RC 1566765

SUMMARY OF PRODUCT CHARACTERISTICS

1. Name of the medicinal product

TABALON 400mg
Ibuprofen caplet 400mg

2. Qualitative and quantitative composition

Each caplet contains Ibuprofen BP 400mg
For excipients see section 6.1.

3. Pharmaceutical form

Caplet: White, oblong, tablets

4. Clinical particulars

4.1 Therapeutic indications

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 (see section 4.4). 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 400 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 1200mg in any 24-hour period.

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

Children under 12:
The daily dosage of Ibuprofen is 20 mg/kg of body weight in divided doses.

For young children, more suitable formulations are available.

In Juvenile Rheumatoid Arthritis, up to 40 mg/kg of body weight daily in divided doses may be taken.

Not recommended for children weighing less than 7kg.

Elderly:
The elderly are at increased risk of serious consequences of adverse reactions. If an NSAID is considered necessary, the lowest effective dose should be used and

for the shortest possible duration. The patient should be monitored regularly for GI bleeding during NSAID therapy.

Method of administration

For oral administration. To be taken preferably with or after food, with a glass of water. Ibuprofen 400mg 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 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:
Bronchospasms 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 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 the 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. ≤ 1200 mg/ 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 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 (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 serious 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.

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 anticoagulants 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.

Masking of symptoms of underlying infections:
Ibuprofen can mask symptoms of infection, which may lead to delayed initiation of appropriate treatment and thereby worsening the outcome of the infection. This has been observed in bacterial community acquired pneumonia and bacterial complications to varicella. When Ibuprofen is administered for fever or pain relief in relation to infection, monitoring of infection is advised. In non-hospital settings, the patient should consult a doctor if symptoms persist or worsen.

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 NSAIDs (see section 4.8). Patients appear to be at the highest risk of these reactions early in the course of therapy, with 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.

The leaflet will include:

This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium-free'.

If you have been told by your doctor that you have an intolerance to some sugars, talk to your doctor before taking these tablets.

These tablets contain sunset yellow (E110), which can cause allergic-type reactions including asthma. Allergy is more common in those people who are allergic to aspirin.

<u>The label will include:</u>

Please read the enclosed leaflet carefully before taking this medicine.

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.

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

- have asthma, diabetes, high cholesterol, high blood pressure, had a stroke, liver, heart, kidney or bowel problem.
- are a smoker.
- are pregnant.

If symptoms do not get better or get worse or if you get new symptoms, talk to your doctor.

4.5 Interaction with other medicinal products and other forms of interaction

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 Fertility, Pregnancy and 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. (See section 4.3).

Breast-feeding
In limited studies, Ibuprofen appears in breast milk in a very low concentration and is unlikely to affect the breastfed 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 Undesirable effects

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

Frequencies are defined as: very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1000 to <1/100), rare (≥1/10,000 to <1/1000), very rare (<1/10,000) and not known (cannot be estimated from the available data). Within each frequency grouping, adverse events are presented in order of decreasing seriousness.

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.

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

System Organ Class	Frequency	Adverse Event
Blood and Lymphatic System Disorders	Very rare	Haematopoietic disorders
Immune System Disorders	Uncommon Very rare	Hypersensitivity with urticaria and pruritus Severe hypersensitivity reactions, including facial, tongue and throat swelling, dyspnoea, tachycardia and hypotension (anaphylaxis, angioedema or severe shock).
Nervous System Disorders	Uncommon Very rare	Headache Aseptic meningitis
Cardiac Disorders	Not Known	Cardiac failure and oedema
Vascular Disorders	Not Known	Hypertension
Respiratory, Thoracic and Mediastinal Disorders	Not Known	Respiratory tract reactivity comprising asthma, bronchospasm or dyspnoea
Gastrointestinal Disorders	Uncommon Rare Very rare Not Known	Abdominal pain, nausea and dyspepsia Diarrhoea, flatulence, constipation and vomiting Peptic ulcer, gastrointestinal perforation or gastrointestinal haemorrhage, melaena and haematemesis[6]. Mouth ulceration and gastritis Exacerbation of colitis and Crohn's disease
Hepatobiliary Disorders	Very rare	Liver disorder

Skin and Subcutaneous Tissue Disorders	Uncommon Very rare Not known	Skin rash Bullous reactions, including Stevens-Johnson syndrome, erythema multiforme and toxic epidermal necrolysis[2] Drug reaction with eosinophilia and systemic symptoms (DRESS syndrome) Acute generalised exanthematous pustulosis (AGEP) photosensitivity reactions
Renal and Urinary Disorders	Very rare	Acute renal failure
Investigations	Very rare	Haemoglobin decreased

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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 NAFDAC pharmacovigilance Yellow form or contact the Pharmacovigilance person for Sygen Pharma.

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 400 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 Pharmacodynamic properties

ATC Code: M01A E01
Group – Anti-inflammatory and anti-rheumatic products, non-steroids.

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 inhibit the effect of low dose aspirin on platelet aggregation when they are dosed concomitantly. In one study, when a single dose of ibuprofen 400mg 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 thromboxane or platelet aggregation occurred. However, the limitations of these data and the uncertainties regarding the 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
No relevant information additional to that already contained elsewhere in the SmPC.

6. PHARMACEUTICAL PARTICULARS
6.1 List of excipients
- Corn starch,
- Polyvinylpyrrolidone 2500,
- Colloidal anhydrous silica
- Carboxymethyl Cellulose
- Avicel 101

6.2 Incompatibilities
None stated.

6.3 Shelf life
5 years.

6.4 Special precautions for storage
Blister pack - This medicinal product does not require any special storage conditions. Store in a dry place below 30°C.

6.5 Nature and contents of the container
Ibuprofen Tablets are available in blister packs of 10 tablets.

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.

7. Marketing authorisation holder
SYGEN PHARMACEUTICALS LIMITED
KM. 38, LAGOS ABEOKUTA EXPRESSWAY, SANGO OTA, OGUN STATE.

8. Marketing authorisation number(s)
NAFDAC REG. No.: 04 -0758.

9. Date of first authorisation/renewal of the authorisation
04/04/2018.

10. Date of revision of the text
01/06/2023