

Artwork Document Information		Artwork Type [Please Tick /]		Sign / Stamp	
Product : T - DUOCOXIB F/C TABLET [FRONT] SAP No. : Date : 23 October 2025		☐ Unit Box ☐ Outer Box ☐ Label		☒ Leaflet ☐ Fix-A-Form ☐ Shipper Carton	
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Remarks		Colour			
1. Font : Helvetica Condensed Regular (Spacing - 8pt / Size - 7pt) 2. Dimension : 210mm(w) x 297mm(h)		Black			
		Colours shown on this proof are to indicate correct colour separations.			

DUOCOXIB FILM COATED TABLET

Duocoxib Film Coated Tablet 120mg
The tablet contains 120mg of Etoricoxib.

Duocoxib Film Coated Tablet 90mg
The tablet contains 90mg of Etoricoxib.

DESCRIPTION:
Duocoxib Film Coated Tablet 120mg: Apple shape, pale green, biconvex with “120” marking on one side and plain on the other side, film-coated tablet.

Duocoxib Film Coated Tablet 90mg: Apple shape, white, biconvex with “90” marking on one side and plain on the other side, film coated tablet.

PHARMACODYNAMICS: Etoricoxib is a nonsteroidal anti-inflammatory drug (NSAID) that exhibits anti-inflammatory, analgesic and antipyretic activities in animal models. Etoricoxib is a potent, orally active and highly selective cyclooxygenase-2 (COX-2) inhibitor. Two isoforms of cyclooxygenase have been identified: cyclooxygenase-1 (COX-1) and cyclooxygenase-2 (COX-2). (COX-1) is responsible for prostaglandin-mediated normal physiologic functions such as gastric cytoprotection and platelet aggregation. Inhibition of COX-1 by nonselective NSAIDs has been associated with gastric damage and platelet inhibition. COX-2 shown to be primarily responsible for the synthesis of prostanoid mediators of pain, inflammation and fever. Selective inhibition of COX-2 by etoricoxib decreases GI toxicity and without causes effects on platelet function. There was no inhibition of *ex vivo* arachidonic acid- or collagen induced platelet aggregation at steady state with doses of Etoricoxib up to 150mg.

PHARMACOKINETICS:
Absorption
Orally administered etoricoxib is well absorbed. A standard meal had no effect on the extent or rate of absorption of a dose of etoricoxib 120mg.

Distribution
Etoricoxib is approximately 92% bound to human plasma protein over the range of concentrations of 0.05 to 5 mcg/ml. The volume of distribution at steady state (V_{des}) is approximately 120 L in humans. Etoricoxib crosses the placenta in rats and rabbits and the blood-brain barrier in rats.

Metabolism
Etoricoxib is extensively metabolized 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 cytochrome P450 (CYP) enzymes. Five metabolites have been identified in man. The principal metabolite is in the 6-carboxylic acid derivative of etoricoxib formed by further oxidation of the 6-hydroxymethyl derivative. These principal metabolites either demonstrate no measurable activity or are not weakly active as COX-2 inhibitors. 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 7 days of once daily administration of 120mg, with an accumulation ratio of approximately 2, corresponding to an accumulation half-life of approximately 22 hours. The plasma clearance is estimated to be approximately 50mL/min.

INDICATIONS:
Duocoxib is indicated for:

- Acute and chronic treatment of the signs and symptoms of osteoarthritis (OA) and rheumatoid arthritis (RA)
- Treatment of ankylosing spondylitis (AS)
- Treatment of acute gouty arthritis
- Treatment of acute pain, including that related to primary dysmenorrhea and minor dental procedures.

The decision to prescribe a selective COX-2 inhibitor should be based on an assessment of the individual patient's overall risks. (See PRECAUTIONS).

DOSAGE AND ADMINISTRATION:
Duocoxib is administered orally. Duocoxib may be taken with or without food and should not be split into half. Duocoxib should be administered for the shortest duration possible and the lowest effective daily dose should be used.

<i>Osteoarthritis</i>	The recommended dose is 30mg or 60mg daily.
<i>Rheumatoid arthritis</i>	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 stabilized, down-titration to a 60mg once daily dose may be appropriate. In the absence of an increase in therapeutic benefit, other therapeutic options should be considered.
<i>Ankylosing spondylitis</i>	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. In the absence of an increase in therapeutic benefit, other therapeutic options should be considered.
<i>Acute pain</i>	In the following acute painful conditions, Duocoxib should be used only for the acute symptomatic period, limited to a maximum of 8 days treatment: <i>Acute Gouty Arthritis</i> The recommended dose is 120mg once daily <i>Primary Dysmenorrhea</i> The recommended dose is 120mg once daily

	Minor Dental Procedures The dose for minor dental procedures should not exceed 90mg daily. Doses greater than those recommended for each indication have either not demonstrated additional efficacy or have not been studied. Therefore: The dose for OA should not exceed 60mg daily. The dose for RA should not exceed 90mg daily. The dose of ankylosing spondylitis should not exceed 90mg daily. The dose for acute gout should not exceed 120mg daily. The dose for acute pain and primary dysmenorrhea should not exceed 120mg daily. The dose for minor dental procedures should not exceed 90mg daily. As the cardiovascular risks of selective COX-2 inhibitors may increase with dose and duration of exposure, the shortest duration possible and the lowest effective daily dose should be used. The patient needs for symptomatic relief and response to therapy should be reevaluated periodically (See PRECAUTIONS).
<i>Elderly, Gender, Race</i>	No dosage adjustment in Duocoxib is necessary for elderly or based on gender or race.
<i>Hepatic Insufficiency</i>	In patients with mild hepatic insufficiency (Child-Pugh score 5 – 6), a dose of 60mg once daily should not be exceeded. In patients with moderate hepatic insufficiency (Child-Pugh score 7 - 9), the dose should be reduced, a dose of 60 mg every other day should not be exceeded, administration of 30mg once daily can also be considered. There are no pharmacokinetic data in patients with severe hepatic insufficiency (Child-Pugh score > 9) (See PRECAUTIONS).
<i>Renal Insufficiency</i>	In patients with advance renal disease (creatinine clearance <30 mL/min), treatment with Duocoxib is not recommended. No dosage adjustment is necessary for patients with lesser degrees of renal insufficiency (creatinine clearance ≥30mL/min)(See PRECAUTIONS).

CONTRAINDICATIONS:
Duocoxib is contraindicated in patients with:

- Hypersensitivity to any component of this product.
- Congestive heart failure (NYHA II-IV).
- Hypertension (high blood pressure) whose blood pressure is not under control
- Established ischemic heart disease, peripheral arterial disease and/or cerebrovascular disease (including patients who have recently undergone coronary artery bypass graft surgery or angioplasty)
- Pregnancy

PRECAUTIONS:
Given the association between cardiovascular risk and exposure to COX—2 Inhibitors, doctors are advised to use the lowest effective dose for the shortest possible duration of treatment.

Selective COX-2 inhibitors are not a substitute for aspirin for cardiovascular prophylaxis because of their lack of effect on platelets. Because etoricoxib, a member of this class, does not inhibit platelet aggregation, antiplatelet therapies should not be discontinued. There is a further increase in the risk of gastrointestinal adverse effects (gastrointestinal ulceration or other gastrointestinal complication) for etoricoxib, other selective COX-2 inhibitors and NSAIDs, when taken concomitantly with acetylsalicylic acid (even at low doses). The relative difference in gastrointestinal safety between selective COX-2 inhibitors + acetylsalicylic acid vs. NSAIDs + acetylsalicylic acid has not been adequately evaluated.

In patients with advanced renal disease, treatment with Duocoxib is not recommended. If therapy with this product must be initiated in such patient, close monitoring of the patient's renal function is advisable.

Long term administration of NSAIDs has resulted in renal papillary necrosis and other renal injury. Renal prostaglandins may play a compensatory role in the maintenance of renal perfusion. Therefore, under condition of compromised renal perfusion, administration of Duocoxib may cause a reduction in prostaglandin formation and, secondarily, in renal blood flow, and thereby impair renal function. Patients at greatest risk of this response are those with pre-existing significantly impaired renal function, uncompensated heart failure, or cirrhosis. Monitoring of renal function in such patients should be considered.

Caution should be used when initiating treatment with Duocoxib in patients with considerable dehydration. It is advisable to rehydrate patients prior to starting therapy with Duocoxib.

As with other drugs known to inhibit prostaglandin synthesis, fluid retention, edema and hypertension have been observed in some patients taking etoricoxib. The possibility of fluid retention, edema or hypertension should be taken into consideration when Duocoxib is used in patients with preexisting edema, hypertension, or heart failure. All Nonsteroidal Anti-inflammatory Drugs (NSAIDs), including etoricoxib, can be associated with new onset or recurrent congestive heart failure. (See Side Effects). Etoricoxib may be associated with more frequent and severe hypertension than some other NSAIDs and selective COX-2 inhibitors, particularly at high doses.

Therefore, special attention should be paid to blood pressure monitoring during treatment with etoricoxib. If blood pressure rises significantly, alternative treatment should be considered.

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[DUOPHARMA MANUFACTURING (BANGI) SDN BHD]

Physicians should be aware that individual patients may develop upper gastrointestinal (GI) ulcers / ulcer complications irrespective of treatment. This event can occur at any time during used and without warning symptom. Independent of treatment, patients with a prior history of GI perforation, ulcers and bleeding (PUB) and patients greater than 65 years of age are known to be at a higher risk for a PUB.

A patient with symptoms and/or signs suggesting liver dysfunction, or in whom an abnormal liver function test has occurred, should be evaluated for persistently abnormal liver function tests. If persistently abnormal liver function tests (three times the upper limit of normal) are detected, Duocoxib should be discontinued.

Duocoxib should be used with caution in patients who have previously experienced acute asthmatic attacks, urticaria, or rhinitis which were precipitated by salicylates or non-selective cyclooxygenase inhibitors. Since the pathophysiology of these reactions is unknown, physicians should weigh the potential benefits of prescribing Duocoxib versus the potential risks.

When using etoricoxib in the elderly and in patients with renal, hepatic or cardiac dysfunction, medically appropriate supervision should be maintained. If these deteriorate during treatment, appropriate measures should be taken, including discontinuation of therapy.

Serious skin reactions, some of them fatal, including exfoliative dermatitis, Steven-Johnson syndrome, and toxic epidermal necrolysis, have been reported very rarely in association with the use of NSAIDs and some selective COX-2 inhibitors during post-marketing surveillance. These serious events may occur without warning. Patients appear to be at highest risk of these reactions early in the course of therapy: the onset of the reactions (such as anaphylaxis and angioedema) have been reported in patients receiving etoricoxib. 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.

Duocoxib may mask fever, which is a sign of infection. The physician should be aware of this when using Duocoxib in patients being treated for infection.

WARNINGS:
RISK OF GI ULCERATION, BLEEDING AND PERFORATION WITH NSAIDS

Serious GI toxicity such as bleeding, ulceration and perforation can occur at any time, with or without warning symptoms, in patients treated with NSAIDs therapy. Although minor upper GI problems (e.g., dyspepsia) are common, usually developing early in therapy, prescribers should remain alert for ulceration and bleeding in patients treated with NSAIDs even in the absence of previous GI tract symptoms.

Patients with prior history of serious adverse events and other risk factors associated with peptic ulcer disease (e.g., alcoholism, smoking and corticosteroid therapy) are at increased risk. Elderly or debilitated patients seem to tolerate ulceration or bleeding less than other individuals and account for most spontaneous reports for fatal GI events.

Warning to prescriber when prescribing COX-2 Inhibitors to patients with risk factors of heart disease, hypertension (high blood pressure), hyperlipidemia, diabetes, smoking patient and patient with peripheral arterial disease.

DRUG INTERACTIONS:
Warfarin: Standard monitoring of INR (International Normalized Ratio) value should be conducted when therapy with Duocoxib is initiated or changed, particularly in the first few days, in patients receiving warfarin or similar agents.

Rifampin: Co-administration of Duocoxib with rifampin, a potent inducer of hepatic metabolism, produced a 65% decrease in etoricoxib plasma area under the curve (AUC). This interaction should be considered when Duocoxib is coadministered with rifampin.

Methotrexate: Monitoring for methotrexate-related toxicity should be considered when Duocoxib at doses greater than 90 mg daily and methotrexate are administered concomitantly.

Diuretic, angiotensin converting enzyme (ACE) inhibitors and angiotensin II antagonist (AIIAs): NSAIDs including selective COX-2 inhibitors may diminish the antihypertensive effect of diuretics, ACE inhibitors and AIIAs. This interaction should be given consideration in patients taking Duocoxib concomitantly with these products.

In some patients with compromised renal function (e.g elderly patients or patients who are volume-depleted, including those on diuretic therapy) who are being treated with non-steroidal anti-inflammatory drugs, including selective COX-2 inhibitors, the co-administration of ACE inhibitors or AIIAs may result in a further deterioration of renal function, including possible acute renal failure. These effects are usually reversible. Therefore, the combination should be administered with caution, especially in the elderly.

Lithium: Non-selective NSAIDs and selective COX-2 inhibitors may increase plasma lithium levels. This interaction should be given consideration in patients taking Duocoxib concomitantly with lithium.

Aspirin: Duocoxib can be used concomitantly with low-dose aspirin at doses for cardiovascular prophylaxis. At steady state, etoricoxib 120 mg once daily had no effect on the antiplatelet activity of low-dose aspirin (81 mg once daily). However concomitantly administration of low dose aspirin with Duocoxib increase the rate of GI ulceration or other complications compared to use of Duocoxib alone.

Oral Contraceptives: Etoricoxib may increase Ethinyl Estradiol (EE) which can increase the incidence of adverse event associated with oral contraceptives (e.g., venous thrombo-embolic events in women at risk). The increase in EE concentration should be considered when selecting an appropriate oral contraceptive for use with Duocoxib.

Hormone replacement therapy: The increase in estrogenic concentration should be taken into consideration when selecting post-menopausal hormone therapy for use with this product.

Other: Etoricoxib does not have important effects on the pharmacokinetic of prednisone/prednisolone or digoxin.

Antacids and ketoconazole (a potent inhibitor of CYP3A4) does not have important effects on the pharmacokinetics of etoricoxib.

PREGNANCY & LACTATION
Pregnancy

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

Lactation
Etoricoxib is excreted in the milk of lactating rats. It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk and because of the possible adverse effects of drugs that inhibit prostaglandin synthesis on nursing infants, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

SIDE EFFECTS
Blood and lymphatic system disorders: thrombocytopenia.
Immune system disorders: hypersensitivity reactions, anaphylactic/anaphylactoid reactions including shock.
Metabolism and nutrition disorders: hyperkalemia.
Psychiatric disorders: anxiety, insomnia, confusion, hallucinations, depression, restlessness.
Nervous system disorders: dysgeusia, somnolence.
Eye disorders: blurred vision.
Cardiac disorders: congestive heart failure, palpitations, angina, arrhythmia.
Vascular disorders: hypertensive crisis.
Respiratory, thoracic and mediastinal disorders: bronchospasm.
Gastrointestinal disorders: abnormal pain, oral ulcers, peptic ulcers including perforation and bleeding (mainly in elderly patients), vomiting, diarrhea.
Hepatobiliary disorders: hepatitis, jaundice, hepatic failure.
Skin and subcutaneous tissue disorders: angioedema, pruritis, erythema, rash, Steven-Johnson syndrome, toxic epidermal necrolysis, urticaria, fixed drug eruption.
Renal and urinary disorders: renal insufficiently, including renal failure.

SYMPTOMS AND TREATMENT OF OVERDOSAGE
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 haemodialysis; it is not known whether etoricoxib is dialyzable by peritoneal dialysis.

EFFECTS ON ABILITY OF DRIVE AND USE OF MACHINE
Etoricoxib has no known influence on the ability to drive or use machines. However, when driving or using machines, a careful precaution should be taken into account.

ROUTE OF ADMINISTRATION
Oral

SHELF LIFE
2 Years

PACK SIZE
Duocoxib Film Coated Tablet 90 mg: 3 x 10 tablets, 10 x 10 tablets
Duocoxib Film Coated Tablet 120 mg: 3 x 10 tablets

STORAGE CONDITION
To be stored below 30°C and protected from light and moisture.

PRODUCT REGISTRATION HOLDER
Duopharma Manufacturing (Bangi) Sdn. Bhd.
Lot No. 2, 4, 6, 8, 10, Jalan P/7, Section 13,
Bangi Industrial Estate, 43650,
Bandar Baru Bangi, Selangor, Malaysia.

MANUFACTURER
Duopharma Manufacturing (Bangi) Sdn. Bhd.
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