1.3.1 Summary of Product Characteristics (SmPC)

ENCLOSED BELOW

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Ibuprofen 400 mg & 200mg film-coated and sugar-coated tablets respectively.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated caplet contains 400 mg of Ibuprofen BP.

Each sugar-coated tablet contains 200mg of Ibuprofen BP.

Excipient with known effect: None.

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film-coated & sugar-coated tablets: 400mg & 200mg respectively.

BUFEX 400 (Ibuprofen 400mg) film-coated caplets are orange-coloured, about 16 mm x 9 mm capsule shaped, with a break line on one side and 'BW' on the other; BUFEX 200 tablets are pink-coloured, round biconvex, plain on both sides.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Symptomatic treatment of

- For short term symptomatic treatment of mild to moderate pain such as headache (including migraine), dysmenorrhea (period pain), dental pain, and fever and pain in the common cold.
- Symptomatic treatment of pain and inflammation in arthritic diseases (e.g. rheumatoid arthritis), degenerative arthritic conditions (e.g. osteoarthritis), and in painful swelling and inflammation after soft tissue injuries. ***4.2 Posology and method of administration***

For oral use.

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

The tablet should be swallowed with a glass of water during or after a meal.

The ibuprofen dose depends on the patient's age and body weight.

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

If in children aged from 6 years and in adolescents this medicinal product is required for more than 3 days, or if symptoms worsen a doctor should be consulted.

Mild to moderate pain and fever

Children 6-12 years (>20kg)

Children 6-9 years (20-29 kg):

200 mg 1-3 times a day with intervals of 4 to 6 hours as required. The maximum daily dose should not exceed 600mg.

Children 10-12 years (30-40 kg):

200mg 1-4 times a day with intervals of 4 to 6 hours as required. The maximum daily dose should not exceed 800 mg.

Adults and adolescents older than 12 years (≥40 kg):

200-400 mg given as a single dose or 3 times a day with an interval of 4 to 6 hours. The dosage in migraine headache should be: 400 mg given as a single dose, if necessary 400 mg with intervals of 4 to 6 hours. The maximum daily dose should not exceed 1200 mg.

Primary dysmenorrhoea

Adults and adolescents older than 12 years of age (≥ 40kg)

200-400 mg 1-3 times a day, with an interval of 4-6 hours, as needed. The maximum daily dose should not exceed 1200 mg.

Rheumatic diseases

Adults:
The usual dose is 400-600 mg three times daily. In some patients, maintenance doses of 600 mg-1200 mg per day are effective. In acute and severe disease may be increased to a maximum of 2400 mg in 3 or 4 doses.

Adolescents older than 12 years (> 40 kg):

The recommended dose is 20 mg/kg up to 40 mg/kg body weight per day in 3-4 doses.

Special populations:

Paediatric population:

BUFEXmg film-coated Tablets is contraindicated in children and adolescents younger than 6 years of age (below 20 kg body weight) because this tablet strength is not suitable due to the large amount of active substance.

Older people NSAIDs should be used with particular caution in elderly patients who are more prone to adverse events and are at increased risk of potentially fatal gastrointestinal haemorrhage, ulceration or perforation (see section 4.4). If treatment is considered necessary, the lowest dose for the shortest duration necessary to control symptoms should be used. Treatment should be reviewed at regular intervals and discontinued if no benefit is seen or intolerance occurs.

Impaired renal function

In patients with mild or moderate reduction of renal function, the dose should be kept as low as possible for the shortest duration necessary to control symptoms and renal function monitored. (For patients with severe renal failure see section 4.3).

Impaired liver function

In patients with mild or moderate reduction of liver function the dose should be kept as low as possible for the shortest duration necessary to control symptoms and liver function monitored. (For patients with severe liver failure see section 4.3).

4.3 Contraindications

BUFEX Tablets is contraindicated in patients with:

- hypersensitivity to the active substance or to any of the excipients listed in section 6.1
- previous hypersensitivity reactions (e.g. asthma, rhinitis, urticaria or angioedema) in response to acetylsalicylic acid or other NSAIDs
- history of gastrointestinal bleeding or perforation, related to previous NSAIDs therapy
- active, or history of recurrent peptic ulcer/haemorrhage (two or more distinct episodes of proven ulceration or bleeding)
- severe hepatic or severe renal insufficiency
- severe heart failure (NYHA Class IV)
- last trimester of pregnancy (see section 4.6)
- significant dehydration (caused by vomiting, diarrhoea or insufficient fluid intake)
- cerebrovascular or other active bleeding
- dishaematopoiesis of unknown origin
- children younger than 6 years of age (below 20 kg body weight) because this tablet strength is not suitable due to large amount of active substance.

4.4 Special warnings and precautions for use

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

Undesirable effects may be minimised by using the lowest effective dose for the shortest duration necessary to control symptoms (see section 4.2 and GI and cardiovascular risks below). Patients treated with NSAIDs long term should undergo regular medical supervision to monitor for adverse events.

BUFEX Tablets should only be administered under strict consideration of the benefitrisk ratio in the following conditions:

- Systemic Lupus Erythematosus (SLE) or other autoimmune diseases.
- Congenital disturbance of porphyrin metabolism (e.g. acute intermittent porphyria) - The first and second trimester of pregnancy
- Lactation

Special care has to be taken in the following cases:

- Gastrointestinal diseases including chronic inflammatory intestinal disease (ulcerative colitis, Crohn's disease)
- Cardiac insufficiency and hypertension
- Reduced renal function
- Hepatic dysfunction
- Disturbed haematopoiesis
- Blood coagulation defects
- Allergies, hay fever, chronic swelling of nasal mucosa, adenoids, chronic obstructive airway disease or bronchial asthma
- Immediately after major surgical interventions

Gastrointestinal bleeding, ulceration and perforation

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 medicinal products likely to increase gastrointestinal risk. (See below and section 4.5).

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

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

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

NSAIDs should be given with care to patients with a history of gastrointestinal disease (ulcerative colitis, Crohn’s disease) as their condition may be exacerbated. (See section 4.8).

Older people

The elderly have an increased frequency of adverse reactions to NSAIDs, especially gastrointestinal bleeding and perforation which may be fatal (see section 4.2).

Cardiovascular and cerebrovascular effects

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

Clinical studies suggest that use of ibuprofen, particularly at high doses (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. Similar consideration should be made before initiating longer-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.

Severe skin reactions

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

Renal effect

Ibuprofen may cause the retention of sodium, potassium and fluid in patients who have not previously suffered from renal disorders because of its effect on renal perfusion. This may cause oedema or even lead to cardiac insufficiency or hypertension in predisposed patients.

As with other NSAIDs, the prolonged administration of ibuprofen to animals has resulted in renal papillary necrosis and other pathological renal changes. In humans, there have been reports of acute interstitial nephritis with haematuria, proteinuria and occasionally nephrotic syndrome. Cases of renal toxicity have also been observed in patients in whom prostaglandins play a compensatory role in the maintenance of renal perfusion. In these patients, administration of NSAIDs may cause a dose-dependent reduction in prostaglandin formation and, secondarily, in renal blood flow, which may precipitate overt renal decompensation. Patients at greatest risk of suffering this reaction are those with renal dysfunction, heart failure, hepatic dysfunction, those taking diuretics and ACE inhibitors and the elderly. Discontinuation of NSAID treatment is generally followed by recovery to the pre-treatment state.

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.

Other precautions
Bronchospasm, urticaria or angioedema may be precipitated in patients suffering from or with a previous history of bronchial asthma, chronic rhinitis, sinusitis, nasal polyps, adenoids or allergic diseases.
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 the habitual intake of analgesics, particularly the combination use of different analgesic substances, may cause permanent renal damage and a risk of renal failure (analgesics nephropathy).

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

Ibuprofen may temporarily inhibit platelet aggregation and prolong the bleeding time. Therefore, patients with coagulation defects or on anticoagulant therapy should be observed carefully.

In case of long-term treatment with ibuprofen a periodical monitoring of hepatic and renal function as well as the blood count is necessary, especially in high risk patients.

Consumption of alcohol should be avoided since it may intensify side effects of NSAIDs, especially if affecting the gastrointestinal tract or the central nervous system.

Patients on ibuprofen should report to their doctor signs or symptoms of gastro-intestinal ulceration or bleeding, blurred vision or other eye symptoms, skin rash, weight gain or oedema.

There is some evidence that medical products which inhibit cyclo- oxygenase/prostaglandin synthesis may cause impairment of female fertility by an effect on ovulation. This is reversible on withdrawal of treatment.

Patients with rare hereditary problem of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction

Concomitant use of ibuprofen and the following substances should be avoided:

Acetylsalicylic acid: Concomitant administration of ibuprofen and acetylsalicylic acid is not generally recommended because of the potential of increased adverse effects. Experimental data suggest that ibuprofen may competitively inhibit the effect of low dose acetylsalicylic acid on platelet aggregation when they are dosed concomitantly. Although there are uncertainties regarding extrapolation of these data to the clinical situation, the possibility that regular, long-term use of ibuprofen may reduce the cardioprotective effect of low-dose acetylsalicylic acid cannot be excluded. No clinically relevant effect is considered to be likely for occasional ibuprofen use (see section 5.1)

Other NSAIDs: As a result of synergistic effects, the concurrent use of several NSAIDs can increase the risk of gastrointestinal ulcers and haemorrhage. Co-administration of ibuprofen with other NSAIDs should therefore be avoided (see section 4.4).

Anti-coagulants: NSAIDs may enhance the effects of anticoagulants, such as warfarin or heparin (see section 4.4). In case of simultaneous treatment, monitoring of the coagulation state is recommended.

Ticlopidin: NSAIDs should not be combined with ticlopidine due to a risk of an additive effect in the inhibition of the platelet function.

Methotrexate: NSAID inhibits the tubular secretion of methotrexate and certain metabolic interactions can occur resulting in decreased clearance of methotrexate. The administration of BUFEXTablets within 24 hours before or after the administrationof methotrexate can lead to an elevated concentration of methotrexate and an increase in its toxic effects. Therefore, concomitant use of NSAIDs and high doses of methotrexate should be avoided. Also, the potential risk of interactions in low dose treatment with methotrexate should be considered, especially in patients with impaired renal function. In combined treatment, renal function should be monitored.

Ibuprofen (like other NSAIDs) should be taken only with caution in combination with the following substances:

Moclobemide: Enhances the effect of ibuprofen.

Phenytoin, lithium and digoxin The concomitant use of ibuprofen with digoxin, phenytoin or lithium preparations may increase serum levels of these medicinal products. A check of serum-lithium is required, a check of serum digoxin and serum-phenytoin is recommended.

Diuretics and antihypertensives: Diuretics and ACE-inhibitors can increase the nephrotoxicity of NSAIDs. NSAIDs can reduce the effect of diuretics and antihypertensives including ACE-inhibitors and beta-blockers. In patients with reduced kidney function (e.g. dehydrated patients or elderly patients with reduced kidney function), the concomitant use of an ACE inhibitor and angiotension II antagonist with a cyclooxygenase-inhibiting medicinal product can lead to further impairment of kidney function and through to acute renal failure. This is usually reversible. Such combination should therefore only be used with caution, especially in elderly patients. The patients have to be instructed to drink

sufficient liquid and periodic monitoring of the kidney values should be considered for the time immediately after the start of the combination therapy.

*The concomitant administration of BUFEX*and potassium sparing diuretics or ACE inhibitors can result in hyperkalaemia.

Captopril: Experimental studies indicate that ibuprofen counteracts the effect of captopril of increased sodium excretion.

Aminoglycosides: NSAIDs can slow down the elimination of aminoglycosides and increase their toxicity.

Selective serotonin reuptake inhibitors (SSRIs): Increased risk of gastrointestinal bleeding (see section 4.4).

Ciclosporine: The risk of kidney damage by ciclosporin is increased by the concomitant administration of certain NSAIDs. This effect cannot be ruled out for the combination of ciclosporine and ibuprofen, either.

Cholestyramine: Concomitant treatment with cholestyramine and ibuprofen results in prolonged and reduced (25%) absorption of ibuprofen. The medicinal products should be administered with at least one hour interval.

Tacrolimus: Elevated risk of nephrotoxicity.

Zidovudine: There is evidence of an increased risk of haemarthrosis and haematoma in HIV positive haemophilia patients receiving concurrent treatment with zidovudine and ibuprofen. There may be an increased risk of haematotoxicity during concomitant use of zidovudine and NSAIDs. Blood counts 1-2 weeks after starting use together are recommended.

Ritonavir: May increase the plasma concentrations of NSAIDs.

Mifepristone: If NSAIDs are used within 8-12 days after mifepristone administration they can reduce the effect of mifepristone.

Probenecid or sulfinpyrazone: May cause a delay in the elimination of ibuprofen. The uricosuric action of these substances is decreased.

Quinolone antibiotics: Patients taking NSAIDs and quinolones may have an increased risk of developing convulsions.

Sulphonylureas: NSAIDs can increase the hypoglycemic effect of sulphonylureas. In the case of simultaneous treatment, monitoring of blood glucose levels is recommended.

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

Anti-platelet aggregation agents (e.g. clopidogrel and ticlopidine): Increase the risk of gastrointestinal bleeding (see section 4.4).

Alcohol, bisphosphonates and oxpentifylline (pentoxyfylline): May potentiate the GI side-effects and the risk of bleeding and ulceration.

Baclofen: Elevated baclofen toxicity.

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 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. During the first and second trimester of pregnancy, BUFEXTablets should not be given unless clearly necessary. If BUFEXTablets 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 treatmentas short as possible.

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

- cardiopulmonary toxicity (with premature closure of the ductus arteriosus and pulmonary hypertension);
- renal dysfunction, which may progress to renal failure with oligo-hydramniosis, 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 BUFEX Tablets (Ibuprofen 400mg) is contraindicated during the last trimester of pregnancy.

Breast-feeding

Ibuprofen is excreted in breast milk, but with therapeutic doses during short term treatment, the risk for influence on infant seems unlikely. If, however, longer treatment is prescribed, early weaning should be considered.

Fertility

The use of ibuprofen may impair 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.

4.7 Effects on ability to drive and use machines

Ibuprofen generally has no adverse effects on the ability to drive and use machinery. However since at high dosage side effects such as fatigue, somnolence, vertigo (reported as common) and visual disturbances (reported as uncommon) may be experienced, the ability to drive a car or operate machinery may be impaired in individual cases. This effect is potentiated by simultaneous consumption of alcohol.

4.8 Undesirable effects

The most commonly observed adverse events are gastrointestinal in nature. Peptic ulcers, perforation or GI bleeding, sometimes fatal, particularly in the elderly, may occur (see section 4.4). Nausea, vomiting, diarrhoea, flatulence, constipation, dyspepsia, abdominal pain, melaena, heamatemesis, ulcerative stomatits, exacerbation of colitis and Crohn's disease (see section 4.4) have been reported following administration. Less frequently, gastritis has been observed.

Undesirable effects are mostly dose-dependent. Especially the risk for the occurrence of gastrointestinal bleedings depends on the dosage range and duration of the treatment. Other known risk factors, see section 4.4.

Clinical studies suggest that use of ibuprofen, particularly at high dose (2400 mg/day) may be associated with a small increased risk of arterial thrombotic events (for example myocardial infarction or stroke) (see section 4.4).

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

The undesirable effects are less frequent when the maximum daily dose is 1200 mg.

Assessment of adverse reactions is normally based on the following occurrence frequency:

Very common (≥1/10)

Common (≥1/100 to <1/10)

Uncommon (≥1/1,000 to <1/100)

Rare (≥1/10,000 to <1/1,000)

Very rare (<1/10,000)

Not known (cannot be estimated from the available data)

Body System	Undesirable Effect	Frequency

Investigations	increase of blood urea nitrogen, serum transaminases and alkaline phosphatase, decrease in haemoglobin and haematocrit values, inhibition of platelet aggregation, prolonged bleeding time, decrease of serum calcium, increase in serum uric acid	Rare
Cardiac disorders	palpitations, heart failure, myocardial infarction, acute pulmonary oedema, oedema	Very rare
Blood and lymphatic system disorders	haematopoietic disorders (anaemia, leucopoenia, thrombocytopenia, pancytopenia, agranulocytosis). The first symptoms or signs may include: fever, sore throat, surface mouth ulcers, flu-like symptoms, severe fatigue, nasal and skin bleeding	Very rare
Nervous System disorders	headache, somnolence, vertigo, fatigue, agitation, dizziness, insomnia, irritability	Common
	aseptic meningitis	Very rare
Eye disorders	visual disturbances	Uncommon
	toxic amblyopia	Rare
Ear and labyrinth disorders	Tinnitus	Very rare
Respiratory, thoracic and mediastinal disorders	rhinitis, bronchospasm	Uncommon
Gastrointestinal disorders	Gastrointestinal disorders such as heartburn, dyspepsia, abdominal pain and nausea, vomiting, flatulence, diarrhoea, constipation	Very common

	gastrointestinal ulcers, sometimes with bleeding and perforation (see section 4.4), occult blood loss which may lead to anaemia, melaena, haematemesis, ulcerative stomatitis, colitis, exacerbation of inflammatory bowel disease, complications of colonic diverticula (perforation, fistula)	Common
	Gastritis	Uncommon
	oesophagitis, pancreatitis, intestinal strictures.	Very rare
Renal and urinary disorders	development of oedema especially in patients with arterial hypertension or renal insufficiency, nephrotic syndrome, interstitial nephritis which can be associated with renal failure	Uncommon
	renal papillary necrosis in long-term use (see section 4.4)	Very rare
Skin and subcutaneous tissue disorders	photosensitivity	Uncommon
	severe forms of skin reactions (erythema multiforme, exfoliative dermatitis, bullous reactions including Stevens-Johnson syndrome and toxic epidermal necrolysis, alopecia, necrotising fascitis	Very rare
	Drug reaction with eosinophilia and systemic symptoms (DRESS syndrome), Acute generalised exanthematous pustulosis (AGEP)	Not known
	Fixed drug eruptions	Not known

Vascular disorder	hypertension	Very rare
Immune System disorders	hypersensitivity reactions such as urticaria, pruritus, purpura and exanthema as well as asthma attacks (sometimes with hypotension)	Uncommon
	Lupus erythematosus syndrome	Rare

	severe hypersensitivity reactions. The symptoms may include: facial oedema, swelling of the tongue, internal laryngeal swelling with constriction of the airways, dyspnoea, tachycardia, fall of blood pressure to the point of life-threatening shock.	Very rare
Hepatobiliary disorders	liver dysfunction, liver damage, especially in long-term use, liver failure, acute hepatitis, jaundice	Very rare
Psychiatric disorder	depression, confusion, hallucinations	Rare

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 national reporting system

(To be completed nationally)

4.9 Overdose

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, or more rarely, diarrhoea. Tinnitus, headache, dizziness, vertigo and gastrointestinal bleeding may also occur. 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. Children may also develop myoclonic cramps. In serious poisoning metabolic acidosis may occur and the prothrombin time/INR may be prolonged, probably due to the actions of circulating clotting factors. Acute renal failure, liver damage, hypotension, respiratory depression and cyanosis may occur. Exacerbation of asthma is possible in asthmatics.

Treatment

Treatment should be symptomatic and supportive and include the maintenance of a clear airway and monitoring of cardiac and vital signs until stable. Gastric emptying or oral administration of activated charcoal is indicated if the patient presents within one hour of ingestion of more than 400 mg per kg of body weight. If BUFEX Tablets has already been absorbed, alkaline substances should be administered to promote the excretion of the acid ibuprofen in the urine. If frequent or prolonged, convulsions should be treated with intravenous diazepam or lorazepam. Bronchodilators should be given for asthma. No specific antidote is available.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Anti-inflammatory and antirheumatic products, non-steroids; propionic acid derivatives. ATC code: M01AE01

Ibuprofen is a NSAID that possesses anti-inflammatory, analgesic and antipyretic activity. Animal models for pain and inflammation indicate that ibuprofen effectively inhibits the synthesis of prostaglandins. In humans, ibuprofen reduces pain possibly caused by inflammation or connected with it, swelling and fever. Ibuprofen exerts an inhibitory effect on prostaglandin synthesis by inhibiting the activity of cyclo-oxygenase. In addition ibuprofen has an inhibitory effect on ADP (adenosine diphosphate) or collagen-stimulated platelet aggregation.

Experimental data suggest that ibuprofen may competitively inhibit the effect of low dose acetylsalicylic acid on platelet aggregation when they are dosed concomitantly. Some pharmacodynamic studies show that when single doses of ibuprofen 400 mg were taken within 8 h before or within 30 min after immediate release acetylsalicylic acid dosing (81 mg), a decreased effect of acetylsalicylic acid on the formation of thromboxane or platelet aggregation occurred. Although there are uncertainties regarding extrapolation of these data to the clinical situation, the possibility that regular, long-term use of ibuprofen may reduce the cardioprotective effect of low-dose acetylsalicylic acid cannot be excluded. No clinically relevant effect is considered to be likely for occasional ibuprofen use (see section 4.5).

Ibuprofen inhibits prostaglandin synthesis in the uterus, thereby reducing intrauterine rest and active pressure, the periodic uterine contractions and the amount of prostaglandins released into the circulation. These changes are assumed to explain the alleviation of menstrual pain. Ibuprofen inhibits renal prostaglandin synthesis which can lead to renal insufficiency; fluid retention and heart failure in risk patients (see section 4.3).

Prostaglandins are connected with ovulation and the use of medicinal products inhibiting prostaglandin synthesis may therefore affect the fertility of women (see section 4.4, 4.6 and 5.3).

5.2 Pharmacokinetic properties

Absorption

Ibuprofen is rapidly absorbed from the gastrointestinal tract. Peak serum concentrations occur one to two hours after administration

Distribution

Ibuprofen is rapidly distributed throughout the whole body. The plasma protein binding is approximately 99%.

Metabolism

Ibuprofen is metabolised in the liver (hydroxylation, carboxylation). *Elimination*

The elimination half-life is approximately 2.5 hours in healthy individuals.
Pharmacologically inactive metabolites are mainly excreted (90%) by the kidneys but also in bile.

5.3 Preclinical safety data

There are no preclinical data considered relevant to clinical safety beyond data included in other sections of this Summary of product characteristics.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

The core tablet contains:

- Corn starch
- Dicalcium phosphate
- Sodium starch glycollate
- Colloidal anhydrous silica (aerosol)
- Polyvinyl povidone (PVPk.30)
- Purified talc
- Magnesium stearate
- Methyl paraben
- Propyl paraben

The tablet coating (sugar coating) contains:
Sugar, shellac, talc, starch, sunset Yellow supra, calcium carbonate, gelatine, acacia, sodium benzoate, titanium dioxide, carnauba wax and beeswax (with isopropyl alcohol and carbon tetrachloride as volatile solvents).

6.2 Incompatibilities

Not applicable

6.3 Shelf life

3 years

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of primary container

PVC/Al blister packs of 1x10 caplets and round tablets. ***6.6***

Special precautions for disposal <and other handling>

No special requirements.

7. MARKETING AUTHORISATION HOLDER

< Blueworld Pharmaceuticals, Foods & Cosmetics Ltd. (In view) >

8. MARKETING AUTHORISATION NUMBER(S)

< In view>

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

N/A

10. DATE OF REVISION OF THE TEXT

N/A

*Hydroxypropyl methyl cellulose 15 centipoise