19-12-2020
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Ubrof® Injection
(Ibuprofen)

For I.V. use only

WARNING: RISK OF SERIOUS CARDIOVASCULAR AND GASTROINTESTINAL EVENTS

Cardiovascular Thrombotic Events: Non-steroidal anti-inflammatory drugs (NSAIDs) cause an increased risk of serious cardiovascular thrombotic events, including myocardial infarction and stroke, which can be fatal. This risk may occur early in treatment and may increase with duration of use. **UBROF** is contraindicated in the setting of coronary artery bypass graft (CABG) surgery.

Gastrointestinal Bleeding, Ulceration and Perforation: NSAIDs cause an increased risk of serious gastrointestinal (GI) adverse events including bleeding, ulceration, and perforation of the stomach or intestines, which can be fatal. These events can occur at any time during use and without warning symptoms. Elderly patients and patients with a prior history of peptic ulcer disease and/or GI bleeding are at greater risk for serious GI events.

QUALITATIVE AND QUANTITATIVE COMPOSITION

Ubrof® Injection 800mg/8ml
Each 8ml contains:
Ibuprofen USP.....800mg

PHARMACEUTICAL FORM

Injection

CLINICAL PARTICULARS

THERAPEUTIC INDICATIONS:

Ubrof® is indicated in adults for the management of mild to moderate pain and the management of moderate to severe pain as an adjunct to opioid analgesics.
Ubrof® is indicated for the reduction of fever in adults where an intravenous route of administration is considered clinically necessary.

POSOLOGY AND METHOD OF ADMINISTRATION

Posology: Use the lowest effective dose for the shortest duration consistent with individual patient treatment goals. After observing the response to initial therapy. The dose and frequency should be adjusted to suit an individual patient's needs.
Do not exceed a total daily dose of 3200mg ibuprofen. To reduce the risk of renal adverse reactions, patients must be well hydrated prior to administration.
Analgesia (Pain): Administer 400mg to 800mg by intravenously, every 6 hours as necessary or as directed by the physician.
Antipyretic (Fever): Administer 400mg intravenously, followed by 400mg every 4 to 6 hours or as directed by the physician.

Ubrof® must be diluted prior to administration.
Dilute to a final concentration of 4mg/ml or less. Appropriate diluents include 0.9% Sodium Chloride Injection USP (normal saline), 5% Dextrose Injection USP (D5W), or Lactated Ringers Solution.
800mg dose: Dilute 8ml of **Ubrof®** in at least 200ml of diluent.
For weight-based dosing at 10mg/kg ensure that the concentration of **Ubrof®** is 4mg/ml or less.
Single dose vial, discard any portion of the contents remaining after use.

CONTRAINDICATIONS:

- **Ubrof®** is contraindicated in patients with known hypersensitivity (e.g., anaphylactic reactions and serious skin reactions) to ibuprofen.
- Patients who have experienced asthma, urticaria, or allergic-type reactions after taking aspirin or other NSAIDs. Severe, rarely fatal anaphylactic-like reactions to NSAIDs have been reported in such patient.
- For the treatment of peri-operative pain in the setting of coronary artery bypass graft (CABG) surgery.

SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Duration of Dosage: Use the lowest effective dose for the shortest duration consistent with individual patient treatment goals. After observing the response to initial therapy. The dose and frequency should be adjusted to suit an individual patient's needs. Do not exceed a total daily dose of 3200mg ibuprofen. Use of the recommended maximum dose of 800mg every 6 hours has only been studied for a period of up to 2 days.
Cardiovascular Thrombotic Events: All NSAIDs have been associated with an increased risk of cardiovascular and thrombotic adverse events when taken long term. Patients with known CV disease or risk factors for CV disease may be at greater risk. To minimize the potential risk for an adverse CV event in patients treated with a NSAID, use the lowest effective dose for the shortest duration.
Hypertension: NSAIDs, including ibuprofen, can lead to onset of new hypertension or worsening of preexisting hypertension, either of which may contribute to the increased incidence of CV events. Use NSAIDs, including ibuprofen, with caution in patients with hypertension. Monitor blood pressure closely during the initiation of NSAID treatment and throughout the course of therapy. Patients taking ACE inhibitors, thiazides, or loop diuretics may have an impaired response to these therapies when taking NSAIDs.
Congestive Heart Failure and Edema: Fluid retention and edema have been observed in some patients taking NSAIDs. Use with caution in patients with fluid retention or heart failure.
Gastrointestinal Effects Risk of Ulceration, Bleeding, and Perforation: Serious GI toxicity such as bleeding, ulceration, and perforation of the stomach, small intestine or large intestine, can occur at any time, with or without warning symptoms, in patients treated with NSAIDs. Minor upper GI problems, such as dyspepsia, are common and may also occur at any time during NSAID therapy.
Most reports of spontaneous fatal GI events are in elderly or debilitated patients, and therefore special care should be taken in treating this population. To minimize the potential risk for an adverse GI event in patients treated with a NSAID, use the lowest effective dose for the shortest possible duration.
Serious Skin Reactions: NSAIDs, including ibuprofen, can cause serious skin adverse reactions such as exfoliative dermatitis, Stevens - Johnson syndrome (SJS), and toxic epidermal necrolysis (TEN), which can be fatal. These serious events may occur without warning. Inform patients about the signs and symptoms of serious skin manifestations, and to discontinue at the first appearance of skin rash or any other sign of hypersensitivity.
Pre-existing Asthma: Patients with asthma may have aspirin-sensitive asthma. The use of aspirin in patients with aspirin-sensitive asthma has been associated with severe bronchospasm, which can be fatal. Since cross-reactivity between aspirin and NSAIDs has been reported in such aspirin sensitive patients, including bronchospasm.

Ubrof® is contraindicated in patients with this form of aspirin sensitivity and should be used with caution in all patients with pre-existing asthma.
Ophthalmological Effects: Blurred or diminished vision, scotomata, and changes in color vision have been reported with oral ibuprofen. Discontinue ibuprofen if a patient develops such complaints, and refer the patient for an ophthalmologic examination that includes central visual fields and color vision testing.
Use in hepatic impairment: Borderline elevations of one or more liver tests may occur in some patients taking NSAIDs, including ibuprofen. These laboratory abnormalities may progress, may remain unchanged, or may be transient with continuing therapy. Notable elevations of ALT or AST (approximately three or more times the upper limit of normal) have been reported in small numbers of patients in clinical trials with NSAIDs.
In addition, rare cases of severe hepatic reactions have been reported, including jaundice, fulminant hepatitis, liver necrosis and hepatic failure, some with fatal outcomes. If clinical signs and symptoms consistent with liver disease develop, or if systemic manifestations occur (e.g., eosinophilia, rash, etc.), ibuprofen should be discontinued.
Use in renal impairment: Long-term administration of NSAIDs has resulted in renal papillary necrosis and other renal injury. Renal toxicity has also been seen in patients in whom renal prostaglandins have a compensatory role in the maintenance of renal perfusion. Caution is also recommended in patients with pre-existing renal disease.
Aseptic Meningitis: Aseptic meningitis with fever and coma has been observed in patients on oral ibuprofen therapy. Although it is probably more likely to occur in patients with systemic lupus erythematous and related connective tissue diseases, it has been reported in patients who do not have underlying chronic disease. If signs or symptoms of meningitis developing a patient on ibuprofen, give consideration to whether or not the signs or symptoms are related to ibuprofen therapy.
Hematological Effects: Anemia may occur in patients receiving NSAIDs, including ibuprofen. This may be due to fluid retention, occult or gross GI blood loss, or an incompletely described effect on erythropoiesis. In patients on long-term treatment with NSAIDs, including ibuprofen, check hemoglobin or hematocrit if they exhibit any signs or symptoms of anemia or blood loss.
NSAIDs inhibit platelet aggregation and have been shown to prolong bleeding time in some patients. Unlike aspirin, their effects on platelet function are less severe quantitatively, of shorter duration, and reversible. Carefully monitor patients who may be adversely affected by alterations in platelet function, such as those with coagulation disorders or patients receiving anticoagulants.
Masking Inflammation and Fever: The pharmacological activity of ibuprofen in reducing fever and inflammation may diminish the utility of these diagnostic signs in detecting complications of presumed non-infectious, painful conditions.
Anaphylactoid Reactions: As with other NSAIDs, anaphylactoid reactions may occur in patients without known prior exposure to ibuprofen. Ibuprofen is contraindicated in patients with the aspirin triad. This symptom complex typically occurs in asthmatic patients who experience rhinitis with or without nasal polyps, or who exhibit severe, potentially

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fatal bronchospasm after taking aspirin or other NSAIDs.
Patients Receiving Spinal or Epidural Analgesia: As potential bleeding around the spinal cord has serious consequences, caution should be exercised when treating patients undergoing spinal and epidural analgesia.
Monitoring: Serious GI tract ulcerations and bleeding can occur without warning symptoms, therefore physicians should monitor for signs or symptoms of GI bleeding
Use in the Elderly: Clinical studies of ibuprofen did not include sufficient numbers of subjects 65 years of age and over to determine whether they respond differently from younger subjects. Dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy. Elderly patients are at increased risk for serious GI adverse events.
As with any NSAIDs, caution should be exercised when treating the elderly (65 years and older)
Paediatric use: Safety and effectiveness of ibuprofen for management of pain and reduction of fever has not been established in paediatric patients. Should only be used in persons 18 years and above.

INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORM OF INTERACTIONS
Aspirin: When ibuprofen is administered with aspirin, ibuprofen's protein binding is reduced, although the clearance of free ibuprofen is not altered. The clinical significance of this interaction is not known; however, as with other NSAIDs, concomitant administration of ibuprofen and aspirin is not generally recommended because of the potential for increased adverse effects.
Anticoagulants: The effects of warfarin and NSAIDs on GI bleeding are synergistic, such that the users of both drugs together have a higher risk of serious GI bleeding than users of either drug alone.
Combination use of ACE inhibitors or angiotensin receptor antagonists: Anti-inflammatory drugs and thiazide diuretics NSAIDs may diminish the antihypertensive effect of ACE inhibitors. This interaction should be given consideration in patients taking NSAIDs concomitantly with ACE inhibitors.
Diuretics: Clinical studies and post marketing observations have shown that ibuprofen can reduce the natriuretic effects of furosemide and thiazides in some patients. This response has been attributed to inhibition of renal prostaglandin synthesis. During concomitant therapy with NSAIDs, observe patients closely for signs of renal failure, as well as to assure diuretic efficacy.
Lithium: Ibuprofen should be avoided in patients taking lithium as NSAIDs have produced elevations of plasma lithium levels and a reduction in renal lithium clearance.
Methotrexate: NSAIDs may enhance the toxicity of methotrexate. Use caution when NSAIDs are administered concomitantly with methotrexate.

PREGNANCY AND LACTATION:
Pregnancy; Use in pregnancy - Category C: Prior to week 30 of pregnancy, ibuprofen should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. From week 30 of pregnancy, Ibuprofen and other NSAIDs can cause fetal harm and should be avoided by pregnant women.
The effects of Ibuprofen on labor and delivery in pregnant women are unknown but, based on the known pharmacology of ibuprofen, administration is not recommended as the onset of labor may be delayed and the duration increased with a greater bleeding tendency in both mother and child.
Use in lactation: It is not known whether ibuprofen and/or its metabolites are excreted in human milk. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants, a decision should be made whether to discontinue nursing or discontinue ibuprofen treatment, taking into account the importance of the drug to the mother.

UNDESIRABLE EFFECTS:
The following serious adverse reactions are discussed under warnings & precautions
- Cardiovascular events
- Gastrointestinal (GI) effects, hepatic effects,
- Hypertension
- Congestive heart failure and edema
- Renal effects,
- Anaphylactoid reactions
- Serious skin reactions
- The most common treatment emergent adverse effects reported in clinical studies are nausea, flatulence, vomiting, and headache. The most common reason for discontinuation of due to adverse events in controlled trials is pruritus (<1%)

OVERDOSE:
The following signs and symptoms have occurred in individuals following an overdose of oral ibuprofen: abdominal pain, nausea, vomiting, drowsiness, and dizziness. In serious poisoning metabolic acidosis may occur. There are no specific measures to treat acute over dosage. There is no known antidote to ibuprofen.

PHARMACOLOGICAL PROPERTIES
PHARMACOTHERAPEUTIC GROUP: Anti-inflammatory, non-steroid, propionic acid derivative. Ibuprofen has analgesic, antipyretic and anti-inflammatory properties Ibuprofen inhibits prostaglandin synthesis.
ATC code: M01A E01

MECHANISM OF ACTION:
Ibuprofen's mechanism of action, like that of other NSAIDs, is not completely understood but may be related to prostaglandin synthetase inhibition. Ibuprofen possesses anti-inflammatory, analgesic, and antipyretic activity.

PHARMACOKINETICS:
Ibuprofen, like most NSAIDs, is highly protein bound (>99% bound at 20mcg/ml). Protein binding is saturable, and at concentrations >20 mcg/ml binding is nonlinear. Based on oral dosing data, there is an age or fever related change in volume of distribution for ibuprofen.

SHELF LIFE
See expiry on the pack.

AVAILABILITY
Ubrof® injection 800mg/8ml (100mg/ml) in a pack of 1's

INSTRUCTIONS
Dosage: As advised by the physician.
To be sold on the prescription of registered medical practitioner.
Keep out of reach of children.
Avoid exposure to heat, light and freezing.
Store between 20 to 25°C
Improper storage may deteriorate the medicine.
Injection should not be used if container is leaking, solution is cloudy or it contains undissolved particle(s)

Manufactured by:
SAMI Pharmaceuticals (Pvt.) Ltd.
F-95, S.I.T.E., Karachi-Pakistan
www.samipharmapk.com
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یوبروف® انجکشن
(آئبوپروفن)

صرف وریدی استعمال کیلئے

خوراک: ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔
صرف رجسٹرڈ ڈاکٹر کے نسخے کے مطابق فروخت کریں۔
دوا کو گرمی، روشنی اور منجمد ہونے سے محفوظ ۲۰ سے ۲۵ ڈگری
سینٹی گریڈ کے درمیان میں رکھیں ورنہ دوا خراب ہوجائیگی۔
انجکشن کے لیک ہونے، دُھندلا ہونے یا اس میں کوئی غیر حل
پزیر شے نظر آنے کی صورت میں ہرگز استعمال نہ کریں۔

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