Size: 280 (L) x 420 (H) mm
Final folding size: 68 x 35 mm
Carton size: 52 x 25 x 125 mm
55 x 25 x 132 mm
Pharma Print Paper 35-50 gsm

MANUAL PACKING

Back side
280 mm

Font type: Times New Roman
Font size: 8 pts.

420 mm

The use of Etoricoxib, as with any medicinal product known to inhibit cyclooxygenase / prostaglandin synthesis, is not recommended in women attempting to conceive.

Lactose
Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicinal product.

INTERACTIONS WITH OTHER MEDICAMENTS
Pharmacodynamic interactions
Oral anticoagulants: Concurrent use of Etoricoxib and warfarin may result in increased prothrombin time International Normalized Ratio (INR).
Patients receiving oral anticoagulants should be closely monitored for their prothrombin time INR, particularly in the first few days when therapy with Etoricoxib is initiated or the dose of Etoricoxib is changed.
Diuretics, ACE inhibitors and Angiotensin II Antagonists: NSAIDs may reduce the effect of diuretics and other antihypertensive drugs. In some patients with compromised renal function (e.g., dehydrated patients or elderly 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. These interactions should be considered in patients taking Etoricoxib concomitantly with ACE inhibitors or angiotensin II antagonists. Therefore, the combination should be administered with caution, especially in the elderly. Patients should be adequately hydrated and consideration should be given to monitoring of renal function after initiation of concomitant therapy, and periodically thereafter.

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. Concomitant administration of Etoricoxib with doses of acetylsalicylic acid above those for cardiovascular prophylaxis or with other NSAIDs is not recommended.

Cyclosporin and tacrolimus: Coadministration of cyclosporin or tacrolimus with any NSAID may increase the nephrotoxic effect of cyclosporin or tacrolimus. Renal function should be monitored when Etoricoxib and either of these drugs is used in combination.

Pharmacokinetic interactions
The effect of Etoricoxib on the pharmacokinetics of other drugs.
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: Concurrent use of Etoricoxib and methotrexate may result in increased methotrexate plasma concentrations and toxicity. Adequate monitoring for methotrexate-related toxicity is recommended when Etoricoxib and methotrexate are administered concomitantly.

Oral contraceptives: Concurrent use of Etoricoxib and ethinyl estradiol (Oral contraceptives) may result in increased plasma concentration of ethinyl estradiol.

This increase in EE concentration should be considered when selecting an oral contraceptive for use with Etoricoxib. An increase in EE exposure can increase the incidence of adverse events associated with oral contraceptives (e.g., venous thrombo-embolic events in women at risk).

Hormone Replacement Therapy (HRT): Concurrent use of Etoricoxib and conjugated estrogens or Hormone Replacement Therapy may result in increased conjugated estrogen exposure. These increases in estrogenic concentration should be taken into consideration when selecting post-menopausal hormone therapy for use with Etoricoxib because the increase in oestrogen exposure might increase the risk of adverse events associated with HRT.

Prednisone/prednisolone: Etoricoxib did not have clinically important effects on the pharmacokinetics of prednisone/ prednisolone.

Digoxin: 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. While knowledge about effects of multiple sulfotransferases is presently limited and the clinical consequences for many drugs are still being examined, 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. CYP2D6, CYP2C9, CYP1A2 and CYP2C19 also can catalyse the main metabolic pathway, but their quantitative roles have not been studied.
Ketoconazole: Ketoconazole, a potent inhibitor of CYP3A4 did not have any clinically important effect on the single-dose pharmacokinetics of 60 mg Etoricoxib.

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: Coadministration of Etoricoxib with rifampicin, a potent inducer of CYP enzymes, produced a decrease in Etoricoxib plasma concentrations. This interaction may result in recurrence of symptoms when Etoricoxib is co-administered with rifampicin. While this information may suggest an increase in dose, doses of Etoricoxib greater than those listed for each indication are not recommended.

Antacids: Antacids do not affect the pharmacokinetics of Etoricoxib to a clinically relevant extent.

PREGNANCY AND LACTATION
Pregnancy
The use of Etoricoxib, as with any drug known to inhibit COX-2, is not recommended in women attempting to conceive.
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 drugs inhibiting prostaglandin synthesis, may cause uterine inertia and premature closure of the ductus arteriosus during the last trimester. Etoricoxib is contra-indicated in all trimesters of pregnancies. If a woman becomes pregnant during treatment, Etoricoxib should be discontinued.

Breast-feeding
It is not known whether Etoricoxib is excreted in human milk. Etoricoxib is excreted in the milk of lactating rats. Women who use Etoricoxib should not breast feed.

SIDE EFFECTS
Tabulated list of adverse reactions

System Organ Class	Adverse Reactions	Frequency Category
Infections and infestations	Alveolar osteitis	Common
	Gastroenteritis, upper respiratory infection, urinary tract infection	Uncommon
Blood and lymphatic system disorders	Anaemia (primarily associated with gastrointestinal bleeding), leukopenia, thrombocytopenia	Uncommon
Immune system disorders	Hypersensitivity	Uncommon
	Angioedema/anaphylactic /anaphylactoid reactions including shock	Rare
Metabolism and nutrition disorders	Oedema/fluid retention	Common
	Appetite increase or decrease, weight gain	Uncommon
Psychiatric disorders	Anxiety, depression, mental acuity decreased, hallucinations	Uncommon
	Confusion, restlessness	Rare
Nervous system disorders	Dizziness, headache	Common
	Dysgeusia, insomnia, paresthaesia/hypaesthesia, somnolence	Uncommon
Eye disorders	Blurred vision, conjunctivitis	Uncommon
Ear and labyrinth disorders	Tinnitus, vertigo	Uncommon
Cardiac disorders	Palpitations, arrhythmia	Common
	Atrial fibrillation, tachycardia, congestive heart failure, non-specific ECG changes, angina pectoris, myocardial infarction	Uncommon
Vascular disorders	Hypertension	Common
	Flushing, cerebrovascular accident, transient ischaemic attack, hypertensive crisis, vasculitis	Uncommon
Respiratory, thoracic and mediastinal disorders	Bronchospasm	Common
	Cough, dyspnoea, epistaxis	Uncommon
Gastrointestinal disorders	Abdominal pain	Very common
	Constipation, flatulence, gastritis, heartburn/acid reflux, diarrhea, dyspepsia/epigastric discomfort, nausea, vomiting, oesophagitis, oral ulcer	Common
	Abdominal distention, bowel movement pattern change, dry mouth, gastroduodenal ulcer, peptic ulcers including gastrointestinal perforation and bleeding, irritable bowel syndrome, pancreatitis	Uncommon
Hepatobiliary disorders	ALT increased, AST increased	Common
	Hepatitis	Rare
	Hepatic failure, jaundice	Rare
Skin and subcutaneous tissue disorders	Ecchymosis	Common
	Facial oedema, pruritus, rash, erythema, urticaria	Uncommon
	Stevens-Johnson syndrome, toxic epidermal necrolysis, fixed drug eruption	Rare
Musculoskeletal and connective tissue disorders	Muscular cramp/spasm, musculoskeletal pain/ stiffness	Uncommon
Renal and urinary disorders	Proteinuria, serum creatinine increased, renal failure/ renal insufficiency	Uncommon
General disorders and administration site conditions	Asthenia/fatigue, flu-like disease	Common
	Chest pain	Uncommon
Investigations	Blood urea nitrogen increased, creatine phosphokinase increased, hyperkalaemia, uric acid increased	Uncommon
	Blood sodium decreased	Rare

The following serious undesirable effects have been reported in association with the use of NSAIDs and cannot be ruled out for Etoricoxib: nephrotoxicity including interstitial nephritis and nephrotic syndrome.

SYMPTOMS AND TREATMENT OF OVERDOSE
Administration of Etoricoxib at single doses 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 experience were consistent with the safety profile for Etoricoxib. (e.g. gastrointestinal events, renovascular events).
In the event of overdose, it is reasonable to employ the usual supportive measures, e.g., remove unabsorbed material from the gastrointestinal tract, employ clinical monitoring, and institute supportive therapy, if required.
Etoricoxib is not dialyzable by hemodialysis; it is not known whether Etoricoxib is dialyzable by peritoneal dialysis.

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.

INSTRUCTIONS FOR USE
Etoricoxib is administered orally and may be taken with or without food. Etoricoxib should be administered for the shortest duration possible and the lowest effective daily dose should be used.

STORAGE CONDITIONS
Store below 30°C. Store in the original packaging to protect from the light and moisture.

DOSAGE FORMS AND PACKAGING AVAILABLE
Film coated Tablets
Alu-Alu Blister (Alu-OPA/Alu/PVC) pack of 10's Count, pack of 30s (3x10s)

NAME AND ADDRESS OF MANUFACTURER/ PRODUCT REGISTRATION HOLDER
Manufactured by:
MICRO LABS LIMITED
Plot No. S-155 to S-159 & N1,
Phase-III & IV, Verna Industrial Estate,
Verna Salcette Goa IN-403 722, INDIA.

Product Registration Holder:
HEALOL PHARMACEUTICALS SDN. BHD.
74-3, Jalan Wangsa Delima 6, KLSC,
Wangsa Maju-53300, Kuala Lumpur, Malaysia.

DATE OF REVISION OF PI
Apr. 2025

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PHARMACODE READING DIRECTION