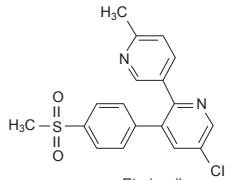
# Starcox™
[ E t o r i c o x i b ]

# اسٹارکوکس

Tablets 60mg, 90mg & 120mg

Starcox (Etoricoxib) is a member of a new class of arthritis/analgesia medications called Coxibs. Chemically, etoricoxib is described as, 5-Chloro-6'-methyl-3-[p-(methylsulfonyl) phenyl]-2, 3'-bipyridine. The molecular formula is $C_{18}H_{15}ClN_2O_2S$ & the structural formula is:



Etoricoxib

**QUALITATIVE AND QUANTITATIVE COMPOSITION**
Starcox (Etoricoxib) is available for oral administration as:

Starcox Tablets 60mg
Each film-coated tablet contains:
Etoricoxib…60mg

Starcox Tablets 90mg
Each film-coated tablet contains:
Etoricoxib…90mg

Starcox Tablets 120mg
Each film-coated tablet contains:
Etoricoxib…120mg

**CLINICAL PHARMACOLOGY**
**Mechanism of Action**
Etoricoxib is an oral, selective cyclo-oxygenase-2 (COX-2) inhibitor. Etoricoxib produced dose-dependent inhibition of COX-2 without inhibition of COX-1 at doses up to 150mg daily. Etoricoxib does not inhibit gastric prostaglandin synthesis and has no effect on platelet function.
Selective inhibition of COX-2 by etoricoxib decreases the synthesis of prostanoid mediators of pain, inflammation and fever with decreased potential for GI toxicity and effects on platelet aggregation.

**Pharmacokinetics**
*Absorption*
Etoricoxib is well absorbed from the gastrointestinal tract after oral doses. The absolute bioavailability is 100%. Peak plasma concentrations are reached in about 1 hour in fasted adults.

*Effect of food:* Food delays absorption by about 2 hours, although it has no effect on the extent of absorption. The onset of the effect of medicinal product may be faster when administered without food. This should be considered when rapid symptomatic relief is needed.

*Distribution*
Etoricoxib is approximately 92% bound to human plasma protein over the range of concentrations of 0.05 to 5mcg/mL. The volume of distribution at steady state ($V_{dss}$) was approximately 120L.

*Metabolism*
Etoricoxib is extensively metabolized with less than 1% of a dose recovered in the urine as the parent drug. The major route of metabolism is via cytochrome P450 isoenzymes including CYP3A4 to form the 6'-hydroxymethyl derivative of etoricoxib, which is then oxidised to the 6'-carboxylic acid derivative, the major metabolite. Both are inactive or only weak cyclo-oxygenase-2 (COX-2) inhibitors.

*Excretion*
Excretion is mainly via the urine (70%) with only 20% of a dose appearing in the feces, mostly as metabolites. Less than 2% is recovered as unchanged drug. Steady state concentrations of etoricoxib are reached within seven days of once daily administration of 120mg. At steady state the half-life of etoricoxib is about 22hours.

**Special Population**
*Hepatic Impairment*
Patients with mild hepatic dysfunction (Child-Pugh score 5-6) administered etoricoxib 60mg once daily has an approximately 16% higher mean AUC as compared to healthy subjects given the same regimen. Patients with moderate hepatic dysfunction (Child-Pugh score 7-9) administered etoricoxib 60mg every other day has similar mean AUC to the healthy subjects given etoricoxib 60mg once daily.

**THERAPEUTIC INDICATIONS**
Starcox (Etoricoxib) is indicated for:
- Symptomatic relief of osteoarthritis (OA) and rheumatoid arthritis (RA)
- The management of ankylosing spondylitis (AS)
- Treatment of acute gouty arthritis
- Relief of acute pain
- Relief of chronic musculoskeletal pain
- Treatment of primary dysmenorrhea
- Treatment of moderate to severe acute post-operative pain associated with dental surgery
- Treatment of moderate to severe acute post-operative pain associated with abdominal gynecological surgery

**DOSAGE AND ADMINISTRATION**
*Osteoarthritis*
The recommended dose is 30mg once daily. In some patients with insufficient relief from symptoms, an increased dose of 60mg once daily may increase efficacy. The dose should not exceed 60mg daily.

*Rheumatoid Arthritis & Ankylosing Spondylitis*
The recommended dose is 60mg once daily. In some patients with insufficient relief from symptoms, an increased dose of 90mg once daily may increase efficacy. Once the patient is clinically stabilised, down-titration to a 60mg once daily dose may be appropriate. The dose should not exceed 90mg daily.

*Acute Gouty Arthritis*
The recommended dose is 120mg once daily. Etoricoxib should not exceed 120mg daily, limited to a maximum of 8 days treatment.

*Acute Pain*
The recommended dose is 120mg once daily. Etoricoxib should be used only for the acute symptomatic period, limited to a maximum of 8 days treatment.

*Chronic Musculoskeletal Pain*
The recommended dose is 60mg once daily. Etoricoxib should be used only for the acute symptomatic period, limited to a maximum of 8 days treatment.

*Primary Dysmenorrhea*
The recommended dose is 120mg once daily.

*Post-Operative Dental Surgery Pain*
The recommended dose is 90mg once daily. It should not exceed 90mg daily, limited to a maximum of 3 days.

*Post-Operative Gynecological Pain*
The recommended dose is 90mg once daily. The initial dose should be administered shortly before surgery. The dose can be increased to a maximum 120mg once daily.

Starcox (Etoricoxib) Tablets may be taken with or without food. Cardiovascular risks of etoricoxib may increase with dose and duration of exposure, the shortest duration possible and the lowest effective daily dose should be used. The patient's need for symptomatic relief and response to therapy should be re-evaluated periodically, especially in patients with osteoarthritis.

**Special Population**
*Hepatic Impairment*
Regardless of indication, in patients with mild hepatic dysfunction (Child-Pugh score 5-6) a dose of 60mg once daily should not be exceeded. In patients with moderate hepatic dysfunction (Child-Pugh score 7-9) regardless of indication, the dose of 30mg once daily should not be exceeded.

**ADVERSE REACTIONS**
*Common*
Alveolar osteitis, edema/fluid retention, dizziness, headache, palpitations, arrhythmia, hypertension, bronchospasm, constipation, flatulence, gastritis, acid reflux, diarrhea, dyspepsia, epigastric discomfort, nausea, vomiting, ALT increased, AST increased, ecchymosis, asthenia/fatigue and flu-like disease.

*Uncommon*
Gastroenteritis, upper respiratory infection, urinary tract infection, anemia, leukopenia, thrombocytopenia, hypersensitivity, increase or decrease appetite, weight gain, anxiety, depression, mental acuity decreased, hallucinations, dysgeusia, insomnia, paresthaesia/hypaesthesia, somnolence, blurred vision, conjunctivitis, tinnitus, vertigo, atrial fibrillation, tachycardia, congestive heart failure, non-specific ECG changes, angina pectoris, myocardial infarction, flushing, cerebrovascular accident, transient ischemic attack, hypertensive crisis, vasculitis, cough, dyspnea, epistaxis, abdominal distention, bowel movement pattern change, constipation, dry mouth, gastroduodenal ulcer, peptic ulcer, irritable bowel syndrome, pancreatitis, facial edema, pruritus, rash, erythema, urticaria, muscular cramp/spasm, musculoskeletal pain/stiffness, proteinuria, serum creatinine increased, renal failure/renal insufficiency, chest pain, blood urea nitrogen increased, creatine phosphokinase increased, hyperkalemia and uric acid increased.

*Rare*
Angioedema/anaphylactic/anaphylactoid reactions including shock, confusion, restlessness, hepatitis, hepatic failure, jaundice, Stevens-Johnson syndrome, toxic epidermal necrolysis, fixed drug eruption and blood sodium decreased.

**"To report SUSPECTED ADVERSE REACTIONS to Getz Pharma's Pharmacovigilance Section, please contact at dsafety@getzpharma.com or +92-21-38636363"**

**CONTRAINDICATIONS**
Etoricoxib is contraindicated in:
- Hypersensitivity to active substance or to any of the excipient of the product.
- Active peptic ulceration or active gastrointestinal (GI) bleeding.
- Patients who have experienced bronchospasm, acute rhinitis, nasal polyps, angioneurotic edema, urticaria or allergic-type reactions after taking acetylsalicylic acid or NSAIDs including COX-2 (cyclooxygenase-2) inhibitors.
- Severe hepatic dysfunction (serum albumin <25 g/L or Child-Pugh score ≥ 10).
- Estimated renal creatinine clearance < 30mL/min.
- Children and adolescents under 16 years of age.
- Inflammatory bowel disease.
- Congestive heart failure (NYHA II-IV).
- Patients with hypertension whose blood pressure is persistently elevated above 140/90mmHg and has not been adequately controlled.
- Established ischemic heart disease, peripheral arterial disease and/or cerebrovascular disease.

**PRECAUTIONS**
*Gastrointestinal effects*
Caution is advised with treatment of patients most at risk of developing a gastrointestinal complication with NSAIDs; the elderly, patients using any other NSAID or acetylsalicylic acid concomitantly or patients with a prior history of gastrointestinal disease, such as ulceration and GI bleeding.

*Cardiovascular effects*
Patients with significant risk factors for cardiovascular events (e.g., hypertension, hyperlipidemia, diabetes mellitus, smoking) should only be treated with etoricoxib after careful consideration.

*Aspirin substitution*
COX-2 selective inhibitors are not a substitute for acetylsalicylic acid for prophylaxis of cardiovascular thrombo-embolic diseases because of their lack of antiplatelet effect. Therefore antiplatelet therapies should not be discontinued.

*Renal effects*
In compromised renal perfusion, administration of etoricoxib may cause a reduction in prostaglandin formation and secondarily, in renal blood flow and thereby impair renal function. Monitoring of renal function in such patients should be considered.

*Fluid retention, edema and hypertension*
Fluid retention, edema and hypertension have been observed in patients taking etoricoxib. All Nonsteroidal Anti-inflammatory Drugs (NSAIDs), including etoricoxib, can be associated with new onset or recurrent congestive heart failure. Caution should be exercised in patients with a history of cardiac failure, left ventricular dysfunction or hypertension and in patients with pre-existing edema from any other reason. If blood pressure raises significantly, alternative treatment should be considered.

*Hepatic effects*
Patients should be monitored with signs and symptoms of liver dysfunction or with abnormal liver function test. If signs of hepatic insufficiency occur or if persistently abnormal liver function tests (three times the upper limit of normal) are detected, etoricoxib should be discontinued.

*Hypersensitivity*
Etoricoxib should be used with caution in patients who have previously experienced acute asthmatic attacks, urticaria or rhinitis precipitated by salicylates or non-selective cyclooxygenase inhibitors.

*General*
Some selective COX-2 inhibitors have been associated with an increased risk of skin reactions in patients with a history of any drug allergy. Etoricoxib should be discontinued at the first appearance of skin rash, mucosal lesions or any other sign of hypersensitivity.
Caution should be used when initiating treatment with etoricoxib in patients with considerable dehydration. It is advisable to rehydrate patients prior to starting therapy with etoricoxib.

**Pregnancy**
Etoricoxib is contraindicated in pregnancy. If a woman becomes pregnant during treatment, etoricoxib must be discontinued.

**Nursing Mother**
Women who use etoricoxib must not breast feed.

**DRUG INTERACTIONS**
*Oral anticoagulants*
Patients receiving chronic warfarin therapy, the administration of etoricoxib 120mg daily is associated with an increase in prothrombin time International Normalized Ratio (INR). Therefore patient receiving oral anticoagulants should be closely monitored for their prothrombin time INR.

*Diuretics, ACE inhibitors and Angiotensin II antagonists*
In patients with compromised renal function the co-administration of an ACE inhibitor or Angiotensin II antagonist and agents that inhibit cyclo-oxygenase may result in further deterioration of renal function, including possible acute renal failure, which is usually reversible. Therefore, the combination should be administered with caution especially in the elderly.

*Acetylsalicylic Acid*
Concomitant administration of low-dose acetylsalicylic acid with etoricoxib may result in an increased rate of GI ulceration or other complications compared to use of etoricoxib alone.

*Ciclosporin and Tacrolimus*
Coadministration of Ciclosporin or Tacrolimus with any NSAID may increase the nephrotoxic effect of Ciclosporin or Tacrolimus.

*Lithium*
NSAIDs decrease lithium renal excretion and therefore increase lithium plasma levels. If necessary, monitor blood lithium closely and adjust the lithium dosage while the combination is being taken and when the NSAID is withdrawn.

*Methotrexate*
Adequate monitoring for methotrexate-related toxicity is recommended when etoricoxib and methotrexate are administered concomitantly.

*Oral contraceptives*
Etoricoxib given concomitantly with oral contraceptive containing ethinyl estradiol and norethindrone increase the steady state AUC of ethinyl estradiol. This increase in concentration should be considered when selecting an appropriate oral contraceptive for use with etoricoxib.

*Hormone Replacement Therapy (HRT)*
Administration of etoricoxib with hormone replacement therapy increases the mean steady state AUC of unconjugated estrone, equilin and 17-ß-estradiol. These increase in oestrogenic concentration should be taken into consideration when selecting post-menopausal hormone therapy for use with etoricoxib.

*Digoxin*
Coadministration of etoricoxib with digoxin, increase digoxin $C_{max}$. Therefore, patients at high risk of digoxin toxicity should be monitored when etoricoxib and digoxin are administered concomitantly.

*Sulfotransferases*
Caution should be considered when administering etoricoxib concurrently with other drugs primarily metabolised by human sulfotransferases (e.g., oral salbutamol and minoxidil).

*Rifampicin*
Coadministration of etoricoxib with rifampicin, decrease etoricoxib plasma concentrations. This interaction may result in recurrence of symptoms when etoricoxib is coadministered with rifampicin.

**OVERDOSAGE**
*Symptoms:*
The most frequently observed adverse experiences are consistent with the safety profile for etoricoxib (e.g., gastrointestinal events, cardiorenal events).

*Treatment:*
In the event of overdose, it is reasonable to employ the usual supportive measures, e.g., remove unabsorbed material from the GI tract, employ clinical monitoring and institute supportive therapy, if required. Etoricoxib is not dialysable by haemodialysis; it is not known whether etoricoxib is dialysable by peritoneal dialysis.

**HOW SUPPLIED**
Starcox (Etoricoxib) Tablets 60mg are available in blister pack of 10's.
Starcox (Etoricoxib) Tablets 90mg are available in blister pack of 14's.
Starcox (Etoricoxib) Tablets 120mg are available in blister pack of 7's.

**STORAGE**
Store at 25°C (Excursions permitted between 15°C - 30°C).
Protect from sunlight and moisture.

The expiration date refers to the product correctly stored at the required conditions.

***Keep out of reach of children.***

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

**Please read the contents carefully before use.**
**This package insert is continually updated from time to time.**

Manufactured by:
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