1 NAME OF THE MEDICINAL PRODUCT

Migrafen 400 mg coated tablets (P product)
Ibuprofen 400 mg coated tablets (P product)

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each Sugar-coated tablet contains Ibuprofen 400 mg

Excipient with known effect: Sucrose (up to 206 mg per tablet).

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Coated tablet

Pink sugar-coated tablets.

4.1 Therapeutic indications

For the POM product (Ebufac):

Ibuprofen 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 is indicated in pain relief of periarticular conditions such as frozen shoulder (capsulitis), bursitis, tendonitis, tenosynovitis and low back pain; ibuprofen can also be used in the pain relief of soft tissue injuries such as sprains & strains and lowering of body temperature in feverish conditions.

Ibuprofen 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.

For the P product (Migrafen 400):

a) The symptomatic relief of migraine, headaches, rheumatic pain, muscular pain, backache, period pain, dental pain, neuralgia, colds and flu.
b) The lowering of body temperature in feverish conditions.

4.2 Posology and method of administration

For the POM product:

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

Posology

Adults:
The recommended dosage of ibuprofen is 1200 to 1800 mg daily in divided doses. Some patients can be maintained on 600 to 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 dosage does not exceed 2400 mg even in divided doses.

Paediatric population

Children over 12 years of age:
The daily dosage of ibuprofen is 20 mg/kg of body weight in divided doses. For juvenile rheumatoid arthritis, up to 40 mg/kg of body weight daily in divided doses may be taken.

Children under 12 years of age:
Not recommended for children under the age of 12 years.

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.

Renal impairment:
Patients with mild to moderate renal impairment, (see section 4.4 - Special warnings and precautions for use) and patients with severe renal insufficiency (see section 4.3 – Contraindications).

Hepatic impairment:
For patients with mild to moderate hepatic impairment (see section 4.4 Special warnings and precautions for use) and patients with severe hepatic dysfunction (see section 4.3-Contraindications).

For the P product:

Adults and children over 12 years: 1 tablet to be taken with water. Subsequently, 1 tablet every four to six hours.

If in 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.

Maximum daily dose: three tablets in 24 hours. To be taken preferably after food.

Children under 12 years of age: Not to be given to children under 12 years of age.

Method of administration

For oral administration. It is recommended that patients with sensitive stomachs take Ibuprofen with food. If taken shortly after eating, the onset of action of Ibuprofen 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 Contra-indications

Ibuprofen is contraindicated in patients with hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

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

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

Ibuprofen is contraindicated during the last trimester of pregnancy (see section 4.6).

Not for use by children under the age of 12 without medical advice if sold as a P product.

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).

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).

The diagnosis of medication overuse headache (MOH) should be suspected in patients who have frequent or daily headaches despite (or because of) the regular use of analgesic medication. Patients with medication overuse headache should not be treated by increasing the dose of the analgesic. In such cases the use of analgesic should be discontinued.
The concomitant consumption of excessive alcohol with NSAIDs, including ibuprofen may increase the risk of adverse effects on the gastrointestinal tract, such as GI haemorrhage or the central nervous system, possibly due to an additive effect.

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, have been reported for 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 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, e.g. 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.

Cardiovascular, 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 (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.

Renal effects

Caution should be used when initiating treatment with ibuprofen in patients with considerable dehydration. There is a risk of renal impairment in dehydrated children, adolescents and the elderly.

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 in whom renal prostaglandins have a compensatory role in the

maintenance of renal perfusion. In these patients, administration of an NSAID may cause a dose-dependent 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 disease there is an increased risk of aseptic meningitis (see section 4.8 Undesirable effects).

Severe skin reactions:

Serious skin reactions, some of them fatal, including exfoliative dermatitis, Stevens-Johnson syndrome, and toxic epidermal necrolysis have been reported rarely in association with the use of NSAIDSs (see section 4.8). Patients appear to be at highest risk of these reactions early in the course of therapy, the onset of the reaction occurring in the majority of cases within the first month of treatment. Acute generalised exanthematous pustulosis (AGEP) has been reported in relation to ibuprofen-containing products. Ibuprofen should be discontinued, at the first appearance of signs and symptoms of severe skin reactions, such as skin rash, mucosal lesions, or any other sign of hypersensitivity.

In exceptional cases, varicella can be at the origin of serious cutaneous and soft tissues 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 Ibuprofen in case of varicella.

Masking of symptoms of underlying infections:

'Migrafen 400 / Ebufac' 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 'Migrafen 400 / Ebufac' 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.

Haematological effects

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

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.

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.

Excipients

Iboprufen tablets contain sucrose and should not be given to patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction

Concurrent aspirin or other NSAIDs may result in an increased incidence of adverse reactions.

Acetylsalicylic acid: Concomitant administration of ibuprofen and acetylsalicylic acid 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).

Anti-coagulants: May enhance the effects of anti-coagulants.

Anti-hypertensives: NSAIDs may diminish the effect of anti-hypertensives.

Diuretics: Reduced diuretic effect. Diuretics can increase the risk of nephrotoxicity of NSAIDs.

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

Cyclosporin: Increased risk of nephrotoxicity.

Mifepristone: NSAIDs should not be used for 8-12 days after mifepristone administration as they can reduce the effect of mifepristone.

Corticosteroids: Increased risk of GI bleeding.

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.

Frusemide: Ibuprofen reduces the natriuretic effect of frusemide and thiazide diuretics. This is thought to be due to the inhibition of renal prostaglandin synthesis. Patients being treated concomitantly with ibuprofen and thiazides or frusemide should be closely monitored.

Lithium: Patients receiving ibuprofen and lithium should be observed for signs of lithium toxicity because ibuprofen has been shown to produce an elevation of plasma lithium levels and a reduction in renal lithium clearance.

Methotrexate: When methotrexate is used concomitantly with ibuprofen, enhanced toxicity of methotrexate may ensue due to a reduction of renal tubular secretion of methotrexate. Exercise caution in these circumstances.

4.6 Pregnancy and lactation

Whilst no teratogenic effects have been demonstrated in animal studies, ibuprofen should be avoided during pregnancy. Congenital abnormalities have been reported in association with ibuprofen administration in man associated; however, these are low in frequency and do not appear to follow any discernible pattern. In view of the known effects of NSAIDS on the foetal cardiovascular system, closure of ductus arteriosus, use in late pregnancy should be avoided. The onset of labour may be delayed and the duration of labour increased. Ibuprofen appears in breast milk at very low concentrations and is unlikely to affect the breast fed infant adversely.

4.7 Effects on ability to drive and use machines

Migrafen 400/Ebufac' does not affect the ability to drive or use machines.

4.8 Undesirable effects

Gastrointestinal disorders: The most commonly observed adverse events are gastrointestinal 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 and 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 have been observed.
Immune system disorders: Hypersensitivity reactions have been reported following treatment with NSAIDs. These may consist of (a) non-specific allergic reaction 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, angioedema and, very rarely, erythema multiforme, bullous dermatoses (including StevensJohnson 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 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 autoimmune disorders, such as systemic lupus erythematosus and mixed connective tissue disease) with symptoms of stiff neck, headache, nausea, vomiting, fever or disorientation (see section 4.4). Exacerbation of infectionrelated 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 (≥1/10), Common (≥1/100 to <1/10), Uncommon (≥1/1,000 to <1/100), Rare (≥1/10,000 to <1/1,000), Very rare (<1/10,000) and Not known (cannot be estimated from the available data).

System organ class	**Frequency**	**Adverse reacon**
Infections and infestaons	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	Uncommon Rare	Hypersensivity Anaphylactic reacon
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

System organ class	**Frequency**	**Adverse reacon**
Ear and labyrinth disorders	Uncommon	Hearing impaired, tinnitus, vertigo
Respiratory, thoracic and mediastinal disorders	Uncommon	Asthma, bronchospasm, dyspnoea
Gastrointestinal disorders	Common	Dyspepsia, diarrhoea, nausea, vomiting, abdominal pain, flatulence, constipation, melaena, haematemesis, gastrointestinal haemorrhage
	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	Nephrotoxity in various forms e.g.Tubulointersal nephris, nephrotic syndrome

System organ class	Frequency	Adverse reacon
	Very rare	Acute renal failure
	Not known	Ureteric colic, dysuria Renal tubular acidosis*
General disorders and administraon site condions	Common	Fatigue
	Rare	Oedema
Cardiac disorders	Very rare	Cardiac failure, myocardial infarction (also see secon 4.4)
	Not known	Kounis syndrome
Vascular disorders	Very rare	Hypertension
Metabolism and Nutrition Disorders	Not known	Decreased Appetite, Hypokalaemia*

*Renal tubular acidosis and hypokalaemia have been reported in the post-marketing setting typically following prolonged use of the ibuprofen component at higher than recommended doses.

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).

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme at www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple 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 been rarely reported. 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.

Prolonged use at higher than recommended doses or overdoses may result in hypokalaemia and renal tubular acidosis. Symptoms may include reduced level of consciousness and generalised weakness (see section 4.4 and section 4.8).

Disorientation, excitation, fainting and cardiovascular toxicity, including hypotension, bradycardia and tachycardia have been reported. Large overdoses are generally well tolerated when no other drugs are being taken.

Therapeutic measures

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

Ibuprofen is a phenylpropionic acid derivative with analgesic, anti-inflammatory and antipyretic actions. Ibuprofen inhibits prostaglandin synthesis.

It is a white powder with characteristic odour and a melting point 75°-77.5°C. Ibuprofen is practically insoluble in water but soluble in 1.5 of alcohol and 1 of chloroform, 1 in 2 of ether and 1 in 1.5 of acetone. Soluble in aqueous solutions of alkali hydroxides and carbonates.

Experimental data suggest that ibuprofen may competitively inhibit the effect of low dose acetylsalicylic acid on platelet aggregation when they are dosed concomitantly. Some pharmacodynamic studies show that when single doses of ibuprofen 400 mg were taken within 8 h before or within 30 min after immediate release acetylsalicylic acid dosing (81 mg), a decreased effect of acetylsalicylic acid 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

Ibuprofen is absorbed from the gastro-intestinal tract. Peak plasma concentrations occur about one to two hours after ingestion. The drug is extensively bound to plasma proteins and has a half life of about 2 hours. It is rapidly excreted in the urine, mainly in the form of metabolites and their conjugates. About 1% is excreted in urine as unchanged Ibuprofen and about 14% as conjugated Ibuprofen.

5.3 Preclinical safety data

Not applicable.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

In the core:

Pregelatinised starch

Crospovidone

Purified Talc

Colloidal anhydrous silica

Stearic acid

Magnesium stearate

In the coating:

Shellac

Purified Talc

Povidone K 25

PB-640013 Pink (contains quinoline yellow aluminum lake E104, erythrosin aluminum lake E127, titanium dioxide E171)

Titanium dioxide

Sucrose

Yellow beeswax

Carnuba wax

6.2 Incompatibilities

No known incompatibilities other than those stated in 4.4 and 4.5 above.

6.3 Shelf life

The shelf-life of Ibuprofen tablets 400mg as packaged for sale is:

36 months in plastic containers

24 months in blister-packs

6.4 Special precautions for storage

Container: Store below 25°C in a dry place in well closed containers.

Blister packs: Do not store above 25°C. Store in the original package.

6.5 Nature and contents of container

1. High density polystyrene with polythene lids and/or polypropylene containers with polypropylene or polythene lids and polyurethane or polythene inserts. Packs of 3, 6, 12, 24, 28, 30, 50, 56,100, 500, 1000 tablets.

2. PVC aluminium foil blister packs, composed of 25 micron PVC glass clear/bluish rigid PVC (pharmaceutical grade) and 20 micron hard-tempered aluminium foil coated on the pull side with 6.7gsm heat-seal lacquer and printed on the bright side. The blister strips are enclosed in outer cardboard cartons. Blister-packs are of 3, 6, 12, 24, 28, 48, 84, 96, 100, 500, 1000 tablets.

The label for the P product will state: “Do not use if you have ever had a stomach ulcer or are allergic to ibuprofen or aspirin. If you are allergic to, or are taking any other pain killer, are pregnant or suffer from asthma, speak to your doctor before taking ‘Migrafen 400’”.

The leaflet for the P Product will state: “If your symptoms persist, consult your doctor of pharmacist.”

6.6 Special precautions for disposal

No special instructions.

7 MARKETING AUTHORISATION HOLDER

Chelonia Healthcare Limited
11 Boumpoulinas Street,
3rd floor, 1060 Nicosia
Cyprus

8 MARKETING AUTHORISATION NUMBER(S)

PL 33414/0050

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

04 December 1979

10 DATE OF REVISION OF THE TEXT

13/10/2024