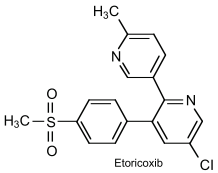
ETOGESIC
(ETORICOXIB)
60mg Tablets

ایٹوجیزک (ایٹوریکوکسب)

DESCRIPTION:
Etogesic (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 C18H15ClN2O2S & the structural formula is:



Etoricoxib

QUALITATIVE & QUANTITATIVE COMPOSITION
Etogesic (Etoricoxib) is available for oral administration as:

Etogesic Tablets 60mg
Each film-coated tablet contains:
Etoricoxib ... 60mg

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 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.
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 (Vdss) was approximately 120L.
Metabolism
Etoricoxib is extensively metabolized with less than 2% of a dose recovered in the urine as the parent drug. The major route of metabolism is via cytochrome P450 is oenzymes 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
Etogesic (Etoricoxib) is indicated for:
- Symptomatic relief of osteoar thr itis (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 & ADMINISTRATION
Osteoarthritis
The recommended dose is 30mg or 60mg once daily.
Rheumatoid Arthritis & Ankylosing Spondylitis
The recommended dose is 90mg once daily.
Acute Gouty Arthritis
The recommended dose is 120mg once daily. Etoricoxib 120mg should be used only for the acute symptomatic period, limited to a maximum of 8 days treatment.
Acute Pain
The recommended dose is 120mg once daily. Etoricoxib 120mg 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.
Primary Dysmenorrhea
The recommended dose is 120mg once daily.
Post-Operative Dental Pain
The recommended dose is 90mg once daily.
Post-Operative Gynecological Pain
The recommended dose is 90mg once daily. The initial dose should be administered shortly before surgery. The dose can be incr eased to a maximum 120mg once daily.
Etogesic (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 60mg every other day should not be exceeded; administration of 30mg once daily can also be considered.

ADVERSE REACTIONS
Common
Alveolar osteitis, oedema/ fluid retention, dizziness, headache, palpitations, hypertension, gastrointestinal disorders (e.g., abdominal pain, flatulence, heartburn) diarrhea, dyspepsia, epigastric discomfort, nausea, ALT increased, AST increased, ecchymosis, asthenia/fatigue and flu-like disease.
Uncommon
Gastroenteritis, upper respiratory infection, urinary tract infection, anemia, leukopenia, thrombocytopenia, increase or decrease appetite, weight gain, anxiety, depression, mental acuity decreased, dysgeusia, insomnia, paresthaesia/hypaesthesia, somnolence, blurred vision, conjunctivitis, tinnitus, vertigo, atrial fibrillation, congestive heart failure, non specific ECG changes, angina pectoris, myocardial infarction, flushing, cerebrovascular accident, transient ischemic attack, cough, dyspnea, epistaxis, abdominal distention, acid reflux, bowel movement pattern change, constipation, dry mouth, gastroduodenal ulcer, irritable bowl syndrome, oesophagitis, oral ulcer, vomiting, gastritis, facial oedema, pruritus, rash, muscular cramp/spasm, musculoskeletal pain/stiffness, proteinuria, serum creatinine increased, chest pain, blood urea nitrogen increased, creatine phosphokinase increased, hyperkalemia and uric acid increased.

Rare
Erythema and blood sodium decreased.

Very Rare
Hypersensitivity reactions including angioedema, anaphylactic/anaphylactoid reactions including shock, confusion, hallucinations, hypertensive crisis, bronchospasm, pepticulcers including gastrointestinal perforation and bleeding, hepatitis, urticaria, Stevens-Johnson syndrome, toxic epidermal necrolysis and renal insufficiency including renal failure.

CONTRAINDICATIONS
Etoricoxib is contraindicated in:

- Hypersensitivity to active substance or to any of the excipients.
- Active peptic ulceration or active gastrointestinal (GI) bleeding.
- Patients who have experienced bronchospasm, acute rhinitis, nasal polyps, angioneurotic oedema, 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 hypertens ion 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.

Pregnancy
Etoricoxib is contraindic ated in pregnancy. If a woman becomes pregnant during treatment, etoricoxib must be discontinued.
Nursing Mother Women who use etoricoxib must not breast feed.

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 Patient s with signific ant 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. Caution should be used when initia ting treatment with etoricoxib in patients with considerable dehydration. It is advisable to rehydrate patients prior to starting therapy with etoricoxib.
Fluid retention, oedema and hypertension
Fluid retention, oedema 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 oedema from any other reason. Etoricoxib should be stopped if the patient's blood pressure is persistently raised.
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.
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 poss ible 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 norethindr one increase the steady state AUC of ethiny l 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 Cmax. 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.

OVER DOSAGE
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 hemodialysis, it is not known whether etoricoxib is dialysable by peritoneal dialysis.
STORAGE
Store below 30°C
Protect from sunlight and moisture.
The expiration date refers to the product correctly stored at the required conditions.
HOW SUPPLIED
Etogesic (Etoricoxib) Tablets 60mg are available in blister pack of 10's.

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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