VEELAM® COUGH SYRUP.

(IBUPROFEN BP 100MG/5ML AND PSEUDOEPHEDRINE HYDROCHLORIDE 15MG/5ML)

SUBMITTED BY: NALIS PHARMACEUTICALS LTD

R67-68 NEKEDE-NAZE
INDUSTRIAL CLUSTERS,
NEKEDE, OWERRI,
IMO STATE, NIGERIA.
TEL: +2348085784400, +2349026044603

Email: info@nalispharma.com, www.nalispharma.com

SUMMARY OF PRODUCT CHARACTERISTICS

(SmPC)

1. NAME OF THE DRUG PRODUCT

Veelam® Cough Syrup.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5ml contains:

Ibuprofen BP……..100 mg

Pseudoephedrine Hydrochloride BP…..15mg
Excipients……qs

3. PHARMACEUTICAL FORM

Oral suspension

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Veelam Cough Syrup is indicated for the relief of symptoms of the common cold and flu such as headache, fever, sore throat, minor aches and pain when associated with blocked nose (nasal congestion) and sinuses (sinusitis) in adults and adolescents over 12 years of age.

4.2 Posology and method of administration

Posology
For oral administration and short-term use only.
This combination product should be used where both, the decongestant action of pseudoephedrine hydrochloride and the analgesic and/or anti-inflammatory action of ibuprofen are required. If one symptom (either nasal congestion or headache and/or fever) predominates, single-agent therapy is preferable.

Dosage

Adults
Take 10ml in any 24 hour period.

Paediatric population

Children over 12 years of age:

Take 5ml in any 24 hour period.

In case of more intense symptoms, 20ml (200 mg ibuprofen/30 mg pseudoephedrine hydrochloride) may be taken at a time. The dose can be repeated, if necessary, at six-hour intervals without exceeding a maximum daily dose of (1200 mg of ibuprofen and 180 mg of pseudoephedrine hydrochloride)
The lowest effective dose should be used for the shortest duration necessary to relieve the symptoms (see section 4.4).
Undesirable effects may be minimised by using the lowest effective dose for the shortest duration necessary to control symptoms (see section 4.4). Maximum duration of treatment is 5 days unless instructed otherwise by a doctor

Method of administration
For oral administration only.

4.3 Contradindications

- **Use in children under 12 years of age.**
- **Hypersensitivity to the active substances or to any of the excipients listed in Section 6.1.**
- **Patients with allergy to aspirin or other Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) or with a history of hypersensitivity reactions (e.g. asthma, bronchospasm, rhinitis, angioedema or urticaria) in response to ibuprofen, aspirin or NSAIDs.**
- **History of gastrointestinal bleeding or perforation, related to previous NSAIDs therapy.**
- **Active or history of recurrent peptic ulcer/haemorrhage (two or more distinct episodes of proven ulceration or bleeding).**
- **Patients with phaeochromocytoma, closed angle glaucoma, diabetes or thyroid disease.**
- **Patients with history of haemorrhagic stroke.**
- **Patients suffering from heart disease, circulatory problems, prostatic hypertrophy, hypertension, coronary artery disease, angina pectoris, tachycardia or haemorrhagic diathesis.**
- **Patients taking other NSAIDs including cyclooxygenase-2 selective inhibitors, pain-relievers or decongestants.**
- **Patients receiving tricyclic antidepressants.**
- **Patients currently receiving, or who have within the last two weeks received, monoamine oxidase inhibitors.**
- **Patients with severe heart failure (NYHA Class IV), renal failure or hepatic failure (see section 4.4).**
- **During pregnancy and breast-feeding. (see section 4.6).**

4.4 Special warnings and precautions for use

- **The use of Veelam Cough Syrup with concomitant NSAIDs including cyclooxygenase-2 selective inhibitors should be avoided (see section 4.3 and 4.5).**
- **Undesirable effects may be minimized by using the minimum effective dose for the shortest duration necessary to control symptoms (see GI and cardiovascular risks below).**
- **If symptoms get worse or last more than 3 days or patients experience any other symptoms not related to the original condition, treatment should be stopped unless directed otherwise by a doctor or healthcare professional.**
- **Elderly: The elderly have an increased frequency of adverse reactions to NSAIDs especially gastrointestinal bleeding and perforation which may be fatal (see section 4.2)**
- **Patients suffering from asthma, hypertension, heart disease, diabetes, liver cirrhosis, renal or hepatic impairment, thyroid disease or prostatic hypertrophy should consult their doctor before using this product (see section 4.3 and 4.8).**

- There is a risk of renal impairment in dehydrated adolescents or young persons, between the age of 12 and 17 years.
- Bronchospasm may be precipitated in patients suffering from or with a previous history of bronchial asthma or allergic disease.
- The use of NSAIDs may impair female fertility (see section 4.6). There is limited evidence that drugs which inhibit cyclo-oxygenase/prostaglandin synthesis may cause impairment of female fertility by an effect on ovulation. This is reversible upon withdrawal of treatment.
- Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.
- Contains parabens, that may cause allergic reactions possibly delayed.
- This medicine contains less than 1 mmol sodium (23 mg) per coated tablet, that is to say essential 'sodium-free'.
- Consumption of alcohol should be avoided during treatment. Pseudoephedrine hydrochloride may cause a positive reaction in tests conducted during anti-doping checks.
- Ischaemic optic neuropathy Ischaemic optic neuropathy has been reported with pseudoephedrine.Pseudoephedrine should be discontinued if sudden loss of vision or decreased visual acuity such as scotoma occurs.
- Masking of symptoms of underlying infections Advil Cold & Flu can mask symptoms of infection, which may lead to a 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 of varicella. When Advil Cold & Flu 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.

Gastrointestinal effects

- Gastrointestinal bleeding, ulceration and perforation: 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 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. Combination therapy with protective agents (e.g. misoprostol or proton pump inhibitors) should be considered for these patients and also for patients requiring concomitant low dose aspirin or other drugs likely to increase gastrointestinal risk (see below and section 4.5)
- 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 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 Advil Cold & Flu, the treatment should be withdrawn.
- NSAIDs should be given with care to patients with a history of gastrointestinal disease (e.g. ulcerative colitis and Crohn's disease) as their condition may be exacerbated (see section 4.8 – undesirable effects).
- Ischaemic colitis: Some cases of ischaemic colitis have been reported with pseudoephedrine. Pseudoephedrine should be discontinued and medical advice sought if sudden abdominal pain, rectal bleeding or other symptoms of ischaemic colitis develop.

Cardiovascular and cerebrovascular effects:

- In patients with cardiac or renal dysfunction, caution is required since the use of NSAIDs may result in deterioration in renal function.
- Clinical studies suggest that use of some NSAIDs (ibuprofen) particularly at a high dose (2400 mg/day) and in longterm 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/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 and smoking), particularly if high doses of ibuprofen (2400 mg/day) are required.
- As NSAIDs can interfere with platelet function, they should be used with caution in patients with intra-cranial haemorrhage and bleeding diathesis.

Dermatological Effects:

- 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 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. Advil Cold & Flu should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity.
- Systemic Lupus Erythematosus and mixed connective tissue disease – increase risk of aseptic meningitis (see section 4.8).
- Severe skin reaction such as acute generalised exanthematous pustulosis (AGEP) may occur with ibuprofen and pseudoephedrine-containing products. This acute pustular eruption may occur within the first 2 days of treatment,with fever, and numerous, small, mostly non-follicular pustules arising on a widespread oedematous erythema andmainly localized on the skin folds, trunk, and upper extremities. Patients should be carefully monitored. If signs and symptoms such as pyrexia, erythema, or many small pustules are observed, administration of Advil Cold & Flu should be discontinued and appropriate measures taken if needed.
- Exceptionally, varicella can be at the origin of serious cutaneous and soft tissue infectious complications. To date, the contributing role of NSAIDs in the worsening of these infections cannot be ruled out. Thus, it is advisable to avoid use of Advil Cold & Flu in case of varicella.

4.5 Interaction with other drug products and other forms of interaction

It is considered unsafe to take Ibuprofen in combination with warfarin or heparin unless under direct medical supervision.

Not recommended combinations:
Acetylsalicylic acid

Concomitant administration of ibuprofen and acetylsalicylic acid is not generally recommended because of the potential of increased adverse effects.

Animal studies show that acetylsalicylic acid reduces the plasma concentrations of Ibuprofen.
Ibuprofen should not be used with other pain relievers such as NSAIDs.
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.

Combinations requiring precautions:
Care should be taken in patients treated with any of the following drugs as interactions have been reported.

Anticoagulants, antihypertensives or thiazide diuretics:
NSAIDs may enhance the effects of anticoagulants and diminish the effects of antihypertensive or thiazide diuretics.
Diuretics: Reduced diuretic effect. Diuretics can increase the risk of nephrotoxicity of
NSAIDs.
Cardiac Glycosides: NSAIDs may exacerbate cardiac failure, reduce GFR and increase
plasma cardiac glycoside levels. Serum digitalis concentrations should therefore be monitored in patients with decreased renal function or congestive heart failure.
Phenytoin: Ibuprofen may increase the pharmacologically active free phenytoin. Patients
taking Ibuprofen for long-term use should be monitored.
Lithium: Decreased elimination of lithium. This may result in clinically significant increases
in lithium concentrations.
Methotrexate: Concomitant administration of Ibuprofen with moderate and high doses of
methotrexate may lead to serious and fatal methotrexate toxicity. Patients with reduced renal function may be at additional risk of toxicity from the combination even when low doses of methotrexate (20 mg/week) are used.
Antacids: Certain antacids may increase the gastrointestinal absorption of Ibuprofen. This is considered to be of clinical relevance particularly during long-term use of Ibuprofen.
Cyclosporin: Increased risk of nephrotoxicity with NSAIDs.
Corticosteroids: Increased risk of gastro-intestinal bleeding or ulceration.
Anti-platelet agents and selective serotonin reuptake inhibitors (SSRIs): Increased risk of
gastrointestinal bleeding.
Aminoglycosides: Reduction in renal function in susceptible individuals decreased elimination of aminoglycosides and increased plasma concentrations.

Pseudoephedrine:
Pseudoephedrine may interact with:
The actions of other sympathomimetic drugs.
The antibacterial agent furazoline.
The action of Pseudoephedrine may be reduced by:
Guanethidine.

Reserpine.
Methyldopa.
The action of Pseudoephedrine may be reduced or enhanced by:
Tricyclic antidepressants.
Pseudoephedrine may reduce the action of:
Guanethidine.
Pseudoephedrine may increase the possibility of arrhythmias in patients taking:
Digitalis.
Quinidine.
Tricyclic antidepressants.

4.6 Fertility, pregnancy and lactation

Advil Cold & Flu is contraindicated during pregnancy and breastfeeding (see section 4.3).

Pregnancy:

Ibuprofen:
Whilst no teratogenic effect has been demonstrated in animal experiments, use of ibuprofen during pregnancy should be avoided.
During the third 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 an increased bleeding tendency in both mother and child (see Section 4.3).

Pseudoephedrine:
Data on pregnancy outcomes after maternal exposure to pseudoephedrine are limited. Two analyses of health maintenance organisation pharmacy data identified 9 malformed infants among 902 first-trimester pseudoephedrine exposures suggesting no specific association with birth defects overall. However the related compounds epinephrine, ephedrine and phenylephrinehave been associated with haemorrhages and cardiovascular and limb malformations in animal models. The vasoconstrictive effects of these drugs may indicate that their use in early pregnancy might increase the risk of vascular disruption defects.

Fertility

There is some evidence that drugs which inhibit cyclo-oxygenase / prostaglandin synthesis may cause impairment of female fertility by an effect on ovulation. This is reversible on withdrawal of treatment.
The use of NSAIDs may impair female fertility and is not recommended in women attempting to conceive. In women who havedifficulties conceiving and who are undergoing investigation of infertility, withdrawal of the product should be considered.

Lactation:

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

Pseudoephedrine:
Pseudoephedrine is excreted in breast milk in small quantities, but the effect of this on breast-fed infants is not known. It is estimated that 0.4% to 0.7% of a single dose of pseudoephedrine ingested by the mother will be excreted in breast milk over 24 hours.

In summary, the use of this product is contraindicated during pregnancy and breastfeeding.

4.7 Effects on ability to drive and use machines

Advil Cold & Flu has no or negligible influence on the ability to drive and use machines at recommended doses and duration of therapy.

Patients who experience dizziness, hallucinations, unusual headaches and visual or hearing disturbances should avoid driving or using machinery. Single administration or short-term use of this medicine does not usually warrant the adoption of any special precautions.

4.8 Undesirable effects

The most common observed adverse events are gastrointestinal in nature. Peptic ulcers, perforation or GI bleeding, sometimesfatal in the elderly, may occur (see section 4.4). Nausea, vomiting, diarrhoea, flatulence, constipation, dyspepsia, abdominal pain, abdominal distension, mouth ulcerations, melaena, haematemesis, ulcerative stomatitis, exacerbation of colitis andCrohn's disease (see section 4.4) have been reported following administration. Less frequently, gastritis has been observed Hypersensitivity reactions have been reported following treatment with Ibuprofen. These may consist of:

1. non-specific allergic reaction and anaphylaxis,
2. Breathing: respiratory tract reactivity comprising of asthma, aggravated asthma, bronchospasm or dyspnoea, Skin:assorted skin disorders, including rashes of various types, bruising pruritis, urticaria, purpura, angiodema and, lesscommonly, exfoliative and bullous dermatoses (including epidermal necrolysis and erythema multiforme).
3. Very rarely, bullous reactions including Steven's – Johnson syndrome and toxic epidermal necrolysis.

Clinical studies suggest that 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) (see section 4.4). Oedema, hypertension, angina pectoris and cardiac failure have been reported in association with NSAID treatment.

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

Patients should be informed that they should stop taking Advil Cold & Flu tablets immediately and consult a doctor if they experience a serious adverse drug reaction.

Very common (≥1/10)
Common (≥1/100 **to <1/10)**
Uncommon (≥1/1000 **to <1/100)**
Rare (≥1/10000 **to <1/1000)**
Very rare (<1/10000)
Not known (cannot be estimated from the available data)

Infections andinfestations	**Ibuprofen**	**Very rare**	**Exacerbation of infectious inflammations (e.g. necrotizing fasciitis), Aseptic meningitis (stiffness of the neck, headache, nausea, vomiting, fever or disorientation in patients with pre-existent autoimmune**
			diseases (SLE, mixed connective tissue disease)
Blood and lymphaticsystem disorders	**Ibuprofen**	**Very rare**	**Haematopoietic disorders (e.g. anaemia, leucopenia, thrombocytopenia,pancytopenia, agranulocytosis)**

Immune system disorders	Ibuprofen	Uncommon	Hypersensitivity reactions with urticaria, pruritus and asthma attacks (with drop in blood pressure)
	Ibuprofen and pseudoephedrine hydrochloride	Very rare	Severe generalised hypersensitivity reactions, signs may be facial oedema, angioedema, dyspnoea, tachycardia, drop in blood pressure,anaphylactic shock
Psychiatric disorders	Ibuprofen	Very rare	Psychotic reactions, depression
	Pseudoephedrine hydrochloride	Not known	Agitation, hallucination, anxiety, abnormal behaviour, insomnia,excitability, irritability, nervousness, restlessness
Nervous systemdisorders	Ibuprofen	Uncommon	Central nervous system disturbances such as headache, dizziness,sleeplessness, agitation, irritability or tiredness
	Pseudoephedrine hydrochloride	Not known	Haemorhagic stroke, ischemic stroke, convulsion, headache, insomnia, nervousness, anxiety, agitation, tremor, hallucinations.
Eye disorders	Ibuprofen	Uncommon	Visual disturbances
	Pseudoephedrine hydrochloride	Not known	Ischaemic optic neuropathy
Ear and labyrinth disorders	Ibuprofen	Rare	Tinnitus
	Ibuprofen	Not known	Vertigo
Cardiac disorders	Ibuprofen	Very rare	Palpitations, heart failure, myocardial infarction, edema, hypertention
	Pseudoephedrine hydrochloride	Not known	Palpitations, tachycardia, chest pain, arrythmia
Vascular disorders	Ibuprofen	Very rare	Arterial hypertension
	Pseudoephedrine hydrochloride	Not known	Hypertension
Respiratory,thoracic andmediastinal disorders	Pseudoephedrine hydrochloride	Rare	Exacerbation of asthma or hypersensitivity reaction with bronchospasm
Gastrointestinaldisorders	Ibuprofen	Common	Dyspepsia, abdominal pain, nausea, vomiting, flatulence, diarrhoea, constipation, anorexia, minor gastrointestinal blood loss in rare cases leading to anaemia
	Ibuprofen	Uncommon	Gastric ulcer with bleeding and/or perforation, gastritis, ulcerous stomatitis, exacerbation of colitis and Crohn's disease (see section 4.4)
	Ibuprofen	Very rare	Oesophagitis, pancreatitis, intestinal diaphragm-like stricture
	Pseudoephedrine hydrochloride	Not known	Dry mouth, thirst, nausea, vomiting

	Pseudoephedrine hydrochloride	Not known	Ischaemic colitis
Hepatobiliarydisorders	Ibuprofen	Very rare	Hepatic dysfunction, hepatic damage, particularly in long-term therapy,hepatic failure, acute hepatitis
Skin and subcutaneous tissue disorders	Ibuprofen	Uncommon	Various skin rashes
	Ibuprofen	Very rare	Bullous exanthema such as Stevens-Johnson syndrome and toxic epidermal necrolysis (Lyell syndrome), alopecia, severe skin infections, soft-tissue complications in a varicella infection
	Ibuprofen	Not known	Drug reaction with eosinophilia and systemic symptoms (DRESS syndrome)
	Pseudoephedrine hydrochloride	Not known	Rash, urticaria, pruritus, hyperhidrosis.
	Ibuprofen and Pseudoephedrine hydrochloride	Not known	Severe skin reactions, including acute generalized exanthematous pustulosis (AGEP)
Renal and Urinary disorders	Ibuprofen	Rare	Kidney-tissue damage (papillary necrosis) and elevated uric acid concentrations in the blood
	Ibuprofen	Very rare	Oedemas (particularly in patients with arterial hypertension or renal insufficiency), nephrotic syndrome, interstitial nephritis, acute renal insufficiency
	Pseudoephedrine hydrochloride	Not known	Difficulty in micturition (Urinary retention in men with urethra-prostatic disorders.)
Investigations	Ibuprofen	Not Known	Haematocrit decreased and haemoglobin decreased

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 to the regulatory bodies such as NAFDAC.

4.9 Overdose

In children ingestion of more than 400 mg/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

Over dosage may result in nervousness, agitation, anxiety, irritability, restlessness, dizziness, tremor, vertigo, insomnia, nausea, abdominal pain, vomiting, epigastric pain, diarrhoea, bradycardia, palpitation, tachycardia, tinnitus, headache and gastrointestinal bleeding. Hyperkalemia, hypertension or hypotension are also possible signs of overdose. Toxicity may manifest as drowsiness, excitation, disorientation or coma. The patient may develop convulsions. Hepatic function may be abnormal. In serious poisoning metabolic acidosis may occur and the prothrombin time/INR may be prolonged. Acute renal failure and liver damage may occur. In asthmatics, exacerbationof asthma is possible.

Management

Due to the rapid absorption of the two active ingredients from the gastro-intestinal tract, emetics and gastric lavage must be instituted within four hours of overdosage to be effective. Charcoal is effective only if given within one hour. Cardiac status should be monitored and the serum electrolytes measured.

If there are signs of cardiac toxicity, propanolol may be administered intravenously. A slow infusion of a dilute solution of potassium chloride should be initiated in the event of a drop in the serum potassium level. Despite hypokalaemia, the patient is unlikely to be potassium depleted, therefore overload must be avoided. Continued monitoring of the serum potassium is advisable for several hours after administration of the salt. For delirium or convulsions, intravenous administration of diazepamis indicated.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic propertie

Ibuprofen is a non steroidal anti-inflammatory agent belonging to the Propionic Acid class of drugs. It has analgesic, antipyretic and anti-inflammatory properties. Pseudoephedrine Hydrochloride is a sympathomimetic agent which causes vasoconstriction of nasal mucosa, thereby reducing rhinorrhoea and nasal congestion.

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 400 mg were taken within 8 h before or within 30 min after immediate release aspirin (acetylsalicylic acid) dosing (81mg), a decreased effect of ASA 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 acetylsalicyclic acid cannot be excluded. No clinically relevanteffect is considered to be likely for occasional ibuprofen use.

5.2 Pharmacokinetic properties

In adults, Ibuprofen from oral dosing is absorbed from the gastrointestinal tract and peak plasma concentrations occur about 1 to 2 hours after ingestion. Ibuprofen is primarily metabolised in the liver to 2-Hydroxyibuprofen and 2- carboxyibuprofen..Ibuprofen is 90 to 99% bound to plasma proteins and has a plasma half-life of about 2 hours. It is rapidlyexcreted in the urine mainly as metabolites and their conjugates. About 1% is excreted in the urine as unchanged ibuprofenand about 14% as conjugated ibuprofen

In limited studies, ibuprofen appears in the breast milk at very low concentrations.

Pseudoephedrine Hydrochloride is rapidly absorbed from the gasto-intestinal tract with peak plasma levels at 1-3 hours. It is partly metabolised in the liver like most sympathomimetics, but is mainly excreted unchanged in the urine.

5.3 Preclinical safety data

Repeated dose toxicity studies on combinations of ibuprofen and pseudoephedrine have not been conducted. The combination was not mutagenic.

Sub-chronic and chronic toxicity studies have been conducted on ibuprofen alone with a 6 month NOAEL of 60 mg/kg in rats. Toxicity occurred in the form of lesions and ulcerations in the gastro-intestinal tract. Ibuprofen is not mutagenic nor was it carcinogenic in chronic rodent bioassays.

Sub-chronic or chronic toxicity studies have not been performed with pseudoephedrine alone. Combination ibuprofen and pseudoephedrine was not mutagenic. A human screening study of over 3,000 pseudoephedrine users showed no increase in cancer over 7.5 years

Reprotoxicity studies in animals with individual ingredients indicated that they were not teratogenic, however use of the product in pregnancy should if possible be avoided.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

S/N	Raw Materials	Specification
1.	Sodium CMC	B.P
2.	Methyl paraben	B.P
3.	Propyl paraben	B.P
4.	Glycerine	B.P
5.	Sugar	B.P
6.	Orange flavour	B.P
8.	Sunset Yellow Colour	B.P
9.	Sodium benzoate	B.P
10	Xanthan gum	BP
11	Tween 80	BP
12	Treated water	B.P

6.2 Incompatibilities

None known

6.3 Shelf life

Three years from the date of manufacture.

6.4 Special precautions for storage

Do not store above 30°C. Store in a dry place.

6.5 Nature and contents of container

100ml HDPE amber pet bottles.
28mm ROPP caps.

6.6 Special precautions for disposal of used medicinal product or waste materials derived from such medicinal product and other handling of the product

No special requirements.

7. APPLICANT/HOLDER OF CERTIFICATE OF PRODUCT REGISTRATION

NAME:
NALIS PHARMACEUTICALS LTD

ADDRESS:

R67-68 Nekede-Naze
Industrial Clusters,
Nekede, Owerri,
IMO State, Nigeria.
Tel: +2348085784400, +2349026044603

Email: info@nalispharma.com, www.nalispharma.com

8. DRUG PRODUCT MANUFACTURER

NAME:
NALIS PHARMACEUTICALS LTD

ADDRESS:

R67-68 Nekede-Naze
Industrial Clusters,
Nekede, Owerri,
IMO State, Nigeria.
Tel: +2348085784400, +2349026044603

Email: info@nalispharma.com, www.nalispharma.com

9. NAFDAC REGISTRATION NUMBER(S):

A11-100333