CLEAN PROPOSED PROFESSIONAL INFORMATION FOR MEDICINES FOR HUMAN USE

SCHEDULING STATUS

S1

1. NAME OF THE MEDICINE

IBUCARE PERIOD PAIN Tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains ibuprofen 400 mg.

Contains sugar (lactose monohydrate)

Each IBUCARE PERIOD PAIN tablet contains 16,00 mg lactose monohydrate.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablets.

White capsule shaped film-coated tablets, plain on both the sides.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

IBUCARE PERIOD PAIN is indicated for the relief of menstrual pain.

4.2 Posology and method of administration

Posology

Use the lowest effective dose for the shortest possible duration of treatment.

Adults and children over 12 years:

The recommended dosage of **IBUCARE PERIOD PAIN** is 1200 mg daily in divided doses, that is, one tablet three times a day.

Do not exceed 3 tablets in any 24 hours.

If symptoms persist for more than 7 days or worsen, or if new symptoms occur, consult your doctor.

Method of administration

IBUCARE PERIOD PAIN is for oral use.

Paediatric population

Not to be given to children under 12 years.

4.3 Contraindications

- Hypersensitivity to ibuprofen or to any of the ingredients of IBUCARE PERIOD PAIN
- History of gastrointestinal perforation, ulceration or bleeding (PUBs) related to previous NSAIDs, including IBUCARE PERIOD PAIN.
- Active or recurrent ulcer/ haemorrhage/ perforations.
- Patients sensitive to aspirin or another nonsteroidal anti-inflammatory drugs (NSAIDs).
- History of severe allergic reactions such as anaphylaxis or angio-edema induced by aspirin or other NSAIDs because of the possibility of cross-sensitivity due to structural relationships which exist among non-steroidal anti-inflammatory medicines, acute allergic reactions are likely to occur in patients who have exhibited allergic reactions to these compounds.
- Aspirin-induced nasal polyps associated with bronchospasm.
- Children under the age of 1-2 years.
- Pregnancy and during labour (see section 4.4 and 4.6)
- Safety in lactation has not been established.
- Patients with severe heart failure (NYHA Class IV), hepatic failure or renal failure (see section 4.4)

4.4 Special warnings and precautions for use

Undesirable effects may be minimised by using the lowest effective dose for the shortest duration necessary to control symptoms (see section 4.2, and GI and cardiovascular risks below).

Caution is advised in the following groups of patients

- Caution is required in patients with a history of hypertension and/or heart failure as fluid retention and oedema have been reported in association with IBUCARE PERIOD PAIN therapy. In view of IBUCARE PERIOD PAIN's inherent potential to cause fluid retention, heart failure may be precipitated in some compromised patients.
- Patients receiving coumarin anticoagulants.
- Patients with collagen disease (mixed connective tissue disorders) and systemic lupus erythematosus may be at risk of developing aseptic meningitis.
- Patients with mild reactions such as allergic rhinitis, urticaria or skin rash induced by aspirin or other NSAIDs.
- Asthma sufferers should only take IBUCARE PERIOD PAIN after consulting a doctor. Caution is required if IBUCARE PERIOD PAIN is administered to patients suffering from, or with a previous history of, bronchial asthma, chronic rhinitis, bronchospasm or allergic diseases since NSAIDs have been reported to precipitate bronchospasm, urticaria or angioedema in such patients.
- Patients with anaemia.

Concomitant use with other NSAIDs

Use of IBUCARE PERIOD PAIN with concomitant NSAIDs including cyclo-oxygenase-2 specific inhibitors should be avoided due to the increased risk of ulceration or bleeding (see section 4.5).

Medication overuse headache

The diagnosis of medication overuse headache (MOH) should be suspected in patients who have frequent or daily headaches despite (or because of) the regular use of analgesic medication. Patients with medication overuse headache should not be treated by increasing the dose of the analgesic. In such cases the use of analgesics should be discontinued.

Concomitant alcohol

The concomitant consumption of excessive alcohol with NSAIDs, including ibuprofen may increase the risk of adverse effects on the gastrointestinal tract, such as GI haemorrhage or the central nervous system, possibly due to an additive effect.

Cardiovascular and cerebrovascular effects

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

Clinical studies suggest that use of ibuprofen, particularly at a high dose (2400 mg/ day) may be associated with a small increased risk of arterial thrombotic events such as myocardial infarction or stroke. Overall, epidemiological studies do not suggest that low dose ibuprofen (e.g. ≤ 1200mg/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 IBUCARE PERIOD PAIN 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.

Risk of foetal renal dysfunction

The use of nonsteroidal anti-inflammatory drugs (NSAIDs), including ibuprofen such as in IBUCARE

PERIOD PAIN around 20 weeks gestation or later in pregnancy may cause foetal renal dysfunction leading to oligohydramnios and, in some cases, neonatal renal impairment. Oligohydramnios is often, but not always, reversable with treatment discontinuation. Complications of prolonged oligohydramnios may include limb contractures and delayed lung maturation (see section 4.3 and 4.6). Invasive procedures such as exchange transfusion or dialysis may be required. If IBUCARE PERIOD PAIN treatment is deemed necessary between 20 to 30 weeks of pregnancy, limit use to the lowest effective dose and shortest duration possible. Consider ultrasound monitoring of amniotic fluid if IBUCARE PERIOD PAIN treatment extends beyond 48 hours. Discontinue IBUCARE PERIOD PAIN if oligohydramnios occurs and follow up according to clinical practice (see section 4.3 and 4.6).

Closure of foetal ductus arteriosus

Regular use of NSAIDs such as IBUCARE PERIOD PAIN during the third trimester of pregnancy, may result in premature closure of the foetal ductus arteriosus in utero and possibly, in persistent pulmonary hypertension of the new-born. The onset of labour may be delayed and its duration increased.

Masking of symptoms of underlying infections

The antipyretic, analgesic and anti-inflammatory action of ibuprofen may mask symptoms of the occurrence or worsening 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 bacteria complications to varicella.

When IBUCARE PERIOD PAIN 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.

Renal effects

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

As with other NSAIDs, long-term administration of ibuprofen, such as in IBUCARE PERIOD PAIN has resulted in renal papillary necrosis and other renal pathologic changes. Patients with congestive heart failure, cirrhosis, diuretic-induced volume depletion, or renal insufficiency require local synthesis of vasodilating prostaglandins to maintain renal perfusion, and therefore these patients are at greater risk of developing renal dysfunction due to NSAID-induced inhibition of renal prostaglandin synthesis. Other patients at risk include those with liver dysfunction, those taking diuretics and ACE inhibitors and the elderly.
For these patients, use the lowest effective dose, for the shortest possible duration and monitor renal function especially in long-term treated patients (see also section 4.3).

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

Gastrointestinal (GI) bleeding and perforation

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

Patients with a history of gastrointestinal disease, particularly when elderly, should report any unusual abdominal symptoms (especially gastrointestinal bleeding) particularly in the initial stages of treatment. Caution should be advised in patients receiving concomitant medicines which could increase the risk of ulceration or bleeding, such as oral corticosteroids, anticoagulants such as warfarin, selective serotonin-reuptake inhibitors or antiplatelet medicines such as aspirin (see section 4.5).

When gastrointestinal bleeding or ulceration occurs in patients receiving IBUCARE PERIOD PAIN, treatment with IBUCARE PERIOD PAIN should be stopped.

IBUCARE PERIOD PAIN should be given with caution to patients with a history of gastrointestinal disease (e.g. ulcerative colitis, Crohn's disease, hiatus hernia, gastro-oesophageal reflux disease, angiodysplasia) as the condition may be exacerbated.

Severe Skin Reactions

Serious skin reactions, some of them fatal, including exfoliative dermatitis, Stevens-Johnson syndrome, and toxic epidermal necrolysis have been reported.

Patients appear to be at highest risk of these reactions early in the course of therapy, the onset of the reaction occurring within the first month of treatment in the majority of cases. Acute generalised exanthematous pustulosis (AGEP) has been reported in relation to ibuprofen-containing products.

IBUCARE PERIOD PAIN should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity.

In exceptional cases, varicella can be at the origin of serious cutaneous and soft tissues infectious complications. To date, the contributing role of NSAIDs in the worsening of these infections cannot be ruled out. Thus, it is advisable to avoid use of IBUCARE PERIOD PAIN in case of varicella.

See DRESS syndrome below.

Drug Reaction with Eosinophillia and Systemic Symptoms (DRESS)

DRESS has been reported in patients taking NSAIDs such as IBUCARE PERIOD PAIN. Some of these events have been fatal or life-threatening. DRESS typically, although not exclusively, presents

with fever, rash, lymphadenopathy, and/or facial swelling. Other clinical manifestations may include hepatitis, nephritis, haematological abnormalities, myocarditis, or myositis. Sometimes symptoms of DRESS may resemble an acute viral infection. Eosinophillia is often present. Because this disorder is variable in its presentation, other organ systems not noted here may be involved. It is important to note that early manifestations of hypersensitivity, such as fever or lymphadenopathy, may be present even though rash is not evident. If such signs or symptoms are present, discontinue IBUCARE PERIOD PAIN and evaluate the patient immediately.

Changes in vision

IBUCARE PERIOD PAIN should be discontinued in patients who experience blurred or diminished vision, or changes in colour vision.

Ulcerative stomatitis

Patients may develop ulcerative stomatitis.

Haematological effects

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

Aseptic meningitis

Aseptic meningitis has been observed in patients on ibuprofen therapy, such as IBUCARE PERIOD PAIN. 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.

Excipients: lactose

IBUCARE PERIOD PAIN contains lactose:

Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take IBUCARE PERIOD PAIN.

Elderly

The elderly have an increased frequency of adverse reactions to NSAIDs including IBUCARE PERIOD PAIN, especially gastrointestinal perforation, ulceration and bleeding (PUBs) which may be fatal. IBUCARE PERIOD PAIN should be given with care to the elderly.

Paediatric population

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

4.5 Interaction with other medicines and other forms of interaction

- Anticoagulants – Enhancement of anticoagulant effect and the possibility of gastrointestinal ulceration or bleeding. IBUCARE PERIOD PAIN may enhance the effects of anti-coagulants such as warfarin.
- Anti-platelet medicines and selective serotonin re-uptake inhibitors (SSRIs): Increased risk of gastrointestinal bleeding.
- Alcohol, corticosteroids, clopidogrel, ticlopidine, bisphosphonates, oxpentifylline – Increased risk of gastrointestinal bleeding and ulceration.
- Antidiabetic medicines including sulphonylureas – Hypoglycaemic effects of these medicines may be increased.
- Digoxin (cardiac glycosides) – May exacerbate cardiac failure, reduce GFR and increase in serum digoxin concentrations.
- Lithium – Increase in the steady-state concentration of lithium.
- Methotrexate – Increased and prolonged methotrexate plasma concentration and an increased risk of methotrexate toxicity.
- Nephrotoxic medicines e.g – ciclosporin – Increased risk of nephrotoxicity.

- Anti-hypertensives, beta-blockers or diuretics – Reduction or reversal of the anti-hypertensive effect may occur. Diuretics can also increase the risk of nephrotoxicity of IBUCARE PERIOD PAIN.
- Bone marrow depressants – The leucopenic and/or thrombocytopenic effects of these medicines may be increased.
- Corticosteroids: Increased risk of gastrointestinal perforation, ulceration or bleeding (PUBs).
- NSAIDs: Use of two or more NSAIDs, including cox-2 inhibitors concomitantly could result in an increase in side effects.
- Aspirin (Acetylsalicylic acid): As with other products containing NSAIDs, concomitant administration of IBUCARE PERIOD PAIN and aspirin 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 aspirin 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 use.
- Cholestyramine: The concomitant administration of ibuprofen and cholestyramine may reduce the absorption of ibuprofen in the gastrointestinal tract. However, the clinical significance is unknown.
- Mifepristone: A decrease in the efficacy can theoretically occur due to the anti-prostaglandin properties of IBUCARE PERIOD PAIN. Limited evidence suggests that coadministration of IBUCARE PERIOD PAIN 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.
- Quinolone antibiotics: Animal data indicates that NSAIDs can increase the risk of convulsions associated with quinolone antibiotics. Patients taking IBUCARE PERIOD PAIN and quinolones may have an increased risk of developing convulsions.
- Aminoglycosides: IBUCARE PERIOD PAIN may decrease the excretion of aminoglycosides.

- Herbal extracts: Ginkgo biloba may potentiate the risk of bleeding with IBUCARE PERIOD PAIN.
- Tacrolimus: Possible increase 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.
- CYP2C9 Inhibitors: Concomitant administration of ibuprofen such as in IBUCARE PERIOD PAIN 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

Use of IBUCARE PERIOD PAIN in pregnancy and during labour is contraindicated.

Inhibition of prostaglandin synthesis may adversely affect the pregnancy and/or embryo/foetal development. Data from epidemiological studies suggest an increased risk of miscarriage and of cardiac malformation and gastroschisis after the use of a prostaglandin synthesis inhibitor in early pregnancy. The risk is believed to increase with dose and duration of therapy.

The use of NSAIDs, such as IBUCARE PERIOD PAIN used at 20 weeks gestation or later may cause serious kidney problems in an unborn baby.
After around 20 weeks of pregnancy, the unborn babies' kidneys produce most of the amniotic fluid. Amniotic fluid provides a protective cushion and helps the unborn babies' lungs, digestive system, and muscles develop. Foetal renal dysfunction can lead to oligohydramnios due to the low levels of amnionic fluid. Complications of prolonged oligohydramnios may include limb contractures and

delayed lung maturation (see section 4.2 and 4.4).

Regular use of NSAIDs such as IBUCARE PERIOD PAIN during the third trimester of pregnancy, may result in premature closure of the foetal ductus arteriosus in utero, and possibly, in persistent pulmonary hypertension of the new-born. The onset of labour may be delayed and its duration increased (see section 4.4).

Lactation

In the limited studies so far available, NSAIDs can appear in the breast milk in very low concentrations. NSAIDs should, if possible, be avoided when breastfeeding.

Fertility

The use of IBUCARE PERIOD PAIN 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 IBUCARE PERIOD PAIN should be considered.

4.7 Effects on ability to drive and use machines

Undesirable effects such as dizziness, drowsiness, fatigue and visual disturbances are possible after taking IBUCARE PERIOD PAIN. If affected, patients should not drive or operate machinery.

4.8 Undesirable effects

Tabulated list of adverse reactions

The table below shows all adverse drug reactions (ADRs) observed during reported clinical trials and recorded post-market spontaneous reports with ibuprofen.

System Organ Class	**Frequency**		
	Frequent	**Less Frequent**	**Not known**
Infections and infestations		Rhinitis, aseptic meningitis	
Blood and lymphatic system disorders		Agranulocytosis, thrombocytopenia, aplastic anaemia, haemolytic anaemia, neutropenia, eosinophilia, leukopenia.	
Immune system disorders		Hypersensitivity, anaphylactic reactions	
Psychiatric disorders		Insomnia, anxiety, depression, confusional state.	
Nervous system disorders	Headache, dizziness	Nervousness, paraesthesia, somnolence, optic neuritis, and drowsiness.	
Eye disorders		Blurred vision, visual impairment, changes in visual	

		colour perception and other toxic amblyopia.	
Ear and labyrinth disorders		Hearing impaired, tinnitus, vertigo.	
Cardiac disorders		Tachycardia, cardiac failure, myocardial infarction.	
Vascular disorders		Flushing, hypertension.	
Respiratory, thoracic and mediastinal disorders		Asthma, bronchospasm, dyspnoea.	
Gastrointestinal disorders	Abdominal discomfort, peptic ulceration, gastrointestinal bleeding, nausea, vomiting, abdominal cramps and pain, dyspepsia, diarrhoea, haematemesis, flatulence,	Gastritis, duodenal ulcer, gastric ulcer, mouth ulceration, gastrointestinal perforation, pancreatitis.	Exacerbation of colitis and Crohn's disease.

	constipation, melaena.		
Hepatobiliary disorders		Hepatitis, jaundice, abnormal hepatic function, hepatic failure, hepatotoxicity.	Abnormal liver function tests.
Skin and subcutaneous tissue disorders	Rash	Urticaria, pruritus, purpura, angioedema, photosensitivity reaction, allergic dermatitis, erythema multiforme, bullous reactions, including Stevens-Johnson syndrome and toxic epidermal necrolysis.	[a)]Drug reaction with eosinophilia and systemic symptoms (DRESS syndrome), acute generalised exanthematous pustulosis (AGEP)
Renal and urinary disorders		Impairment of renal function, acute reversible renal failure, interstitial nephritis and nephrotic syndrome.	Cystitis, haematuria.
General disorders and administration	Fatigue	Oedema, fever.	

site conditions			

[a)]Drug reaction with eosinophilia and systemic symptoms (DRESS syndrome) (see section 4.4)

Description of selected adverse reactions

Gastrointestinal disorders: The most frequently observed adverse events are gastrointestinal in nature. Peptic ulcers, perforation or GI bleeding, sometimes fatal, particularly in the elderly, may occur (see section 4.4). Nausea, vomiting, diarrhoea, flatulence, constipation, dyspepsia, abdominal pain, melaena, haematemesis, ulcerative stomatitis, gastrointestinal haemorrhage and exacerbation of colitis and Crohn's disease (see section 4.4) have been reported following ibuprofen administration. Less frequently, gastritis, duodenal ulcer, gastric ulcer and gastrointestinal perforation have been observed.

Immune system disorders: Hypersensitivity reactions have been reported following treatment with NSAIDs. These may consist of (a) non-specific allergic reaction and anaphylaxis, (b) respiratory tract reactivity comprising asthma, aggravated asthma, bronchospasm or dyspnoea, or (c) assorted skin disorders, including rashes of various types, pruritus, urticaria, purpura, angioedema and, very rarely, erythema multiforme, bullous dermatoses (including Stevens- Johnson syndrome and toxic epidermal necrolysis).

Cardiac disorders and vascular disorders: Oedema, hypertension and cardiac failure have been reported in association with NSAID treatment. Clinical studies suggest that use of ibuprofen, particularly at high dose (2400 mg/day) may be associated with a small increased risk of arterial thrombotic events such as myocardial infarction or stroke (see section 4.4).

Infections and infestations: Rhinitis and aseptic meningitis (especially in patients with existing autoimmune disorders, such as systemic lupus erythematosus and mixed connective tissue disease) with symptoms of stiff neck, headache, nausea, vomiting, fever or disorientation (see section 4.4).

Exacerbation of infection-related inflammations coinciding with the use of NSAIDs has been described. If signs of an infection occur or get worse during use of Ibuprofen the patient is therefore recommended to go to a doctor without delay.

Skin and subcutaneous tissue disorders: In exceptional cases, severe skin infections and soft-tissue

complications may occur during a varicella infection (see also "Infections and infestations").

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions to SAHPRA via the “6.04 Adverse Drug Reaction Reporting Form”, found online under SAHPRA’s publications: https://www.sahpra.org.za/Publications/Index/8

4.9 Overdose

Symptoms

Most patients who have ingested significant amounts of ibuprofen will manifest symptoms within 4 to 6 hours. The most likely symptoms of overdosage are epigastric pain, nausea, vomiting, lethargy and drowsiness.

Central nervous system (CNS) effects include headache, tinnitus, dizziness, convulsion, and loss of consciousness. Nystagmus, metabolic acidosis, hypothermia, renal effects, gastrointestinal bleeding, coma, apnoea, diarrhoea and depression of the CNS and respiratory system have also been rarely reported. In serious poisoning metabolic acidosis may occur. Disorientation, excitation, fainting and cardiovascular toxicity, including hypotension, bradycardia and tachycardia have been reported. In cases of significant overdose, renal failure and liver damage are possible. Large overdoses are generally well tolerated when no other medicines are being taken.

Management

Patients should be treated symptomatically as required. Within one hour of ingestion of a potentially toxic amount, activated charcoal should be considered. Electrolytes may be corrected by intravenous infusions if necessary.

Good urine output should be ensured.

Renal and liver function should be closely monitored.

Patients should be observed for at least four hours after ingestion of potentially toxic amounts.

Frequent or prolonged convulsions should be treated with intravenous diazepam. Other measures may be indicated by the patient's clinical condition. There is no specific antidote for IBUCARE PERIOD PAIN.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacological Classification/ Category and Class: A 2.7 Antipyretic or antipyretic and anti-inflammatory analgesic.

Pharmacotherapeutic group**:** Propionic acid derivatives.

ATC Code: M01AE01

Ibuprofen has analgesic, antipyretic and anti-inflammatory activities. Its analgesic activity is exerted through a peripheral action of blocking pain-impulse generation. The peripheral action of ibuprofen may also be due to inhibition of prostaglandin synthesis or to inhibition of the synthesis or actions of other substances that sensitize pain receptors to mechanical or chemical stimulation. Ibuprofen exerts its antipyretic effects by acting centrally on the hypothalamic heat-regulating center to produce peripheral vasodilation resulting in increased blood flow through the skin, sweating and heat loss. Ibuprofen exerts its anti-inflammatory action peripherally in inflamed tissue by reducing prostaglandin activity and by inhibiting synthesis and/ or actions of other local mediators of the inflammatory response.

5.2 Pharmacokinetic properties

Rapidly absorbed after oral administration. Onset of action for pain relief is 30 minutes and the time for peak effect for fever is 2 to 4 hours. The half-life of Ibuprofen is about 2 hours and the duration of action for fever is 6 to 8 hours or more and is 4 to 6 hours for pain. The excretion of ibuprofen is rapid and complete with more than 90 % of an ingested dose excreted in the urine as metabolites or their conjugates.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core:

Colloidal anhydrous silica

Croscarmellose sodium

Lactose monohydrate

Magnesium stearate

Maize starch

Microcrystalline cellulose

Polyvinyl povidone

Sodium lauryl sulphate

Film-coating:

Hydroxypropyl cellulose

Hydroxypropyl methyl cellulose

Polyethylene glycol

Titanium dioxide

6.2 Incompatibilities

Not applicable

6.3 Shelf life

3 years

6.4 Special precautions for storage

Store in a dry place at or below 25 °C. Protect from light.

Keep blister packs in carton until required for use.

6.5 Nature and contents of container

Opaque Aluminium/PVC blister packs of 1 x 10, 1 x 12, 2 x 10, 2 x 12.

6.6 Special precautions for disposal and other handling

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Austell Laboratories (Pty) Ltd.

52 Mineral Crescent

Crown ext. 3,

Johannesburg, 2092

South Africa

8. REGISTRATION NUMBER

42/3.1/0062

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

09 October 2009

10. DATE OF REVISION OF THE TEXT

To be allocated by the Authority