

Indrufen اندروفن

(Ibuprofen)
400mg/100ml Infusion
400mg/4ml Injection.

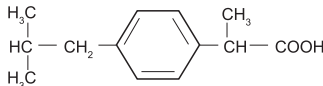
400مليگرام في 100ملي ليتر انفيوزن
400مليگرام في 4ملي ليتر انجكشن

COMPOSITION
Indrufen Infusion 400mg/4ml
Each ml Injection contains:
Ibuprofen (BP).....100mg.
Finished Product Specs.: Innovator's Specification.

Indrufen Infusion 400mg/100ml
Each 100ml vial contains:
Ibuprofen (BP).....400mg.
Finished Product Specs.: Innovator's Specification.

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.
• Indrufen 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.

DESCRIPTION
Indrufen (Ibuprofen) is a nonsteroidal anti-inflammatory drug, available as an Injection (400mg/4ml) and as an Infusion (400mg/100ml) for intravenous administration. The chemical name is Ibuprofen, which is (+)-2-(4-isobutylphenyl) propionic acid. It has a molecular weight of 206.28. The structural formula of Ibuprofen is:



CLINICAL PHARMACOLOGY
Mechanism of Action
Ibuprofen has analgesic, anti-inflammatory, and antipyretic properties. The mechanism of action of Ibuprofen, 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 and its mode of action may be due to a decrease of prostaglandins in peripheral tissues.

Pharmacokinetics
Ibuprofen is a racemic mixture of (-)- and (+)-isomers. In which (+)-isomer is responsible for clinical activity, while (-)-form is pharmacologically inactive and is slowly and incompletely (~60%) interconverted into the active (+) species in adults. The (-)-isomer serves as a circulating reservoir to maintain levels of active drug. The pharmacokinetic parameters of Ibuprofen determined in a study with volunteers are presented below.

Pharmacokinetic Parameters of Intravenous Ibuprofen		
	400mg* Ibuprofen Mean (CV%)	800mg* Ibuprofen Mean (CV%)
Number of Patients	12	12
AUC (mcg·h/ml)	109.3 (26.4)	192.8 (18.5)
Cmax (mcg/ml)	39.2 (15.5)	72.6 (13.2)
KCL (1/h)	0.32 (17.9)	0.29 (12.8)
T1/2 (h)	2.22 (20.1)	2.44 (12.9)

AUC = Area-under-the-curve
Cmax = Peak plasma concentration
CV = Coefficient of Variation
KEL = First-order elimination rate constant
T1/2 = Elimination half-life
* = 60 minute Infusion time

Ibuprofen 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.

INDICATIONS AND USAGE
Indrufen is indicated in adults and pediatric patients six months and older for the management of acute mild to moderate and moderate to severe post-operative pain with adjunctive reduced opioid analgesics,

intravenously. Intravenous route of administration is considered clinically necessary for fever reduction in adults.

DOSAGE AND ADMINISTRATION

Dosage:

Injection:

Indrufen Injection must be diluted prior to administration.

Adult Pain: 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.

Adult Fever: 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 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 400mg max	Every 4 to 6 hours as necessary	10 minutes	*40 mg/Kg or 2,400 mg
12 to 17 years	400mg	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.

Method of administration

Dilute to a final concentration of 4 mg/ml or less. Appropriate diluents include 0.9% Sodium Chloride Injection USP (normal saline) or 5% Dextrose Injection USP (D5W), or Lactated Ringers Solution, 400mg dose. Dilute 4ml of Indrufen Injection in at least 100ml of diluent.

- For weight-based dosing at 10 mg/kg ensure that the concentration of Indrufen Injection is 4 mg/ml or less.
- After observing the response to initial therapy with Indrufen, the dose and frequency should be adjusted to suit an individual patient's needs. Do not exceed 3200 mg total daily dose in adults. Do not exceed 40 mg/kg or 2,400 mg, whichever is less, total daily dose in pediatric patients less than 17 years of age.
- Visually inspect Indrufen for particulate matter and discoloration prior to administration. If visibly opaque particles, discoloration or other foreign particulates are observed, the solution should not be used.
- Diluted solutions are stable for up to 24 hours at ambient temperature (approximately 20 to 25° C) and room lighting.

Dosage:

Infusion:

Adults:

Treatment of moderate pain and fever:

The recommended dose is 400 mg of Indrufen Infusion every 6 to 8 hours as necessary, without exceeding the maximum daily recommended dose of 1200 mg.

- The lowest effective dose should be used for the shortest duration necessary to relieve symptoms and to avoid side effects.
- Make sure that patient had enough fluids in order to minimize the risk of side effects to the kidney.
- Use should be limited to situations where oral administration is inappropriate. Patients must switch to oral treatment as soon as this is possible.
- This medicine is indicated for short-term acute treatment only and should not be used for more than 3 days.
- Precautions should be necessary, if patient has an infection consult a doctor without delay if symptoms such as fever and pain are persisted or worsen.

Children and Adolescents

Indrufen Infusion should not be used in children and adolescents (below 18 years of age).

Method of administration

Intravenous use:

- Indrufen Infusion should be administered as an intravenous Infusion for 30 minutes.
- Indrufen Infusion is restricted to hospital use only.
- Indrufen Infusion will be given by doctor or nurse.

CONTRAINDICATIONS

Ibuprofen is contraindicated in the following patients:

- Known hypersensitivity (e.g., anaphylactic reactions and serious skin reactions) to Ibuprofen or any components of the drug.
- 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.
- In the setting of coronary artery bypass graft (CABG) surgery.

ADVERSE REACTIONS

It includes:

- Cardiovascular Thrombotic Events
- GI Bleeding, Ulceration and Perforation
- Hepatotoxicity
- Hypertension
- Heart Failure and Edema
- Renal Toxicity and Hyperkalemia
- Anaphylactic reactions
- Serious Skin Reactions
- Hematologic Toxicity

WARNINGS AND PRECAUTIONS

Duration of Dosage

Use the lowest effective dose for the shortest duration. Do not exceed a total daily dose of 3200mg Ibuprofen Injection.

Cardiovascular Thrombotic Events

Patients with known Cardiovascular (CV) disease or risk factors had a higher absolute incidence of excess serious CV thrombotic events.

Status Post Coronary Artery Bypass Graft (CABG) Surgery

In Patients with CABG found an increased incidence of myocardial infarction and stroke.

Post-MI Patients

Patients treated with NSAIDs in the post-MI period are at increased risk of reinfarction, CV-related death, and all-cause mortality beginning in the first week of treatment. Avoid the use of Ibuprofen in patients with a recent MI unless the benefits are expected to outweigh the risk of recurrent CV thrombotic events. If Ibuprofen 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 gastrointestinal (GI) adverse events including inflammation, bleeding, ulceration, and perforation of the esophagus, stomach, small intestine, or large intestine, which can be fatal.

Hepatotoxicity

Elevations of ALT or AST (less than three times ULN) may occur in up to 15% of patients treated with NSAIDs, including Ibuprofen. Inform patients of the warning signs and symptoms of hepatotoxicity (e.g., nausea, fatigue, lethargy, diarrhea, pruritus, jaundice, right upper quadrant tenderness, and "flu-like" symptoms).

Hypertension

NSAIDs, including Ibuprofen, 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

Avoid the use of Ibuprofen in patients with severe heart failure unless the benefits are expected to outweigh the risk of worsening heart failure. If Ibuprofen 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. Renal toxicity has also been seen in patients in whom renal prostaglandins have a compensatory role in the maintenance of renal perfusion. In these patients, administration of an NSAID may cause a dose dependent reduction in prostaglandin formation and, secondarily, in renal blood flow, which may precipitate overt renal decompensation.

Hyperkalemia

Increases in serum potassium concentration, including hyperkalemia, have been reported with use of NSAIDs, even in some patients without renal impairment. In patients with normal renal function, these effects have been attributed to a hyporeninemic-hypoaldosteronism state.

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

When Ibuprofen is used in patients with pre-existing 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.

Premature Closure of Fetal Ductus Arteriosus

Ibuprofen may cause premature closure of the fetal ductus arteriosus. Avoid use of NSAIDs, including Ibuprofen, in pregnant women starting at 30 weeks of gestation (third trimester).

Hematologic Toxicity

NSAIDs, including Ibuprofen may increase the risk of bleeding events. Concomitant use of warfarin and other anticoagulants, antiplatelet agents (e.g., aspirin), and serotonin reuptake inhibitors (SSRIs) and serotonin norepinephrine reuptake inhibitors (SNRIs) may increase this risk. Infusion of the drug product without dilution can cause hemolysis.

Masking of Inflammation and Fever

The pharmacological activity of Ibuprofen in reducing inflammation, and possibly fever, may diminish the utility of diagnostic signs in detecting infections.

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

- The concomitant use of Ibuprofen and anticoagulants have an increased risk of serious bleeding compared to the use of either drug alone.
- Concomitant use of drugs that interfere with serotonin reuptake and an NSAID may potentiate the risk of bleeding more than an NSAID alone.

Aspirin

Concomitant use of an NSAID and aspirin was associated with a significantly increased incidence of GI adverse reactions as compared to use of the NSAID alone.

ACE Inhibitors, Angiotensin Receptor Blockers, and Beta-blockers

• NSAIDs may diminish the antihypertensive effect of angiotensin converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs), or beta-blockers (including propranolol).

• In patients who are elderly, volume-depleted (including those on diuretic therapy), or have renal impairment, co-administration of an NSAID with ACE inhibitors or ARBs may result in deterioration of renal function, including possible acute renal failure. These effects are usually reversible.

Diuretics

NSAIDs reduced the natriuretic effect of loop diuretics (e.g., furosemide) and thiazide diuretics in some patients. This effect has been attributed to the NSAID inhibition of renal prostaglandin synthesis.

Digoxin

The concomitant use of Ibuprofen with digoxin has been reported to increase the serum concentration and prolong the half-life of digoxin.

Lithium

NSAIDs have produced elevations in plasma lithium levels and reductions in renal lithium clearance. The mean minimum lithium concentration increased 15%, and the renal clearance decreased by approximately 20%. This effect has been attributed to NSAID inhibition of renal prostaglandin synthesis.

Methotrexate

Concomitant use of NSAIDs and methotrexate may increase the risk for methotrexate toxicity (e.g., neutropenia, thrombocytopenia, renal dysfunction).

Cyclosporine

Concomitant use of Ibuprofen and cyclosporine may increase cyclosporine's nephrotoxicity.

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.

Pemetrexed

Concomitant use of Ibuprofen and pemetrexed, may increase the risk of pemetrexed-associated myelosuppression, renal, and GI toxicity.

USE IN SPECIFIC POPULATIONS

Pregnancy

Avoid use of NSAIDs, including Ibuprofen, in pregnant women starting at 30 weeks gestation (third trimester) due to increases the risk of premature closure of the fetal ductus arteriosus.

Females and Males of Reproductive Potential

The use of prostaglandin-mediated NSAIDs, including Ibuprofen, may delay or prevent rupture of ovarian follicles, which has been associated with reversible infertility in some women.

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.

OVERDOSAGE

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, but were rare.

Manage patients with symptomatic and supportive care following an NSAID overdosage. There are no specific antidotes. Consider emesis and/or activated charcoal 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, alkalization of urine, hemodialysis, or hemoperfusion may not be useful due to high protein binding.

STORAGE

Store below 30°C.
Protect from heat and light.

PRESENTATION

Indufen (Ibuprofen) Injection 400mg/4ml is available as pack of 4mlx10's.
Indufen (Ibuprofen) Infusion 400mg/100ml is available as pack of 1Vial of 100mL

To be sold on prescription of a registered medical practitioner only.

Keep all medicines out of the reach of children



Manufactured by :

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