

# Straza

(Piroxicam-β-Cyclodextrin)

اسٹرازا  
(پیروکسیم-بیٹا-سائیکلوڈیکسٹرین)

## COMPOSITION

Each **Straza** Piroxicam-β-Cyclodextrin 20mg tablet contains 20mg of Piroxicam-β-Cyclodextrin complex 191.2mg eq. to Piroxicam 20mg  
"Product contains Lactose"

## DESCRIPTION

**Straza** (Piroxicam-β-Cyclodextrin) tablet contain Piroxicam which is a member of the oxicam group of nonsteroidal anti-inflammatory drugs (NSAIDs).

## CLINICAL PHARMACOLOGY

### Mechanism of Action:

Piroxicam tablet are a nonsteroidal anti-inflammatory drug (NSAID) that exhibits anti-inflammatory, analgesic, and antipyretic activities in animal models. The mechanism of action of Piroxicam, like that of other NSAIDs, is not completely understood but may be related to prostaglandin synthetase inhibition.

## PHARMACOKINETICS

**Absorption:** Piroxicam is well absorbed following oral administration. Drug plasma concentrations are proportional for 10 and 20 mg doses and generally peak within three to five hours after medication. The prolonged half-life (50 hours) results in the maintenance of relatively stable plasma concentrations throughout the day on once daily doses and to significant accumulation upon multiple dosing. A single 20 mg dose generally produces peak Piroxicam plasma levels of 1.5 to 2 mcg/mL, while maximum drug plasma concentrations, after repeated daily ingestion of 20 mg Piroxicam tablet, usually stabilize at 3-8 mcg/mL. Most patients approximate steady state plasma levels within 7-12 days. Higher levels, which approximate steady state at two to three weeks, have been observed in patients in whom longer plasma half-lives of Piroxicam occurred.

With food there is a slight delay in the rate but not the extent of absorption following oral administration. The concomitant administration of antacids (aluminum hydroxide or aluminum hydroxide with magnesium hydroxide) have been shown to have no effect on the plasma levels of orally administered Piroxicam.

**Distribution:** The apparent volume of distribution of Piroxicam is approximately 0.14 L/kg. Ninety-nine percent of plasma Piroxicam is bound to plasma proteins. Piroxicam is excreted into human milk. The presence in breast milk has been determined during initial and long-term conditions (52 days). Piroxicam appeared in breast milk at about 1% to 3% of the maternal concentration. No accumulation of Piroxicam occurred in milk relative to that in plasma during treatment.

**Metabolism:** Metabolism of Piroxicam occurs by hydroxylation at the 5 position of the pyridyl side chain and conjugation of this product; by cyclodehydration; and by a sequence of reactions involving hydrolysis of the amide linkage, decarboxylation, ring contraction, and N-demethylation. In vitro studies indicate cytochrome P4502C9 (CYP2C9) as the main enzyme involved in the formation to the 5'-hydroxy-Piroxicam, the major metabolite (see Pharmacogenetics, and Special Populations, Poor Metabolizers of CYP2C9 Substrates). The biotransformation products of Piroxicam metabolism are reported to not have any anti-inflammatory activity.

**Excretion:** Piroxicam and its biotransformation products are excreted in urine and feces, with about twice as much appearing in the urine as in the feces. Approximately 5% of a Piroxicam dose is excreted unchanged. The plasma half-life (T<sub>1/2</sub>) for Piroxicam is approximately 50 hours.

## INDICATIONS AND USAGE

Carefully consider the potential benefits and risks of Piroxicam tablet and other treatment options before deciding to use Piroxicam tablet. Use the lowest effective dose for the shortest duration consistent with individual patient treatment goals. Piroxicam tablet are indicated:

- For relief of the signs and symptoms of osteoarthritis.
- For relief of the signs and symptoms of rheumatoid arthritis.

## DOSAGE AND ADMINISTRATION

Carefully consider the potential benefits and risks of Piroxicam tablet and other treatment options before deciding to use Piroxicam tablet. Use the lowest effective dose for the shortest duration consistent with individual patient treatment goals. After observing the response to initial therapy with Roxam tablet, the dose and frequency should be adjusted to suit an individual patient's needs.

For the relief of rheumatoid arthritis and osteoarthritis, the recommended dose is 20 mg given orally once per day. If desired, the daily dose may be divided. Because of the long half-life of Piroxicam tablet, steady-state blood levels are not reached for 7-12 days. Therefore, although the therapeutic effects of Piroxicam are evident early in treatment, there is a progressive increase in response over several weeks and the effect of therapy should not be assessed for two weeks.

## ADVERSE REACTIONS

In patients taking Piroxicam tablet or other NSAIDs, the most frequently reported adverse experiences occurring in approximately 1-10% of patients are:

**Cardiovascular System:** Edema.

**Digestive System:** Anorexia, abdominal pain, constipation, diarrhea, dyspepsia, elevated liver enzymes, flatulence, gross bleeding/perforation, heartburn, nausea, ulcers (gastric/duodenal), vomiting.

**Hemic and Lymphatic System:** Anemia, increased bleeding time.

**Nervous System:** Dizziness, headache.

**Skin and Appendages:** Pruritus, rash.

**Special Senses:** Tinnitus.

**Urogenital System:** Abnormal renal function.

Additional adverse experiences reported occasionally include:

**Body As a Whole:** Fever, infection, sepsis.

**Cardiovascular System:** Congestive heart failure, hypertension, tachycardia, syncope.

**Digestive System:** Dry mouth, esophagitis, gastritis, glossitis, hematemesis, hepatitis, jaundice, melena, rectal bleeding, stomatitis.

**Hemic and Lymphatic System:** Echinomiasis, eosinophilia, epistaxis, leukopenia, purpura, petechial rash, thrombocytopenia.

**Metabolic and Nutritional:** Weight changes, fluid retention.

**Nervous System:** Anxiety, asthenia, confusion, depression, dream abnormalities, drowsiness, insomnia, malaise, nervousness, paresthesia, somnolence, tremors, vertigo.

**Respiratory System:** Asthma, dyspnea.

**Skin and Appendages:** Alopecia, bruising, desquamation, erythema, photosensitivity, sweat.

**Special Senses:** Blurred vision.

**Urogenital System:** Cystitis, dysuria, hematuria, hyperkalemia, interstitial nephritis, nephrotic syndrome, oliguria/polyuria, proteinuria, renal failure, glomerulonephritis.

Other adverse reactions which occur rarely are:

**Body As a Whole:** Anaphylactic reactions, appetite changes, death, flu-like syndrome, pain (colic), serum sickness.

**Cardiovascular System:** Arrhythmia, exacerbation of angina, hypotension, myocardial infarction, palpitations, vasculitis.

**Digestive System:** Eruption, liver failure, pancreatitis.

**Hemic and Lymphatic System:** Agranulocytosis, hemolytic anemia, aplastic anemia, lymphadenopathy, pancytopenia.

**Hypersensitivity:** Positive ANA.

**Metabolic and Nutritional:** Hyperglycemia, hypoglycemia.

**Nervous System:** Akathisia, convulsions, coma, hallucinations, meningitis, mood alterations.

**Respiratory:** Respiratory depression, pneumonia.

**Skin and Appendages:** Angioedema, toxic epidermal necrosis, erythema multiforme, exfoliative dermatitis, onycholysis, Stevens-Johnson Syndrome, urticaria, vesiculobullous reaction.

**Special Senses:** Conjunctivitis, hearing impairment, swollen eyes.

**Reproductive system and breast disorders:** Female fertility decreased.

## DRUG INTERACTIONS

**Highly Protein Bound Drugs:** Piroxicam is highly protein bound and, therefore, might be expected to displace other protein bound drugs. Physicians should closely monitor patients for a change in dosage requirements when administering Piroxicam tablet to patients on other highly protein bound drugs.

**Aspirin:** When Piroxicam is administered with aspirin, its protein binding is reduced, although the clearance of free Piroxicam is not altered. Plasma levels of Piroxicam are depressed to approximately 80% of their normal values when Piroxicam is administered (20 mg/day) in conjunction with aspirin (3900 mg/day). The clinical significance of this interaction is not known; however, as with other NSAIDs, concomitant administration of Piroxicam and aspirin is not generally recommended because of the potential for increased adverse effects.

**Methotrexate:** NSAIDs have been reported to competitively inhibit methotrexate accumulation in rabbit kidney slices. This may indicate that they could enhance the toxicity of methotrexate. Caution should be used when NSAIDs are administered concomitantly with methotrexate.

**ACE-Inhibitors:** Reports suggest that NSAIDs may diminish the antihypertensive effect of ACE-inhibitors. This interaction should be given consideration in patients taking NSAIDs concomitantly with ACE-inhibitors. In patients who are elderly, volume-depleted (including those on diuretic therapy), or with compromised renal function, co-administration of NSAIDs, including selective COX-2 inhibitors, with ACE inhibitors, may result in deterioration of

renal function, including possible acute renal failure. These effects are usually reversible. **Diuretics:** Clinical studies, as well as postmarketing observations, have shown that Piroxicam tablet can reduce the natriuretic effect of furosemide and thiazides in some patients. This response has been attributed to inhibition of renal prostaglandin synthesis. During concomitant therapy with NSAIDs, the patient should be observed closely for signs of renal failure as well as to assure diuretic efficacy.

**Lithium:** NSAIDs have produced an elevation of plasma lithium levels and a reduction in renal lithium clearance. The mean minimum lithium concentration increased 15% and the renal clearance was decreased by approximately 20%. These effects have been attributed to inhibition of renal prostaglandin synthesis by the NSAID. Thus, when NSAIDs and lithium are administered concurrently, subjects should be observed carefully for signs of lithium toxicity. **Warfarin:** The effects of warfarin and NSAIDs on GI bleeding are synergistic, such that users of both drugs together have a risk of serious GI bleeding higher than users of either drug alone.

## Carcinogenesis, Mutagenesis, Impairment of Fertility

Piroxicam has not been adequately evaluated for carcinogenicity.

Piroxicam was not mutagenic in an Ames bacterial reverse mutation assay, or in a dominant lethal mutation assay in mice, and was not clastogenic in an in vivo chromosome aberration assay in mice. Reproductive studies in which rats were administered Piroxicam at doses of 2, 5, or 10 mg/kg/day (up to 5 times the maximum recommended human dose [MRHD] of 20 mg based on dog/m<sup>2</sup> 2 body surface area [BSA]) revealed no impairment of male or female fertility.

## USE IN SPECIFIC POPULATIONS

**Pregnancy:** Pregnancy Category C First and Second Trimester

**Pregnancy Category D Third Trimester:** There are no adequate and well-controlled studies of Piroxicam in pregnant women. Use of NSAIDs, including Piroxicam, during the third trimester of pregnancy increases the risk of premature closure of the ductus arteriosus. During the first and second trimesters of pregnancy, use Piroxicam only if the potential benefit justifies the potential risk to the fetus. During the third trimester of pregnancy, the patient should be apprised of the potential hazard to a fetus.

**Labor and Delivery:** The effects of Piroxicam on labor or delivery in pregnant women are unknown. In rat studies with Piroxicam, as with other drugs known to inhibit prostaglandin synthesis, delayed parturition and an increased incidence of stillbirth were noted at doses equivalent to the MRHD of Piroxicam.

**Nursing Mothers:** Piroxicam is present in human milk at about 1% to 3% of the maternal concentration. No accumulation of Piroxicam occurred in milk relative to that in maternal plasma during treatment. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for Piroxicam and any potential adverse effects on the breastfed child from the drug or from the underlying maternal condition. Exercise caution when Piroxicam is administered to a nursing woman.

**Pediatric Use:** Safety and effectiveness in pediatric patients have not been established.

**Geriatric Use:** As with any NSAID, caution should be exercised in treating the elderly (65 years and older). Most spontaneous reports of fatal GI events with NSAIDs are in the elderly or debilitated patients and, therefore, care should be taken in treating this population. In addition to a past history of ulcer disease, older age and poor general health status (among other factors) may increase the risk for GI bleeding. To minimize the potential risk of an adverse GI event, the lowest effective dose should be used for the shortest possible duration.

## WARNINGS AND PRECAUTIONS

**General:** Piroxicam tablet cannot be expected to substitute for corticosteroids or to treat corticosteroid insufficiency. Abrupt discontinuation of corticosteroids may lead to disease exacerbation. Patients on prolonged corticosteroid therapy should have their therapy tapered slowly if a decision is made to discontinue corticosteroids. The pharmacological activity of Piroxicam tablet in reducing fever and inflammation may diminish the utility of these diagnostic signs in detecting complications of presumed noninfectious, painful conditions.

**Hepatic Effects:** Borderline elevations of one or more liver tests may occur in up to 15% of patients taking NSAIDs, including Piroxicam tablet. 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 approximately 1% of patients in clinical trials with NSAIDs. In addition, rare cases of severe hepatic reactions, including jaundice and fatal fulminant hepatitis, liver necrosis and hepatic failure, some of them with fatal outcomes have been reported.

A patient with symptoms and/or signs suggesting liver dysfunction, or in whom an abnormal liver test has occurred, should be evaluated for evidence of the development of more severe hepatic reaction while on therapy with Piroxicam tablet. If clinical signs and symptoms consistent with liver disease develop, or if systemic manifestations occur (e.g., eosinophilia, rash, etc.), Piroxicam tablet should be discontinued.

**Hematological Effects:** Anemia is sometimes seen in patients receiving NSAIDs, including Piroxicam tablet. This may be due to fluid retention, occult or gross GI blood loss, or an incompletely described effect upon erythropoiesis. Patients on long-term treatment with NSAIDs, including Piroxicam tablet, should have their hemoglobin or hematocrit checked if they exhibit any signs or symptoms of anemia.

NSAIDs inhibit platelet aggregation and have been shown to prolong bleeding time in some patients. Unlike aspirin, their effect on platelet function is quantitatively less, of shorter duration, and reversible. Patients receiving Piroxicam tablet who may be adversely affected by alterations in platelet function, such as those with coagulation disorders or patients receiving anticoagulants, should be carefully monitored.

**Ophthalmologic Effects:** Because of reports of adverse eye findings with nonsteroidal anti-inflammatory agents, it is recommended that patients who develop visual complaints during treatment with Piroxicam tablet have ophthalmic evaluations.

**Preexisting 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, including bronchospasm, between aspirin and other nonsteroidal anti-inflammatory drugs has been reported in such aspirin-sensitive patients, Piroxicam tablet should not be administered to patients with this form of aspirin sensitivity and should be used with caution in patients with preexisting asthma.

## REVERSIBLE DELAYED OVULATION

Based on the mechanism of action, the use of prostaglandin-mediated NSAIDs, including Piroxicam, may delay or prevent rupture of ovarian follicles, which has been associated with reversible infertility in some women. Animal studies have shown that administration of prostaglandin synthesis inhibitors has the potential to disrupt prostaglandin-mediated follicular rupture required for ovulation. Small studies in women taking NSAIDs have also shown a reversible delay in ovulation. Therefore, in women who have difficulties conceiving or who are undergoing investigation of infertility, withdrawal of NSAIDs, including Piroxicam, should be considered.

## CONTRAINDICATIONS

Piroxicam tablet are contraindicated in patients with known hypersensitivity to Piroxicam. Piroxicam tablet should not be given to 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 patients.

## OVERDOSAGE

Symptoms following acute NSAID overdoses are usually limited to lethargy, drowsiness, nausea, vomiting, and epigastric pain, which are generally reversible with supportive care. Gastrointestinal bleeding can occur. Hypertension, acute renal failure, respiratory depression, and coma may occur, but are rare. Anaphylactoid reactions have been reported with therapeutic ingestion of NSAIDs, and may occur following an overdose.

Patients should be managed by symptomatic and supportive care following an NSAID overdose. There are no specific antidotes. Emesis and/or activated charcoal (60-100 g in adults, 1-2 g/kg in children) and/or osmotic cathartic may be indicated. The long plasma half-life of Piroxicam should be considered when treating an overdose with Piroxicam. Experiments in dogs have demonstrated that the use of multiple-dose treatments with activated charcoal could reduce the half-life of Piroxicam by more than 50% and systemic bioavailability by as much as 37% when activated charcoal is given as late as 6 hours after ingestion of Piroxicam. Forced diuresis, alkalization of urine, hemodialysis, or hemoperfusion may not be useful due to high protein binding.

## PRESENTATION

**Straza** 20mg Tablets : 2 x 10's/pack.

## DOSAGE

As directed by the physician.

## INSTRUCTIONS

Store below 30°C.  
Protect from sunlight and moisture.  
Keep out of reach of children.

Detailed prescribing information is available on request.

Manufactured by:  
**AsianContinental (Pvt.) Ltd.**  
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Karachi-Pakistan.



An ISO Certified Company

LF7/049/00

خوراک:  
ڈاکٹری ہدایت کے مطابق استعمال کریں۔  
ہدایات:  
دوا کو ۳۰ ڈگری سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔  
صوبہ اوڈیسی سے بچائیں۔  
بچوں کی پہنچ سے دور رکھیں۔