

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Extra Strength Ibuprofen 400mg Tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 400mg of Ibuprofen.

Excipients with known effect:

Each tablet contains: 100.28 mg sucrose

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Coated tablet

Round white sugar coated tablet

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

Adults, elderly and Children over 12 years: For symptomatic relief of Rheumatic or muscular pain, pain of non-serious arthritic conditions, back ache, neuralgia, migraine, headache, dental pain, dysmenorrhoea.

Ibuprofen relieves pain and reduces inflammation and temperature as well as relieving headaches and other types of pain. It also relieves cold and flu symptoms

4.2 Posology and method of administration

For oral administration and short term use only.

The lowest effective dose should be used for the shortest duration necessary to relieve symptoms (see section 4.4).

Adults and the elderly: If this medicinal product is required for more than 10 days, or if symptoms persist or worsen, consult your doctor.

Children and Adolescents (age range: ≥ 12 years to < 18 years): If this medicinal product is required for more than 3 days, or if symptoms persist or worsen, consult your doctor.

400mg (1 tablet) to be taken with water up to three times a day as required.

Adult: Take 1 capsule with water, up to three times a day as required.

Leave at least four hours between doses and do not take more than 1200mg (3 tablets) in any 24 hour period.

Children under 12 years of age: Not recommended.

4.3 Contraindications

Hypersensitivity to ibuprofen or any of the excipients listed in section 6.1.

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, relating to previous NSAIDs therapy.

Use with concomitant NSAIDs, including cyclo-oxygenase-2 specific inhibitors-increased risk of adverse reactions (see section 4.5)

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

Severe heart failure (NYHA Class IV), renal failure or hepatic failure (see section 4.4)

During last trimester of pregnancy as there is a risk of premature closure of the fetal 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 4.6)

4.4 Special warnings and precautions for use

Paracetamol:

The hazards of paracetamol overdose are greater in patients with non-cirrhotic alcoholic liver disease. Immediate medical advice should be sought in the event of an overdose, even if the patient feels well, because of the risk of delayed, serious liver damage.

Do not take with any other paracetamol containing products. Immediate medical advice should be sought if this occurs, even if you feel well as this can result in an overdose (see section 4.9).

Caution is advised if paracetamol is administered concomitantly with flucloxacillin due to increased risk of high anion gap metabolic acidosis (HAGMA), particularly in patients with severe renal impairment, sepsis,

malnutrition and other sources of glutathione deficiency (e.g. chronic alcoholism), as well as those using maximum daily doses of paracetamol. Close monitoring, including measurement of urinary 5-oxoproline, is recommended.

Ibuprofen:

Undesirable effects may be minimised by using the lowest effective dose for the shortest possible duration necessary to control symptoms (see GI and cardiovascular risks below) and by patients taking the dose with food (see Section 4.2).

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

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)..

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 due to the increased risk of ulceration or bleeding and other side effects (see section 4.5).

SLE and mixed connective tissue disease:

Systemic lupus erythematosus (SLE) and mixed connective tissue disorders- 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.

Renal:

Renal impairment as renal function may further deteriorate (see sections 4.3 and 4.8). 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 in whom renal prostaglandins have a compensatory role in the maintenance of renal perfusion. In these patients, the administration of an NSAID may cause a dose dependent reduction in prostaglandin formation and precipitate renal failure. Patients at greatest risk of this reaction are those with impaired renal function, cardiac impairment, liver dysfunction, those taking diuretics and ACE inhibitors and the elderly. Renal function should be monitored in these patients (see section 4.3 and 4.8).

Discontinuation of NSAID therapy is usually followed by recovery to the pre-treatment state.

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 (see sections 4.3 and 4.8).

Cardiovascular and cerebrovascular effects:

Caution (discussion with doctor or pharmacist) is required prior to starting treatment in patients with a history of hypertension and/or mild to moderate 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 (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. ≤ 1200 mg/day) is associated with an increased risk of myocardial infarction.

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.

Haematological effects: Ibuprofen, like other NSAIDs, can interfere with platelet aggregation and has been shown to prolong bleeding time in normal subjects.

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.

Impaired female fertility:

There is limited evidence that drugs which inhibit cyclo-oxygenase/prostaglandin synthesis may cause impairment of female fertility by an effect on ovulation. The use of ibuprofen therefore, 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 is reversible upon withdrawal of treatment.

Gastrointestinal effects:

NSAIDs should be given with care to patients with a history of gastrointestinal disease (ulcerative colitis, Crohn's disease) as these 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 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 acetylsalicylic acid, or other drugs likely to increase gastrointestinal risk (see below and 4.5).

Patients with a history of GI toxicity, particularly when elderly, should report any unusual abdominal symptoms (especially GI bleeding) particularly in the initial stages of treatment.

Caution should be advised in patients receiving concomitant medications which could increase the risk of ulceration or bleeding, such as oral corticosteroids, anticoagulants such as warfarin, selective serotonin-reuptake inhibitors or anti-platelet agents such as aspirin (see section 4.5)

When GI bleeding or ulceration occurs in patients receiving 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), and 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).

Paediatric Population:

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

Masking of symptoms of underlying infections:

Ibuprofen 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 Ibuprofen is administered for fever or pain relief in relation to infection, monitoring of infection is advised.

In nonhospital settings, the patient should consult a doctor if symptoms persist or worsen.

Important information regarding the ingredients in this medicine

Sucrose: This medicine contains sucrose. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrose-isomaltase insufficiency should not take this medicine.

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

The label will include:

Read the enclosed leaflet before taking this product.

Do not use if you:

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

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.
- are a smoker.
- are pregnant.

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

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.

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 aspirin (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 effects (see section 4.4).

Ibuprofen should be used with caution in combination with:

Corticosteroids: Increased risk of gastrointestinal ulceration or bleeding (see section 4.4).

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

Anti-hypertensives, (ACE inhibitors and angiotensin II Antagonists)and diuretics: Since NSAIDs may diminish the effect 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.

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 glycoside levels.

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

Lithium: There is evidence for potential increases in plasma levels of lithium due to decreased elimination of lithium.

Methotrexate: There is evidence for the potential increase in plasma levels of methotrexate as NSAIDs may inhibit the tubular secretion of methotrexate and reduce clearance of 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. A decrease in the efficacy of the medicinal product can theoretically occur due to the antiprostaglandin properties of NSAIDs. Limited evidence suggests that co-administration 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.

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.

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

Aminoglycosides: NSAIDs may decrease the excretion of aminoglycosides.

Herbal extracts: Ginkgo 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 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 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.

From the 20th week of pregnancy onward, ibuprofen 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, Ibuprofen should not be given unless clearly necessary. If Ibuprofen 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 Ibuprofen for several days from gestational week 20 onward. Ibuprofen 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 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, Ibuprofen is contraindicated during the third trimester of pregnancy (see sections 4.3 and 5.3).

Breast-feeding:

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

Fertility:

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 events which have been associated with Ibuprofen are given below, listed by system organ class and frequency. Frequencies are defined as: very common ($\geq 1/10$), common ($\geq 1/100$ to $< 1/10$), uncommon ($\geq 1/1000$ to $< 1/100$), rare ($\geq 1/10,000$ to $< 1/1000$), very rare ($< 1/10,000$) and not known (cannot be estimated from the available data). Within each frequency grouping, adverse events are presented in order of decreasing seriousness.

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

The adverse events observed most often are gastrointestinal in nature. Adverse events are mostly dose-dependent; in particular the risk of occurrence of gastrointestinal bleeding is dependent on the dosage range and duration of treatment.

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) (see section 4.4).

Immune system disorders:

Uncommon: hypersensitivity reactions¹ with urticaria and pruritus

Very rare: 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.

Blood and lymphatic system disorders:

Very rare: Haematopoietic disorders (anaemia, hemolytic anaemia, aplastic anaemia, leucopenia, thrombocytopenia, pancytopenia, agranulocytosis). First signs are: fever, sore throat, superficial mouth ulcers, flu-like symptoms, severe exhaustion, unexplained nose and skin bleeding and bruising.

Skin and subcutaneous tissue disorders:

Uncommon: Various skin rashes

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) and acute generalised exanthematous pustulosis (AGEP), Photosensitivity reactions

Nervous system disorders:

Uncommon: Headache

Very rare: Aseptic Meningitis²

Cardiac disorders:

Not known: Cardiac failure and oedema, angina pectoris, Kounis syndrome

Vascular Disorders:

Not known: Hypertension

Respiratory, thoracic and mediastinal disorders:

Very rare: Asthma, bronchospasm, dyspnoea and wheezing

Gastrointestinal disorders:

Uncommon: Abdominal pain, nausea and dyspepsia

Rare: Diarrhoea, flatulence, constipation and vomiting

Very rare: Peptic ulcer, perforation or gastrointestinal haemorrhage, malaena, haematemesis, sometimes fatal, particularly in the elderly. Ulcerative stomatitis, gastritis

Not known: Exacerbation of ulcerative colitis and Crohn's disease (see section 4.4)

Hepatobiliary disorders:

Very rare: Liver disorders, especially in long-term treatment, hepatitis and jaundice

Metabolism and Nutrition disorders

Not known: Hypokalaemia³, Decreased appetite

Renal and urinary disorders:

Very rare: Acute renal failure, papillary necrosis, especially in long-term use, associated with increased serum urea and oedema. Haematuria, interstitial nephritis, nephrotic syndrome, proteinuria

Not known: Renal insufficiency, Renal tubular acidosis³, Ureteric colic, dysuria

Eye disorders:

Very rare: Visual disturbance

Ear and labyrinth disorders:

Very rare: Tinnitus and vertigo

Psychiatric disorders:

Very rare: Nervousness

General disorders and administration site conditions:

Very rare: peripheral oedema

Investigations:

Very rare: Decreased haematocrit and haemoglobin levels

Description of Selected Adverse Reactions

¹Hypersensitivity 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).

²The 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).

³Renal 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.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorization 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 Website:

www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

Paracetamol

Liver damage is possible in adults who have taken 10 g (equivalent to 20 tablets) or more of paracetamol. Ingestion of 5 g (equivalent to 10 tablets) or more of paracetamol may lead to liver damage if the patient has one or more of the risk factors below:

- a) Is on long term treatment with carbamazepine, phenobarbitone, phenytoin, primidone, rifampicin, St John's Wort or other drugs that induce liver enzymes.
- b) Regularly consumes alcohol in excess of recommended amounts.
- c) Is likely to be glutathione depleted e.g. eating disorders, cystic fibrosis, HIV infection, starvation, cachexia

Symptoms

Symptoms of paracetamol overdose in the first 24 hours include pallor, nausea, vomiting, anorexia and abdominal pain. Liver damage may become apparent 12 to 48 hours after ingestion as liver function tests become abnormal. Abnormalities of glucose metabolism and metabolic acidosis may occur. In severe poisoning, hepatic failure may progress to encephalopathy, haemorrhage, hypoglycaemia, cerebral oedema and death. Acute renal failure with acute tubular necrosis, strongly suggested by loin pain, haematuria and proteinuria, may develop even in the absence of severe liver damage. Cardiac arrhythmias and pancreatitis have been 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 overdose 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).

Management

Immediate treatment is essential in the management of paracetamol overdose. Despite a lack of significant early symptoms, patients should be referred to hospital urgently for immediate medical attention. Symptoms may be limited to nausea or vomiting and may not reflect the severity of overdose or the risk of organ damage. Management should be in accordance with established treatment guidelines.

Treatment with activated charcoal should be considered if the overdose has been taken within 1 hour. Plasma paracetamol concentration should be measured at 4 hours or later after ingestion (earlier concentrations are unreliable).

Treatment with N-acetylcysteine may be used up to 24 hours after ingestion of paracetamol however; the maximum protective effect is obtained up to 8 hours

post ingestion. The effectiveness of the antidote declines sharply after this time.

If required the patient should be given intravenous-N-acetylcysteine, in line with the established dosage schedule. If vomiting is not a problem, oral methionine may be a suitable alternative for remote areas, outside hospital. Patients who present with serious hepatic dysfunction beyond 24 hours from ingestion should be managed in accordance with established guidelines.

Ibuprofen

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. 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.

In serious poisoning metabolic acidosis may occur.

Symptoms

Most patients who have ingested clinically important amounts of NSAIDs will develop no more than nausea, vomiting, epigastric pain, abdominal pain, lethargy or more rarely diarrhoea within 4 to 6 hours. Tinnitus, dizziness, 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, loss of consciousness or coma. Cardiovascular toxicity, including hypotension, bradycardia and tachycardia have been reported. Occasionally patients develop convulsions. Nystagmus, hypothermia, apnoea, 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. In cases of significant overdose acute renal failure and liver damage may occur. Exacerbation of asthma is possible in asthmatics.

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

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. 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.

If frequent or prolonged, convulsions should be treated with intravenous diazepam or lorazepam. Give bronchodilators for asthma.

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

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

M01A E, Anti-inflammatory and anti-rheumatic products, non-steroids, Propionic acid derivatives.

Ibuprofen is a propionic acid derivative NSAID that has demonstrated its efficacy by inhibition of prostaglandin synthesis. In humans ibuprofen reduces inflammatory pain, swellings and fever. Furthermore, ibuprofen reversibly inhibits platelet aggregation.

Clinical evidence demonstrates that when 400 mg of ibuprofen is taken the pain relieving effects can last for up to 8 hours.

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 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 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.

Ibuprofen is metabolised in the liver to two major metabolites with primary excretion via the kidneys, either as such or as major conjugates, together with a negligible amount of unchanged ibuprofen. Excretion by the kidney is both rapid and complete.

The elimination half life of ibuprofen is approximately 2 hours.

No significant differences in pharmacokinetic profile are observed in the elderly. In limited studies ibuprofen appears in the breast milk in very low concentrations.

5.3 Preclinical safety data

There are no pre-clinical data of relevance to the prescriber which are additional to that already included in other sections of the SmPC.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet Core

Colloidal anhydrous silica
Potato Starch
Povidone
Microcrystalline cellulose
Alginic acid
Magnesium stearate
Sodium lauryl sulfate
Sodium starch glycolate
Croscarmellose sodium

Coating Materials

PVAP sealcote (contains polyvinyl acetate phthalate & stearic acid)
Purified talc
Sucrose
Calcium carbonate
Acacia
Titanium dioxide (E171)
Carnauba wax

6.2 Incompatibilities

Not applicable

6.3 Shelf life

3 years

6.4 Special precautions for storage

Do not store above 25°C.

Keep the blister tightly closed and in the outer carton to protect from moisture and light.

6.5 Nature and contents of container

Blister Packs.

Tablets are packed individually in pre-moulded PVC film and sealed with aluminium foil.

Pack sizes: 8, 12, 16, 24, 32, 48, 56, 64, 72, 84, 96.

6.6 Special precautions for disposal

Not applicable

7 MARKETING AUTHORISATION HOLDER

Bristol Laboratories Limited
Unit 3, Canalside,
Northbridge Road,
Berkhamsted,
HP4 1EG

8 MARKETING AUTHORISATION NUMBER(S)

PL 17907/0161

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

23/05/2006

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