**APPROVED PACKAGE INSERT: IBUCARE-200**

**SCHEDULING STATUS:**

S1

**PROPRIETARY NAME AND DOSAGE FORM:**

**IBUCARE-200 Tablets**

**COMPOSITION:**

Each film-coated tablet contains Ibuprofen 200 mg.

**Excipients:**

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.

Contains sugar (lactose monohydrate).

**PHARMACOLOGICAL CLASSIFICATION:**

A 2.7 Antipyretic or antipyretic and anti-inflammatory analgesic.

**PHARMACOLOGICAL ACTION:**

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.

**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.

**INDICATIONS:**

**IBUCARE-200** is indicated for the relief of headache and back pain of musculo-skeletal origin, feverishness, muscular aches and pain, menstrual pain, dental pain and for the relief of pain associated with migraine.

**CONTRAINDICATIONS:**

Allergy to any of the ingredients of **IBUCARE-200**.

- Heart failure
- History of gastrointestinal perforation, ulceration or bleeding (PUBs) related to previous NSAIDs, including **IBUCARE-200**.
- Active or recurrent ulcer/ haemorrhage/ perforations.
- Patients sensitive to aspirin or another nonsteroidal anti-inflammatory medicines (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.
- Safety in pregnancy and lactation has not been established.

**WARNINGS AND SPECIAL PRECAUTIONS:**

- **IBUCARE-200** should not be given to patients with bleeding disorders, cardiovascular disease, peptic ulceration or a history of such ulceration.
- Asthma suffers should only take **IBUCARE-200** after consulting a doctor.
- Caution is advised in patients receiving coumarin anticoagulants.
- Patients who are sensitive to aspirin should not be given **IBUCARE-200**.
- 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-200** therapy. In view of **IBUCARE-200's** inherent potential to cause fluid retention, heart failure may be precipitated in some compromised patients.
- The antipyretic, analgesic and anti-inflammatory action of ibuprofen may mask symptoms of the occurrence or worsening of infection.
- Regular use of NSAIDs such as **IBUCARE-200** 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.
- Elderly: The elderly have an increased frequency of adverse reactions to NSAIDs including **IBUCARE-200**, especially gastrointestinal perforation, ulceration and bleeding (PUBs) which may be fatal.
- The risk of gastrointestinal perforation, ulceration or bleeding (PUBs) is higher with increasing doses of **IBUCARE-200**, in patients with a history of ulcers, and the elderly.
- When gastrointestinal bleeding or ulceration occurs in patients receiving **IBUCARE-200,** treatment with **IBUCARE-200** should be stopped.

- **IBUCARE-200** 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.
- Serious skin reactions, some of them fatal, including exfoliative dermatitis, Stevens-Johnson syndrome, and toxic epidermal necrolysis have been reported. **IBUCARE-200** should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity.
- **IBUCARE-200** should be given with care to the elderly, to patients with bronchospasm, and in liver or renal failure.
- Patient 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.
- **IBUCARE-200** should be discontinued in patients who experience blurred or diminished vision, or changes in colour vision.
- Patients with collagen disease may be at risk of developing aseptic meningitis.
- Mild reactions such as allergic rhinitis, urticaria or skin rash induced by aspirin or other NSAIDs.
- Anaemia.
- Stomatitis.
- Systemic lupus erythematosus.
- Effects on ability to drive and use machines: No studies on the effects of **IBUCARE-200** on the ability to drive and use machines have been performed.
- Excipients of **IBUCARE-200**: Contains lactose. Patients with rare hereditary conditions of galactose intolerance e.g. galactosemia, Lapp lactase deficiency, or glucose-galactose malabsorption should not take **IBUCARE-200**.

**INTERACTIONS:**

- Anticoagulants – Enhancement of anticoagulant effect and the possibility of gastrointestinal ulceration or bleeding.
- Alcohol, corticosteroids, clopidogrel, ticlopidine, bisphosphonates, oxpentifylline – Increased risk of gastrointestinal bleeding and ulceration.
- Antidiabetic medicines – Hypoglycaemic effects of these medicines may be increased.
- Digoxin – 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 – cyclosporin – Increased risk of nephrotoxicity.
- Anti-hypertensives or diuretics – Reduction or reversal of the anti-hypertensive effect may occur.
- 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).
- Anti-coagulants: **IBUCARE-200** 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.
- NSAIDs: Use of two or more NSAIDs concomitantly could result in an increase in side effects.

**PREGNANCY AND LACTATION:**

Safety in pregnant and nursing mothers has not been established.

**DOSAGE AND DIRECTIONS FOR USE:**

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

**Adults and children over 12 years:**

Initial dose 2 tablets taken with water, then if necessary, 1 or 2 tablets every four hours.

Migraine:

Take 2 tablets three times a day.

Do not exceed 6 tablets in any 24 hours. Not to be given to children under 12 years. If symptoms persist for more than 7 days, consult your doctor.

**SIDE EFFECTS**

**Blood and the lymphatic system disorders**

*Less frequent*: Agranulocytosis, thrombocytopenia, anaemias, neutropenia, eosinophilia.

**Immune system disorders**

*Less frequent*: Hypersensitivity reactions (fever, rashes, hepatotoxicity, aseptic meningitis).

**Nervous system disorders**

*Less frequent:* Dizziness, nervousness, depression, insomnia, headache, tinnitus and drowsiness.

**Eye disorders**

*Less frequent:* Blurred vision, changes in visual colour perception and other toxic amblyopia.

**Cardiac disorders**

*Less frequent:* Tachycardia, cardiac failure.

**Vascular disorders**

*Less frequent:* Flushing, oedema, hypertension

**Gastrointestinal disorders**

The most commonly observed adverse events are gastrointestinal in nature. Peptic ulcers, perforation or gastrointestinal bleeding, sometimes fatal. Diarrhoea, flatulence, constipation, dyspepsia, melaena, haematemesis, ulcerative stomatitis, exacerbation of colitis and Crohn's disease, gastritis.

*Frequent:* Abdominal discomfort, peptic ulceration, gastrointestinal bleeding, nausea, vomiting, abdominal cramps and pain.

**Hepato-biliary disorders**

*Less frequent:* Hepatitis.

*Frequency not known:* Abnormal liver function tests.

**Renal and urinary disorders**

*Less frequent:* Impairment of renal function, acute reversible renal failure, interstitial nephritis and nephritic syndrome.

**Skin and subcutaneous tissue disorders**

*Less frequent:* Allergic dermatitis, erythema multiforme, bullous reactions, including Stevens-Johnson syndrome and toxic epidermal necrolysis.

*Frequency not known:* Skin rash, pruritus.

**KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:**

The most likely symptoms of overdosage are epigastric pain and nausea. If recently taken, gastric lavage will remove any unabsorbed **IBUCARE-200**. Electrolytes may be corrected by intravenous infusions if necessary. There is no specific antidote for **IBUCARE-200.**

**IDENTIFICATION:**

White, circular, film coated tablets, plain on both the sides.

**PRESENTATION:**

Opaque Aluminium/PVC blister packs of 1 x 10, 1 x 12, 2 x 10, 2 x 12, 1 x 15, 1 x 16 tablets.

**STORAGE INSTRUCTIONS:**

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

Keep blister packs in carton until required for use.

KEEP OUT OF REACH OF CHILDREN.

**REGISTRATION NUMBER:**

42/3.1/0061

**NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION:**

Austell Laboratories (Pty) Ltd.

52 Mineral Crescent,

Crown ext 3,

Johannesburg, 2092

South Africa.

**DATE OF PUBLICATION OF THE PACKAGE INSERT:**

Date on the registration certificate of the medicine: 09 October 2009