

hovid-Etoricoxib Tablet

VIETO01-M2

DESCRIPTION

hovid-Etoricoxib Tablet 30 mg:

Round, 6.0mm in diameter, red film-coated tablet, bevel-edged and deep convex faces.

hovid-Etoricoxib Tablet 60 mg:

Round, 8.0mm in diameter, red film-coated tablet, bevel-edged and shallow convex faces.

hovid-Etoricoxib Tablet 90 mg:

Round, 9.0mm in diameter, white film-coated tablet, bevel-edged and shallow convex faces.

hovid-Etoricoxib Tablet 120 mg:

Round, 10.0mm in diameter, red film-coated tablet, bevel-edged and shallow convex faces.

COMPOSITION

hovid-Etoricoxib Tablet 30 mg:

Each tablet contains 30 mg of Etoricoxib.

hovid-Etoricoxib Tablet 60 mg:

Each tablet contains 60 mg of Etoricoxib.

hovid-Etoricoxib Tablet 90 mg:

Each tablet contains 90 mg of Etoricoxib.

hovid-Etoricoxib Tablet 120 mg:

Each tablet contains 120 mg of Etoricoxib.

PHARMACODYNAMICS

Etoricoxib is a nonsteroidal anti-inflammatory agent (dipyrindinyl derivative) for oral administration. It is a highly selective inhibitor of cyclooxygenase-2 (COX-2) that exhibits anti-inflammatory, analgesic, and antipyretic activities in animal models.

Two isoforms of cyclooxygenase have been identified: cyclooxygenase-1 (COX-1) and cyclooxygenase-2 (COX-2).

The COX-1 isoenzyme is constitutively expressed in most tissues, and is particularly involved in prostaglandin synthesis in kidneys, platelets, and gastric mucosa; products of COX-1 appear cytoprotective, and inhibition of this isoform has been associated with antiplatelet and gastrointestinal toxicity. The inducible COX-2 isoform is expressed at sites of inflammation, and its inhibition is considered responsible for analgesic and anti-inflammatory properties of nonsteroidal anti-inflammatory agents.

The COX-1-sparing effects of selective COX-2 inhibitors suggest they may be as effective as nonselective inhibitors of both COX-1 and COX-2 (ie, naproxen, ibuprofen, ketorolac) in treating pain and inflammation with a reduced propensity for hematologic and gastrointestinal toxicity.

PHARMACOKINETICS

Absorption: Etoricoxib is well absorbed from the gastrointestinal tract after oral doses. The mean oral bioavailability is approximately 100%.

Peak plasma concentrations occur in about 1 hour in fasted adults; food delays absorption by about 2 hours, although it has no effect on the extent of absorption. Antacids (calcium carbonate, aluminum/magnesium hydroxide) do not significantly affect the absorption of etoricoxib.

Distribution: Plasma protein binding is about 92%.

Etoricoxib may cross the placenta and that some is distributed into breast milk.

Volume of Distribution: 119 L at steady state.

Metabolism: Etoricoxib is extensively metabolized with <2% of a dose recovered in 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.

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.

These principal metabolites either demonstrate no measurable activity or are only weakly active as COX-2 inhibitors.

No metabolites are considered to contribute significantly to COX-2 (or COX-1) inhibition.

Elimination: Etoricoxib is excreted mainly via the urine (70%) with only 20% of a dose appearing in the faeces. At steady state the

half-life of etoricoxib is about 22 hours.

INDICATION

Etoricoxib 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 dysmenorrhoea 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.

CONTRAINDICATIONS

- Hypersensitivity to any component of this product.
- Congestive heart failure (NYHA II-IV)
- 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
- Patients with hypertension whose blood pressure has not been adequately controlled
- Renal impairment associated with a creatinine clearance of less than 30 mL/minute
- Patients with active gastrointestinal ulceration or bleeding
- Patients with a history of bronchospasm with rhinoconjunctivitis or urticaria/angioedema associated with aspirin or other nonsteroidal antiinflammatory agents (adult-onset asthma, chronic rhinitis, nasal polyps, and chronic urticaria/angioedema predispose to these reactions) (risk of anaphylactic-like reactions)
- Patients with inflammatory bowel disease
- Patients who have increased risk of cardiovascular disease (ischemic heart disease and stroke)
- Severe hepatic dysfunction
- Children and adolescents less than 16 years old

WARNINGS AND PRECAUTIONS

Etoricoxib may be associated with an increased risk of thrombotic events (especially MI and stroke). 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.

Etoricoxib should not be used in patients with ischaemic heart disease, peripheral arterial disease, or cerebrovascular disease. It should be used with caution in patients with significant risk factors for cardiovascular disease such as hypertension, hyperlipidaemia, and diabetes mellitus.

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.

Selective COX-2 inhibitors are not a substitute for aspirin for cardiovascular prophylaxis because of their lack of effect on platelets. Hence, antiplatelet therapies should not be discontinued.

There is a further increase in the risk of gastrointestinal adverse effects (gastrointestinal ulceration or other gastrointestinal complications) for etoricoxib when taken concomitantly with acetylsalicylic acid (even at low doses).

In patients with advanced renal disease, treatment with etoricoxib is not recommended. If therapy with etoricoxib must be initiated in such patients, renal function should be monitored closely.

Long-term use of NSAIDs has resulted in renal papillary necrosis and other renal injury. Monitoring of renal function should be considered for those with pre-existing significantly impaired renal function, uncompensated heart failure, or cirrhosis.

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

The possibility of fluid retention, edema or hypertension should be taken into consideration when etoricoxib is used in patients with pre-existing edema, hypertension, or heart failure.

All Nonsteroidal Antiinflammatory Drugs (NSAIDs), including etoricoxib, can be associated with new onset or recurrent congestive heart failure.

Etoricoxib, particularly at high doses, may be associated with more frequent and severe hypertension compared with other NSAIDs and selective cyclo-oxygenase-2 (COX-2) inhibitors; blood pressure monitoring during etoricoxib treatment is recommended. Etoricoxib should not be used in patients with hypertension whose blood pressure is not controlled.

Conditions predisposing to gastrointestinal events (eg, history of peptic ulcer, upper gastrointestinal disease, ulcerative colitis, smoking, advancing age, concurrent aspirin or corticosteroids, alcohol abuse, stress).

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, etoricoxib should be discontinued.

Etoricoxib should be used with caution in patients with history of acute asthmatic attacks, urticaria, or rhinitis, which were caused by salicylates or non-selective cyclooxygenase inhibitors.

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

It should be avoided in patients with severe hepatic impairment (Child-Pugh score of 10 or more). Therapy should be stopped if persistently abnormal liver enzyme values are seen.

Use of etoricoxib is associated with very rare occurrence of serious skin reactions, some of them fatal, including exfoliative dermatitis, Stevens-Johnson syndrome, and toxic epidermal necrolysis. These serious events may occur without warning and patients are at highest risk for these reactions early in the course of therapy.

Patients with history of mild allergic phenomena related to ingestion of other nonsteroidal antiinflammatory drugs (eg, rash) should be treated with caution. Etoricoxib should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity.

Etoricoxib may mask fever, which is a sign of infection.

Risk of GI Ulceration, Bleeding and Perforation with NSAID

Serious GI toxicity such as bleeding, ulceration and perforation can occur at any time, with or without warning symptoms, in patients treated with NSAID 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 GI 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.