

Polmastar

Polmacoxib 2mg

1. Generic Name:

Polmacoxib Capsule 2 mg

2. Qualitative and quantitative composition:

Each Hard Gelatin Capsule contains:

Polmacoxib 2 mg

Excipients: q.s.

Colour: Erythrosine (Used in Capsule Shell)

3. Dosage form and strength:

Capsule of 2mg

4. Clinical particulars

4.1 Therapeutic indication:

It is indicated for treatment of Idiopathic (Primary) Osteoarthritis of Hip/Knee.

4.2 Posology and method of administration:

Posology:

Adult: The recommended dose is 2 mg once a day, and should be administered after meals. The daily dose should not exceed 2 mg. If there is no therapeutic benefit at the recommended dose, this drug should be discontinued and an appropriate alternative treatment should be considered.

Duration of treatment:

The potential risks and benefits of this drug and other alternative therapies should be considered before administering this drug. Cardiovascular risk increases with increasing dose and duration of exposure to this drug, so it should be administered for the shortest possible period of time. The efficacy of this drug for more than 6 weeks and the safety of long-term administration for more than 6 months have not been established, and adverse reactions such as hypertension, angina pectoris, and edema may occur when administering this drug. Therefore, when administering this drug, it is necessary to re-evaluate whether the administration should continue according to the patient's symptom relief and response to the treatment at least every month.

Special populations

Elderly:

The majority of spontaneous reports of fatal gastrointestinal adverse events are of aged persons and weak persons, so special caution should be exercised when administering this drug to these patients.

When this drug is administered to aged persons or patients with cardiac dysfunction. If symptoms worsen during treatment, appropriate measures such as stopping treatment should be taken.

Patients with liver and kidney disease Polmacoxib drug should not be administered as there is no experience with administration.

Renal impairment:

Long-term administration of nonsteroidal anti-inflammatory drugs, including this drug, may cause renal papillary necrosis or other kidney damage. In addition, prostaglandins play an important role in maintaining renal blood flow, so special caution is required in patients with heart failure, renal failure, hepatic failure, patients administering diuretic ACE inhibitors or angiotensin II receptor blockers, and aged persons. When the administration is stopped, most patients return to their state before treatment. Advanced renal disease there have been no controlled clinical trials of this drug in patients with advanced renal disease. Therefore, the administration of this drug is not recommended in patients with advanced renal disease. If the patient needs to start administering this drug, the patient's renal function should be closely monitored.

Hepatic impairment:

Administration of nonsteroidal anti-inflammatory drugs, including this drug, may increase liver function levels. These abnormal test values may worsen, change, or be temporary as treatment continues. In addition, serious hepatic adverse events including jaundice, fatal fulminant hepatitis, hepatic necrosis, and liver failure (some fatal) have been reported rarely with the administration of nonsteroidal anti-inflammatory drugs, including this drug. During the administration period, continuously and carefully monitor for deterioration of liver function in patients with symptoms and/ or signs suggestive of liver dysfunction, or in patients with abnormal liver function test results. If abnormal liver function test results (more than 3 times the upper limit of normal) are continuously observed, or clinical symptoms or systemic symptoms related to liver disease (e.g., eosinophilia, rash) develops, this drug should be discontinued.

Paediatric population:

Safety and efficacy in children under 18 years of age have not been established.

Method of administration:

Oral use.

Adult: The recommended dose is 2 mg once a day, and should be administered after meals.

4.3 Contraindications:

- ⚠ Hypersensitivity reaction to Polmacoxib or a history of it
- ⚠ People allergic to sulphonamides
- ⚠ People with a history of asthma, acute rhinitis, nasal polyps, angioedema urticaria, or allergic reactions to aspirin or other NSAIDs (including COX-2 inhibitors)
- ⚠ Hypertensive patients who are not well controlled despite taking antihypertensive drugs
- ⚠ Patients with edema or fluid retention
- ⚠ Hepatic impairment
- ⚠ Renal impairment
- ⚠ Patients with active peptic ulcer or gastrointestinal bleeding
- ⚠ People with inflammatory bowel disease, such as Crohn's disease or ulcerative colitis
- ⚠ Patients with congestive heart failure (NYHA II-IV)
- ⚠ Patients with established ischemic heart disease, peripheral arterial disease and / or cerebrovascular disease
- ⚠ Women who are pregnant or may be pregnant nursing mother
- ⚠ Treatment of pain before and after coronary artery bypass surgery (CABG)
- ⚠ Patients with hyperkalaemia
- ⚠ Patients with coagulation disorders or receiving anticoagulants

4.4 Special warnings and precautions for use:

The efficacy and safety of this drug for acute pain relief (pain after surgery or tooth extraction) have not been established and should not be administered.

People who regularly drink three or more cups of alcoholic drinks per day should consult their doctor or pharmacist if they need to take this drug or other antipyretic analgesics. If these people take this drug, they may cause gastrointestinal bleeding.

Cardiovascular risk:

Nonsteroidal anti-inflammatory drugs, including this drug, may increase the risk of serious cardiovascular thrombotic reactions, myocardial infarction, and stroke, which can be fatal. This risk may be increased with the duration of administration, dose, and underlying cardiovascular risk factors, and maybe even greater in patients with cardiovascular disease. It should be administered at the lowest effective dose and for the shortest possible period of time to minimize the potential risk of cardiovascular adverse events in patients treated with this drug. The doctor and patient should carefully monitor the development of these.

Advanced renal and hepatic disease: There have been no controlled clinical trials of this drug in patients with advanced renal disease. Therefore, the administration of this drug is not recommended in patients with advanced renal disease. If the patient needs to start administering this drug, the patient's renal function should be closely monitored.

Administration of nonsteroidal anti-inflammatory drugs, including this drug, may increase liver function levels. These abnormal test values may worsen, change, or be temporary as treatment continues. In addition, serious hepatic adverse events including jaundice, fatal fulminant hepatitis, hepatic necrosis, and liver failure (some fatal) have been reported rarely with the administration of nonsteroidal anti-inflammatory drugs, including this drug. During the administration period, continuously and carefully monitor for deterioration of liver function in patients with symptoms and/ or signs suggestive of liver dysfunction, or in patients with abnormal liver function test results. If abnormal liver function test results (more than 3 times the upper limit of normal) are continuously observed, or clinical symptoms or systemic symptoms related to liver disease (e.g., eosinophilia, rash) develops, this drug should be discontinued.

Pseudo-anaphylactic reactions: As with other nonsteroidal anti-inflammatory drugs, pseudo anaphylactic reactions may occur in patients who have never been exposed to the drug. This combination of symptoms typically occurs in patients with asthma who present with or without nasal polyps or severe bronchospasm that is potentially fatal after administration of aspirin or other nonsteroidal anti-inflammatory drugs. When these pseudo-anaphylactic reactions occur,

first aid should be taken.

Skin reactions: This drug is a sulfa-drug and may cause serious skin adverse reactions such as exfoliative dermatitis, mucocutaneous-ocular syndrome (Stevens-Johnson syndrome), and toxic epidermal necrolysis (Riehl Syndrome), which can be fatal. These serious adverse reactions may occur without warning symptoms and may occur in patients without a history of sulfa drug allergy. In most cases, these adverse reactions occur within the first month of administration. Patients should be aware of the signs and symptoms of significant skin manifestations and the drug should be discontinued at the first signs and symptoms of hypersensitivity reactions such as skin rashes, mucosal lesions or blisters, fever, and itching.

Asthma: Some patients with asthma may be sensitive to aspirin. The use of aspirin in patients with aspirin-induced asthma may be associated with severe bronchospasm, which can be fatal. Cross reactivity, including bronchospasm, between aspirin and other nonsteroidal anti-inflammatory drugs, has been reported in these patients with aspirin-induced asthma. Therefore, this drug should not be administered to patients with aspirin-induced asthma and should be used with caution in patients with asthma.

Others

Hemoglobin or hematocrit levels should be tested if symptoms or signs of anaemia or blood loss occur with long-term administration of this drug. Selective COX-2 inhibitors generally do not affect platelet count, prothrombin time (PTI), or partial thromboplastin time (PTT) and do not inhibit platelet aggregation at recommended doses. However, caution should be exercised as adverse reactions of prolonged prothrombin time have been reported as a result of clinical trials with this drug.

Patients administering long-term nonsteroidal anti-inflammatory drugs, including this drug, should have CBC blood tests and physicochemical tests done regularly. If clinical symptoms or systemic symptoms (e.g., eosinophilia, rash) related to liver disease or renal disease develop, or abnormal liver function test or renal function test results persist or worsen, the drug should be discontinued. The pharmacological nature of this drug may cause fever and other symptoms and signs of subclinical inflammation, delaying the diagnosis of infectious complications under painful and non infectious conditions. In patients with severe dehydration, the drug should be administered after hydration and should be carefully observed.

4.5 Drugs interactions:

Since this drug is mainly metabolized by CYP3A4 in the liver, caution should be exercised when administered concurrently with drugs that inhibit CYP3A4.

Interaction with ketoconazole or erythromycin:

When ketoconazole 400 mg was administered concurrently once a day, ketoconazole inhibited the metabolism of this drug through CYP3A4 and increased the AUC of this drug by 1.3 times. Therefore, when starting concomitant administration of this drug, a lower dose than the usual dose should be considered. Also, the T_{max} (median) was 71.9 hours when this drug and ketoconazole were administered concurrently, which was longer than 9 hours when administered alone, so caution should be exercised that treatment response time may be delayed when administered concurrently with ketoconazole.

Interaction with ACE inhibitors or angiotensin II receptor blockers:

Since the antihypertensive effect of an ACE inhibitor or angiotensin II receptor blocker may be reduced by nonsteroidal anti-inflammatory drugs, including this drug, this interaction should be taken into consideration when administering this drug and an ACE inhibitor or angiotensin II receptor blocker in combination. Patients with renal impairment (e.g., dehydrated patients or aged persons) may be at an increased risk of reversible acute renal failure when nonsteroidal anti-inflammatory drugs, including this drug, are administered concurrently with an ACE inhibitor or angiotensin II receptor blocker. Therefore, caution should be exercised when administering this combination, especially to aged persons. Adequate hydration should be provided to patients, and renal function should be monitored regularly after starting such concomitant administration.

Interaction with Diuretic:

In the case of nonsteroidal anti-inflammatory drugs, including this drug, it has been confirmed that the natriuretic effect of furosemide and thiazide diuretics may be reduced in some patients by inhibition of prostaglandin synthesis in the kidney. Therefore, during concomitant administration of these drugs and nonsteroidal anti-inflammatory drugs, including this drug, patients should be closely monitored for signs of renal failure.

Interaction with Aspirin:

There is no consistent evidence that administered concurrently with aspirin may reduce the risk of serious cardiovascular thrombotic reactions associated with the use of nonsteroidal anti-inflammatory drugs, including this drug. Selective COX-2 inhibitors may be administered concurrently with low-dose aspirin (not more than 325 mg per day), but it has been reported that the incidence of gastrointestinal adverse events (gastrointestinal ulcers) or other gastrointestinal complications is higher than when this drug alone is administered. Since this drug has not been studied for its effect on platelets, it cannot be used as a substitute for aspirin as a preventive therapy for the cardiovascular system.

4.6 Use in special populations (such as pregnant women, lactating women, paediatric patients, geriatric patients etc.)

Pregnancy:

Polmacoxib should not be administered to pregnant women or women who may become pregnant. If pregnancy is confirmed while administering this drug, the administration of this drug should be discontinued.

Breast-feeding:

It has been established that this drug may be transferred to the fetus through plasma-like or slightly higher concentrations in the breast milk of rats. Many drugs not only pass into breast milk, but if they do, serious adverse reactions in infants are of concern, so lactation or drug administration should be discontinued considering the importance of drug administration to nursing mothers.

Fertility:

The use of nonsteroidal anti-inflammatory drugs may interfere with or delay follicle rupture due to their mechanism of action, which may cause reversible infertility in some women. Therefore, discontinuation of nonsteroidal anti-inflammatory drugs, including this drug, should be considered in women who have difficulty getting pregnant or are undergoing infertility tests. Inhibition of prostaglandin synthesis may adversely affect pregnancy.

Elderly:

Liver, and especially heart function, so appropriate observation is required when administering this drug to aged persons. In patients with arthritis over 70 years of age, the blood drug concentration of this drug is 1.4 times higher than that in patients with arthritis between 40 and 69 years of age, so it should be administered with caution.

Renal impairment:

There have been no controlled clinical trials of this drug in patients with advanced renal disease. Therefore, the administration of this drug is not recommended in patients with advanced renal disease. If the patient needs to start administering this drug, the patient's renal function should be closely monitored.

Hepatic impairment:

There is no clinical experience in adult patients with hepatic impairment. However, since Polmacoxib is not metabolized and is eliminated as unchanged in urine and faeces, hepatic impairment is not expected to increase systemic exposure above the safety margin in adult patients. Therefore, no dosage adjustment is required in adult patients with hepatic impairment.

4.7 Effects on ability to drive and use machines:

Patients who experience dizziness or drowsiness while taking this medicine should avoid driving or operating machinery.

4.8 Undesirable effects:

All adverse reactions reported in clinical trials of this drug in patients with osteoarthritis regardless of the causal relationship with this drug are as follows. Expression frequency is defined as follows; very common (≥1/10), common (≥1/100, <1/10), uncommon (≥1/1,000, <1/100), rare (≥1/10,000, <1/1,000), very rare (<1/10,000).

Table-Adverse reactions reported in clinical trials of this drug:

Expression in organs	Adverse Reactions	Expression Frequency
Infection	Nasopharyngitis	Common
	Pneumonia, athlete's foot, bronchitis, cellulitis, boils, herpes zoster, influenza, syphilis, urinary tract infection, nail fungus	Uncommon
Benign and malignant neoplasms	Colorectal adenoma	Uncommon
Blood and lymphatic system disorders	Anaemia	Common
	Skin papilloma	Uncommon
Immune system disorders	Eosinophilia, hypersensitivity reaction	Uncommon
Metabolism and nutritional system	Chemical allergy, diabetes, hypercholesterolemia, hyperkalaemia	Uncommon

Side A: L-148 x H-297 mm

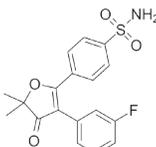
Mental disorders	Depressed mood, major depression	Uncommon
Nervous system disorders	Headache	Common
	Insomnia, paraesthesia, conscious depression, dizziness, drowsiness, dullness, Alzheimer's type dementia, tremor	Uncommon
Visual impairment	Periorbital edema, eyelid edema, blepharitis, blepharospasm, dry eyes, keratitis, macular hole	Uncommon
Ear and labyrinthine disturbance	Ear discomfort, postural dizziness	Uncommon
Heart disorders	Palpitation, angina pectoris, right bundle branch block, myocardial ischemia	Uncommon
Vascular disorders	Increase of blood pressure	Common
	Heart arrhythmia, hypertension, facial flushing, abnormal blood pressure levels	Uncommon
Respiratory, thoracic and mediastinal disorders	Cough, shortness of breath	Common
	Asthma, runny nose, sore throat, productive cough, rhinitis, allergic rhinitis	Uncommon
Gastrointestinal disorders	Epigastric pain, diarrhea, indigestion, nausea, abdominal pain	Common
	Vomiting, intestinal motility disorder, irritable bowel syndrome, stool color changes, food poisoning, gastric ulcer, gingivitis, dental problems, dry mouth, enteritis, epigastric discomfort, gastritis, abdominal discomfort, lower abdominal pain, Aphthous stomatitis, constipation, gastroesophageal reflux disease, colorectal polyp, esophagitis	Uncommon
Liver and biliary tract disorders	Hyperbilirubinemia	Uncommon
Skin and subcutaneous tissue disorders	Swollen face, urticaria, erythema, neurodermatitis, pruritus, systemic pruritus, eczema	Uncommon
Musculoskeletal and connective tissue disorders	Arthralgia, back pain, flat feet, joint swelling, neck pain, limb pain, plantar fasciitis, musculoskeletal pain, intervertebral disc herniation, muscle cramps	Uncommon
Kidney and urinary tract	Frequent urination, chronic renal failure, microalbuminuria, urolithiasis	Uncommon
Reproductive and mammary system	Breast pain	Uncommon
Systemic and site of administration	Chest discomfort, facial edema, edema, peripheral edema	Common
	Fatigue, generalized edema, influenza-like illness, weight gain, asthenia, thirst, bruises, abrasions, lacerations, traffic accidents, vertebral compression fractures, chills, fever, insect bites, concussion, ligament ruptures, ligament sprains, cuts, wrist fractures	Uncommon
Examination	Heat sensation, drug overdose, neutrophil increased, unsaturated iron binding capacity decreased, prothrombin time extended, hemoglobin decreased, alanine aminotransferase (ALT) increased, aspartate aminotransferase increased, creatine phosphokinase increased, creatinine in the blood increased	Uncommon

7. Description:

Drug Substance: Polmacoxib

Chemical Name: 4-[3-(3-fluorophenyl)-5,5-dimethyl-4-oxofuran-2-yl]benzenesulfonamide

Structure:



Molecular Weight: 361.4g/mol

Molecular Formula: C₁₇H₁₅FNO₅S

Dosage Form: Capsule

8. Pharmaceutical particulars:

8.1 Incompatibilities:

Not applicable

8.2 Shelf life:

Please see manufacturing date/expiry date printed on pack. Do not use the product after the expiry date which is stated on the packaging. The Expiry date refers to the last day of the month.

8.3 Packaging information:

Alu-Alu blister pack of 10 capsules

8.4 Storage and handling instructions:

Do not store above 30°C. Protect from direct sunlight and moisture.

Keep all medicines out of reach of children.

9. Patient counselling information:

In general, healthcare professionals may counsel their patients and/or their relatives about the special warnings and precautions for use, drug interactions, undesirable effects, and any relevant contraindications of the medicine. Patients may also be informed about posology, method of administration, and storage/handling information as applicable.



10. Manufactured for:

Dawa Limited
Plot No. 7879/8, Baba Dogo Road, Ruaraka.
P.O Box 16633-00620, Nairobi, Kenya.

11. Manufactured by:

Precise Biopharma Private Limited
Mumbai -400078, Maharashtra, India
At: East African (India) Overseas
8 & 8A, Pharmacy, Selaqui, Dehradun-Uttarakhand-248011, India
Mfg. Lic. No. : 20/UA/LL/2019

As a result of comparing the expression frequency of adverse reactions according to the administration period of this drug, the expression frequency of pain and chest discomfort such as nasopharyngitis, anaemia, headache, and epigastric pain increased by more than 1% when administered for 24 weeks compared to when administered for 6 weeks, and the expression frequency of palpitations, angina pectoris, hypertension, increased blood pressure, and blood pressure abnormalities also seemed to increase.

4.9 Overdose:

Symptoms caused by an overdose of nonsteroidal anti-inflammatory drugs are generally lethargy, drowsiness, nausea, vomiting, and epigastric pain, which are recoverable with adjuvant therapy. Gastrointestinal bleeding may also occur, rarely hypertension, acute renal failure, respiratory depression, and coma. Therapy is usually symptomatic and adjuvant, and there is no specific antidote. If symptoms appear within 4 hours of taking the drug or if a very large dose is taken, vomiting, medicinal carbon (60-100 g for adults, 1-2 g per kg for children), and osmotic diarrhea can be used. Treatments such as hemodialysis, forced diuresis, urinary alkalization, and hemoperfusion are not useful because of the high protein binding rate of this drug.

5. Pharmacological properties:

Relief of symptoms or signs of osteoarthritis (degenerative arthritis)

5.1 Mechanism of Action:

Polmacoxib is a selective COX-2 inhibitor. Polmacoxib is a first-in-class dual COX2/carbonic anhydrase I/II inhibitor, a potential non-steroidal anti-inflammatory drug (NSAID) with postulated attenuated cardiovascular risk compared to selective COX2 inhibiting NSAIDs.

5.2 Pharmacodynamic properties:

Unlike other NSAIDs, polmacoxib has a dual mode of action: inhibition of COX-2 and binding to carbonic anhydrase (CA) with high affinity. A key function of CA is to regulate the pH level in the body through the interconversion between carbon dioxide and bicarbonate. Where COX-2 and CA coexist, the high-affinity binding of polmacoxib to CA reduces the COX-2 inhibitory activity of polmacoxib. Since the CV side effects of traditional NSAIDs and COX-2 inhibitors are associated with COX-2 inhibition in the CV system where CA is abundant it is theoretically possible that the dual action mechanism of polmacoxib may minimize the adverse CV effects of COX-2 inhibition.

5.3 Pharmacokinetic properties

Absorption: Test drug Polmacoxib Tab. 2 mg and control drug polmacoxib Capsule 2 mg were administered in a crossover test each to a total of 32 healthy adult subjects on an empty stomach. After administration, the pharmacokinetic parameters C_{max} and AUC, were evaluated. Variable(unit)

Variable(unit)	Reference drug	Test drug
C _{max} (ng/mL)	295.41 ± 40.79 (13.81)	321.36 ± 36.09 (11.23)
AUC _{0-∞} (ng-hr/mL)	68544.30 ± 15046.80 (21.95)	72423.10 ± 15241.00 (21.04)
AUC _{0-t} (ng-hr/mL)	75886.70 ± 19347.50 (25.50)	79956.30 ± 20741.10 (25.94)
t _{1/2} (hr)	187.35 ± 39.76 (39.76)	183.29 ± 46.70 (46.70)
T _{max} (hr) median (range)*	4.00 [2.000~10.000]	3.50 [1.000~24.100]
[Arithmetic mean ± SD (CV%) †Median value [Minimum value~Maximum value]		

Distribution: At this time, the mean steady-state C_{max} was 2,054 ng/mL in whole blood and 40 to 51 ng/mL in plasma

Metabolism: This drug is mainly metabolized by CYP3A4

Excretion: Mainly through feces, less through urine

Elderly: In patients with arthritis over 70 years of age, the blood drug concentration of this drug is 1.4 times higher than that in patients with arthritis between 40 and 69 years of age, so it should be administered with caution.

6. Nonclinical properties:

6.1 Animal Toxicology or Pharmacology:

In animal studies (rabbits and rats), administration of this drug has been shown to have reproductive toxicity, including teratogenesis, but the potential risk to human pregnancy is unknown.

In animal studies, the administration of drugs that inhibit prostaglandin synthesis has been shown to increase implantation failure. This drug was found to significantly reduce the mean number of corpus luteum, implantation, and viable embryos in rats when administered at a dose of 1 mg/kg/day or more.

It has been established that this drug may be transferred to the fetus through plasma-like or slightly higher concentrations in the breast milk of rats. Many drugs not only pass into breast milk, but if they do, serious adverse reactions in infants are of concern, so lactation or drug administration should be discontinued considering the importance of drug administration to nursing mothers.