1.3.1 SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

PRODUCT NAME: Ibuprofen 200 mg Tablets BP

BRAND NAME: Inbu-200

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

PRODUCT NAME: Ibuprofen 200 mg Tablets BP

Each coated tablet contains:
Ibuprofen BP ……200 mg
Excipients……..q.s.

For complete list of excipients refer section 6.1.

3. *PHARMACEUTICAL FORM:*

Tablet

Pink coloured oval shaped coated tablets, plain on both sides

4. *CLINICAL PARTICULARS*

4.1 Therapeutic Indication:

For the relief of mild to moderate pain including rheumatic or muscular pain, pain of non-serious arthritic conditions, backache, headache, dental pain, migraine, neuralgia, dysmenorrhoea, feverishness and for the relief of symptoms of colds and influenza.

4.2 Posology and method of administration:

For oral administration and short-term use only.

Adults, the elderly and children over 12 years:

The lowest effective dose should be used for the shortest duration necessary to relieve symptoms. The patient should consult a doctor if symptoms persist or worsen, or if the product is required for more than 10 days.

Not to be used for children under 12 years of age

Ibuprofen 200 mg to be taken up to three times a day as required.

Leave at least four hours between doses and do not take more than 1200 mg in any 24hour period.

Method of administration

For oral administration. To be taken preferably with or after food, with a glass of water. Ibuprofen 200mg tablets should be swallowed whole and not chewed, broken, crushed or sucked on to avoid oral discomfort and throat irritation.

4.3 Contraindications:

• Hypersensitivity to Ibuprofen or any of the excipients listed in section 6.1.

• Patients who have previously shown hypersensitivity reactions (e.g. asthma, rhinitis, angioedema or urticaria) in response to aspirin or other non-steroidal anti-inflammatory drugs.

• 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.

• Severe hepatic failure, renal failure or heart failure (See section 4.4)

• Last trimester of pregnancy (See section 4.6).

4.4 Special warning and precautions for use

Undesirable effects may be minimized 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.

Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malsabsorption should not take this medicine.

Respiratory:

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

Other NSAIDs:

The use of Ibuprofen with concomitant NSAIDs including cyclo-oxygenase-2 selective inhibitors should be avoided (see section 4.5).

SLE and mixed connective tissue disease:

Caution is required in certain conditions like systemic lupus erythematosus and mixed connective tissue disease due to increased risk of aseptic meningitis (see section 4.8).

Renal:

Renal impairment as renal function may further deteriorate (see section 4.3 and 4.8)

Hepatic:

Hepatic dysfunction (see section 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, fluid retention, hypertension, oedema and/or cardiac impairment have been reported in association with NSAID therapy (see Section 4.8).

Clinical trial and epidemiological data suggest that use of ibuprofen, particularly at high doses (2200 mg daily) and in long-term treatment 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. ≤ 1200 mg daily) is associated with an increased risk of myocardial infarction.

Impaired female fertility:

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

Gastrointestinal:

NSAIDs should be given with care to patients with a history of gastrointestinal disease and chronic inflammatory intestinal 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 anytime during treatment, with or without warning symptoms or a previous history of serious 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 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 oral corticosteroids, or anti-coagulants such as warfarin or selective serotonin reuptake inhibitors or anti-platelet agents such as aspirin (See section 4.5 Interactions).

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

Dermatological:

Severe skin reactions

Serious skin reactions, some of them fatal, including exfoliative dermatitis, Stevens-Johnson syndrome, and toxic epidermal necrolysis have been reported rarely in association with the use of NSAIDSs (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. Acute generalised exanthematous pustulosis (AGEP) has been reported in relation to ibuprofen-containing products. Ibuprofen should be discontinued, at the first appearance of signs and symptoms of severe skin reactions, such as skin rash, mucosal lesions, or any other sign of hypersensitivity.

Paediatric population

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

4.5 Drug Interactions

Ibuprofen should not be used in combination with:

Aspirin: Unless low-dose aspirin (not above 75 mg daily) has been advised by a doctor, as this may increase the risk of adverse reactions (See section 4.4).

Experimental data suggest that ibuprofen may inhibit the effect of low dose aspirin on platelet aggregation when they are dosed concomitantly. However, the limitations of these data and the uncertainties regarding extrapolation of ex vivo data to the clinical situation imply that no firm conclusions can be made for regular ibuprofen use, and 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:

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

Antihypertensives and diuretics: NSAIDs may diminish the effect of these drugs.

Diuretics can increase the risk of nephrotoxicity of NSAIDs.

Corticosteroids: Increase the risk of gastrointestinal ulceration or bleeding (see section 4.4)

Anti-platelet agents and selective serotonin reuptake inhibitors (SSRIs): increased 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 increases in plasma levels of lithium. Methotrexate: There is a potential for an increase in plasma 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 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 of 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.

4.6 Pregnancy & Lactation

Pregnancy

Whilst no teratogenic effects have been demonstrated in animal experiments, the use of Ibuprofen in pregnancy 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 the duration increased with an increased bleeding tendency in both the mother and child.

Breast-feeding

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

Fertility

See section 4.4 regarding female fertility.

4.7 Effects on ability to drive and use machines:

Undesirable effects such as dizziness, drowsiness, fatigue and visual disturbances are possible after taking NSAIDs. If affected, patients should not drive or operate machinery.

4.8 Adverse Effects

Hypersensitivity reactions have been reported and these may consist of: -

Non-specific allergic reaction and anaphylaxis:

• Respiratory tract reactivity, e.g. asthma, aggravated asthma, bronchospasm or dyspnoea

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

The following list of 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.

Blood and lymphatic disorders:

Very rare: Haematopoietic disorders (anaemia, haemolytic anaemia, aplastic anaemia, leukopenia, thrombocytopenia, and agranulocytosis). First signs are: fever, sore throat, superficial mouth ulcers, flu-like symptoms, severe exhaustion, bleeding and bruising.

Immune system disorders:

Uncommon: hypersensitivity reactions with urticaria and pruritus.

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 a stiff neck, headache, nausea, vomiting, fever or disorientation have been observed (See section 4.4).

Severe hypersensitivity reactions symptoms could be: facial, tongue and laryngeal swelling, dyspnoea, tachycardia, hypotension, (anaphylaxis, angioedema or severe shock).

Exacerbation of asthma and bronchospasm.

Nervous system:

Uncommon: Headache

Very rare: Aseptic meningitis – single cases have been reported very rarely.

Ear and labyrinth disorders

Very rare: Tinnitus and vertigo

Cardiac disorders

Cardiac failure has been reported in association with NSAID treatment.

Clinical trial and epidemiological data suggest that use of ibuprofen (particularly at high doses 2200 mg daily) and in long-term treatment may be associated with a small increased risk of arterial thrombotic events (for example myocardial infarction or stroke), (see section 4.4).

Vascular disorders

Very rare: Hypertension

Gastrointestinal disorders:

The most commonly-observed adverse events are gastrointestinal in nature. Uncommon: Abdominal pain, nausea and dyspepsia.

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).

Ulcerative stomatitis, gastritis, exacerbation of ulcerative colitis and Crohn's disease (See section 4.4).

Hepatobiliary disorders:

Very rare: Liver disorders, abnormal liver function, hepatic failure, hepatitis and jaundice

Skin and subcutaneous tissue disorders:

Uncommon: Various skin rashes.

Very rare: Severe forms of skin reactions such as bullous reactions, including Stevens-Johnsons Syndrome, erythema multiforme and toxic epidermal necrolysis can occur.

Not known: Acute generalised exanthematous pustulosis (AGEP)

Renal and urinary disorders:

Very rare: Impaired renal function and toxic nephropathy in various forms, including interstitial nephritis, nephrotic syndrome, acute renal failure, papillary necrosis, especially in long-term use, associated with increased serum urea and oedema.

General disorders and administration site conditions

Very rare: Oedema

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 or search for MHRA yellow card in the Google play or Apple play store.

4.9 Overdose

Toxicity

Signs and symptoms of toxicity have generally not been observed at doses below 100 mg/kg in children or adults. However, supportive care may be needed in some cases. Children have been observed to manifest signs and symptoms of toxicity after ingestion of 200 mg/kg or greater. 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 significant amounts of ibuprofen will manifest symptoms within 4 to 6 hours.

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, dizziness, occasionally excitation, nystagmus and disorientation or coma. Occasionally patients develop convulsions, fainting, hypothermia, apnoea and respiratory or CNS depression, cardiovascular toxicity resulting in hypotension, bradycardia or tachycardia. 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 Pharmacodynamics properties

Pharmacotherapeutic group: NSAIDs

ATC code: M01A E01

Mechanism of action:

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

Experimental data suggest that ibuprofen may inhibit the effect of low dose aspirin on platelet aggregation when they are dosed concomitantly. In one study, when a single dose of ibuprofen 200mg was taken within 8 hours before or within 30 minutes after immediate release aspirin dosing (81mg), a decreased effect of aspirin on the formation of throm-boxane or platelet aggregation occurred. However, the limitations of these data and the uncertainties regarding extrapolation of ex vivo data to the clinical situation imply that no firm conclusions can be made for regular ibuprofen use, and 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 breast milk in very low concentrations.

5.3 Preclinical Safety Data:

None

6. *PHARMACEUTICAL PARTICULARS*

6.1 List of excipients

Ibuprofen 200 mg Tablets BP

List of Excipients:

- Maize Starch (Dried)
- Gelatin
- Propyl Hydroxy benzoate
- Methyl Paraben
- Purified Talc
- Colloidal anhydrous silica
- Maize Starch (for Paste)
- Magnesium stearate
- Calcium carbonate
- Sucrose
- Titanium Dioxide
- Sodium Benzoate
- Sunset Yellow
- Carnauba Wax
- Purified water

6.2 Incompatibilities

Not Applicable

6.3 Shelf Life

36 Months.

6.4 Special precautions for storage:

Do not store above 30°C. Protect from light.
Keep the medicine out of reach of children.

6.5 Nature and contents of container

A blister of 10 tablets in a clinical carton of 50 cartons per printed outer carton.
1000 tablets packed inside HDPE jar.

NAFDAC Reg.No.: 04-2568

6.6 Special precautions for disposal and other handling
Any unused product or waste material should be disposed of in accordance with local requirements

7. *APPLICANT*

Name of the Applicant:
SAGAR VITACEUTICALS NIGERIA LIMITED

Business Address:
Plot 2, Ladipo Oluwole Street,
Off Oba-Akran Avenue, Ikeja.
Lagos,
NIGERIA

Manufactured by:

SAGAR VITACEUTICALS NIGERIA LIMITED.
Plot 2, Ladipo Oluwole Street,
Off Oba-Akran Avenue, Ikeja.
Lagos,
NIGERIA

8. *WHO PREQUALIFICATION REFERENCE NUMBER*
Not applicable

9. *DATE OF PREQUALIFICATION / RENEWAL OF PREQUALIFICATION*
Not applicable

10. *DATE OF REVISION OF THE TEXT*
Not applicable