TORXIB 60mg

(E t o r i c o x i b)

Tablets

ٹورزیب ۶۰ ملی گرام

(ایٹوریکوکسب) ٹیبلٹس

QUALITATIVE AND QUANTITATIVE COMPOSITION

Torxib Tablets 60mg

Each film-coated tablet contains:

Etoricoxib……60 mg

Innovator's Specification

DESCRIPTION:

Etoricoxib is a new COX-2 selective inhibitor. Etoricoxib selectively inhibits isoform 2 of cyclooxygenase enzyme (COX-2). This reduces the generation of prostaglandins (PGs) from arachidonic acid.

CLINICAL PHARMACOLOGY:

Mechanism of Action: Etoricoxib is an oral, selective cyclo-oxygenase-2 (COX-2) inhibitor within the clinical dose range. Across clinical pharmacology studies, Torxib produced dose-dependent inhibition of COX-2 without inhibition of COX-1 at doses up to 150 mg daily. Etoricoxib did not inhibit gastric prostaglandin synthesis and had no effect on platelet function. **Pharmacokinetics: Absorption:** Orally administered etoricoxib is well absorbed. The absolute bioavailability
is approximately 100%. The pharmacokinetics of etoricoxib are linear across the clinical dose range. Dosing with food (a high-fat meal) had no effect on the extent of absorption of etoricoxib after administration of a 120mg dose. **Distribution:** Etoricoxib is approximately 92% bound to human plasma protein over the range of concentrations of 0.05 to 5 μg/ml. The volume of distribution at steady state (Vdss) was approximately 120L in humans. Etoricoxib crosses the placenta in rats and rabbits, and the blood-brain barrier in rats. **Biotransformation:** Etoricoxib is extensively metabolised with <1% of a dose recovered in urine as the parent drug. The major route of metabolism to form the 6'-hydroxymethyl derivative is catalyzed by CYP enzymes. Five metabolites have been identified in man. The principal metabolite is the 6'-carboxylic acid derivative of etoricoxib formed by further oxidation of the 6'-hydroxymethyl derivative. None of these metabolites inhibit COX-1. **Elimination:** Elimination of etoricoxib occurs almost exclusively through metabolism followed by renal excretion. Steady state concentrations of etoricoxib are reached within seven days of once daily administration of 120 mg, with an accumulation ratio of approximately 2, corresponding to a half-life of approximately 22 hours. The plasma clearance after a 25-mg intravenous dose is estimated to be approximately 50 ml/min. **Pharmacodynamics:** Etoricoxib is an oral, selective cyclo-oxygenase-2 (COX-2) inhibitor, cyclooxygenase is responsible for generation of prostaglandins. Two isoforms, COX-1 and COX-2, have been identified. COX-2 is the isoform of the enzyme that has been shown to be induced by pro-inflammatory stimuli and has been postulated to be primarily responsible for the synthesis of prostanoid mediators of pain, inflammation, and fever. COX-2 is also involved in ovulation, implantation and closure of the ductus arteriosus, regulation of renal function, and central nervous system functions (fever induction, pain perception and cognitive function). It may also play a role in ulcer healing. COX-2 has been identified in tissue around gastric ulcers in man but its relevance to ulcer

healing has not been established.

INDICATIONS AND USAGE:

Etoricoxib is indicated in adults and adolescents 16 years of age and older for the symptomatic relief of osteoarthritis (OA), rheumatoid arthritis (RA), ankylosing spondylitis, and the pain and signs of inflammation associated with acute gouty arthritis. Etoricoxib is indicated in adults and adolescents 16 years of age and older for the short-term treatment of moderate pain associated with dental surgery. **Contraindications:** Hypersensitivity to the active substance or to any of the excipients.• Active peptic ulceration or active gastro-intestinal (GI) bleeding. • Patients who, after taking acetylsalicylic acid or NSAIDs including COX-2 (cyclooxygenase-2) inhibitors, experience bronchospasm, acute rhinitis, nasal polyps, angioneurotic oedema, urticaria, or allergic-type reactions. • Pregnancy and lactation. • Severe hepatic dysfunction (serum albumin <25 g/l or Child-Pugh score ≥10). • Estimated renal creatinine clearance <30 ml/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 140/90 mmHg and has not been adequately controlled.• Established ischaemic heart disease, peripheral arterial disease, and/or cerebrovascular disease.

INTERACTIONS:

Drug Interactions: Pharmacodynamic interactions: Oral anticoagulants(warfarin): Torxib when administered with warfarin increases 13%, prothrombin time (INR). **Diuretics, ACE inhibitors and Angiotensin II Antagonists:** NSAIDs may reduce the effect of diuretics and other antihypertensive drugs. **Acetylsalicylic Acid:** Etoricoxib can be used concomitantly with acetylsalicylic acid at doses used for cardiovascular prophylaxis (low-dose acetylsalicylic acid). However, 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. **Cyclosporin and tacrolimus:** Coadministration of cyclosporin or tacrolimus with any NSAID may increase the nephrotoxic effect of cyclosporin or tacrolimus. **Pharmacokinetic interactions: 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:** etoricoxib 120 mg increased methotrexate plasma concentrations by 28% and reduced renal clearance of methotrexate by 13%. Adequate monitoring for methotrexate-related toxicity is recommended when etoricoxib and methotrexate are administered concomitantly. **Oral contraceptives:** Etoricoxib 60 mg given concomitantly with an oral contraceptive containing 35 micrograms ethinyl estradiol (EE) and 0.5 to 1 mg norethindrone for 21 days increased the steady state AUC0-24hr of EE by 37%. Etoricoxib 120 mg given with the same oral contraceptive concomitantly or separated by 12 hours, increased the steady state AUC0-24hr of EE by 50 to 60%. This increase in EE concentration should be considered when selecting an oral contraceptive for use with etoricoxib. **Hormone Replacement Therapy (HRT):** Administration of etoricoxib 120 mg with hormone replacement therapy consisting of conjugated estrogens (0.625 mg Etoricoxib for 28 days, increased the mean steady state AUC0-24hr of unconjugated estrone (41%), equilin (76%), and 17-β-estradiol (22%). **Prednisone/prednisolone:** Etoricoxib did not have clinically important effects on the pharmacokinetics of prednisone/prednisolone. **Digoxin:** Etoricoxib 120 mg when administered with digoxin, there was an increase in digoxin Cmax (approximately 33%). Patients at high risk of digoxin toxicity should be monitored for this when etoricoxib and digoxin are administered concomitantly.
Effect of etoricoxib on drugs metabolised by sulfotransferases: Etoricoxib is an inhibitor of human sulfotransferase activity, particularly SULT1E1, and has been shown to increase the serum concentrations of ethinyl estradiol. It may be prudent to exercise care when administering etoricoxib concurrently with other drugs primarily metabolised by human sulfotransferases (e.g., oral salbutamol and minoxidil).Effect of

etoricoxib on drugs metabolised by CYP isoenzymes: etoricoxib is not expected to inhibit cytochromes P450 (CYP) 1A2, 2C9, 2C19, 2D6, 2E1 or 3A4. **Effects of other drugs on the pharmacokinetics of etoricoxib:** The main pathway of etoricoxib metabolism is dependent on CYP enzymes. CYP3A4 appears to contribute to the metabolism of etoricoxib in vivo. In vitro studies indicate that CYP2D6, CYP2C9, CYP1A2 and CYP2C19 also can catalyse the main metabolic pathway, but their quantitative roles have not been studied in vivo. **Ketoconazole:** Ketoconazole, a potent inhibitor of CYP3A4, dosed at 400 mg once a day for 11 days to healthy volunteers, did not have any clinically important effect on the single-dose pharmacokinetics of 60 mg etoricoxib (43% increase in AUC). **Voriconazole and Miconazole:** Co-administration of either oral voriconazole or topical miconazole oral gel, strong CYP3A4 inhibitors, with etoricoxib caused a slight increase in exposure to etoricoxib, but is not considered to be clinically meaningful based on published data. **Rifampicin:** Co-administration of etoricoxib with rifampicin, a potent inducer of CYP enzymes, produced a 65% decrease in etoricoxib plasma concentrations.
Antacids: Antacids do not affect the pharmacokinetics of etoricoxib to a clinically relevant extent.

USE IN SPECIFIC POPULATION:

Conception and contraception: Long term use of some NSAIDs is associated with reduced female fertility, which is reversible on stopping treatment.
Pregnancy: Teratogenic in animal studies. Avoid during the third trimester (risk of closure of fetus ductus arteriosus in utero and possibly persistent by pulmonary hypertension of the newborn); onset of labour may be delayed and duration may be increased. **Breast Feeding:** Use with caution during breastfeeding present in milk in animal studies. **Hepatic Impairment Use with caution;** there is an increased risk of gastro-intestinal bleeding and fluid retention. Avoid in severe liver disease. **Dose Adjustment:** Max. 60mg daily in mild impairment Max.60 mg on alternate days or 30mg once daily in moderate impairment. **Renal Impairment:** Avoid if possible or use with caution. In adults: Avoid if eGFR less than 30mL/minute/1.73m^2. In children: Avoid if eGFR less than 30mL/minute/1.73m^2. **Dose Adjustment:** The lowest effective dose should be used for the shortest possible duration. **Monitoring:** In renal impairment monitor renal function; sodium and water retention may occur and renal function may deteriorate, possibly leading to renal failure. **Monitoring Requirements:** Monitor blood pressure before treatment, 2 weeks after initiation and periodically during treatment.

PRECAUTIONS:

Allergic disorders, cardiac impairment (NSAIDs may impair renal function), coagulation defects, connective-tissue disorders, Crohn's disease (may be exacerbated), dehydration, elderly (risk of serious side effects and fatalities). History of cardiac failure, hypertension, left ventricular dysfunction, oedema, risk factors for cardiovascular events, ulcerative colitis (may be exacerbated).

DOSAGE AND ADMINISTRATION:

Pain and inflammation in osteoarthritis: By Mouth: Child 16-17 years: 30mg once daily, increased if necessary to 60 mg once daily. **Adult:** 30mg once daily, increased if necessary to 60mg once daily. Pain and inflammation in rheumatoid arthritis Ankylosing spondylitis: **By Mouth:** Child 16-17 years: 60mg once daily, increased if necessary to 90 mg once daily. **Adult:** 60mg once daily, increased if necessary to 90mg once daily. **Acute Gout: By Mouth:** Child 16-17 years: 120mg once daily for maximum 8 days. Adult: 120mg once daily for maximum 8 days. **Acute pain conditions:** For acute pain conditions, etoricoxib should be used only for the acute symptomatic period. **Postoperative dental surgery pain:** The recommended dose is 90 mg once daily, limited to a maximum of 3 days. Some patients may require other postoperative analgesia in addition to etoricoxib during the three-day treatment period. Doses greater than those recommended for each indication have either not demonstrated additional efficacy or have not been studied. **Overdosage:** 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.

ADVERSE REACTIONS:

• **Common or very common:** Ecchymosis, fatigue, influenza like symptoms, palpitation. • Uncommon: Anxiety, appetite change, arthralgia, arterial fibrillation, chest pain, cough, dry mouth dyspnoea, electrolyte disturbances, epistaxis, flushing, mental acuity impaired, mouth ulcer, myalgia, paraesthesia, taste disturbance, transient ischemic attack, weight change. • **Rare:** Alveolitis, asceptic meningitis (patients with connective tissue disorders such as systemic lupus erythematosus may be especially susceptible), hepatic damage, intestinal fibrosis associated with NSAIDs can lead to renal failure, pancreatitis, papillary necrosis associated with NSAIDs can lead to renal failure, pulmonary eosinophilia, Stevens-Johnson syndrome, toxic epidermal necrolysis, visual disturbances. • **Very rare:** Confusion, hallucinations.• **Frequency Not Known:** Angioedema, blood disorders, bronchospasm, colitis (induction of or exacerbation of), Crohn's disease (induction of or exacerbation of), depression, diarrhoea, dizziness, drowsiness, fluid retention (rarely precipitating congestive heart failure), gastro intestinal bleeding, gastrointestinal discomfort, gastrointestinal ulceration, haematuria, headache, hearing disturbances, hypersensitivity reactions, insomnia, nausea, nervousness, photosensitivity, raised blood pressure, rashes, renal failure (especially in patients with pre-existing renal impairment), tinnitus, vertigo.

INSTRUCTIONS

Dosage as directed by the physician.
Store below 30°C.
Protect from heat, light and moisture.
Keep all medicines out of the reach of children.

PRESENTATION

Torxib (Etoricoxib) Tablets 60 mg are available in Alu-Alu blister pack of 1x10's.

علامات/طریقہ استعمال:

ٹورزیب ٹیبلٹس ہڈیوں اور جوڑوں کے درد اور سوزش میں مبتلا ارتھرائیٹس، عارضی گٹھیا کے مریضوں کے لیے تجویز کردہ ہے۔

ٹورزیب ٹیبلٹس دانتوں کی سرجری سے منسلک درد اور سوزش کے علاج میں بھی استعمال کی جاسکتی ہے۔

مختلف امراض کے لحاظ سے خوراک ڈاکٹر کی ہدایت کے مطابق تجویز کردہ ہے۔

مضر اثرات:

اختلاج قلب، تھکن، انفلوئنزا، بے چینی، سینے کا درد، کھانسی، منہ کا خشک ہونا، جگر کی خرابی، معدے کی تکلیف، نیند کی کمی اور چکر آنا۔

احتیاطی تدابیر:

حاملہ خواتین اور دودھ پلانے والی مائیں صرف مستند ڈاکٹر کی ہدایت پر ہی استعمال کریں۔

جگر، گردے اور دل کے مریضوں میں احتیاط سے استعمال کریں۔

ہدایات:

خوراک ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔

۳۰ ڈگری سینٹی گریڈ سے کم پر رکھیں۔

روشنی، گرمی اور نمی سے محفوظ رکھیں۔

For detailed information:

Genix Pharma (Pvt.) Ltd.

44,45-B, Korangi Creek Road, Karachi-75190, Pakistan.
UAN: +92-21-111-10-10-11, **Email:** info@genixpharma.com

ISO 9001:2015 ISO 14001:2015 ISO 45001:2018

www.genixpharma.com