



EVANS BAROQUE LIMITED

SUMMARY OF PRODUCT CHARACTERISTICS
(SmPC)
ALGAFEN SUSPENSION

1. NAME OF THE MEDICINAL PRODUCT

{(Algafen Suspension) Ibuprofen 100mg/5ml Oral Suspension}

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

[Ibuprofen 100mg/5ml contains:

{For a full list of excipients, see section 6.1}

3. PHARMACEUTICAL FORM

Oral Suspension

4. Clinical particulars

4.1 Therapeutic indications

{Algafen Suspension, Ibuprofen 100mg/5ml} is used as an analgesic for relief of mild to moderate muscular pain, post-immunisation pyrexia, symptomatic relief of headache, earache, dental pain and backache. It can also be used in minor injuries such as sprains and strains. Ibuprofen 100 mg / 5 ml Oral Suspension is effective in the relief of feverishness and symptoms of colds and influenza.

4.2 Posology and method of administration

Posology

Pediatric population

For pain and fever - 20mg/kg/day in divided doses (including OTC use).

Infants 3-6 months weighing more than 5 kg: One 2.5 ml dose may be taken 3 times in 24 hours. Do not use for more than 24 hours

Infants 6 months-1 year: 2.5ml three to four times a day

Children 1-4 years: 5ml three times a day

Children 4-7 years: 7.5ml three times a day

Children 7-12 years: 10ml three times a day

4.3 Contraindications

Hypersensitivity to ibuprofen or any of the constituents in the product

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 (NYHA Class IV) (see section 4.4, Special warnings and precautions for use)

Patients with rare hereditary problems of fructose intolerance should not take this medicine. Significant dehydration (caused by vomiting, diarrhoea or insufficient fluid intake)

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 section 4.2 GI and cardiovascular risks below).

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 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.

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 cyclooxygenase-2 selective inhibitors should be avoided (see section 4.5).

SLE and mixed connective tissue disease: Systemic lupus erythematosus as well as those with mixed connective tissue disease—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). There is a risk of renal impairment in dehydrated children and adolescents.

Hepatic: Hepatic dysfunction (see sections 4.3 and 4.8).

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 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 ulceration or bleeding, such as oral corticosteroids, anticoagulants such as warfarin, selective serotonin-reuptake inhibitors or antiplatelet agents such as aspirin (see section 4.5).

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

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.

Additional Warnings for OTC use

Do not give to babies aged 3-6 months for more than 24 hours.

Do not give to children aged 6 months and older for more than 3 days.

Consult your doctor promptly if symptoms persist or worsen.

Do not exceed the stated dose.

Not recommended for children under 3 months

4.5 Interaction with other medicinal products and other forms of interaction

Ibuprofen (like other NSAIDs) should be avoided in combination with:

Aspirin (Acetylsalicylic Acid):

Concomitant administration of ibuprofen and acetylsalicylic acid is not generally recommended because of the potential of increased adverse effects unless low-dose aspirin (not above 75mg daily) has been advised by a doctor, (see section 4.4).

Experimental data suggest that ibuprofen may competitively inhibit the effect of low dose 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 acetylsalicylic acid cannot be excluded. 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 reactions (see section 4.4).

Ibuprofen should be used with caution in combination with:

Corticosteroids: as these may increase the risk of gastrointestinal ulceration or bleeding (see section 4.4).

Antihypertensives and diuretics: Since NSAIDs may diminish the effects of these drugs. In some patients with compromised renal function (e.g. dehydrated patients or elderly patients with compromised renal function) the co-administration of an ACE inhibitor or Angiotensin II antagonist and agents that inhibit cyclo-oxygenase may result in further deterioration of renal function, including possible acute renal failure, which is usually reversible. These interactions should be considered in patients taking a coxib concomitantly with ACE inhibitors or angiotensin II antagonists. Therefore, the combination should be administered with caution, especially in the elderly. Patients should be adequately hydrated and consideration should be given to monitoring of renal function after initiation of concomitant therapy, and periodically thereafter.

Diuretics can increase the risk of nephrotoxicity of NSAIDs. Anticoagulants: NSAIDs may enhance the effects of anti-coagulants, such as warfarin (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 cardiac glycoside levels.

Lithium: There is evidence for potential increases in plasma levels of lithium.

Methotrexate: There is evidence for the potential 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 and Lactation

Pregnancy

Whilst no teratogenic effects have been demonstrated in animal experiments the use of Ibuprofen 100mg/5ml Oral Suspension, 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 mother and child (see section 4.3

Contraindications).

Lactation/Breastfeeding

In limited studies, ibuprofen appears in breast milk in very low concentration and is unlikely to affect the breast-fed infant adversely. See section 4.4 regarding female fertility.

4.7 Effects on ability to drive and use machines

None expected at recommended doses and duration of therapy

4.8 Undesirable effects

ADVERSE REACTIONS

Please note that Algafen tablets can prolong bleeding time.

There have been reports of high blood pressure and heart failure as well as worsening of ulcers in the large intestine and Crohn's disease (inflammatory bowel disease) in treatment with pain-relieving medicines (NSAIDs).

Exceptional serious infections of the skin in case of varicella. Exacerbation of infection-related inflammations (e.g. development of necrotising fasciitis) coinciding with the use of NSAIDs has been described.

Medicines like Algafen tablets may entail a slightly increased risk of heart attack or stroke.

Children and adolescents

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

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

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, occasionally excitation and disorientation or coma. Occasionally patients develop convulsions. 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: {Anti-inflammatory and anti-rheumatic product, non-steroid, propionic acid derivative {Non-steroidal Anti-inflammatory Drugs; NSAIDs}, ATC code:{ M01A E01}

Mechanism of action

Ibuprofen works by non-selectively inhibiting the enzyme called cyclooxygenase (COX), which is required for the synthesis of prostaglandins via the arachidonic acid pathway. COX converts arachidonic acid to prostaglandin H₂ (PGH₂) in the body. PGH₂, in turn, is converted by other enzymes to several other prostaglandins (which are mediators of pain, inflammation, and fever) and to thromboxane A₂ (which stimulates platelet aggregation, leading to the formation of blood clots).

Ibuprofen is a nonselective COX inhibitor, in that it inhibits two isoforms of cyclooxygenase, COX-1 and COX-2. The inhibition of COX by ibuprofen therefore lowers the level of prostaglandins made by the body. The prostaglandins that are formed from PGH₂ are important mediators of sensations such as pain and processes such as fever and inflammation, pain, fever and swelling. The antipyretic effects may arise as a result of action on the hypothalamus leading to vasodilation, an increased peripheral blood flow and subsequent heat dissipation.

Pharmacodynamic effects

Ibuprofen works by blocking the production of prostaglandins, substances that the body releases in response to illness and injury. Prostaglandins cause pain and swelling, or inflammation. They are released in the brain, and they can also cause fever. Ibuprofen's painkilling effects begin soon after taking a dose>

Clinical efficacy and safety

Clinical Pharmacology of Ibuprofen

Ibuprofen is supplied as tablets with a potency of 200 to 800 mg. The usual dose is 400 to 800 mg three times a day. It is almost insoluble in water having pK_a of 5.3. It is well absorbed orally; peak serum concentrations are attained in 1 to 2 hours after oral administration. It is rapidly bio-transformed with a serum half life of 1.8 to 2 hours. The drug is completely eliminated in 24 hours after the last dose and eliminated through metabolism. The drug is more than 99% protein bound, extensively metabolized in the liver and little is excreted unchanged.

Although highly bound to plasma proteins (90-99%), displacement interactions are not clinically

significant, hence the dose of oral anti-coagulants and oral hypoglycemic needs not be altered.¹ More than 90% of an ingested dose is excreted in the urine as metabolites or their conjugates, the major metabolites are hydroxylated and carboxylated compounds.

Old age has no significant effects on the elimination of ibuprofen. Renal impairment also has no effect on the kinetics of the drugs, rapid elimination still occur as a consequence of metabolism. The administration of ibuprofen tablets either under fasting conditions or immediately before meals yield quiet similar serum concentrations-time profile. When it is administered immediately after a meal, there is a reduction in the rate of absorption but no appreciable decrease in the extent of absorption.>

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 elimination half-life of Ibuprofen is about 2 hours.

In limited studies Ibuprofen appears in the breast milk in very low concentrations

BIOAVAILABILITY/BIOEQUIVALENCE

Ibuprofen is rapidly absorbed from the gastrointestinal tract with a bioavailability of 80-90%. Peak serum concentrations occur one to two hours after administration. If administered with food, peak serum concentrations are lower and achieved more slowly than when taken on an empty stomach Food does not affect markedly total bioavailability.

Excretion by the kidney is both rapid and complete. The elimination half-life is approximately 2 hours. The excretion of ibuprofen is virtually complete 24 hours after the last dose.>

5.3 Preclinical safety data

No relevant information additional to that contained elsewhere in the SPC

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

[List all excipients **except solvents removed during processing.**]

[NAME OF EACH INGREDIENT]

Raw Material	Raw material
Ibuprofen	Glycerol
Maltitol liquid	Polysorbate 80
Croscarmellose Sodium	Saccharin sodium
Citric acid monohydrate	Sodium methylhydroxybenzoate
Sodium propylhydroxybenzoate	Purified water
Colorcoat FC4W-H	Flavour

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years

6.4 Special precautions for storage

How to store Algafen Suspension

Store below 30°C, away from light, Keep all medicines out of the reach of children

6.5 Nature and contents of container <and special equipment for use, administration or implantation>

HDPE bottle sealed with child resistant, tamper evident cap. Pack size: 100ml

6.6 Special precautions for disposal <and other handling>

Shake well before use. Any unused product or waste material should be disposed of in accordance with local requirements.

7. APPLICANT/MANUFACTURER

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