FUBU

40mg, 80mg Tablets

[Febuxostat]

فیوبو

۴۰ ملی گرام، ۸۰ ملی گرام گولیاں۔

DESCRIPTION:
FUBU (Febuxostat) is a non-purine selective inhibitor of xanthine oxidase. Febuxostat is chemically described as 2-[3-cyano-4-(2-methylpropoxy) phenyl]-4-methylthiazole 5-carboxylic acid. Its molecular formula is $C_{16}H_{16}N_2O_3S$ with molecular weight of 316.38.

QUALITATIVE AND QUANTITATIVE COMPOSITION:
FUBU (Febuxostat) is available for oral administration as:

1. FUBU Tablet 40mg
Each film coated tablet contains:
Febuxostat.....40mg
(Product Specs.: Sigma)

2. FUBU Tablet 80mg
Each film coated tablet contains:
Febuxostat.....80mg
(Product Specs.: Sigma)

CLINICAL PHARMACOLOGY:

Mechanism of Action:
Febuxostat is a potent, non-purine, selective inhibitor of xanthine oxidase (XO) that achieves its therapeutic effect of decreasing serum uric acid by selectively inhibiting xanthine oxidase. Uric acid is the end product of purine metabolism and is generated in the cascade of hypoxanthine → xanthine → uric acid. Both steps in the transformation are catalyzed by xanthine oxidase. Febuxostat has been shown to potently inhibit both the oxidized and reduced forms of xanthine oxidase. At therapeutic concentrations febuxostat does not inhibit other enzymes involved in purine or pyrimidine metabolism, namely, guanine deaminase, hypoxanthine guanine phosphoribosyltransferase, orotate phosphoribosyltransferase, orotidine monophosphate decarboxylase or purine nucleoside phosphorylase.

Pharmacokinetics:

Absorption:
Febuxostat is rapidly and extensively absorbed following oral dose administration, with a tmax at approximately 1.0 to 1.5 hours and about 84% absorbed.
Febuxostat may be taken without regard to food.

Distribution:
The mean apparent steady state volume of distribution (Vss/F) of febuxostat was approximately 50L. The plasma protein binding of febuxostat is approximately 99.2 %,(primarily to albumin), and is constant over the concentration range achieved with 40mg and 80mg doses.

Metabolism:
Febuxostat is extensively metabolized by conjugation via uridine diphosphate glucuronosyltransferase (UDPGT) enzyme system and oxidation via the cytochrome P450 (CYP) system. Four pharmacologically active hydroxyl metabolites have been identified, of which three occur in plasma of humans. In vitro studies with human liver microsomes showed that those oxidative metabolites were formed primarily by CYP1A1, CYP1A2, CYP2C8 or CYP2C9 and febuxostat glucuronide was formed mainly by UGT 1A1, 1A8, and 1A9.

Excretion:
Febuxostat is eliminated by both hepatic and renal pathways. Following an 80mg oral dose of ^{14}C-labeled febuxostat, approximately 49% of the dose was recovered in the urine. In addition to the urinary excretion, approximately 45% of the dose was recovered in the feces. The apparent mean terminal half-life ($t_{1/2}$) of febuxostat was approximately 5 to 8 hours.

Special Populations:

Renal Impairment:
Following multiple doses of 80mg of febuxostat in patients with mild, moderate or severe renal insufficiency, the Cmax of febuxostat did not change, relative to subjects with normal renal function.

Hepatic Impairment:
Following multiple doses of 80mg of febuxostat in patients with mild (Child-Pugh Class A) or moderate (Child-Pugh Class B) hepatic insufficiency, the Cmax and AUC of febuxostat and its metabolites did not change significantly compared to subjects with normal hepatic function.

THERAPEUTIC INDICTAIONS:
FUBU (Febuxostat) is indicated for the chronic management of hyperuricemia in patients with gout.

DOSAGE AND ADMINISTRATION:
For treatment of hyperuricemia in patients with gout, **FUBU** (Febuxostat) is recommended at 40mg or 80mg once daily. The recommended starting dose of **FUBU** (Febuxostat) is 40mg once daily. For patients who do not achieve a serum uric acid (sUA) less than 6mg/dL after 2 weeks with 40mg, **FUBU** (Febuxostat) 80mg is recommended.
FUBU (Febuxostat) can be taken without regard to food or antacid use.

Tumor Lysis Syndrome:
The recommended oral dose of **FUBU** is 120mg once daily without regard to food.
FUBU should be started two days before the beginning of cytotoxic therapy and continued for a minimum of 7 days, however treatment may be prolonged up to 9 days according to chemotherapy duration as per clinical judgment.

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

WARNING:
There was increased risk of cardiovascular (CV) death with febuxostat, Physician should advise patients to seek medical attention right away if they experience symptoms like chest pain, shortness of breath, and irregular heartbeat while taking the drug. Febuxostat use should be limited to patients who do not respond to or cannot tolerate allopurinol.

PRECAUTIONS:
-Treatment with febuxostat in patients with ischemic heart disease or congestive heart failure is not recommended.
- After initiation of febuxostat, an increase in gout flares is frequently observed. In order to prevent gout flares when febuxostat is initiated, concurrent prophylactic treatment with an NSAID or colchicine is recommended.
- As with other urate lowering medicinal products, in patients in whom the rate of urate formation is greatly increased the absolute concentration of xanthine in urine could, in rare cases, rise sufficiently to allow deposition in the urinary tract. As there has been no experience with febuxostat, its use in these populations is not recommended.
- Laboratory assessment of liver function is recommended at, for example 2 and 4 months following initiation of febuxostat and periodically thereafter.

Pregnancy:
Febuxostat should not be used during pregnancy.

Nursing mothers:
Febuxostat should not be used while breast feeding.

DRUG INTERACTIONS:

Xanthine oxidase substrate drugs:
Drugs metabolized by XO are contraindicated with febuxostat. Inhibition of XO by Febuxostat may cause increased plasma concentrations of these drugs leading to toxicity and hematological adverse effects.

Naproxen and other inhibitors of glucuronidation:
Febuxostat metabolism depends on Uridine Glucuronosyl Transferase UGT enzymes. Medicinal products that inhibit glucuronidation, such as NSAIDs and probenecid, could affect the elimination of febuxostat. In healthy subjects concomitant use of febuxostat and naproxen 250mg BID was associated with an increase in febuxostat exposure. Febuxostat can be co-administered with naproxen with no dose adjustment of febuxostat or naproxen being necessary.

Inducers of glucuronidation:
Potent inducers of UGT enzymes might possibly lead to increased metabolism and decreased efficacy of febuxostat. Monitoring of serum uric acid is therefore recommended 1-2 weeks after start of treatment with a potent inducer of glucuronidation. Conversely, cessation of treatment of an inducer might lead to increased plasma levels of febuxostat.

ADVERSE REACTIONS:
The following adverse drug reactions have been reported during therapy with Febuxostat:

Common:
Headache, diarrhea, nausea, rash and LFT abnormalities.

Uncommon:
Blood amylase increase, platelet count decrease, blood creatinine increase, hemoglobin decrease, blood urea increase , LDH increase, triglycerides increase, dizziness, paraesthesia, somnolence, altered taste, abdominal pain, gastro-oesophageal reflux disease, vomiting, dry mouth, dyspepsia, constipation, frequent stools, flatulence, gastrointestinal discomfort, nephrolithiasis, hematuria, polakiuria, dermatitis, urticaria, pruritus, arthralgia, arthritis, myalgia, muscle cramp, musculoskeletal pain, weight increase, increased appetite, hypertension, flushing, hot flush, fatigue, edema, influenza like symptoms and libido decreased.

Rare:
Palpitations, renal insufficiency, asthenia, thirst, nervousness and insomnia.

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

INSTRUCTIONS:
- Store below 30°C.
- Protect from light & moisture.
- Keep out of reach of children.

To be sold on prescription of a registered medical practitioner.

HOW SUPPLIED:
FUBU (Febuxostat) 40mg Tablets are available in pack of 20's.
FUBU (Febuxostat) 80mg Tablets are is available in pack of 20's.

خوراک: ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔
ہدایت: دوا کو بچوں کی پہنچ سے دور رکھیں۔
روشنی اور نمی سے بچائیں۔ بچوں کی پہنچ سے دور رکھیں۔
صرف رجسٹرڈ ڈاکٹر کے نسخے کے مطابق فروخت کریں۔

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