Boots Ibuprofen and Codeine 200mg/12.8mg Film-Coated Tablets

Summary of Product Characteristics Updated 29-Aug-2024 | THE BOOTS COMPANY PLC

1. Name of the medicinal product

Ibuprofen and Codeine 200mg/12.8mg film-coated Tablets

2. Qualitative and quantitative composition

Active ingredient	mg/tablet
Ibuprofen	200 mg
Codeine Phosphate Hemihydrate	12.8 mg
Excipients with known effect	mg/tablet
Sodium Starch Glycolate (Type A)	45 mg (11 mg Sodium)

For the full list of excipients, see section 6.1

3. Pharmaceutical form

Film Coated Tablet (Tablet)

White capsule-shaped tablet embossed with 'I +'

4. Clinical particulars

4.1 Therapeutic indications

This medicine is indicated in patients older than 12 years of age.

For the short term treatment of acute moderate pain which is not considered to be relieved by other analgesics (e.g. paracetamol, ibuprofen or aspirin) alone, such as: rheumatic and muscular pain, backache, neuralgia, migraine, headache, dental pain, dysmenorrhoea.

4.2 Posology and method of administration

For oral administration and short-term use only.

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

Recommended dosage:

Adults over 18 years: One or two tablets every four to six hours.

Do not take more than 6 tablets in 24 hours.

Leave at least four hours between doses.

Children aged 12 years to 18 years: The recommended dose for children 12 years and older is one or two tablets every 6 hours when necessary up to a maximum of 6 tablets in 24 hours.

Children under 12 years: This medicine should not be used in children below the age of 12 years because of the risk of opioid toxicity due to the variable and unpredictable metabolism of codeine to morphine (see sections 4.3 and 4.4).

Elderly:

No special dosage modifications are required for elderly patients, unless renal or hepatic function is impaired, in which case dosage should be assessed individually.

Do not take for more than 3 days continuously without medical review.

The patient should consult a doctor if symptoms persist or worsen, or if the product is required for more than 3 days.

4.3 Contraindications

Hypersensitivity to ibuprofen, codeine or any of the excipients in the product.

Patients who have previously shown hypersensitivity reactions (e.g. asthma, rhinitis, angioedema, or urticaria) in response to aspirin or other non-steroidal anti-inflammatory drugs.

Active or history of recurrent peptic ulcer/haemorrhage (two or more distinct episodes of proven ulceration or bleeding).

History of upper gastrointestinal bleeding or perforation, related to previous NSAIDs therapy.

Severe hepatic failure, renal failure or heart failure (NYHA Class IV) (See section 4.4, special warnings and precautions for use).

Third trimester of pregnancy (See section 4.6 Pregnancy and lactation).

Respiratory depression, chronic constipation.

In all paediatric patients (0-18 years of age) who undergo tonsillectomy and/or adenoidectomy for obstructive sleep apnoea syndrome due to an increased risk of developing serious and life threatening adverse reactions (see section 4.4).

In women during breastfeeding (see section 4.6).

In patients for whom it is known they are CYP2D6 ultra-rapid metabolisers.

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, Posology and method of administration and GI and cardiovascular risks below).

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

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

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 and Codeine Tablets 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.

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 this medicine with concomitant NSAIDs including cyclooxygenase-2 selective inhibitors should be avoided (see section 4.5).

SLE and mixed connective tissue disease:

Systemic lupus erythematosus and mixed connective tissue disease -increased risk of aseptic meningitis (see section 4.8 Undesirable effects).

Renal:

Renal impairment as renal function may further deteriorate (see section 4.3 and 4.8). There is a risk of renal impairment in dehydrated children and adolescents.

Severe hypokalaemia and renal tubular acidosis have been reported due to prolonged use of ibuprofen at higher than recommended doses. This risk is increased with the use of codeine/ibuprofen as patients may become dependent on the codeine component (see warning on Opioid use disorder, section 4.8 and section 4.9). Presenting signs and symptoms included reduced level of consciousness and generalised weakness. Ibuprofen induced renal tubular acidosis should be considered in patients with unexplained hypokalaemia and metabolic acidosis.

Hepatic:

Hepatic dysfunction (See section 4.3 and Section 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 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. ≤ 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 be made before initiating long-term treatment of patients with risk factors for cardiovascular events (e.g. hypertension, hyperlipidaemia, diabetes mellitus, smoking), particularly if high doses of ibuprofen (2400 mg/day) are required.

Cases of Kounis syndrome have been reported in patients treated with ibuprofen. 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. 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 (See section 4.8 Undesirable effects).

GI bleeding, ulceration or perforation, which can be fatal, has been reported with all NSAIDs at anytime during treatment, with or without warning symptoms or a previous history of serious GI events.

The risk of GI bleeding, ulceration or perforation is higher with increasing NSAID doses, in patients with a history of ulcer, particularly if complicated with haemorrhage or perforation (see section 4.3), and in the elderly. These patients should commence treatment on the lowest dose available. Combination therapy with protective agents (e.g. misoprostol or proton pump inhibitors) should be considered for these patients, and also for patients requiring concomitant low dose aspirin, or other drugs likely to increase gastrointestinal risk (see below and section 4.5).

Patients with a history of 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 gastrotoxicity or bleeding, such as corticosteroids, selective serotonin-reuptake inhibitors, anti-platelet agents such as aspirin or anticoagulants such as warfarin. In patients receiving anticoagulant therapy, prothrombin time should be monitored daily for the first few days of combined treatment (see section 4.5 Interactions).

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

Dermatological:

Severe cutaneous adverse reactions (SCARs)

Severe cutaneous adverse reactions (SCARs) including exfoliative dermatitis, erythema multiforme, Stevens-Johnson syndrome (SJS), Toxic Epidermal Necrolysis (TEN), Drug Reactions with Eosinophilia and Systemic Symptoms (DRESS syndrome), and acute generalised 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 this medicine should be withdrawn immediately and an alternative treatment considered (as appropriate).

Exceptionally, varicella can be at the origin of serious cutaneous and soft tissue 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 this medicine in case of varicella.

Codeine should be used with caution in those with hypotension and/or hypothyroidism. The tablets should be used with caution in patients with raised intracranial pressure or head injury. The effects of CNS depressants (including alcohol) may be potentiated by codeine.

Opioid use disorder (abuse and dependence):

Tolerance, physical and psychological dependence and opioid use disorder (OUD) may develop upon repeated administration of opioids such as codeine. Abuse or intentional misuse of Ibuprofen and Codeine Tablets may result in overdose and/or death.

Serious clinical outcomes, including fatalities, have been reported in association with abuse and dependence with codeine/ibuprofen combinations, particularly when taken for prolonged periods at higher than recommended doses. These have included reports of gastrointestinal perforations, gastrointestinal haemorrhages, severe anaemia, renal failure, renal tubular acidosis and severe hypokalaemia associated with the ibuprofen component.

Patients should be informed about the risks and signs of OUD as well as serious clinical outcomes. If these signs occur, patients should be advised to contact their doctor.

Withdrawal symptoms, such as restlessness and irritability may occur once the drug is stopped.

CYP2D6 metabolism

Codeine is metabolised by the liver enzyme CYP2D6 into morphine, its active metabolite. If a patient has a deficiency or is completely lacking this enzyme an adequate analgesic effect will not be obtained. Estimates indicate that up to 7% of the Caucasian population may have this deficiency. However, if the patient is an extensive or ultra-rapid metaboliser there is an increased risk of developing side effects of opioid toxicity even at commonly prescribed doses. These patients convert codeine into morphine rapidly resulting in higher than expected serum morphine levels.

General symptoms of opioid toxicity include confusion, somnolence, shallow breathing, small pupils, nausea, vomiting, constipation and lack of appetite. In severe cases this may include symptoms of circulatory and respiratory depression, which may be life threatening and very rarely fatal. Estimates of prevalence of ultra-rapid metabolisers in different populations are summarised below:

Population	Prevalence %
African/Ethiopian	29%
African American	3.4% to 6.5%
Asian	1.2% to 2%
Caucasian	3.6% to 6.5%
Greek	6.0%
Hungarian	1.9%
Northern European	1% to 2%

Post operative use in children

There have been reports in the published literature that codeine given post-operatively in children after tonsillectomy and/or adenoidectomy for obstructive sleep apnoea, led to rare, but life threatening adverse events including death (see also section 4.3). All children received doses of codeine that were within the appropriate dose range; however there was evidence that these children were either ultra-rapid or extensive metabolisers in their ability to metabolise codeine to morphine.

Children with compromised respiratory function

Codeine is not recommended for use in children in whom respiratory function might be compromised including neuromuscular disorders, severe cardiac or respiratory conditions, upper respiratory or lung infections, multiple trauma or extensive surgical procedures. These factors may worsen symptoms of morphine toxicity.

The label will state:

Front of pack

• Can cause addiction

• For three days use only

Back of pack

Read the enclosed leaflet before taking this product.

• List of indications as agreed in 4.1 of the SPC

• If you need to take this medicine continuously for more than 3 days you should see your doctor or pharmacist

• This medicine contains codeine which can cause addiction if you take it continuously for more than 3 days. If you take this medicine for headaches for more than 3 days it can make them worse

Do not take 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, liver, heart, kidney or bowel problems

• are a smoker

• are pregnant

If symptoms persist or worsen, consult your doctor.

The leaflet (or combined label/leaflet) will state:

'Headlines' section (to be prominently displayed)

• This medicine can be used for… ..(indications)

• You should only take this product for a maximum of 3 days at a time. If you need to take it for a longer than 3 days you should see your doctor or pharmacist for advice

• This medicine contains codeine which can cause addiction if you take it continuously for more than 3 days. This can give you withdrawal symptoms from the medicine when you stop taking it

• If you take this medicine for headaches for more than 3 days it can make them worse

'What this medicine is for' section

• Succinct description of the indications from 4.1 of the SPC

'Before you take this medicine' section

• This medicine contains codeine which can cause addiction if you take it continuously for more than 3 days. This can give you withdrawal symptoms from the medicine when you stop taking it

• If you take a painkiller for headaches for more than 3 days it can make them worse

'How to take this medicine' section

• Do not take for more than 3 days. If you need to use this medicine for more than 3 days you must speak to your doctor or pharmacist

• This medicine contains codeine and can cause addiction if you take it continuously for more than 3 days. When you stop taking it you may get withdrawal symptoms. You should talk to your doctor or pharmacist if you think you are suffering from withdrawal symptoms

'Possible side effects' section

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet.

You can also report side effects directly via the Yellow Card Scheme Website: www.mhra.go.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. By reporting side effects you can help provide more information on the safety of this medicine.

'How do I know if I am addicted?' section

If you take the medicine according to the instructions on the pack it is unlikely that you will become addicted to the medicine. However, if the following apply to you it is important that you talk to your doctor:

• You need to take the medicine for longer periods of time

• You need to take more than the recommended amount

• When you stop taking the medicine you feel very unwell but you feel better if you start taking the medicine again

4.5 Interaction with other medicinal products and other forms of interaction

Ibuprofen should not be used in combination with:

Acetylsalicylic acid (aspirin): Unless low-dose aspirin (not above 75mg daily) has been advised by a doctor, 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 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).

Codeine:

Interacts with monoamine oxidase inhibitors. Therefore caution should be exercised in patients taking monoamine oxidase inhibitors.

Ibuprofen should be used with caution in combination with:

Anticoagulants:

NSAIDS may enhance the effects of anti-coagulants, such as warfarin (See section 4.4).

Antihypertensives and diuretics:

NSAIDs may diminish the effect of these drugs. Diuretics can increase the risk of nephrotoxicity of NSAIDs.

Corticosteroids:

Increased risk of gastrointestinal ulceration or bleeding (See section 4.4 Special warnings).

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.

Lithium:

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

Methotrexate:

There is a potential for an increase in plasma methotrexate.

Ciclosporin:

Increased risk of nephrotoxicity.

UK SPC only: **Mifepristone:**

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

Tacrolimus:

Possible increased risk of nephrotoxicity when NSAIDs are given with tacrolimus.

Zidovudine:

Increased risk of haematological toxicity when NSAIDs are given with zidovudine. There is evidence of an increased risk of haemarthroses and haematoma in HIV(+) haemophiliacs receiving concurrent treatment with zidovudine and ibuprofen.

Quinolone antibiotics:

Animal data indicate that NSAIDs can increase the risk of convulsions associated with quinolone antibiotics. Patients taking NSAIDs and quinolones may have an increased risk of developing convulsions.

4.6 Fertility, pregnancy and lactation

Female fertility:

See section 4.4 regarding female fertility

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);

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).

Lactation:

Codeine

Codeine should not be used during breastfeeding (see section 4.3).

At normal therapeutic doses codeine and its active metabolite may be present in breast milk at very low doses and is unlikely to adversely affect the breast fed infant. However, if the patient is an ultra-rapid metaboliser of CYP2D6, higher levels of the active metabolite, morphine, may be present in breast milk and on very rare occasions may result in symptoms of opioid toxicity in the infant, which may be fatal.

Ibuprofen

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

4.7 Effects on ability to drive and use machines

Patients may become dizzy or sedated with this medicine. If affected, patients should not drive or operate machinery.

This medicine can impair cognitive function and can affect a patient's ability to drive safely. This class of medicine is in the list of drugs included in regulations under 5a of the Road Traffic Act 1988. When prescribing this medicine, patients should be told:

• The medicine is likely to affect your ability to drive

• Do not drive until you know how the medicine affects you

• It is an offence to drive while under the influence of this medicine

• However, you would not be committing an offence (called a 'statutory defence') if:

- The medicine has been prescribed to treat a medical or dental problem and

- You have taken it according to the instructions given by the prescriber and in the information provided with the medicine and

- It was not affecting your ability to drive safely

4.8 Undesirable effects

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)

Ibuprofen:

Hypersensitivity reactions:

Uncommon: Hypersensitivity reactions 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).

Exacerbation of asthma and bronchospasm.

Gastrointestinal:

The most commonly-observed adverse events are gastrointestinal in nature.

Uncommon: abdominal pain, nausea and 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.

Exacerbation of colitis and Crohn's disease (see section 4.4).

Nervous System:

Uncommon: Headache, blurred vision

Very rare: Aseptic meningitis – single cases have been reported very rarely.

Renal and urinary disorders:

Very rare: Acute renal failure, papillary necrosis, especially in long-term use, associated with increased serum urea and oedema.

Not known: Renal tubular acidosis (reported in the post-marketing setting typically following prolonged use at higher than recommended doses due to dependence on the codeine component)

Hepatic:

Very rare: liver disorders.

Haematological:

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.

Skin and subcutaneous tissue disorders:

Uncommon: Various skin rashes

Very rare: Severe cutaneous adverse reactions (SCARs) (including erythema multiforme, exfoliative dermatitis, Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN)).

Not known: Drug reaction with eosinophilia and systemic symptoms (DRESS syndrome).

Not known: Acute generalised exanthematous pustulosis (AGEP).

Not known: Photosensitivity reactions

Immune System:

In patients with existing auto-immune disorders (such as systemic lupus erythematosus, mixed connective tissue disease) during treatment with ibuprofen, single cases of symptoms of aseptic meningitis, such as stiff neck, headache, nausea, vomiting, fever or disorientation have been observed (see section 4.4).

Cardiovascular and Cerebrovascular:

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

Not known: Kounis syndrome

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 Special warnings and precautions for use).

Metabolism and nutrition disorders:

Not known: Hypokalaemia (reported in the post-marketing setting typically following prolonged use at higher than recommended doses due to dependence on the codeine component)

Codeine

Side effects to codeine include constipation, respiratory depression, cough suppression, nausea and drowsiness.

Regular prolonged use of codeine is known to lead to addiction and symptoms of restlessness and irritability may result when treatment is then stopped.

Prolonged use of a pain killer for headache can make them worse.

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

4.9 Overdose

Overuse of this product, defined as consumption of quantities in excess of the recommended dose, or consumption for a prolonged period, may lead to physical or psychological dependency. Symptoms of restlessness and irritability may result when treatment is stopped.

Symptoms of overdose with ibuprofen include;

In children ingestion of more than 400 mg/kg may cause symptoms. In adults the dose response effect is less clear cut. The half-life in overdose is 1.5-3 hours.

Symptoms

Most patients who have ingested clinically important amounts of NSAIDs will develop no more than nausea, vomiting, epigastric pain, or more rarely diarrhoea. Tinnitus, headache and gastrointestinal bleeding are also possible. In more serious poisoning, toxicity is seen in the central nervous system, manifesting as drowsiness, occasionally excitation and disorientation or coma. Occasionally patients develop convulsions. In serious poisoning metabolic acidosis may occur and the prothrombin time/ INR may be prolonged, probably due to interference with the actions of circulating clotting factors. Acute renal failure and liver damage may occur.

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

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.

Symptoms of overdose with codeine include;

Nausea and vomiting are prominent features. Respiratory depression, excitability, convulsions, hypotension and loss of consciousness may occur with large codeine overdose.

The stomach should be emptied. If severe CNS depression has occurred, artificial respiration, oxygen and parenteral naloxone may be needed. Imbalance in electrolyte levels should be considered.

5. Pharmacological properties

5.1 Pharmacodynamic properties

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.

Codeine is a centrally acting weak analgesic. Codeine exerts its effect through μ opioid receptors, although codeine has low affinity for these receptors, and its analgesic effect is due to its conversion to morphine. Codeine, particularly in combination with other analgesics, has been shown to be effective in acute nociceptive pain.

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 hours before or within 30 minutes after immediate release acetylsalicylic acid dosing (81 mg), a decreased effect of acetylsalicylic acid on the formation of thromboxane or platelet aggregation occurred. However 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

The elimination half-life of both ibuprofen and codeine is approximately three hours, and both drugs are given three to four times daily. The combination of the two drugs is therefore appropriate from a pharmacokinetic viewpoint; the tablet exhibits normal release characteristics for both active substances.

5.3 Preclinical safety data

There are no preclinical data of relevance to the prescriber which are additional to that already included.

6. Pharmaceutical particulars

6.1 List of excipients

Tablet Core:

Cellulose, Microcrystalline

Hypromellose

Sodium Starch Glycloate (Type A)

Maize Starch, Pregelatinised

Film Coat:

Hypromellose

Titanium dioxide (E171)

Talc

6.2 Incompatibilities

Not applicable

6.3 Shelf life

36 months.

6.4 Special precautions for storage

This medicine does not require any special storage conditions.

6.5 Nature and contents of container

White 250 micron PVC/60gsm PVdC/20 micron hard temper aluminium foil.

Pack sizes:

6, 8, 10, 12, 14, 16, 18, 20, 24, 28, 30, 32

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

No special requirements.

7. Marketing authorisation holder

The Boots Company PLC

1 Thane Road West

Nottingham

NG2 3AA.

8. Marketing authorisation number(s)

PL00014/0662

9. Date of first authorisation/renewal of the authorisation

03/11/2010

10. Date of revision of the text

20/08/2024

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