NAME OF THE MEDICINAL PRODUCT

Nurofen Express 400 mg Liquid Capsules

PRODUCT DESCRIPTION

Capsule, soft. A clear red oval soft gelatin capsule printed with an identifying logo in white

PHARMACODYNAMIC

Ibuprofen is a nonsteroidal anti-inflammatory drug (NSAID) that in the conventional animal-experiment inflammation models has proven to be effective via prostaglandin-synthesis inhibition. In humans, ibuprofen reduces inflammatory-related pain, swellings and fever. Furthermore,ibuprofen reversibly inhibits ADP-and collagen-induced platelet aggregation. Experimental data suggests that ibuprofen may inhibit the effect of low dose aspirin on platelet aggregation when they are dosed concomitantly. In one study, when a single dose of ibuprofen 400mg was taken within 8 h before or within 30 min after immediate release dosing (81 mg), a decreased effect of ASA on the formation of thromboxane of platelet aggregation occurred. Although there are uncertainties regarding extrapolation of these date 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.

PHARMACOKINETICS

On oral application, ibuprofen is partly absorbed in the stomach and then completely in the small intestine.

Following hepatic metabolisation (hydroxylation, carboxylation), the pharmacologically inactive metabolites are completely eliminated, mainly renally (90 %), but also with the bile. The elimination half-life in healthy individuals and those with liver and kidney diseases is 1.8 -3.5 hours, plasma-protein binding about 99 %.

Peak plasma levels following oral administration of a normal-release pharmaceutical form (tablet) are reached after 1-2 hours. However, ibuprofen is absorbed more rapidly from the gastrointestinal tract following oral administration of Nurofen Express Liquid Capsules. In 2 pharmacokinetic studies, the times to peak plasma levels (Tmax) for ibuprofen acid tablets were 60 and 90 min compared with 35 and 40 min respectively for Nurofen Express Liquid Capsules. An average Cmax is achieved in half the time taken for Nurofen Express Liquid Capsules compared with normal-release pharmaceutical form (tablet Nurofen). Ibuprofen is detected in the plasma for more than 8 hours after administration of Nurofen Express Liquid Capsules.

INDICATIONS

Nurofen Express Liquid Capsules are indicated for the relief of pain such as headache, dental pain, period pain, rheumatic pain, muscular pain and backache. They also relieve fever such as fever associated with cold & flu.

POSOLOGY AND METHOD OF ADMINISTRATION

For oral use and short-term use only. Capsules should not be chewed.

The lowest effective dose should be used for the shortest duration necessary to relieve symptoms.

<u>Adults and children over 12 years</u>

Single dose: 1-2 liquid capsules of 200mg respectively.
1 liquid capsule of 400mg

If necessary, take additional doses of 1 or 2 capsules (200 mg or 400 mg ibuprofen) but do not exceed a total dose of 1200mg ibuprofen in any 24-hour period. The dosing interval should not be below 4 hours for the 200 mg dose and not below 6 hours for the 400 mg dose.

If this product is required for more than 3 days in the case of fever or for more than 4 days for pain relief, or if the symptoms worsen the patient is advised to consult a doctor.

It is recommended that patients with sensitive stomachs take Nurofen Express Liquid Capsules with food.

If taken shortly after eating, the onset of action of Nurofen Express Liquid Capsules may be delayed. If this happens do not take more Nurofen Express Liquid Capsules than recommended or until the correct re-dosing interval has passed.

ROUTE OF ADMINISTRATION
Oral

CONTRAINDICATIONS

- Hypersensitivity to ibuprofen, ponceau 4R (E124) or to any of the excipients
- Patients with a history of hypersensitivity reactions (e.g. bronchospasm, asthma, rhinitis, angioedema or urt icaria) associated with the intake of acetylsalicylic acid (ASA) or other non-steroidal anti-inflammatory drugs (NSAIDs)
- Active, or history of recurrent peptic ulcer/haemorrhage (two or more distinct episodes of proven ulceratio n or bleeding)
- History of gastrointestinal bleeding or perforation, related to previous NSAIDs therapy
- Patients with severe hepatic failure, severe renal failure, coronary heart disease or severe heart failure (see also section Warnings and Precautions)
- Adolescents weighing less than 40 kg or children under 12 years of age.
- In patients with cerebrovascular or other active bleeding
- In patients with unclarified blood-formation disturbances
- In patients with severe dehydration (caused by vomiting, diarrhoea or insufficient fluid intake)
- The last trimester of pregnancy (see section Pregnancy and Lactation)

WARNINGS AND PRECAUTIONS

Undesirable effects may be minimised by using the lowest effective dose for the shortest duration necessary to control symptoms (see GI and cardiovascular risks below).

- Congenital disorder of porphyrin metabolism (e.g. acute intermittent porphyria) gastrointestinal disorders and chronic inflammatory intestinal disease (ulcerative colitis, Crohns disease) (see section Side Effects)
- Hypertension and/or cardiac impairment as renal function may deteriorate. (see sections Contraindications and Side Effects)
- Directly after major surgery
- In patients who react allergically to other substances, as an increased risk of hypersensitivity reactions occurring also exists for them on use of Nurofen Express Liquid Capsules
- In patients who suffer from hayfever, nasal polyps or chronic obstructive respiratory disorder as an increased risk exists for them of allergic reactions occurring.
- These may present as asthma attacks (so called analgesic asthma). Quincke's oedema or urticaria

The elderly have an increased frequency of adverse reactions to NSAIDs, especially gastrointestinal bleeding and perforation, which may be fatal.

Respiratory:

Bronchospasm may be precipitated in patients suffering from, or with a history of, bronchial asthma or allergic disease.

Other NSAIDs:

The use of ibuprofen with concomitant NSAIDs including cyclooxygenase-2 selective inhibitors should be avoided.

SLE and mixed connective tissue disease:

Systemic lupus erythematosus as well as those with mixed connective tissue disease – increased risk of aseptic meningitis.

Renal:

Renal impairment as renal function may further deteriorate.

There is a risk of renal impairment in dehydrated children and adolescents
Renal tubular acidosis and hypokalaemia may occur following acute overdose and in patients taking ibuprofen products over long periods at high doses (typically greater than 4 weeks), including doses exceeding the recommended daily dose.

Hepatic:

Hepatic dysfunction.

Cardiovascular and cerebrovascular effects

Cases of Kounis syndrome have been reported in patients treated with Nurofen Extra Strength 400 mg Liquid Capsules/Nurofen Express 400 mg Liquid Capsules. 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.

Caution (discussion with doctor or pharmacist) is required prior to starting treatment in patients with a history of hypertension and/or heart failure as fluid retention, hypertension and oedema have been reported in association with NSAID therapy.

Clinical studies suggest that 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. $\leq$ 1200 mg/day) is associated with an increased risk of arterial thrombotic events.

Patients with uncontrolled hypertension, congestive heart failure (NYHA II-III), established ischaemic heart disease, peripheral arterial disease, and/or cerebrovascular disease should only be treated with ibuprofen after careful consideration and high doses (2400 mg/day) should be avoided.

Careful consideration should also be exercised before initiating long-term treatment of patients with risk factors for cardiovascular events (e.g. hypertension, hyperlipidaemia, diabetes mellitus, smoking), particularly if high doses of ibuprofen (2400 mg/day) are required.

Impaired female fertility:

There is limited evidence that drugs which inhibit cyclooxygenase/ prostaglandin synthesis may cause impairment of female fertility by an effect on ovulation. This is reversible upon withdrawal of treatment.

Gastrointestinal:

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

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 and in the elderly. These patients should commence treatment on the lowest dose available.

Patients with a history of GI toxicity, particularly the 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.

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

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).

Masking of symptoms of underlying infections

This medicinal product 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 this medicine is administered for pain or fever in relation to infection, monitoring of infection is advised. In non-hospital settings, the patient should consult a doctor if symptoms persist or worsen.

This medicine contains 27.9 mg potassium per capsule. To be taken into consideration by patients with reduced kidney function or patients on a controlled potassium diet.

Contains Sorbitol. Patients with rare hereditary problems of fructose intolerance should not take this medicine.

Also contains Ponceau 4R (E124) which may cause allergic reactions.

The label will include: Read the enclosed leaflet before taking this product

Do not take if you:

- have (or have had two or more episodes of) a stomach ulcer, perforation or bleeding
- are allergic to ibuprofen, to any of the ingredients, or to aspirin or other painkillers
- are taking other NSAID pain killers or aspirin with a daily dose above 75 mg

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

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

If symptoms persist or worsen, or if new symptoms occur, consult your doctor or pharmacist.

Other notes

Severe acute hypersensitivity reactions (for example anaphylactic shock) are observed very rarely. At the first signs of hypersensitivity reaction after taking/administering Nurofen Express Liquid Capsules therapy must be stopped. Medically required measures, in line with the symptoms, must be initiated by specialist personnel.

Ibuprofen, the active substance of Nurofen Express Liquid Capsules may temporarily inhibit the blood-platelet function (thrombocyte aggregation). Therefore, it is recommended to monitor patients with coagulation disturbances carefully.

In prolonged administration of Nurofen Express Liquid Capsules regular checking of the liver values, the kidney function, as well as of the blood count, is required.

Prolonged use of any type of painkiller for headaches can make them worse. If this situation is experienced or suspected, medical advice should be obtained and treatment should be discontinued. 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 headache medications.

In general terms, the habitual intake of painkillers, particularly on combination of several pain-relieving active substances, may lead to permanent renal damage with the risk of renal failure (analgesic nephropathy). This risk may be increased under physical strain associated with loss of salt and dehydration.

Therefore, it should be avoided.

Through concomitant consumption of alcohol, active substance-related undesirable effects, particularly those that concern the gastrointestinal tract or the central nervous system, may be increased on use of NSAIDs.

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.

INTERACTION WITH OTHER MEDICINAL PRODUCTS

Concomitant use of ibuprofen with:	Possible effects:
Other NSAIDs, including salicylates	The concomitant administration of several NSAIDs may increase the risk of gastrointestinal ulcers and bleeding due to a synergistic effect. The concomitant use of ibuprofen with other NSAIDs should therefore be avoided.
Digoxin, phenytoin, lithium	The concomitant use of Nurofen Express Liquid Capsules with digoxin, phenytoin or lithium preparations may increase serum levels of these medicinal products. A check of serum-digoxin, serum- lithium and serum-phenytoin is not as a rule required on correct use (maximum over 4 days).
Corticosteroids	Corticosteroids as these may increase the risk of adverse reactions, especially of the gastrointestinal tract (gastrointestinal; ulceration or bleeding) (see section Contraindications)
Anti-platelet agents and Selective serotonin reuptake inhibitors (SSRIs):	Increased risk of gastrointestinal bleeding (see section Warnings and Precautions)
Acetylsalicylic acid (low dose):	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 clinical relevant effect is considered to be likely for occasional ibuprofen use (see section 5.1).
Anticoagulants:	NSAIDs may enhance the effect of anti-coagulants, such as warfarin (see section Warnings and Precautions)
Probenecid and sulfinpyrazone:	Medicinal products that contain probenecid or sulfinpyrazone may delay the excretion of ibuprofen.
Diuretics, ACE inhibitors, beta receptor- blockers and angiotensin-II antagonists:	NSAIDs may reduce the effect of diuretics and other antihypertensive medicinal products. 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, beta receptor-blockers or angiotensin-II antagonists and agents that inhibit cyclo-oxygenase may result in further deterioration of renal function, including possible acute renal failure, which is usually reversible. Therefore, the combination should be administered with caution, especially in the elderly. Patients should be adequately hydrated and considered should be given to monitoring of renal function after initiation of concomitant therapy, and periodically thereafter.
Potassium sparing diuretics:	The concomitant administration of Nurofen Express Liquid Capsules and potassium- sparing diuretics may lead to hyperkalaemia (check of serum potassium is recommended).
Methotrexate:	The administration of Nurofen Express Liquid Capsules within 24 hours before or after administration of methotrexate may lead to elevated concentrations of methotrexate and an increase in its toxic effect.
Ciclosporin:	The risk of a kidney-damaging effect due to ciclosporin in increased through the concomitant administration of certain nonsteroidal anti-inflammatory drugs. This effect also cannot be ruled out for a combination of ciclosporin with ibuprofen.
Tacrolimus:	The risk of nephrotoxicity is increased if the two medicinal products are administered concomitantly.
Zidovudine:	There is evidence of an increased risk of haemarthroses and haematoma in HIV (+) haemophiliacs receiving concurrent treatment with zidovudine and ibuprofen. Increased risk of haematological toxicity when NSAIDs are given with zidovudine.
Sulphonylureas	Clinical investigations have shown interactions between nonsteroidal anti-inflammatory drugs and antidiabetics (sulphonylureas). Although interactions between ibuprofen and sulphonylureas have not been described to date, a check of blood glucose values is recommended as a precaution on concomitant intake.
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.
Mifepristone:	NSAIDs should not be used for 8-12 days after mifepristone administration as NSAIDs can reduce the effect of mifepristone.
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 and fluconazole.

PREGNANCY AND LACTATION

Pregnancy:

Inhibition of prostaglandin synthesis may adversely affect the pregnancy and/or the embryo/foetal development. Data from epidemiological studies suggest an increased risk of miscarriage and of cardiac malformation and gastroschisis after use of a prostaglandin synthesis inhibitor in early pregnancy. The absolute risk for cardiovascular malformation was increased from less than 1%, up to approximately 1.5%. The risk is believed to increase with dose and duration of therapy.

In animals, administration of a prostaglandin synthesis inhibitor has been shown to result in increased pre- and post-implantation loss and embryofoetal lethality. In addition, increased incidences of various malformations, including cardiovascular, have been reported in animals given a prostaglandin synthesis inhibitor during the organogenetic period.

From the 20th week of pregnancy onward, Nurofen use may cause oligohydramnios resulting from foetal renal dysfunction. This may occur shortly after treatment initiation and is usually reversible upon discontinuation. In addition, there have been reports of ductus arteriosus constriction following treatment in the second trimester, most of which resolved after treatment cessation, therefore during the first and second trimester of pregnancy, Nurofen should not be given unless clearly necessary.

If Nurofen is used by a woman attempting to conceive, or during the first and second trimester of pregnancy, the dose should be kept as low and duration of treatment as short as possible. Antenatal monitoring for oligohydramnios and ductus arteriosus constriction should be considered after exposure to Nurofen for several days from gestational week 20 onward. Nurofen should be discontinued if oligohydramnios or ductus arteriosus constriction are found.

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

- cardiopulmonary toxicity (premature constriction/closure of the ductus arteriosus and pulmonary hypertension);
- renal dysfunction (see above); which may progress to renal failure with oligohydroamniosis;

the mother and the neonate, at the end of the pregnancy, to:

- possible prolongation of bleeding time, an anti-aggregating effect which may occur even at very low doses;
- inhibition of uterine contractions resulting in delayed or prolonged labour.

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

Lactation:

Ibuprofen and its metabolites can pass in low concentrations into the breast milk. No harmful effects to infants are known to date, so for short-term treatment with the recommended dose for pain and fever interruption of breast-feeding would generally not be necessary.

UNDESIRABLE EFFECTS

The list of the following undesirable effects comprises all undesirable effects that have become known under treatment with ibuprofen, also those under high-dose long-term therapy in rheumatism patients. The stated frequencies, which extend beyond very rare reports, refer to the short-term use of daily doses up to a maximum of 1200 mg ibuprofen for oral dosage forms and a maximum of 1800 mg for suppositories.

With the following adverse drug reactions, it must be accounted for that they are predominantly dose-dependent and vary inter individually.

The most commonly observed adverse reactions are gastrointestinal in nature. Peptic ulcers, perforation GI bleeding, sometimes fatal, particularly in the elderly may occur (see section Warnings and Precautions). Nausea, vomiting, diarrhoea, flatulence, constipation, dyspepsia, abdominal pain, melaena, haematemesis, ulcerative stomatitis, exacerbation of colitis and Crohn's disease (see section Warnings and Precautions) have been reported following administration. Less frequently, gastritis has been observed. Particularly the risk of gastrointestinal bleeding occurring is dependent on the dose range and the duration of use.

Oedema, hypertension and cardiac failure have been reported in association with NSAID treatment.

Clinical trial and epidemiological data suggest that use of ibuprofen, particularly at high dose (2400 mg daily), and in long term treatment may be associated with a small increased risk of arterial thrombotic events (for example myocardial infarction or stroke) (see section Warnings and Precautions).

Please note that within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1000 to <1/100), rare (≥1/10,000 to <1/1000), very rare (<1/10,000) and not known (cannot be estimated from the available data)

Hypersensitivity reactions have been reported and these may consist of:

a) non-specific allergic reactions and anaphylaxis
b) respiratory tract reactivity, e.g. asthma, aggravated asthma, bronchospasm, dyspnoea
c) various skin reactions, e.g. pruritus, urticaria, angioedema and more rarely exfoliative and bullous dermatoses (including epidermal necrolysis and erythema multiforme)

The patient is to be instructed to inform a doctor at once and to stop taking Nurofen Express if they experience any of the above.

System Organ Class	Frequency	Adverse Event
Blood and Lymphatic System Disorders	Very rare:	Haematopoietic disorders (anaemia, leucopenia, thrombocytopenia, pancytopenia, agranulocytosis). First signs are: fever, sore throat, superficial mouth ulcers, flu-like symptoms, severe exhaustion, unexplained bleeding and bruising.
Immune System Disorders	 Uncommon Very rare	Hypersensitivity reactions consisting of[1]: Urticaria and pruritus Severe hypersensitivity reactions. Symptoms could be facial, tongue and laryngeal swelling, dyspnoea, tachycardia, hypotension (anaphylaxis, angioedema or severe shock).

	Not known	Respiratory tract reactivity comprising asthma, aggravated asthma, bronchospasm or dyspnoea.
Nervous System Disorders	Uncommon	Headache
	Very rare	Aseptic meningitis[2]
Cardiac Disorders	Not known	Cardiac failure and oedema
	Not known	Kounis syndrome
Vascular Disorders	Not known	Hypertension
Gastrointestinal Disorders	Uncommon	Abdominal pain, nausea, dyspepsia
	Rare	Diarrhoea, flatulence, constipation and vomiting
	Very rare	Peptic ulcer, perforation or gastrointestinal haemorrhage, melaena, haematemesis, sometimes fatal, particularly in the elderly. Ulcerative stomatitis, gastritis
	Not known	Exacerbation of colitis and Crohn's disease
Hepatobiliary Disorders	Very rare	Liver disorders
Skin and Subcutaneous Tissue Disorders	Uncommon	Various skin rashes
	Very rare	Severe cutaneous adverse reactions (SCARs) (bgullous reactions, including erythema multiforme, exfoliative dermatitis, Stevens-Johnson syndrome, and toxic epidermal necrolysis2)

	Not known	Drug reaction with eosinophilia and systemic symptoms (DRESS syndrome) Acute generalised exanthematous pustulosis (AGEP) **<u>Photosensitivity reactions</u>**
Metabolism and Nutrition Disorders	Not known Not known	Decreased Appetite Hypokalaemia*
Renal and Urinary Disorders	Very rare Not known Not known Not known	Acute renal failure, papillary necrosis, especially in long-term use, associated with increased serum urea and oedema. Renal insufficiency Ureteric colic, dysuria Renal tubular acidosis*
Investigations	Very rare	Decreased haemoglobin levels

Description of Selected Adverse Reactions

[1] Hypersensitivity reactions have been reported following treatment with ibuprofen. These may consist of (a) non-specific allergic reactions and anaphylaxis, (b) respiratory tract activity comprising asthma, aggravated asthma, bronchospasm, dyspnoea or (c) assorted skin disorders, including rashes of various types, pruritus, urticaria, purpura, angioedema and more rarely exfoliative and bullous dermatoses (including epidermal necrolysis and erythema multiforme).

[2]The pathogenic mechanism of drug-Induced aseptic meningitis is not fully understood. However, the available data on NSAID-related aseptic meningitis points to a hypersensitivity reaction (due to a temporal relationship with drug intake, and disappearance of symptoms after drug discontinuation). Of note, single cases of symptoms of aseptic meningitis (such as stiff neck, headache, nausea, vomiting, fever or disorientation) have been observed during treatment with ibuprofen, in patients with existing auto-immune disorders (such as systemic lupus erythematosus, mixed connective tissue disease).

*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.

OVERDOSE

Symptoms and treatment of overdose:

In children ingestion of more than 400 mg/kg ibuprofen may cause symptoms. In adults the dose response effect is less clear cut. Symptoms of an overdose:

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 dizziness, 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. No special antidote is available

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

Patients who experience dizziness, drowsiness, vertigo or visual disturbances while they are taking ibuprofen, should avoid driving or using machinery. Single administration or short term use of ibuprofen does not usually warrant the adoption of any special precautions. This applies to a greater extent in combination with alcohol.

SHELF LIFE

24 months.

STORAGE CONDITION

Store below 30°C. store in original package.

ATC CODE

M01A E01 Propionic acid derivative

MANUFACTURER

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