For Medical Professional only

boschofen

(Ibuprofen B.P. 400mg)
100ml I.V. Infusion

بوشوفن (آئبو پروفین بی۔پی ۴۰۰ ملی گرام) ۱۰۰ ملی لیٹر انفیوژن

DESCRIPTION:
boschofen (ibuprofen) Injection is a nonsteroidal anti-inflammatory drug. The chemical name is ibuprofen, which is (±)-2-(p-isobutylphenyl) propionic acid. Ibuprofen is a white powder with a melting point of 74-77°C. It has a molecular weight of 206.28.

COMPOSITION:
Each 100 mL vial contains:
Ibuprofen B.P. …….. 400mg
(Product Specs.: Innovator's)

CLINICAL PHARMACOLOGY:
Pharmacodynamic Properties:
Pharmacotherapeutic group: **boschofen** has analgesic, anti-inflammatory, and antipyretic properties, ATC-Code: MO1AE01

Mechanism of action:
The mechanism of action of **boschofen**, like that of other NSAIDs, is not completely understood but involves inhibition of cyclooxygenase (COX-1 and COX-2). Ibuprofen is a potent inhibitor of prostaglandin synthesis in vitro. Ibuprofen concentrations reached during therapy have produced in vivo effects. Prostaglandins sensitize afferent nerves and potentiate the action of bradykinin in inducing pain in animal models. Prostaglandins are mediators of inflammation. Because ibuprofen is an inhibitor of prostaglandin synthesis, its mode of action may be due to a decrease of prostaglandins in peripheral tissues.

Pharmacokinetic Properties:
The pharmacokinetic parameters of **boschofen** determined in a study with febrile pediatric patients are presented in Table 1. It was observed that the median Tmax was at the end of the infusion and that **boschofen** had a shorter elimination half-life in pediatric patients compared to adults. The volume of distribution and clearance increased with age.

Table 1: Pharmacokinetic Parameters of 10 mg/kg Intravenous Ibuprofen, Pediatric Patients, by Age Group

	6 months to <2 years Mean (CV%)	2 years to <6 years Mean (CV%)	6 years to 16 years Mean (CV%)
Number of Patients	5	12	25
AUC (mcg•h/mL)	71.1 (37.1)	79.2 (37.0)	80.7 (36.9)
Cmax (mcg/mL)	59.2 (34.8)	64.2 (34.3)	61.9 (26.6)
Tmax (min)*	10 (10-30)	12 (10-46)	10 (10-40)
T1/2 (h)	1.8 (29.9)	1.5 (41.8)	1.55 (26.4)
Cl (mL/h)	1172.5 (38.9)	1967.3 (56.0)	4878.5 (71.0)
Vz (mL)	2805.7 (20.1)	3695.8 (30.0)	10314.2 (67.4)
Cl/WT# (mL/hr/kg)	133.7 (58.6)	130.1 (82.4)	109.2 (41.6)
Vz/WT# (mL/kg)	311.2 (35.4)	227.2 (41.7)	226.8 (30.4)

*Median (minimum-maximum)
#WT: body weight (kg)

Ibuprofen, like most NSAIDs, is highly protein bound (>99% bound at 20 mcg/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.

THERAPEUTIC INDICATIONS:
boschofen is indicated in adults and pediatric patients six months and older for the:
- Management of mild to moderate pain and the management of moderate to severe pain as an adjunct to opioid analgesics
- Reduction of fever

DOSAGE AND ADMINISTRATION:

Adults
For Analgesia (pain):
The dose is 400 mg to 800 mg intravenously every 6 hours as necessary. Infusion time must be at least 30 minutes. Maximum daily dose is 3,200 mg.
For Fever:
The dose is 400 mg intravenously, followed by 400 mg every 4 to 6 hours or 100 mg to 200 mg every 4 hours as necessary. Infusion time must be at least 30 minutes. Maximum daily dose is 3,200 mg.

Pediatric Patients
For Analgesia (pain) and Fever
Ages 12 to 17 years of age
The dose is 400 mg intravenously every 4 to 6 hours as necessary. Infusion time must be at least 10 minutes. Maximum daily dose is 2,400 mg.

Ages 6 months to 12 years of age
The dose is 10 mg/kg intravenously up to a maximum single dose of 400 mg every 4 to 6 hours as necessary. Infusion time must be at least 10 minutes. Maximum daily dose is 40 mg/kg or 2,400 mg, whichever is less.

Pediatric Dosing as Necessary for Fever and Pain

Age Group	Dose	Dosing Interval	Min. Infusion Time	Max Daily Dose
6 months to less than 12 years	10 mg/kg up to 400 mg max	Every 4 to 6 hours as Necessary	10 minutes	*40 mg/Kg or 2,400 mg
12 to 17 years	400 mg	Every 4 to 6 hours as Necessary	10 minutes	2,400 mg

Maximum daily dose is 40 mg/kg or 2,400 mg, whichever is less

Renal insufficiency
Precautions should be taken when NSAIDs are used in patients with renal insufficiency. In patients with mild or moderate renal impairment the initial dose should be reduced and be kept as low as possible for the shortest duration necessary to control symptoms and renal function monitored. This medicinal product is contraindicated in patients with severe renal insufficiency.

Hepatic insufficiency
Precautions should be taken when NSAIDs are used in this population although differences in the pharmacokinetic profile have not been observed. Patients with mild or moderate hepatic insufficiency should start the treatment with reduced doses, the dose should be kept as low as possible for the shortest duration necessary and they should be carefully monitored. This medicinal product is contraindicated in patients with severe hepatic insufficiency.

Method of administration:
For intravenous use. Ibuprofen should only be administered by qualified healthcare professionals in an environment where appropriate equipment is available (during treatment).
The solution should be administered as an intravenous infusion over 30 minutes

CONTRAINDICATIONS:
boschofen is contraindicated in the following patients:
- Known hypersensitivity (e.g., anaphylactic reactions and serious skin reactions) to ibuprofen or any components of the drug product.
- History of asthma, urticaria, or other allergic-type reactions after taking aspirin or other NSAIDs. Severe, sometimes fatal, anaphylactic reactions to NSAIDs have been reported in such patients.
- Conditions involving an increased tendency or active bleeding such as thrombocytopenia;
- Active, or history of recurrent peptic ulcer/haemorrhage (two or more distinct episodes of proven ulceration or bleeding);
- History of gastrointestinal bleeding or perforation, related to previous NSAIDs therapy;
- Cerebrovascular or other active bleeding;
- Severe hepatic or renal insufficiency;
- Severe heart failure (NYHA Class IV);
- Severe dehydration (caused by vomiting, diarrhoea or insufficient fluid intake);
- Pregnancy, in the last trimester.

WARNINGS AND PRECAUTIONS:
Cardiovascular Thrombotic Events
Several COX-2 selective and nonselective NSAIDs of up to three years duration have shown an increased risk of serious cardiovascular (CV) thrombotic events, including myocardial infarction (MI) and stroke, which can be fatal. To minimize the potential risk for an adverse CV event in NSAID-treated patients, use the lowest effective dose for the shortest duration possible. Patients should be informed about the symptoms of serious CV events and the steps to take if they occur.
The concurrent use of aspirin and an NSAID, such as ibuprofen, increases the risk of serious gastrointestinal (GI) events.

Status Post Coronary Artery Bypass Graft (CABG) Surgery
COX-2 selective NSAID for the treatment of pain in the first 10-14 days following CABG surgery found an increased incidence of myocardial infarction and stroke. NSAIDs are contraindicated in the setting of CABG.

Post-MI Patients
If **boschofen** is used in patients with a recent MI, monitor patients for signs of cardiac ischemia.

Gastrointestinal Bleeding, Ulceration, and Perforation
NSAIDs, including ibuprofen, cause serious gastrointenstinal (GI) adverse events including inflammation, bleeding, ulceration, and perforation of the esophagus, stomach, small intestine, or large intestine, which can be fatal. These serious adverse events can occur at any time, with or without warning symptoms, in patients treated with **boschofen**. Other factors that increase the risk for GI bleeding in patients treated with NSAIDs include longer duration of NSAID therapy; concomitant use of oral corticosteroids, aspirin, anticoagulants, or selective serotonin reuptake inhibitors (SSRIs); smoking; use of alcohol; older age; and poor general health status.

Hepatotoxicity
Elevations of ALT or AST (three or more times the upper limit of normal [ULN]) have been reported in approximately 1% of NSAID- treated patients.Elevations of ALT or AST (less than three times ULN) may occur in up to 15% of patients treated with NSAIDs, including ibuprofen.

Hypertension
NSAIDs, including **boschofen**, can lead to new onset or worsening of pre-existing hypertension, either of which may contribute to the increased incidence of CV events. Patients taking angiotensin converting enzyme (ACE) inhibitors, thiazide diuretics, or loop diuretics may have impaired response to these therapies when taking NSAIDs. Monitor blood pressure (BP) during the initiation of NSAID treatment and throughout the course of therapy.

Heart Failure and Edema
Fluid retention and edema have been observed in some patients treated with NSAIDs. Avoid the use of **boschofen** in patients with severe heart failure unless the benefits are expected to outweigh the risk of worsening heart failure. If **boschofen** is used in patients with severe heart failure, monitor patients for signs of worsening heart failure.

Renal Toxicity and Hyperkalemia
Renal Toxicity
Long-term administration of NSAIDs has resulted in renal papillary necrosis and other renal injury.
Avoid the use of **boschofen** in patients with advanced renal disease unless the benefits are expected to outweigh the risk of worsening renal function. If **boschofen** is used in patients with advanced renal disease, monitor patients for signs of worsening renal function.

Hyperkalemia
Increases in serum potassium concentration, including hyperkalemia, have been reported with use of NSAIDs, even in some patients without renal impairment.

Anaphylactic Reactions
Ibuprofen has been associated with anaphylactic reactions in patients with and without known hypersensitivity to ibuprofen and in patients with aspirin-sensitive asthma.

Exacerbation of Asthma Related to Aspirin Sensitivity
A subpopulation of patients with asthma may have aspirin-sensitive asthma which may include chronic rhinosinusitis complicated by nasal polyps; severe, potentially fatal bronchospasm; and intolerance to aspirin and other NSAIDs. Because cross-reactivity between aspirin and other NSAIDs has been reported in such aspirin-sensitive patients, When **boschofen** is used in patients with preexisting asthma (without known aspirin sensitivity), monitor patients for changes in the signs and symptoms of asthma.

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 reactions, and to discontinue the use of **boschofen** at the first appearance of skin rash or any other sign of hypersensitivity.

Hematologic Toxicity
Anemia has occurred in NSAID-treated patients. This may be due to occult or gross GI blood loss, fluid retention, or an incompletely described effect on erythropoiesis. If a patient treated with **boschofen** has any signs or symptoms of anemia, monitor hemoglobin or hematocrit.
NSAIDs, including **boschofen** may increase the risk of bleeding events. Concomitant use of warfarin and other anticoagulants, antiplatelet agents, and serotonin reuptake inhibitors (SSRIs) and serotonin norepinephrine reuptake inhibitors (SNRIs) may increase this risk. Monitor these patients for signs of bleeding.

Ophthalmological Effects:
Blurred or diminished vision, scotomata, and changes in color vision have been reported with oral ibuprofen. Discontinue ibuprofen if the patient develops such complaints, and refer the patient for an ophthalmologic examination that includes central visual fields and color vision testing.

Laboratory Monitoring
Because serious GI bleeding, hepatotoxicity, and renal injury can occur without warning symptoms or signs, consider monitoring patients on long-term NSAID treatment with a CBC and a chemistry profile periodically.

DRUG INTERACTIONS:
Drugs That Interfere with Hemostasis:
Monitor patients with concomitant use of **boschofen** with anticoagulants (e.g., warfarin), antiplatelet agents (e.g. aspirin), selective serotonin reuptake inhibitors (SSRIs), and serotonin norepinephrine reuptake inhibitors (SNRIs) for signs of bleeding.

Aspirin
Concomitant use of **boschofen** and analgesic doses of aspirin is not generally recommended because of the increased risk of bleeding.

ACE Inhibitors, Angiotensin Receptor Blockers, Beta-blockers & Diuretics
During concomitant use of **boschofen** and ACE-inhibitors, ARBs, or beta- blockers, monitor blood pressure to ensure that the desired blood pressure is obtained. During concomitant use of **boschofen** and ACE-inhibitors or ARBs in patients who are elderly, volume-depleted, or have impaired renal function, monitor for signs of worsening renal function.

Digoxin
The concomitant use of ibuprofen with digoxin has been reported to increase the serum concentration and prolong the half-life of digoxin. During concomitant use of **boschofen** and digoxin, monitor serum digoxin levels.

Lithium
NSAIDs have produced elevations in plasma lithium levels and reductions in renal lithium clearance. During concomitant use of **boschofen** and lithium, monitor patients for signs of lithium toxicity.

Methotrexate
Concomitant use of NSAIDs and methotrexate may increase the risk for methotrexate toxicity (e.g., neutropenia, thrombocytopenia, renal dysfunction). During concomitant use of **boschofen** and methotrexate, monitor patients for methotrexate toxicity.

Cyclosporine
Concomitant use of **boschofen** and cyclosporine may increase cyclosporine's nephrotoxicity. During concomitant use of **boschofen** and cyclosporine, monitor patients for signs of worsening renal function.

NSAIDs and Salicylates
Concomitant use of ibuprofen with other NSAIDs or salicylates (e.g., diflunisal, salsalate) increases the risk of GI toxicity, with little or no increase in efficacy. The concomitant use of ibuprofen with other NSAIDs or salicylates is not recommended.

Pemetrexed:
During concomitant use of **boschofen** and and pemetrexed, in patients with renal impairment whose creatinine clearance ranges from 45 to 79 mL/min, monitor for myelosuppression, renal and GI toxicity. NSAIDs with short elimination half-lives (e.g., diclofenac, indomethacin) should be avoided for a period of two days before, the day of, and two days following administration of pemetrexed.

PREGNANCY:
Pregnancy category: C
Use of NSAIDs, including **boschofen**, during the third trimester of pregnancy increases the risk of premature closure of the fetal ductus arteriosus. Avoid use of NSAIDs, including **boschofen**, in pregnant women starting at 30 weeks gestation (third trimester). Use of nonsteroidal antiinflammatory drugs (NSAIDs) around 20 weeks or later in pregnancy may cause rare but serious kidney problems in an unborn baby. This can lead to low levels of amniotic fluid surrounding the baby and possible complications. Health care professionals should limit prescribing NSAIDs between 20 to 30 weeks of pregnancy and avoid prescribing them after 30 weeks of pregnancy. If NSAID treatment is determined necessary, limit use to the lowest effective dose and shortest duration possible and check for oligohydramnios during the treatment.

LACTATION:
No lactation studies have been conducted with ibuprofen. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for **boschofen** and any potential adverse effects on the breastfed infant from the **boschofen** or from the underlying maternal condition.

Pediatric Use
The effectiveness of **boschofen** for the treatment of pain and fever has not been studied in pediatric patients less than 6 months of age.

Geriatric Use
Elderly patients, compared to younger patients, are at greater risk for NSAID-associated serious cardiovascular, gastrointestinal, and/or renal adverse reactions. If the anticipated benefit for the elderly patient outweighs these potential risks, start dosing at the low end of the dosing range, and monitor patients for adverse effects. 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.

ADVERSE EFFECTS:
Common:
Fatigue or sleeplessness, headache, dizziness, Vertigo, Pyrosis, abdominal pain, nausea, vomiting, flatulence, diarrhoea, constipation and slight gastro-intestinal blood losses that may cause anaemia in exceptional cases, Gastrointestinal ulcers, potentially with bleeding and perforation, Ulcerative stomatitis, exacerbation of colitis and Crohn´s disease, Skin eruption, Pain and burning sensation in the administration site.

Uncommon:
Hypersensitivity reactions with skin rashes and itching, as well as asthma attacks (possibly with drop in blood pressure), Anxiety, restlessness, Insomnia, agitation, irritability or tiredness. Aseptic meningitis (stiff neck, headache, nausea, vomiting, fever or confusion). Patients with autoimmune disorders appear to be predisposed, Visual disturbances, Reversible toxic amblyopia, Tinnitus, Gastritis, Urticaria, pruritus, purpura (including allergic purpura), skin rash, reduced urinary excretion and formation of oedemas, particularly in patients with arterial hypertension or renal insufficiency, nephrotic syndrome, interstitial nephritis that may be accompanied by acute renal insufficiency.

Rare:
Psychotic reactions, nervousness, irritability, confusion or disorientation and depression, Hearing disorders, Oesophageal stenosis, exacerbation of diverticular disease, unspecific haemorrhagic colitis, If gastrointestinal bleeding occurs could cause anaemia and haematemesis, Jaundice, hepatic dysfunction, hepatic damage, particularly in long-term therapy, acute hepatitis.

Very Rare:
Exacerbation of infection-related inflammations (e.g. development of necrotising fasciitis) coinciding with the use of non-steroidal anti-inflammatory drugs has been described. This is possibly associated with the mechanism of action of the non-steroidal anti-inflammatory drugs, Disturbances to blood formation (anaemia, agranulocytosis, leukopenia, thrombocytopenia, and pancytopenia). First symptoms are: fever, sore throat, superficial mouth wounds, influenza-like complaints, severe lassitude, nosebleeds and skin bleeding, Systemic lupus erythematosus, severe hypersensitivity reactions, face oedema, swelling of the tongue, swelling of the internal larynx with constriction of the airways, difficulty breathing, palpitations, hypotension and life-threatening (shock), Palpitations, heart failure, myocardial infarction, Bullous reactions including Stevens-Johnson syndrome and toxic epidermal necrolysis (Lyell's syndrome), erythema multiforme, alopecia. Photosensitivity reactions and allergic vasculitis.

OVER DOSAGE:
Symptoms following acute NSAID overdosages have been typically limited to lethargy, drowsiness, nausea, vomiting, and epigastric pain, which have been generally reversible with supportive care. Gastrointestinal bleeding has occurred. Hypertension, acute renal failure, respiratory depression, and coma have occurred. Manage patients with symptomatic and supportive care following an NSAID overdosage. There are no specific antidotes. Consider emesis and/or activated charcoal (60 to 100 grams in adults, 1 to 2 grams per kg of body weight in pediatric patients) and/or osmotic cathartic

in symptomatic patients seen within four hours of ingestion or in patients with a large overdosage (5 to 10 times the recommended dosage). Forced diuresis, alkalinization of urine, hemodialysis, or hemoperfusion may not be useful due to high protein binding.

STORAGE:
Protect from heat, sunlight. Store below 25°C
Do not refrigerate or freeze
The expiration date refers to the product correctly stored at required conditions

Caution:
Infusion should not be used if container is leaking, solution is cloudy or it contains undissolved particle.

Presentation:
1's (100 mL vial)

Instruction:
To be sold on prescription of a registered medical practitioner only.
Keep it out of reach of children.
For single use in one patient only.
Patients and healthcare professionals can also report suspected adverse drug reaction at ade@bosch-pharma.com

خوراک: ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔
- دھوپ اور گرمی سے محفوظ ۲۵°ڈگری سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔
- ریفریجریٹر میں رکھنے یا منجمد ہونے سے بچائیں۔

تنبیہ: انفیوژن کے لیک ہونے ڈھندلا ہونے یا اس میں کوئی غیر حل پزیر شے نظر آنے کی صورت میں ہرگز استعمال نہ کریں۔

ہدایت: صرف مستند ڈاکٹر کے نسخے پر فروخت کریں۔
- بچوں کی پہنچ سے دور رکھیں۔
- ایک بار میں صرف ایک مریض کے استعمال کے لئے۔

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ISO 9001:2015 Certified Company