

# **SUMMARY OF PRODUCT CHARACTERISTICS**

## **1 NAME OF THE MEDICINAL PRODUCT**

Ibuprofen Tablets BP 400 mg

Rofen™

## **2 QUALITATIVE AND QUANTITATIVE COMPOSITION**

Ibuprofen BP 400 mg per tablet.

Excipient with known effect: 76 mg Sucrose

For the full list of excipients, see section 6.1

## **3 PHARMACEUTICAL FORM**

The product is presented in the form of a sugar coated, deep convex tablet imprinted with the marking IBU 400.

## **4 CLINICAL PARTICULARS**

### **4.1 Therapeutic indications**

Ibuprofen Tablets is indicated for its analgesic and anti-inflammatory effects in the treatment of rheumatoid arthritis (including juvenile rheumatoid arthritis or Still's disease), ankylosing spondylitis, osteoarthritis and other non-rheumatoid (seronegative) arthropathies.

In the treatment of non-articular rheumatic conditions, Ibuprofen Tablets is indicated in periarticular conditions such as frozen shoulder (capsulitis), bursitis, tendonitis, tenosynovitis and low back pain; Ibuprofen Tablets can also be used in soft tissue injuries such as sprains and strains.

Ibuprofen Tablets is also indicated for its analgesic effect in the relief of mild to moderate pain such as dysmenorrhoea, dental and post-operative pain and for the symptomatic relief of headache including migraine headache.

## **4.2 Posology and method of administration**

Undesirable effects may be minimised by using the lowest effective dose for the shortest duration necessary to control symptoms (see section 4.4).

### Posology:

#### *Adults and children over 12 years of age:*

The recommended dosage of Ibuprofen Tablets is 1200-1800 mg daily in divided doses. Some patients can be maintained on 600-1200 mg daily. In severe or acute conditions, it can be advantageous to increase the dosage until the acute phase is brought under control, provided that the total daily dose does not exceed 2400 mg in divided doses.

#### *Paediatric population:*

The daily dosage of Ibuprofen Tablets 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 7 kg.

#### *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. If renal or hepatic function is impaired, dosage should be assessed individually.

### Method of administration

For oral administration. It is recommended that patients with sensitive stomachs take Ibuprofen Tablets with food. If taken shortly after eating, the onset of action of Ibuprofen Tablets may be delayed. To be taken preferably with or after food, with plenty of fluid. Ibuprofen 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 to any of the excipients listed on section 6.1.

Should not be used in patients who have previously shown hypersensitivity reactions (e.g. asthma, urticaria, angioedema or rhinitis) after taking ibuprofen, aspirin or other NSAIDs.

Also contraindicated in patients with a history of gastrointestinal bleeding or perforation, related to previous NSAID therapy. Ibuprofen should not be used in patients with active, or history of, recurrent peptic ulcer, or gastrointestinal haemorrhage (two or more distinct episodes of proven ulceration or bleeding).

Ibuprofen should not be given to patients with conditions involving an increased tendency to bleeding.

Ibuprofen Tablets is contraindicated in patients with severe heart failure (NYHA Class IV), hepatic failure and renal failure (see section 4.4).

Ibuprofen Tablets is contraindicated during the 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 section 4.2, and GI and cardiovascular risks below).

Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrose-isomaltase insufficiency should not take this medication.

As with other NSAIDs, ibuprofen may mask the signs of infection.

The use of ibuprofen with concomitant NSAIDs including cyclooxygenase-2 selective inhibitors should be avoided due to the increased risk of ulceration or bleeding (see section 4.5).

#### *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).

*Paediatric population:*

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

*Gastrointestinal bleeding, ulceration and perforation:*

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. 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 gastrointestinal disease, particularly when elderly, should report any unusual abdominal symptoms (especially gastrointestinal 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 ibuprofen, the treatment should be withdrawn.

NSAIDs should be given with care to patients with a history of ulcerative colitis or Crohn's disease as these conditions may be exacerbated (see section 4.8).

*Respiratory disorders and hypersensitivity reactions*

Caution is required if ibuprofen is administered to patients suffering from, or with a previous history of, bronchial asthma, chronic rhinitis or allergic diseases since NSAIDs have been reported to precipitate bronchospasm, urticaria or angioedema in such patients.

*Cardiac, Renal and Hepatic Impairment:*

The administration of an NSAID may cause a dose dependent reduction in prostaglandin formation and precipitate renal failure. The habitual concomitant intake of various similar painkillers further increases this risk. Patients at greatest risk of this reaction are those with impaired renal function, cardiac impairment, liver dysfunction, those taking diuretics and the elderly. For these patients, use the lowest effective dose, for the shortest possible duration and monitor renal function

especially in long-term treated patients (see also section 4.3).

Ibuprofen should be given with care to patients with a history of heart failure or hypertension since oedema has been reported in association with ibuprofen administration.

#### *Cardiovascular and cerebrovascular effects*

Appropriate monitoring and advice are required for patients with a history of hypertension and/or mild to moderate congestive heart failure as fluid retention and oedema have been reported in association with NSAID therapy.

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). Overall, epidemiological studies do not suggest that low dose ibuprofen (e.g. £ 1200mg/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.

Cases of Kounis syndrome have been reported in patients treated with Ibuprofen Tablets. Kounis syndrome has been defined as cardiovascular symptoms secondary to an allergic or hypersensitive reaction associated with constriction of coronary arteries and potentially leading to myocardial infarction.

#### *Renal effects:*

Caution should be used when initiating treatment with ibuprofen in patients with considerable dehydration.

As with other NSAIDs, long-term administration of ibuprofen has resulted in renal papillary necrosis and other renal pathologic changes. Renal toxicity has also been seen in patients whom renal prostaglandins have a compensatory role in the maintenance of renal perfusion. In these patients, administration of an NSAID may cause a dose-dependant reduction in prostaglandin formation and, secondarily, in renal blood flow, which may cause renal failure. Patients at greatest risk of this reaction are those with impaired renal function, heart failure, liver dysfunction, those taking diuretics and ACE inhibitors and the elderly. Discontinuation of NSAID therapy is usually followed by recovery to the pre-treatment state.

*SLE and mixed connective tissue disease:*

In patients with systemic lupus erythematosus (SLE) and mixed connective tissue disorders there may be an increased risk of aseptic meningitis (see section 4.8).

*Aseptic meningitis:*

Aseptic meningitis has been observed on rare occasions in patients on ibuprofen therapy. Although it is probably more likely to occur in patients with systemic lupus erythematosus and related connective tissue diseases, it has been reported in patients who do not have an underlying chronic disease.

*Severe cutaneous adverse reactions (SCARs):*

Severe cutaneous adverse reactions (SCARs), including exfoliative dermatitis, erythema multiforme, Stevens- Johnson syndrome (SJS), Toxic Epidermal Necrolysis (TEN), Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS syndrome), and acute generalized exanthematous pustulosis (AGEP), which can be life-threatening or fatal, have been reported in association with the use of ibuprofen (see section 4.8). Most of these reactions occurred within the first month.

If signs and symptoms suggestive of these reactions appear, ibuprofen should be withdrawn immediately and an alternative treatment considered (as appropriate).

*Haematological effects:*

Ibuprofen, like other NSAIDs, can interfere with platelet aggregation and Prolong bleeding time in normal subjects.

*Impaired female fertility:*

The use of ibuprofen may impair female fertility and is not recommended in women attempting to conceive. In women who have difficulties conceiving or who are undergoing investigation of infertility, withdrawal of ibuprofen should be considered.

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

## **4.5 Interaction with other medicinal products and other forms of interaction**

Care should be taken in patients treated with any of the following drugs as interactions have been reported in some patients.

Antihypertensives, beta-blockers and diuretics: NSAIDs may reduce the effect of anti-hypertensives, such as ACE inhibitors, angiotensin-II receptor antagonists, beta-blockers and diuretics. Diuretics can also increase the risk of nephrotoxicity of NSAIDs..

Cardiac glycosides: NSAIDs may exacerbate cardiac failure, reduce GFR and increase plasma cardiac glycoside levels.

Lithium: decreased elimination of lithium.

Colestyramine: The concomitant administration of ibuprofen and colestyramine may reduce the absorption of ibuprofen in the gastrointestinal tract. However, the clinical significance is unknown.

Methotrexate: NSAIDs may inhibit the tubular secretion of methotrexate and reduce clearance of methotrexate.

Ciclosporin: increased risk of nephrotoxicity.

Mifepristone: A decrease in the efficacy of the medicinal product can theoretically occur due to the antiprostaglandin properties of NSAIDs. Limited evidence suggests that coadministration of NSAIDs on the day of prostaglandin administration does not adversely influence the effects of mifepristone or the prostaglandin on cervical ripening or uterine contractility and does not reduce the clinical efficacy of medicinal termination of pregnancy.

Other analgesics including cyclooxygenase-2 selective inhibitors: avoid concomitant use of two or more NSAIDs, (including Cox-2 inhibitors), as this may result in an increased risk of adverse reactions (see section 4.4).

Aspirin (Acetylsalicylic acid): As with other products containing NSAIDs, concomitant administration of ibuprofen and aspirin is not generally recommended because of the potential of increased adverse effects.

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).

Corticosteroids: increased risk of GI bleeding or ulceration (see section 4.4).

Anticoagulants: NSAIDs may enhance the effects of anticoagulants, such as warfarin (see section 4.4).

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.

Sulfonylureas: NSAIDs may potentiate the effects of sulfonylurea medications. There have been reports of hypoglycaemia in patients on sulfonylurea medications receiving ibuprofen.

Anti-platelet agents and selective serotonin reuptake inhibitors (SSRIs): increased risk of gastrointestinal bleeding (see section 4.4).

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.

Aminoglycosides: NSAIDs may decrease the excretion of aminoglycosides.

Herbal extracts: Gingko biloba may potentiate the risk of bleeding with NSAIDs.

CYP2C9 Inhibitors: Concomitant administration of ibuprofen with CYP2C9 inhibitors may increase the exposure to ibuprofen (CYP2C9 substrate). In a study with voriconazole and fluconazole (CYP2C9 inhibitors), an increased S(+)-ibuprofen exposure by approximately 80 to 100% has been shown. Reduction of the ibuprofen dose should be considered when potent CYP2C9 inhibitors are administered concomitantly, particularly when high-dose ibuprofen is administered with either voriconazole or fluconazole.

## **4.6 Fertility, Pregnancy and lactation**

### Pregnancy:

Inhibition of prostaglandin synthesis may adversely affect the pregnancy and/or embryo/foetal development. Data from epidemiological studies suggest an increased risk of miscarriage and of cardiac malformation and gastroschisis after the use of a prostaglandin synthesis inhibitor in early pregnancy. The risk is believed to increase with dose and duration of therapy. In animals, the administration of a prostaglandin synthesis inhibitor has been shown to result in increased pre- and post-implantation

losses and embryo/foetal lethality. In addition, increased incidences of various malformations, including cardiovascular, have been reported in animals given a prostaglandin synthesis inhibitor during the organogenetic period.

During the first and second trimester of pregnancy, ibuprofen should not be given unless clearly necessary. If ibuprofen is used by a woman attempting to conceive, or during the first or second trimester of pregnancy, the dose should be kept as low and duration of treatment as short as possible.

During the third trimester of pregnancy, all prostaglandin synthesis inhibitors may expose the foetus to the following:

- Cardiopulmonary toxicity (with premature closure of the ductus arteriosus and pulmonary hypertension)
- Renal dysfunction, which may progress to renal failure with oligohydramnios.

At the end of pregnancy, prostaglandin synthesis inhibitors may expose the mother and the neonate to the following:

- Possible prolongation of bleeding time
- Inhibition of uterine contractions, which may result in delayed or prolonged labour.

Consequently, ibuprofen is contraindicated during the third trimester of pregnancy.

#### Breast-feeding:

In the limited studies so far available, NSAIDs can appear in breast milk in very low concentration. NSAIDs should, if possible, be avoided when breastfeeding.

#### Fertility:

See section 4.4 Special warnings and precautions for use, 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**

*Gastrointestinal disorders:* the most commonly observed adverse events are gastro-intestinal in nature. Peptic ulcers, perforation or GI bleeding, sometimes fatal, particularly in the elderly, may occur (see section 4.4). Nausea, vomiting, diarrhoea, flatulence, constipation, dyspepsia, abdominal pain, melaena, haematemesis, ulcerative stomatitis, gastrointestinal haemorrhage, exacerbation of colitis and Crohn's disease (see section 4.4) have been reported following ibuprofen administration. Less frequently, gastritis, duodenal ulcer, gastric ulcer and gastrointestinal perforation have been observed.

*Immune system disorders:* hypersensitivity reactions have been reported following treatment with NSAIDs. These may consist of (a) non-specific allergic reactions and anaphylaxis, (b) respiratory tract reactivity comprising asthma, aggravated asthma, bronchospasm or dyspnoea, or (c) assorted skin disorders, including rashes of various types, pruritus, urticaria, purpura, angiodema and very rarely, erythema multiforme, bullous dermatoses (including Stevens-Johnson syndrome and toxic epidermal necrolysis).

*Cardiac disorders and vascular disorders:* Oedema, hypertension, and cardiac failure, have been reported in association with NSAID treatment.

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 (such as myocardial infarction or stroke) (see section 4.4).

*Infections and infestations:* rhinitis and aseptic meningitis (especially in patients with existing auto-immune disorders, such as systemic lupus erythematosus and mixed connective tissue disease) with symptoms such as stiff neck, headache, nausea, vomiting, fever or disorientation (see section 4.4). Exacerbation of infection-related inflammations coinciding with the use of NSAIDs has been described. If signs of an infection occur or get worse during use of Ibuprofen the patient is therefore recommended to go to a doctor without delay.

*Skin and subcutaneous tissue disorders:* in exceptional cases, severe skin infections and soft-tissue complications may occur during a varicella infection (see also "Infections and infestations").

The following adverse reactions possibly related to ibuprofen and displayed by MedDRA frequency convention and system organ classification. Frequency groupings are classified according to the subsequent conventions: very common ( $\geq 1/10$ ), Common ( $\geq 1/100$  to  $< 1/10$ ), Uncommon ( $\geq 1/1,000$  to  $< 1/100$ ), Rare ( $\geq 1/10,000$  to  $< 1/1,000$ ), Very rare ( $< 1/10,000$ ) and Not known (cannot be estimated from the available data).

<b>System organ class</b>	<b>Frequency</b>	<b>Adverse reaction</b>
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Infections and infestations	Uncommon	Rhinitis
	Rare	Meningitis aseptic (see section 4.4)
Blood and lymphatic system disorders	Rare	Leukopenia, thrombocytopenia, neutropenia, agranulocytosis, aplastic anaemia , haemolytic anaemia
Immune system disorders	Rare	Anaphylactic reaction
Psychiatric disorders	Uncommon	Insomnia, anxiety
	Rare	Depression, Confusional state
Nervous system disorders	Common	Headache, dizziness
	Uncommon	Paraesthesia, somnolence
	Rare	Optic neuritis
Eye disorders	Uncommon	Visual impairment
	Rare	Toxic optic neuropathy
Cardiac disorders	Very rare	Cardiac failure, myocardial infarction (also see section 4.4)
	Not known	Kounis syndrome
Vascular disorders	Very rare	Hypertension
Respiratory, thoracic and mediastinal disorders	Uncommon	Asthma, bronchospasm, dyspnoea
Gastrointestinal disorders	Common	Dyspepsia, diarrhoea, nausea, vomiting, abdominal pain, flatulence, constipation, melaena, haematemesis, gastrointestinal
	Uncommon	Gastritis, duodenal ulcer, gastric ulcer, mouth ulceration, gastrointestinal perforation
	Very rare	Pancreatitis
	Not known	Exacerbation of Colitis and Crohn´s disease

Hepatobiliary disorders	Uncommon	Hepatitis, jaundice, hepatic function abnormal
	Very Rare	Hepatic failure
Skin and subcutaneous tissue disorders	Common	Rash
	Uncommon	Urticaria, pruritus, purpura, angioedema, photosensitivity reaction
	Very rare	Severe cutaneous adverse reactions (SCARs) (including Erythema multiforme, exfoliative dermatitis, Stevens-Johnson syndrome, and toxic epidermal necrolysis)
	Not known	Drug reaction with eosinophilia and systemic symptoms (DRESS syndrome), acute generalised exanthematous pustulosis (AGEP)
Renal and urinary disorders	Uncommon	Nephrotoxicity in various forms e.g. Tubulointerstitial nephritis, nephrotic syndrome and renal failure
General disorders and administration	Common	Fatigue
	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](http://www.mhra.gov.uk/yellowcard) or search for MHRA Yellow Card in the Google Play or Apple App 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 400 mg/kg or greater.

### *Symptoms*

Most patients who have ingested significant amounts of ibuprofen will manifest symptoms within 4 to 6 hours.

The most frequently reported symptoms of overdose include nausea, vomiting, abdominal pain, lethargy and drowsiness. Central nervous system (CNS) effects include headache, tinnitus, dizziness, convulsion, and loss of consciousness. Nystagmus, metabolic acidosis, hypothermia, renal effects, gastrointestinal bleeding, coma, apnoea, diarrhoea and depression of the CNS and respiratory system have also rarely been reported. In serious poisoning metabolic acidosis may occur. Disorientation, excitation, fainting and cardiovascular toxicity, including hypotension, bradycardia and tachycardia have been reported. In cases of significant overdose, renal failure and liver damage are possible. Large overdoses are generally well tolerated when no other drugs are being taken.

### *Management*

Patients should be treated symptomatically as required.

Within one hour of ingestion of a potentially toxic amount, activated charcoal should be considered. Alternatively, in adults, gastric lavage should be considered within one hour of ingestion of a potentially life-threatening overdose.

Good urine output should be ensured.

Renal and liver function should be closely monitored.

Patients should be observed for at least four hours after ingestion of potentially toxic amounts.

Frequent or prolonged convulsions should be treated with intravenous diazepam.

Other measures may be indicated by the patient's clinical condition.

## **5 PHARMACOLOGICAL PROPERTIES**

### **5.1 Pharmacodynamic properties**

Pharmacotherapeutic classification: Anti-inflammatory and antirheumatic products, nonsteroidal; propionic acid derivatives.

ATC code: M01AE01

Ibuprofen is a propionic acid derivative with analgesic, anti-inflammatory and anti-pyretic activity. The drug's therapeutic effects as an NSAID is thought to result from its inhibitory effect on the enzyme cyclo-oxygenase, which results in a marked reduction in prostaglandin synthesis.

Experimental data suggest that ibuprofen may competitively inhibit the effect of low dose aspirin on platelet aggregation when they are dosed concomitantly. Some pharmacodynamic studies show that when single doses of ibuprofen 400mg were 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. 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 4.5).

## **5.2 Pharmacokinetic properties**

### Absorption

Ibuprofen is rapidly absorbed from the gastrointestinal tract, peak serum concentrations occurring 1-2 hours after administration.

### Distribution

Ibuprofen is extensively bound to plasma proteins.

### Biotransformation

Ibuprofen is metabolised in the liver to two inactive metabolites and these, together with unchanged ibuprofen, are excreted by the kidney either as such or as conjugates.

### Elimination

The elimination half-life is approximately 2 hours.  
Excretion by the kidney is both rapid and complete.

## **5.3 Preclinical safety data**

Not applicable.

# **6 PHARMACEUTICAL PARTICULARS**

## **6.1 List of excipients**

Colloidal silicon dioxide USNF

Maize starch BP  
Pregelatinised maize starch BP  
Potable water HSE  
Sodium starch glycollate BP  
Stearic acid BP  
Dextrin HSE  
Talc BP  
Gelatin EP  
Syrup BP  
Nipasept sodium HSE  
Sucrose BP  
Heavy kaolin BP  
Titanium dioxide BP

## **6.2 Incompatibilities**

Not applicable.

## **6.3 Shelf life**

5 years for opaque plastic containers and 2 years for blister packs.

## **6.4 Special precautions for storage**

Protect from heat, light and moisture.

Keep out of reach of children.

## **6.5 Nature and contents of container**

The product marketed in pack sizes of 28, 42, 50, 56, 84, 100, 112, 250, 500, 1000 and bulk tablets are packed in opaque plastic containers (securitainers) and/or in opaque plastic containers composed of either, high density polypropylene or high density polyethylene with tamper evident or child resistant tamper evident closure

composed of high density polyethylene with a packing inclusion of standard polyether foam or polyethylene or polypropylene made filler. The product is also marketed in blister packs of aluminium/opaque PVC, it is subsequently packed in printed box board cartons in pack sizes of 12, 24, 28, 42, 48, 56, 84, 96 and 112 tablets.

#### **6.6 Special precautions for disposal**

No special instructions for use/handling.

### **7 MARKETING AUTHORISATION HOLDER**

HFA HOLDINGS LTD  
Wharley Hall, Barston Lane  
Hampton In Arden,  
West Midlands  
B92 OHS  
England  
United Kingdom

### **8 MARKETING AUTHORISATION NUMBER(S)**

PL 52574/0007

### **9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**

05/03/2009

### **10 DATE OF REVISION OF THE TEXT**

29/01/2024