Hiloric®

(Febuxostat)

Highnoon

COMPOSITION
Hiloric 40mg Tablet:
Each film-coated tablet contains: Febuxostat 40mg
Hiloric 80mgTablet:
Each film-coated tablet contains: Febuxostat 80mg

DESCRIPTION
Hiloric (Febuxostat) is a non-purine, selective inhibitor of xanthine oxidase.

MECHANISM OF ACTION
Febuxostat, a xanthine oxidase inhibitor, achieves its therapeutic effect by decreasing serum uric acid by selectively inhibiting xanthine oxidase, which is needed to make uric acid in the body. By reducing the production of uric acid, Febuxostat can reduce levels of uric acid in the blood and keep them low, stopping crystals from building up. This can reduce the symptoms of gout. Febuxostat is not expected to inhibit other enzymes involved in purine and pyrimidine synthesis and metabolism at therapeutic concentrations.

PHARMACOKINETICS
Febuxostat is rapidly and well absorbed after oral doses. Although, dosage with high fat meal decreases peak plasma concentration and exposure, this is not thought clinically significant, and Febuxostat may be taken with or without food. Plasma protein binding is about 99% (primarily to albumin). Febuxostat is extensively metabolised by conjugation via the uridine diphosphate glucuronosyltransferase (UDPGT) enzyme system, and by the oxidation via the cytochrome P450 isoenzymes system; active metabolised are formed mainly by UGT1A1, UGT1A8, UGT1A9, and by CYP1A1,CYP1A2, CYP2C8, or CYP2C9. Febuxostat has a mean terminal half life about 5 to 8 hours. Febuxostat is eliminated by both hepatic and renal pathways, about half of the doses excreted via the urine, and other half via the faeces.

INDICATIONS AND USAGE
It is indicated for chronic management of hyperuricemia in patients with chronic gout.
It is not recommended for the treatment of asymptomatic hyperuricemia.

DOSAGE AND ADMINISTRATION
For treatment of hyperuricemia in patients with gout, it is recommended at 40mg or 80mg once daily. The recommended starting dose for the treatment of hyperuricemia in patients with gout is 40mg once daily. For patients who do not achieve a serum uric acid (sUA) less than 6 mg/dl after two weeks with 40 mg, the recommended dose is 80 mg..
It can be taken without regard to food or antacid use.

ADVERSE REACTIONS
The most common adverse effects of Febuxostat are liver function abnormalities, arthralgia, dizziness, nausea and rashes. The less commonly reported adverse effects includes: abdominal distention, abdominal pain, dry mouth, frequent stools, gastritis, gingival pain, haematemesis, hyperchlorhydria, hematochezia, mouth ulceration, pancreatitis, peptic ulcer, constipation, dyspepsia, flatulence, gastro esophageal reflux disease, gastrointestinal discomfort, edema, fatigue, thirst, hemiparesis, cerebro- vascular accident, hypoesthesia, hyposmia, lacunar infarction, lethargy, mental impairment, migraine, anxiety, transient ischemic attack, tremor, nervousness, Guillain-Barre syndrome, balance disorder, agitation, depression, flushing, feeling abnormal, paresthesia, somnolence, insomnia, altered taste, vomiting, weight increased, weight decreased, tinnitus, vertigo, hearing loss, blurred vision, hypersensitivity, herpes zoster, dehydration, appetite decrease, appetite increased, hypokalemia, hypertriglyceridemia, hypercholesterolemia, muscle spasms, hyperglycemia, hyperlipidemia, diabetes mellitus, pollakiuria, proteinuria, renal failure, renal insufficiency, urgency & incontinence, nephrolithiasis, hematuria, dermatitis, angio-edema, dermographism, ecchymosis, hair growth abnormal, hyperhidrosis, peeling skin, petechiae, pruritus, purpura, skin lesion, skin odor abnormal, flushing, urticaria, photosensitivity, altered skin pigmentation, pain, joint stiffness, joint swelling, muscle twitching, muscle, tightness, muscle weakness, arthritis, myalgia, anemia, leukopenia / leukocytosis, thrombocytopenia, idiopathic thrombocytopenic purpura, neutropenia, pancytopenia, splenomegaly, abnormal coagulation test (prothrombin time prolonged), cardiovascular death, non-fatal myocardial infarction, non-fatal stroke, atrial fibrillation, atrial flutter, cardiac murmur, ECG abnormalities, sinus bradycardia, tachycardia, angina pectoris, hypotension, hypertension, palpitations, cough, bronchitis, epistaxis, respiratory tract congestion, nasal dryness, sneezing, throat irritation, pharyngeal edema, paranasal sinus hypersecretion, dyspnea, upper respiratory tract infection, libido decrease, erectile dysfunction, breast pain, irritability, panic attack, personality change, cholelithiasis, cholecystitis, hepatic steatosis, hepatitis, gallstone, hepatomegaly, gynecomastia, alteration in hair colors, hot flush, alopecia. headache, contusion, nervousness, influenza-like symptoms, mass, asthenia, gait disturbance, anorexia, eczema and pain. The additional reported adverse events are agranulocytosis, eosinophilia, jaundice, anaphylaxis, anaphylactic reaction, aggressive thoughts and tubulointerstitial nephritis. The laboratory parameters include; activated partial thromboplastin time prolonged, creatine increased, bicarbonate decreased, sodium increased, EEG abnormal, glucose increased, cholesterol increased, triglycerides increased, amylase increased, potassium increased, TSH increased, platelet count decreased, hematocrit decreased, hemoglobin decreased, MCV increased, RBC decreased, creatinine increased, blood amylases increases, blood urea increased, BUN/creatinine ratio increased, creatine phosphokinase (CPK) increased, alkaline phosphatase increased, LDH increased, PSA increased, urine output increased/decreased, lymphocyte count decreased, neutrophil count decreased, WBC increased/decreased, coagulation test abnormal, low density lipoprotein (LDL) increased, prothrombin time prolonged, urinary casts, urine positive for white blood cells and protein.

DRUG INTERACTIONS
- Inhibition of xanthine oxidase is known to increase concentrations of mercaptopurine or azathioprine, so use of Febuxostat with these drugs is not recommended. Similarly, caution is advised when Febuxostat is given with theophylline, and theophylline concentrations should be monitored. Febuxostat is metabolized via the uridine diphosphate glucuronosyltransferase enzyme system, and inhibitor or inducers of this system might affect exposure to Febuxostat. Serum uric acid should be monitored 1 to 2 weeks after starting treatment with a potent inducer of glucuronidation.
- No data are available regarding the safety of Febuxostat during cytotoxic chemotherapy.
- Febuxostat does not have clinically significant interactions with colchicine, naproxen, indomethacin, hydrochlorothiazide, warfarin or desipramine. Therefore, Febuxostat may be used concomitantly with these medications.

CONTRAINDICATIONS
Febuxostat is contraindicated in patients with:
- Hypersensitivity to the active substance or to any of the excipients.
- In patient being treated with azathioprine or mercaptopurine.
- Asymptomatic hyperuricemia.

USE IN SPECIFICPOPULATIONS

Pregnancy
Febuxostat should not be used during pregnancy.

Nursing Mothers
Febuxostat is expected in the milk of rats. It is not known whether this drug is excreted in human milk because many drugs are excreted in human milk, caution should be exercised.

Pediatric Use
Safety and effectiveness in pediatric patients under 18 years of age have not been established.

Geriatric Use
No dose adjustment Is necessary in elderly patients.

Renal impairment
No dose adjustment is necessary in patients with mild to moderate renal impairment (Clcr 30 to 89 mL/min). The recommended starting dose is 40 mg once daily. for patients who do not achieve a sUA less than 6 mg/dL after two weeks with 40 mg, then 80 mg is recommended. For patients with seven renal impairment (Clcr 15 to 29 mL/min), the dose of febuxostat is limited to 40mg once daily.

Hepatic Impairment
No dose adjustment is necessary in patients with mild or moderate hepatic impairment (Child-Pugh Class A or B), No studies have been conducted in patients with severe hepatic impairment (Child-Pugh Class C); therefore, caution should be exercised in these patients.

WARNINGS AND PRECAUTIONS
- No dose adjustment is necessary in patients with mild or moderate renal impairment. There are insufficient data in patients with severe renal impairment therefore, caution should be exercised in these patients.
- No studies have been conducted in patients with secondary hyperuricemia (including organ transplant recipients); Febuxostat is not recommended for use in patients whom the rate of urate formation is greatly increased (e.g., malignant disease and its treatment, Lesch- Nyhan syndrome). The concentration of xanthine in urine could, in rare cases, rise sufficiently to allow deposition in the urinary tract.
- Treatment in patients with ischaemic heart disease or congestive heart failure is not recommended.
- Concomitant ingestion of an antacid containing magnesium hydroxide and aluminum hydroxide delay absorption of Febuxostat, so Febuxostat may be taken without regard to antacid use.
- After initiation of Febuxostat, an increase in gout flares is frequently observed. This increase is due to reduction in serum uric acid levels, resulting in mobilization of urate from tissue deposits. In order to prevent gout flares when Febuxostat is initiated, concurrent prophylactic treatment with an NSAID or colchicine is recommended.
- There was a higher rate of cardiovascular thromboembolic events (cardiovascular deaths, non-fatal myocardial infarctions, and non-fatal strokes) in patients treated with Febuxostat. Monitor for signs and symptoms of myocardial infarction (MI) and stroke.
- There have been reports of fatal and non-fatal hepatic failure in patients taking Febuxostat, although the reports contain insufficient information necessary to establish the probable cause. Increase transaminase elevations greater than three times the upper limit of normal (ULN) were observed. NO dose-effect relationship for these transaminase elevations was noted. Obtain a liver test panel (serum alanine aminotransferase [ALT], aspartate aminotransferase [AST], alkaline phosphatase, and total bilirubin) as a baseline before initiating Febuxostat. Measure liver tests promptly in patients who report symptoms that may indicate liver injury, including fatigue, anorexia, right upper abdominal discomfort, dark urine or jaundice. In this clinical context, if the patient is found to have abnormal liver tests (ALT greater than three times the upper limit of the reference range), Febuxostat treatment should be interrupted, and investigation done to establish the probable cause. Febuxostat should not be restarted in these patients without another explanation for the liver test abnormalities. Patients who have serum ALT greater than three times the reference range with serum total bilirubin greater than two times the reference range without alternative etiologies are at risk for severe drug-induced liver injury and should not be restarted on Febuxostat. For patients with lesser elevations of serum ALT or bilirubin and with an alternate probable cause, treatment with Febuxostat can be used with caution.
- Serious skin and hypersensitivity reactions, including Stevens-Johnson Syndrome, drug reaction with eosinophilia and systemic symptoms (DRESS), and toxic epidermal necrolysis (TEN) have been reported in patients taking Febuxostat. Discontinue Febuxostat if serious skin reactions are suspected. Febuxostat should be used with caution in these patients.

OVERDOSAGE
Patients with an overdose should be managed by symptomatic and supportive care provided.

DOSAGE AND INSTRUCTIONS
To be sold and used on the prescription of a registered medical practitioner only. Keep out of reach of children. Do not store above 30°C. Keep in a dry place. Protect from light.

PRESENTATION
Hiloric 40mg Tablets: Alu. Alu. Blister Pack of 2 x 10's.
Hiloric 80mg Tablets: Alu. Alu. Blister Pack of 2 x 10's.

ہائیلورِک®

(فیبکسوسٹیٹ)

خوراک و ہدایات:

صرف مستند ڈاکٹر کے نسخہ کے مطابق ہی دوا فروخت اور استعمال کی جائے۔

بچوں کی پہنچ سے دور رکھیں۔ 30°C سے زیادہ درجہ حرارت پر نہ رکھیں۔

خشک جگہ پر رکھیں۔ روشنی سے بچائیں۔

Manufactured by
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