1.6 product information
1.6.1 Prescribing information (Summary of product characteristics)
1. Name of the medicinal product
Profen 400 Tablets

2. Qualitative and quantitative composition
Each Film Coated Tablet contains Ibuprofen BP 400mg.

3. Pharmaceutical form
Pink circular, biconvex, film coated tablets scored on one side and plain on reverse. Packed in blisters of 10 x 10`s in a unit box and in 500`s in HDPE container with literature insert.

4. Clinical particulars
4.1 Therapeutic indications
Profen is indicated for the relief of fever and pain.
It is also used in the management of mild to moderate pain in conditions such as dysmenorrhea, migraine and postoperative pain.
It is also used in the management of pain and inflammation in such conditions as ankylosing spondylitis, Osteoarthritis, rheumatoid arthritis and in other musculoskeletal and joint disorders such as sprains and strains.

4.2 Dosage and Administration
Profen is taken orally preferably after meals or with milk.
Adults
- Analgesic dosage for Adults usually is 1.2 to 1.8g daily in 3 – 4 divided doses.
  If necessary, this may be increased to 2.4g. Alower maintainance dose of 0.6 – 1.2g may be adequate in some patients.
- For rheumatoid arthritis and osteoarthritis a dosage of 300 or 400mg every 3 or 4 hours and which may be adjusted according to the patients need will be necessary, the maximum total daily dosage being 3.2g.

Children
- Analgesic dosage is 20mg per kg body weight daily in divided doses, the maximum dose being 500mg for children under 30kg body weight.
- For Juvenile Rheumatoid Arthritis up to 40mg per kg of body weight daily in divide doses may be given.

4.3 Contraindications
Profen should be given under close supervision to patients with gastric ulceration or with history of upper gastrointestinal tract disease.
Caution should also be exercised when it is administered to the elderly, those on anticoagulant therapies and in cases of renal, cardiac or hepatic impairment.
Profen is not recommended during pregnancy and in nursing mothers. Its use is contraindicated in persons known to be hypersensitive to it and in persons with the syndrome of nasal polyps, angioedema and bronchospatic reactivity to aspirin or other NSAIDs.
In case of visual disturbance, treatment with profen should be discontinued and an ophthalmological examination undertaken.

4.4 Special warnings and precautions 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 (see GI and cardiovascular risks below).
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 (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. Ibuprofen should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity.

4.5 Interaction with other medicinal products and other forms of interaction
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.
Antihypertensives 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.

4.6 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 (see section 4.4). 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.

4.9 Overdose

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

Pharmacotherapeutic group: Propionic acid derivatives.

ATC Code: M01AE

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 elsewhere in the SmPC.

6. Pharmaceutical particulars
6.1 List of excipients
Tablet contents:
White Com Starch
Sodium Starch Glycolate
Sodium Methyl Paraben
Povidone K-30
Colloidal Silicon Dioxide
Magnesium Stearate
Hydroxypropyl Methylcellulose (5 Cps) .
Titanium Dioxide
Erythrosine Lake Colour
Purified Talc
Polyethylene Glycol - 6000
Isopropyl Alcohol
Purified Water

6.2 Incompatibilities
None known.

6.3 Shelf life
3 years

6.4 Special precautions for storage
Store in a dry place, below 30°C.
Protect from light,
Keep all medicines out of reach of children

6.5 Nature and contents of container
Pink, circular, biconvex, film coated tablets scored on one side and plain on reverse. Packed in Blister pack of 10 x 10's or 500's in HDPE container with literature insert**.**

6.6 Special precautions for disposal and other handling
Not applicable.

7. Marketing Authorization Holder and Manufacturing Site Addresses Marketing Authorization Holder:
Company name: LABORATORY & ALLIED LTD
Address: PLOT NO: 209/10349 OFF MOMBASA ROAD,
P.O BOX 42875, CODE 00100 NAIROBI, Country: KENYA
Telephone: + 254 – 20-8040306
Telefax: 254 – 020 - 8040309
E-Mail: info@laballied.com

Manufacturing Site Address:
Company name: LABORATORY & ALLIED LTD
Address: PLOT NO: 209/10349 OFF MOMBASA ROAD,
P.O BOX 42875, CODE 00100 NAIROBI, Country: KENYA
Telephone: + 254 – 20-8040306
Telefax: 254 – 020 - 8040309
E-Mail: info@laballied.com

8. Marketing authorisation number(s)
Kenya: H96/424

9. Date of first authorisation/renewal of the authorisation
Kenya: 24/10/1996

10. Date of revision of the text
January 2021

1.6.2 Container labeling

Profen 400 Tablets are packed in blisters of 10 x 10's in a unit box with literature insert and 500's in HDPE containers with literature insert.

Packaging Samples provided in **section 1.6.4 below**

1.6.3 Patient information leaflet (PIL)

Provided in **section 1.6.4 below**

1.6.4 Mock-ups and specimens

Enclosed