ETORICOXIB

RILAXIA

120 mg Film-Coated Tablet
Selective COX-2 Inhibitor

FORMULATION:
Each film-coated tablet contains:
Etoricoxib ..... 120 mg

PRODUCT DESCRIPTION:
White circular, slightly biconvex, film-coated tablet, having breakline on one side and plain on other side.

PHARMACODYNAMIC PROPERTIES:
Pharmacotherapeutic group: Anti-inflammatory and antirheumatic products, non-steroids, coxibs.

Mechanism of Action:
Etoricoxib is an oral, selective cyclo-oxygenase-2 (COX-2) inhibitor within the clinical dose range.
Across clinical pharmacology studies, Etoricoxib 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.
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.

PHARMACOKINETICS:
Etoricoxib is well absorbed from the gastrointestinal tract after oral doses. Peak plasma concentrations are reached in about 1 hour in fasted adults; food delays absorption by about 2 hours, although it has no effect on the extent of absorption. Plasma protein binding is about 92%. At steady state, the half-life of Etoricoxib is about 22 hours. Etoricoxib is extensively metabolised with less than 2% 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 is mainly via the urine (70%) with only 20% of a dose appearing in the faeces. Studies in animals suggest that Etoricoxib may cross the placenta and that some is distributed into breast milk.

INDICATIONS:
For acute treatment of signs and symptoms of osteoarthritis, rheumatoid arthritis and acute gouty arthritis. Also for the management of acute pain associated with inflammation. Use the lowest effective dose for the shortest duration consistent with individual patient treatment goals.

DOSAGE AND ADMINISTRATION:
In osteoarthritis, Etoricoxib is given orally in a usual dose of 30 mg once daily, increased to 60 mg once daily if necessary. The recommended dose in rheumatoid arthritis is 90 mg once daily; higher doses of 120 mg once daily are used in gouty arthritis although such doses should only be used for the acute symptomatic period and for a maximum of 8 days. Or as prescribed by the physician.

CONTRAINDICATION:
Hypersensitivity to the active substance or to any of the excipients.

ABSOLUTE CONTRAINDICATIONS:
Not to be given to those patients who have history of:
- Stroke: Cerebrovascular Accident, (CVA)
- Heart attack: Myocardial infarction, (MI)
- Coronary Artery Bypass Graft (CABG)
- Uncontrolled Hypertension
- Congestive Heart Failure (CHF) NYHA II-IV

ADVERSE DRUG REACTIONS:
The most common adverse effects of NSAIDs are generally gastrointestinal disturbances, such as gastrointestinal discomfort, nausea, and diarrhoea; these are usually mild and reversible but in some patients peptic ulceration and severe gastrointestinal bleeding may occur. It is generally agreed that inhibition of cyclo-oxygenase-1 (COX-1) plays an important role in the gastrointestinal effects of NSAIDs; the selective inhibition of COX-2 improves gastrointestinal tolerance.
CNS-related adverse effects include headache, vertigo, dizziness, nervousness, tinnitus, depression, drowsiness, and insomnia. Hypersensitivity reactions may occur occasionally and include fever; angioedema, bronchospasm, and rashes. Hepatotoxicity and aseptic meningitis which occur rarely, may also be hypersensitivity reactions. Some patients may experience visual disturbance.
Hematological adverse effects of NSAIDs include anemia, thrombocytopenia, neutropenia, eosinophilia, and agranulocytosis. Unlike aspirin, inhibition of platelet aggregation is reversible with other NSAIDs.
Some NSAIDs have been associated with nephrotoxicity such as interstitial nephritis and nephrotic syndrome; renal failure may be provoked by NSAIDs especially in patients with pre-existing renal impairment.
Haematuria has also occurred. Long-term use or abuse of analgesic, including NSAIDs, has been associated with nephropathy.
Fluid retention may occur, rarely precipitating heart failure in susceptible patients.
Other adverse effects include photosensitivity, alveolitis, pulmonary eosinophilia, pancreatitis, Stevens-Johnson syndrome and toxic epidermal necrolysis are other rare adverse effects.

Induction or exacerbation of colitis has also been reported.
Etoricoxib should not be used in patients with hypertension whose blood pressure is not controlled.
Etoricoxib is also contraindicated in patients with inflammatory bowel disease, moderate to severe heart failure, and renal impairment associated with creatinine clearance of less than 30 mL/minute.

DRUG INTERACTIONS:
The metabolism of Etoricoxib is mediated by the cytochrome P450 isoenzyme CYP3A4. Use with other drugs that inhibit or induce this isoenzyme may result in changes in plasma concentration of Etoricoxib. In addition, *in vitro* studies suggest that several other isoenzymes may also mediate the main metabolic pathway of Etoricoxib. Rifampicin, a potent inducer of CYP isoenzymes, has produced decreased plasma concentrations of Etoricoxib.
Etoricoxib is an inhibitor of human sulfotransferase activity and has been shown to increase the plasma concentration of ethinylestradiol. Interactions with other drugs, such as oral salbutamol and minoxidil, also metabolised by this enzyme may be a possibility and licensed product information advises care with such combinations.

WARNINGS AND PRECAUTIONS:
a) COX-2 inhibitors are not to be given to patients with allergy to NSAIDs and those with Asthma.
b) Exercise caution when prescribing Selective COX-2 inhibitors in patients with ischemic heart disease and those with risk factors for heart disease, hypertension, hyperlipidemia, diabetes, smoking and patient with peripheral arterial disease.
c) Considering association between cardiovascular risk and exposure to COX-2 inhibitors, doctors are advised to use the lowest effective dose for the shortest duration of treatment.
d) Intake of COX-2 inhibitors should be stopped with appearance of skin rash and signs of hypersensitivity.
e) If not yet instituted, warning statement should include potential gastrointestinal (gastric and liver) and renal toxicities.

FERTILITY, PREGNANCY AND LACTATION:
Pregnancy
No clinical data on exposed pregnancies are available for etoricoxib. Studies in animals have shown reproductive toxicity. The potential for human risk in pregnancy is unknown. Etoricoxib, as with other medicinal products inhibiting prostaglandin synthesis, may cause uterine inertia and premature closure of the ductus arteriosus during the last trimester. Etoricoxib is contraindicated in pregnancy. If a woman becomes pregnant during treatment, etoricoxib must be discontinued.

Breastfeeding
It is not known whether etoricoxib is excreted in human milk. Etoricoxib is excreted in the milk of lactating rats. Women who use etoricoxib must not breastfeed.

Fertility
The use of etoricoxib, as with any drug substance known to inhibit COX-2, is not recommended in women attempting to conceive.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES:
Patients who experience dizziness, vertigo or somnolence while taking Etoricoxib should refrain from driving or operating machinery.

OVERDOSE AND TREATMENT:
In clinical studies, administration of single doses of etoricoxib up to 500 mg and multiple doses up to 150 mg/day for 21 days did not result in significant toxicity. There have been reports of acute overdosage with etoricoxib, although adverse experiences were not reported in the majority of cases. The most frequently observed adverse experiences were consistent with the safety profile for etoricoxib (e.g. gastrointestinal events, cardiorenal events).

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.

STORAGE CONDITION:
Store at temperatures not exceeding 30ºC.

Keep all medicines out of reach of children.

CAUTION:
Foods, Drugs, Devices, and Cosmetics Act prohibits dispensing without prescription.

For suspected adverse drug reactions, report to the FDA: www.fda.gov.ph
Patient should seek medical attention immediately at the first sign of any adverse drug reaction.

AVAILABILITY:
Alu/PVC Blister Pack x 10's (Box of 30's).

DRP-5488-02
Date of First Authorization: 04 February 2022
Date of Revision of Package Insert: December 2022

417308R/PHL/001-28/09/2022

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