

1.5.1 Prescribing information (Summary of products characteristics):

1. Name of the Medicinal Product: IBUREN TABLETS
Strength: Each film coated tablet contains Ibuprofen BP 200mg
Pharmaceutical form: Tablets

2. Qualitative and Quantitative composition:

Qualitative composition:

Sr. No.	Ingredient	Specification	Uses
1.	Ibuprofen	BP	Active
2.	Lactose	BP	Diluent
3.	Maize starch (mixing)	BP	Diluent
4.	Maize starch (paste)	BP	Binder
5.	Sodium methyl paraben	BP	Preservative
6.	Sodium propyl paraben	BP	Preservative
7.	Maize starch (lubrication)	BP	Lubricant
8.	Sodium starch glycollate	BP	Disintegrant
9.	Magnesium stearate	BP	Lubricant

CTD MODULE 1 ADMINISTRATIVE INFORMATION AND PRODUCT INFORMATION	
Product Name :	**IBUREN TABLETS (Ibuprofen 200mg)**

Quantitative composition:

Component and quality standard (and grade, if applicable)	**Function**	**Strength (label claim)**			
		Each film coated tablet contains Ibuprofen BP 200mg			
		Quantity in mg per tablet	**%**	**Quantity in Kg per 1,000,000 T**	**%**
Contents of **IBUREN TABLETS**					
Ibuprofen	Active	200.00	62.74	200.00	62.74
Lactose	Diluent	18.00	5.65	18.00	5.65
Maize starch (mixing)	Diluent	42.00	13.18	42.00	13.18
Maize starch (paste)	Binder	20.00	6.27	20.00	6.27
Sodium methyl paraben	Preservative	0.5	0.16	0.5	0.16
Sodium propyl paraben	Preservative	0.25	0.08	0.25	0.08
Maize starch (lubrication)	Lubricant	30.00	9.41	30.00	9.41
Sodium starch glycollate	Disintegrant	5.00	1.57	5.00	1.57
Magnesium stearate	Lubricant	3.00	0.94	3.00	0.94
Total	NA	318.75	100.00	318.75	100.00

3. Pharmaceutical form: Tablets

4. Clinical particular's:

4.1 Therapeutic indication:

For the relief of mild to moderate pain including rheumatic and muscular pain, backache, neuralgia, migraine, headache, dental pain, dysmenorrhoea, feverishness and for the relief of the symptoms of cold and influenza.

4.2 Posology and method of administration:

For oral administration and short-term use only. Undesirable effects may be minimized by using the lowest effective dose for the shortest duration necessary to control symptoms.

Adults, the elderly, and children and adolescents over 12 years of age:

If in children and adolescents, between the age of 12 and 18 years, this medicinal product is required for more than 3 days, or if symptoms worsen, a doctor should be consulted.

For adults aged 18 years or older the minimum effective dose should be used for the shortest time necessary to relieve symptoms. If the product is required for more than 10 days or if the symptoms worsen, or persist, the patient should consult a pharmacist or a doctor.

1 or 2 tablets to be taken up to three times a day, as required. The tablets should be taken with water.

Leave at least 4 hours between doses and do not take more than 1200mg (6 tablets) in any 24 hour period.

Not to be given to children under 12 years of age.

Method of Administration: Oral route.

4.3 Contraindication:

Hypersensitivity to Ibuprofen or any of the constituents in the product.

Ibuprofen is contra-indicated in patients who have previously shown hypersensitivity reactions (e.g. asthma, rhinitis, angiodema or urticaria) in response to aspirin or other non-steroidal anti-inflammatory drugs.

Active or previous peptic ulcer (two or more episodes of proven ulceration or bleeding).

History of upper gastrointestinal bleeding or perforation, related to previous NSAID therapy.

Patients with severe hepatic failure, renal failure or severe heart failure (NYHA Class IV).

Use in last trimester of pregnancy.

4.4 Special warning and precaution for use:

Caution is required in patients with certain conditions:

• Systemic lupus erythematosus as well as those with mixed connective tissue disease due to increased risk of aseptic meningitis.

• Gastrointestinal disorders and chronic inflammatory intestinal disease as these conditions may be exacerbated (ulcerative colitis, Crohn's disease).

• Caution is required prior to starting treatment in patients with a history of hypertension and or heart/failure. Oedema, hypertension and/or cardiac impairment as renal function may deteriorate and/or fluid retention occur.

• Renal impairment as renal function may deteriorate.

• Hepatic dysfunction.

Undesirable effects may be minimised by using the minimum effective dose for the shortest possible duration to control symptoms.

The elderly are at increased risk of the serious consequences of adverse reactions especially gastrointestinal bleeding and perforation which may be fatal.

Bronchospasm may be precipitated in patients suffering from or with a previous history of bronchial asthma or allergic disease.

Use with concomitant NSAIDs including cyclo-oxygenase-2 specific inhibitors should be avoided.

Cardiovascular and cerebrovascular effects

Clinical studies suggest that use of ibuprofen, particularly at high doses (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 daily) is associated with an increased risk of arterial thrombotic events.

Patients with uncontrolled hypertension, congestive heart failure (NYHA II-III), established ischaemic heart disease, peripheral arterial disease, and/or cerebrovascular disease should only be treated with ibuprofen after careful consideration and high doses (2400 mg/day) should be avoided.

Careful consideration should also be exercised before initiating long-term treatment of patients with risk factors for cardiovascular events (e.g. hypertension, hyperlipidaemia, diabetes mellitus, smoking), particularly if high doses of ibuprofen (2400 mg/day) are required.

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.

Gastro-intestinal (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 serious GI effects (including ulcerative colitis, Crohn's disease).

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 and in the elderly. These patients should commence treatment on the lowest dose available.

Patients with a history of GI toxicity, particularly when elderly, should report any unusual abdominal symptoms (especially GI bleeding) particularly in the initial stages of treatment.

Caution should be advised in patients receiving concomitant medications which could increase the risk of gastrotoxicity or bleeding, such as corticosteroids, or anticoagulants such as warfarin, selective serotonin uptake inhibitors or anti-platelet agents such as aspirin.

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

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. Patients appear to be at highest risk for these reactions early in the course of therapy: the onset of the reaction occurring in the majority of cases within the first month of treatment. Ibuprofen should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity.

Patients with rare hereditary problems of fructose intolerance should not take this medicine as this product contains sucrose.

Each tablet contains 67mg of sucrose. This should be taken into account in patients with diabetes mellitus.

There is a risk of renal impairment in dehydrated children and adolescents, between the ages of 12-18 year olds.

The label will include:

12-18 years: if symptoms worsen, or persist for more than 3 days, or you get new symptoms consult your doctor.

Adults: if symptoms worsen, or persist for more than 10 days, or you get new symptoms consult your pharmacist or doctor.

Read the enclosed leaflet before taking this product.

Do not take if you:

• have ever had a stomach ulcer, perforation or bleeding

• are allergic to ibuprofen (or anything else in this medicine), aspirin or other related painkillers

• are taking other NSAID painkillers, or aspirin with a daily dose above 75mg

• are in the last 3 months of pregnancy.

Speak to a pharmacist or your doctor before taking if you:

• have asthma, diabetes, high cholesterol, high blood pressure, had a stroke, heart, liver, kidney or bowel problems

• are a smoker

• are pregnant

4.5 Interactions with other medicinal products and other forms of interactions:

Ibuprofen should not be used in combination with:

Acetylsalicylic acid

Concomitant administration of Ibuprofen and aspirin (acetylsalicylic acid) is not generally recommended (unless low-dose aspirin (not above 75mg daily) has been advised by a doctor), as this combination may increase the risk of adverse reactions.

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 aspirin (acetylsalicylic acid) cannot be excluded. No clinically relevant effect is considered to be likely for occasional ibuprofen use.

Other NSAIDs including cyclooxygenase-2 selective inhibitors: as these may increase the risk of adverse effects.

Ibuprofen should be used with caution in combination with:

Corticosteroids: may increase the risk of adverse reactions, especially of the gastrointestinal tract.

Antihypertensive and diuretics: NSAIDs may diminish the effects of these drugs. Diuretics can increase the risk of nephrotoxicity of NSAIDs.

Anticoagulants: NSAIDS may enhance the effects of anticoagulants, such as warfarin.

Anti-platelet agents and selective serotonin-reuptake inhibitors (SSRIs): increased risk of gastrointestinal bleeding.

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 the potential for increased plasma levels of methotrexate.

Ciclosporin: Increased risk of nephrotoxicity.

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

Tacrolimus: Possible increase risk of nephrotoxicity when NSAIDs are given with tacrolimus.

Zidovudine: There is evidence of an increased risk of haemarthroses and haematoma in HIV positive 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.

Additional information on special populations:

Not Applicable

Pediatric population:

Not Applicable

4.6 Fertility, pregnancy and lactation:

Pregnancy:

While no teratogenic effects have been demonstrated in animal experiments, use of Ibuprofen should, if possible, be avoided during the first 6 months of pregnancy.

During the 3rd trimester, ibuprofen is contraindicated, 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 duration of labour increased, with increased bleeding tendency in both mother and child.

Lactation:

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

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

4.8 Undesirable effects:

Hypersensitivity reactions have been reported and these may consist of

a) Non specific allergic reactions and anaphylaxis,

b) Respiratory tract reactivity comprising asthma, aggravated asthma, bronchospasm or dyspnoea or

c) Various skin reactions, e.g. pruritus, urticaria, angioedema, and more rarely, exfoliative and bullous dermatoses (including epidermal necrolysis, and erythema multiforme).

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

Infections and infestations	Very rare:	Aseptic meningitis
Blood and lymphatic disorders	Very rare:	Haematopoietic disorders (anaemia, hemolytic anemia, aplastic anemia), leucopenia, thrombocytopenia, pancytopenia, agranulocytosis). First signs are: fever, sore throat, superficial mouth ulcers, flu-like symptoms, severe exhaustion, nose and skin bleeding.
Immune system disorders	Uncommon:	Hypersensitivity reactions with urticaria and pruritus.
	Very rare:	In patients with existing auto-immune disorders (such as systemic lupus erythematosus, mixed connective tissue disease) during treatment with ibuprofen, single cases of symptoms of aseptic meningitis, such as stiff neck, headache, nausea, vomiting, fever or disorientation have been observed. Severe hypersensitivity reactions. Symptoms could be: facial, tongue and larynx swelling, dyspnoea, tachycardia, hypotension, (anaphylaxis, angioedema or severe shock). Exacerbation of asthma and bronchospasm.

Psychiatric disorders	Very rare:	Nervousness
Nervous System	Uncommon:	Headache
Eye disorders	Very rare:	Visual disturbance
Ear and labyrinth disorders	Very rare:	Tinnitus and vertigo
Cardiac disorders	Very rare:	Cardiac failure
Vascular disorders	Very rare:	Hypertension
Respiratory, thoracic and mediastinal disorders	Very rare:	Asthma, broncospasm, dyspnoea and wheezing
Gastrointestinal disorders	Uncommon:	Abdominal pain, abdominal distension, dyspepsia and nausea.
	Rare:	Diarrhoea, flatulence, constipation and vomiting.
	Very rare:	Peptic ulcer, perforation or gastrointestinal haemorrhage, melaena, haematemesis, sometimes fatal, particularly in the elderly (see section 4.4). Exacerbation of ulcerative colitis and Crohn's disease. Mouth ulceration.
Hepatobiliary disorders	Very rare:	Liver disorders, especially in long-term treatment, hepatitis and jaundice.
Skin and subcutaneous tissue disorders	Uncommon:	Various skin rashes.
	Very rare: Not known:	Severe forms of skin reactions such as bullous reactions, including Stevens-Johnson Syndrome, erythema multiforme and toxic epidermal necrolysis can occur. Drug reaction with eosinophilia and systemic symptoms (DRESS syndrome)
Renal and urinary disorders	Very rare:	Acute renal failure, papillary necrosis, especially in long-term use, associated with increased serum urea and oedema. Haematuria, interstitial nephritis, nephritic syndrome, proteinuria
General disorders and administration site conditions	Very rare:	Oedema, peripheral oedema.
Investigations	Very rare:	Decreased hematocrit and hemoglobin levels.

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) (see section 4.4).

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 and Treatment:

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

Symptoms

Most patients who have ingested clinically important amounts of NSAIDs will develop no more than nausea, vomiting, epigastric pain, or more rarely diarrhoea. Tinnitus, headache and gastrointestinal bleeding are also possible. In more serious poisoning, toxicity is seen in the central nervous system, manifesting as vertigo, headache, respiratory depression, dyspnoea, drowsiness, occasionally excitation and disorientation or coma. Occasionally patents develop convulsions. In serious poisoning, hypotension, hyperkalaemia, and 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

Should be symptomatic and supportive and include 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:

Ibuprofen is a phenylpropionic acid derivative NSAID that has demonstrated its efficacy by inhibition of prostaglandin synthesis. In humans, Ibuprofen reduces inflammatory pain, swelling and fever. Furthermore, Ibuprofen reversibly inhibits platelet aggregation. Experimental data suggest that Ibuprofen may competitively inhibit the effect of low dose aspirin (acetylsalicylic acid) on platelet aggregation when they are dosed concomitantly. Some pharmacodynamics studies show that when single doses of Ibuprofen 400mg were taken within 30 min after immediate release aspirin (acetylsalicylic acid) dosing (81 mg), a decreased effect of aspirin (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 aspirin (acetylsalicylic acid) cannot be excluded. No clinically relevant effect is considered to be likely for occasional Ibuprofen use.

5.2 Pharmacokinetic properties:

Ibuprofen is rapidly absorbed following administration and is rapidly distributed throughout the whole body. The excretion is rapid and complete via the kidneys.
Maximum plasma concentrations are reached 45 minutes after ingestion if taken on an empty stomach. When taken with food, peak levels are observed after 1 to 2 hours. These times may vary with different dosage forms.
The half life of ibuprofen is about 2 hours.
In limited studies, ibuprofen appears in the breast milk in very low concentrations.

5.3 Preclinical safety data:

No relevant information additional to that already contained.

6. Pharmaceutical Particulars:

6.1 List of excipients

Iburen tablets contains the following excipients:

Lactose, Maize starch, Sodium methyl paraben, Sodium propyl paraben, Sodium starch glycollate and Magnesium stearate.

6.2 Incompatibilities

None known

6.3 Shelf life

24Months

6.4 Special precaution for storage

Store in a cool dry place below 30ºC. Protect from light. Keep out of reach of children.

6.5 Nature and contents of container

Aluminium/ transparent PVC blister of 10 tablets and 10 of such tablets are packed in a unit box with pack insert.

6.6 Special precautions for disposal

No special precaution.

7. MARKETING AUTHORISATION HOLDER AND MANUFACTURING SITE ADDRESSES:

Marketing Authorization Holder:
Rene Industries Ltd
Address : PO Box 6034, Plot No.680, Kamuli, Kireka, Kampala, Uganda.

Manufactured by:
Rene Industries Ltd
Address : PO Box 6034, Plot No.680, Kamuli, Kireka, Kampala, Uganda.

8. MARKETING AUTHORISATION NUMBER:

Not Applicable

9. DATE OF FIRST REGISTRATION/RENEWAL OF THE REGISTRATION:

Not Applicable

10. DATE OF REVISION OF THE TEXT:

Not Applicable

11. DOSIMETRY (IF APPLICABLE):

Not Applicable

12. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS (IF APPLICABLE):

Not Applicable