For the use of a Registered Medical Practitioner or a Hospital or a Laboratory only

FEBUGOOD

1. Generic Name

Febuxostat Tablets 40 and 80 mg

2. Qualitative and quantitative Composition:

FEBUGOOD 40

Each film coated tablet contains:

Febuxostat… 40 mg

Excipients… q.s.

Colours: Yellow Oxide of Iron & Titanium Dioxide I.P.

FEBUGOOD 80

Each film coated tablet contains:

Febuxostat… 80 mg

Excipients… q.s.

Colours: Sunset yellow FCF &Titanium Dioxide I.P.

The excipients used are Maize starch, Polyvinyl pyrrolidone K30, Microcrystalline cellulose, Crospovidone, Isopropyl alcohol, Croscarmellose sodium, Aerosil, Magnesium stearate, Hypromellose, Polyethylene Glycol 6000, purified Talc, Titanium dioxide, Yellow Oxide of Iron, Dichloromethane, Sunset yellow FCF Lake.

3. Dosage form and strength

Dosage form: Tablet

Strength: Febuxostat 40 and 80 mg

4. Clinical particulars

4.1. Therapeutic indication

Febuxostat is a Xanthine Oxidase (XO) inhibitor indicated for the treatment of chronic hyperuricemia in conditions where urate deposition has already occurred (including a history, or presence of tophus and / or gouty arthritis).

4.2. Posology and method of administration

Posology

For treatment of hyperuricemia in patients with gout, FEBUGOOD is recommended at 40 mg or 80 mg once daily. The recommended starting dose of FEBUGOOD is 40 mg once daily. For patients who do not achieve a serum uric acid (sUA) less than 6 mg per dL after 2 weeks with 40 mg, FEBUGOOD 80 mg is recommended. Febuxostat works sufficienctly quickly to allow retesting of the serum uric acid after 2 weeks. The theapeutic target is to decrease and maintain serum uric acid below 6 mg/dl (357 μmol/l). FEBUGOOD can be taken without regard to food or antacid use.

Method of administration

These should be swallowed whole with water.

4.3. Contraindications

- Febuxostat is contraindicated in patients being treated with azathioprine, mercaptopurine, or theophylline.
- Hypersensitivity to the active substance or to any of the excipients.

4.4. Special warnings and precautions for use

Cardio-vascular disorders

Treatment with febuxostat in patients with ischemic heart disease or congestive heart failure is not recommended and present evidence states that it increases the cardiovascular-thrombo embolic events (cardiovascular deaths, non-fatal myocardial infarctions, and non-fatal strokes) in those subjects who are on febuxostat than allopurinol. A causal relationship with febuxostat has not been established.

Gout Flare

After initiation of febuxostat therapy, 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. If a gout flare occurs during febuxostat treatment, it should not be discontinued. The gout flare should be managed concurrently with NSAID or colchicine as appropriate for the individual patient. Continuous treatment with febuxostat decreases frequency and intensity of gout flares.

Liver Enzyme Elevations

During randomized controlled studies, transaminase elevations greater than 3 times the upper limit of normal were observed. Hence it is recommended that liver function should be monitored before initiation of therapy and thereafter.

Thyroid disorders

Increased TSH values (>5.5 µIU/ml) were observed in patients on long-term treatment with febuxostat (5.0%) in the long term open label extension studies. Caution is required when febuxostat is used in patients with alteration of thyroid function.

Xanthine deposition

As with other urate lowering medicinal products, in patients in whom the rate of urate formation is greatly increased (e.g. malignant disease and its treatment, Lesch-Nyhan syndrome) 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.

Lactose

Febuxostat tablets contain lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.5. Drugs interactions

Effect of Febuxostat on Other Drugs

Xanthine Oxidase Substrate Drugs-Azathioprine, Mercaptopurine, and Theophylline: Febuxostat is an XO inhibitor. Drug interaction studies of febuxostat with drugs that are metabolized by XO (e.g., theophylline, mercaptopurine, azathioprine) have not been conducted. Inhibition of XO by febuxostat may cause increased plasma concentrations of these drugs leading to toxicity. Febuxostat is contraindicated in patients being treated with azathioprine, mercaptopurine and theophylline. Azathioprine and mercaptopurine undergo

metabolism via three major metabolic pathways, one of which is mediated by XO. Although febuxostat drug interaction studies with azathioprine and mercaptopurine have not been conducted, concomitant administration of allopurinol [a xanthine oxidase inhibitor] with azathioprine or mercaptopurine has been reported to substantially increase plasma concentrations of these drugs. Because febuxostat is a XO inhibitor, it could inhibit the XO-mediated metabolism of azathioprine and mercaptopurine leading to increased plasma concentrations of azathioprine or mercaptopurine that could result in severe toxicity.

Theophylline is a CYP1A2 and XO substrate. Although no febuxostat drug interaction study with theophylline has been conducted, concomitant administration of theophylline with allopurinol, a xanthine oxidase inhibitor at doses ≥ 600 mg per day, has been reported to increase theophylline plasma concentrations. Because febuxostat is a xanthine oxidase inhibitor and theophylline is a low therapeutic index drug, febuxostat could inhibit the XO-mediated metabolism of theophylline leading to increased plasma concentrations of theophylline that could induce severe theophylline toxicity.

P450 Substrate Drugs:

In vitro studies have shown that febuxostat does not inhibit P450 enzymes CYP1A2, 2C9, 2C19, 2D6, or 3A4 and it also does not induce CYP1A2, 2B6, 2C9, 2C19, or 3A4 at clinically relevant concentrations. As such, pharmacokinetic interactions between febuxostat and drugs metabolized by these CYP enzymes are unlikely.

Effect of Other Drugs on febuxostat

Febuxostat is metabolized by conjugation and oxidation via multiple metabolizing enzymes. The relative contribution of each enzyme isoform is not clear. A drug interaction between febuxostat and a drug that inhibits or induces one particular enzyme isoform is in general not expected.

In Vivo Drug Interaction Studies

Colchicine: No dose adjustment is necessary for either febuxostat or colchicine when the two drugs are co-administered. Administration of febuxostat (40 mg once daily) with colchicine (0.6 mg twice daily) resulted in an increase of 12% in Cmax and 7% in AUC24 of febuxostat. In addition, administration of colchicine (0.6 mg twice daily) with febuxostat (120 mg daily) resulted in less than 11% change in Cmax or AUC of colchicine for both AM and PM doses. These changes were not considered clinically significant.

Naproxen: No dose adjustment is necessary for febuxostat or naproxen when the two drugs are co-administered. Administration of febuxostat (80 mg once daily) with naproxen (500 mg twice daily) resulted in a 28% increase in Cmax and a 40% increase in AUC of febuxostat. The increases were not considered clinically significant. In addition, there were no significant changes in the Cmax or AUC of naproxen (less than 2%).

Indomethacin: No dose adjustment is necessary for either febuxostat or indomethacin when these two drugs are co-administered. Administration of febuxostat (80 mg once daily) with indomethacin (50 mg twice daily) did not result in any significant changes in Cmax or AUC of febuxostat or indomethacin (less than 7%).

Hydrochlorothiazide: No dose adjustment is necessary for febuxostat when co-administered with hydrochlorothiazide. Administration of febuxostat (80 mg) with hydrochlorothiazide (50 mg) did not result in any clinically significant changes in Cmax or AUC of febuxostat (less than 4%), and serum uric acid concentrations were not substantially affected.

Warfarin: No dose adjustment is necessary for warfarin when co-administered with febuxostat. Administration of febuxostat (80 mg once daily) with warfarin had no effect on the

pharmacokinetics of warfarin in healthy subjects. INR and Factor VII activity were also not affected by the co-administration of febuxostat.

Desipramine: Co-administration of drugs that are CYP2D6 substrates (such as desipramine) with febuxostat are not expected to require dose adjustment. Febuxostat was shown to be a weak inhibitor of CYP2D6 in vitro and in vivo. Administration of febuxostat (120 mg once daily) with desipramine (25 mg) resulted in an increase in Cmax (16%) and AUC (22%) of desipramine, which was associated with a 17% decrease in the 2-hydroxydesipramine to desipramine metabolic ratio (based on AUC).

4.6. Use in special populations (such as pregnant women, lactating women, paediatric patients, geriatric patients etc.)

No dose adjustment is necessary when administering FEBUGOOD in patients with mild to moderate renal impairment. The recommended starting dose of FEBUGOOD is 40 mg once daily. For patients who do not achieve a sUA less than 6 mg per dL after 2 weeks with 40 mg, FEBUGOOD 80 mg is recommended.

No dose adjustment is necessary in patients with mild to moderate hepatic impairment.

4.7. Effects on ability to drive and use machines

Febugood has no or negligible influence on the ability to drive and use machines.

4.8. Undesirable effects

From randomized clinical trial experience, most common adverse reaction (≥1%) were liver function abnormality, nausea, diarrhea, arthralgia, rash, and dizziness. While less common adverse reaction (≥1%) were as follows:

Blood and Lymphatic System Disorders: Anemia, idiopathic thrombocytopenic purpura, leukocytosis/leukopenia, neutropenia, pancytopenia, splenomegaly, thrombocytopenia.

Cardiac Disorders: Angina pectoris, atrial fibrillation/flutter, cardiac murmur, ECG abnormal, palpitations, sinus bradycardia, tachycardia.

Ear and Labyrinth Disorders: Deafness, tinnitus, vertigo.

Eye Disorders: Vision blurred.

Gastrointestinal Disorders: Abdominal distention, abdominal pain, constipation, dry mouth, dyspepsia, flatulence, frequent stools, gastritis, gastroesophageal reflux disease, gastrointestinal discomfort, gingival pain, haematemesis, hyperchlorhydria, hematochezia, mouth ulceration, pancreatitis, peptic ulcer, vomiting.

General Disorders and Administration Site Conditions: Asthenia, chest pain/discomfort, edema, fatigue, feeling abnormal, gait disturbance, influenza-like symptoms, mass, pain, thirst.

Hepatobiliary Disorders: Cholelithiasis/cholecystitis, hepatic steatosis, hepatitis, hepatomegaly.

Immune System Disorder: Hypersensitivity. Infections and Infestations: Herpes zoster. Procedural Complications: Contusion.

Metabolism and Nutrition Disorders: Anorexia, appetite decreased/increased, dehydration, diabetes mellitus, hypercholesterolemia, hyperglycemia, hyperlipidemia, hypertriglyceridemia, hypokalemia, weight decreased/increased.

Musculoskeletal and Connective Tissue Disorders: Arthritis, joint stiffness, joint swelling, muscle spasms/twitching/ tightness/weakness, musculoskeletal pain/stiffness, myalgia.

Nervous System Disorders: Altered taste, balance disorder, cerebrovascular accident, Guillain-Barré syndrome, headache, hemiparesis, hypoesthesia, hyposmia, lacunar infarction, lethargy, mental impairment, migraine, paresthesia, somnolence, transient ischemic attack, tremor.

Psychiatric Disorders: Agitation, anxiety, depression, insomnia, irritability, libido decreased, nervousness, panic attack, personality change.

Renal and Urinary Disorders: Hematuria, nephrolithiasis, pollakiuria, proteinuria, renal failure, renal insufficiency, urgency, incontinence.

Reproductive System and Breast Changes: Breast pain, erectile dysfunction, gynecomastia.

Respiratory, Thoracic and Mediastinal Disorders: Bronchitis, cough, dyspnea, epistaxis, nasal dryness, paranasal sinus hypersecretion, pharyngeal edema, respiratory tract congestion, sneezing, throat irritation, upper respiratory tract infection.

Skin and Subcutaneous Tissue Disorders: Alopecia, angio-edema, dermatitis, dermographism, ecchymosis, eczema, hair color changes, hair growth abnormal, hyperhidrosis, peeling skin, petechiae, photosensitivity, pruritus, purpura, skin discoloration/altered pigmentation, skin lesion, skin odor abnormal, bursitis, urticaria.

Vascular Disorders: Flushing, hot flush, hypertension, hypotension.

Laboratory Parameters: 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 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, triglyceride increases, prothrombin time prolonged, urinary casts, urine positive for white blood cells and protein.

Reporting of adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Report suspected adverse reactions via any point of contact available at www.torrentpharma.com.

4.9. Overdose

Human experience of overdose with FEBUGOOD is limited.

5. Pharmacological properties

5.1. Mechanism of Action

Febuxostat is xanthine oxidase (XO) inhibitor and shows its action by decreasing serum uric acid level. Febuxostat has been shown to potently inhibit both the oxidized and reduced forms of XO. It is not expected to inhibit other enzymes (like guanine deaminase, hypoxanthine guanine phosphoribosyltransferase, orotate phosphoribosyltransferase, orotidine monophosphate decarboxylase or purine nucleoside phosphorylase.) involved in purine and pyrimidine synthesis and metabolism at therapeutic concentrations.

5.2. Pharmacodynamic properties

Febuxostat shows dose dependent effect on the uric acid level. In healthy subjects it shows dose dependent decrease in 24 hour mean serum uric acid (sUA) level, and increases in the 24-hour mean xanthine concentration. In addition, there was a decrease in the total daily urinary uric acid excretion and also increase in the total daily urinary xanthine excretion. Percent reduction in 24-hour mean serum uric acid concentrations was 40% to 55% for 40mg to 80 mg of daily dosing.

The efficacy of febuxostat was demonstrated in two Phase 3 pivotal studies (APEX study and FACT study described below) that were conducted in 1832 patients with hyperuricemia and gout. In each phase 3 pivotal study, Febuxostat demonstrated superior ability to lower and maintain sUA levels compared to allopurinol. The primary efficacy endpoint in each study was the proportion of patients whose last 3 monthly sUA levels were < 6.0 mg/dl (357 µmol/l). No patients with organ transplant have been included in these studies.

APEX Study: The Allopurinol and Placebo-Controlled Efficacy Study of Febuxostat (APEX) was a Phase 3, randomized, double-blind, multicenter, 28-week study. One thousand and seventy-two (1072) patients were randomized: placebo (n=134),

FEBUXOSTAT 80 mg QD (n=267), FEBUXOSTAT 120 mg QD (n=269),

FEBUXOSTAT 240 mg QD (n=134) or Allopurinol (300 mg QD [n=258] for patients with a baseline serum creatinine ≤ 1.5 mg/dl or 100 mg QD [n=10] for patients with a baseline serum creatinine>1.5 mg/dl and 2.0 mg/dl). Two hundred and forty mg febuxostat (2 times the recommended highest dose) was used as a safety evaluation dose.

The APEX study showed statistically significant superiority of both the FEBUXOSTAT 80 mg QD and the FEBUXOSTAT 120 mg QD treatment arms versus the conventionally used doses of allopurinol 300mg (n = 258) /100mg (n = 10) treatment arm in reducing the sUA below 6 mg/dl (357 µmol/l) (see Table 1).

FACT Study: The Febuxostat Allopurinol Controlled Trial (FACT) Study was a Phase 3, randomized, double-blind, multicenter, 52-week study. Seven hundred sixty (760) patients were randomized: FEBUXOSTAT 80 mg QD (n=256), FEBUXOSTAT 120 mg QD (n=251), or allopurinol 300 mg QD (n=253).

The FACT study showed the statistically significant superiority of both FEBUXOSTAT 80 mg and FEBUXOSTAT 120 mg QD treatment arms versus the conventionally used dose of allopurinol 300 mg treatment arm in reducing and maintaining sUA below 6 mg/dl (357 µmol/l).

Table 1 summarises the primary efficacy endpoint results:

Proportion of Patients with Serum Uric Acid Levels <6.0 mg/dl (357µmol/l) Last Three Monthly Visits

Study	FEBUXOSTAT 80 mg QD	FEBUXOSTAT 120 mg QD	Allopurinol 300/100 mg QD[1]
APEX (28 weeks)	48 % * (n=262)	65% *, # (n=269)	22% (n=268)
FACT (52 weeks)	53%* (n=255)	62%* (n=250)	21% (n=251)
Combined Results	51%* (n=517)	63%*, # (n=519)	22% (n=519)

[1] results from subjects receiving either 100 mg QD (n=10: patients with serum creatinine >1.5 and ≤ 2.0 mg/dl) or 300 mg QD (n=509) were pooled for analyses.

* p < 0.001 vs allopurinol, # p < 0.001 vs 80 mg

The ability of FEBUXOSTAT to lower serum uric acid levels was prompt and persistent. Reduction in serum uric acid level to 1.5 mg/dl and ≤ 2.0 mg/dl). For renally impaired subjects who were randomized to allopurinol, the dose was capped at 100mg QD. FEBUXOSTAT achieved the primary efficacy endpoint in 44% (80 mg QD), 45% (120 mg QD), and 60% (240 mg QD) of patients compared to 0% in the allopurinol 100 mg QD and placebo groups. There were no clinically significant differences in the percent decrease in serum uric acid concentration in healthy subjects irrespective of their renal function (58 % in the normal renal function group and 55% in the severe renal dysfunction group).

Primary endpoint in the sub group of patients with sUA r10 mg/dl Approximately 40% of patients (combined APEX and FACT) had a baseline sUA of r10 mg/dl. In this subgroup FEBUXOSTAT achieved the primary efficacy endpoint in 41% (80 mg QD), 48% (120 mg QD), and 66% (240 mg QD) of patients compared to 9% in the allopurinol 300 mg/100 mg QD and 0 % in the placebo groups.

Clinical Outcomes: proportion of patients requiring treatment for a gout flare and tophi size change

The proportion of subjects requiring treatment for a gout flare (APEX and FACT Study) was numerically lower in the groups that achieved an average post-baseline serum urate level <6.0 mg/dl, <5.0 mg/dl, or <4.0 mg/dl compared to the group that achieved an average post-baseline serum urate level r6.0 mg/dl during the last 32 weeks of the treatment period (Week 20-Week 24 to Week 48 - 52 intervals).

Two years of data from the Phase 3 Open Label Extension study showed that the maintenance of serum urate levels < 6 mg/dl (<357 µmol/l) resulted in a decrease in the incidence of gout flares with less than 3 % of subjects requiring treatment for a flare (i.e. more than 97 % of patients did not require treatment for a flare) at Month 16-24. This was associated with a reduction of tophus size leading to complete resolution in 54% of subjects at Month 24.

During the phase 3 clinical studies, mild liver function test abnormalities were observed in patients treated with febuxostat (3.5%). These rates were similar to the rates reported on allopurinol (3.6%). Increased TSH values (<5.5 µIU/ml) were observed in patients on long-term treatment with febuxostat (5.0%) and patients with allopurinol (5.8%) in the long term open label extension studies.

The total exposure to FEBUXOSTAT in phase 3 pivotal studies and long-term extension studies is greater than 2700 patient-years.

5.3. Pharmacokinetic properties

In healthy subjects, maximum plasma concentrations (Cmax) and AUC of febuxostat increased in a dose proportional manner following single and multiple doses of 10 mg to 120 mg. For doses between 120 mg and 300 mg, a greater than dose proportional increase in AUC is observed for febuxostat. There is no accumulation when therapeutic doses are administered every 24 hours. Febuxostat has an apparent mean terminal elimination half-life (t1/2) of approximately 5 to 8 hours. Febuxostat pharmacokinetic parameters for patients with hyperuricemia and gout estimated by population pharmacokinetic analyses were similar to those estimated in healthy subjects.

Absorption: The absorption of febuxostat following oral dose administration was estimated to be 49% to 84%. Maximum plasma concentrations (tmax) of febuxostat occurred between 1 to 1.5 hours post-dose. Absolute bioavailability of the febuxostat tablet has not been studied.

Following multiple 80 mg once daily doses with a high fat meal, there was a 49% decrease in Cmax and an 18% decrease in AUC, respectively. However, no clinically significant change in the percent decrease in serum uric acid concentration was observed (58% fed vs. 51% fasting). Thus, Febuxostat may be taken with or without food.

Concomitant ingestion of an antacid containing magnesium hydroxide and aluminum hydroxide with an 80 mg single dose of Febuxostat has been shown to delay absorption of febuxostat (approximately 1 hour) and to cause a 31% decrease in Cmax and a 15% decrease in AUC∞. As AUC rather than Cmax was related to drug effect, change observed in AUC was not considered clinically significant. Hence, Febuxostat may be taken without regard to antacid use.

Distribution: The mean apparent steady state volume of distribution (Vss/F) of febuxostat was 29 to 75 L after oral doses of 10mg to 300mg. The plasma protein binding of febuxostat is approximately 99.2%, (primarily to albumin), and is constant over the concentration range achieved with 40 mg and 80 mg doses while for active metabolite value ranges from 82 to 91%.

Metabolism: Febuxostat is extensively metabolized by both conjugation via uridine diphosphate glucuronosyltransferase (UGT) enzymes including UGT1A1, UGT1A3, UGT1A9, and UGT2B7 and oxidation via cytochrome P450 (CYP) enzymes including CYP1A2, 2C8 and 2C9 and non-P450 enzymes. The oxidation of the isobutyl side chain leads to the formation of four pharmacologically active hydroxy metabolites, all of which occur in plasma of humans at a much lower extent than febuxostat. In urine and feces, acyl glucuronide metabolites of febuxostat (~35% of the dose), and oxidative metabolites, 67M-1 (~10% of the dose), 67M-2 (~11% of the dose), and 67M-4, a secondary metabolite from 67M-1, (~14% of the dose) appeared to be the major metabolites of febuxostat in vivo.

Elimination: Febuxostat is eliminated by both hepatic and renal pathways. Following an 80 mg oral dose of 14C-labeled febuxostat, approximately 49% of the dose was recovered in the urine as unchanged febuxostat (3%), the acyl glucuronide of the drug (30%), its known oxidative metabolites and their conjugates (13%), and other unknown metabolites (3%). In addition to the urinary excretion, approximately 45% of the dose was recovered in the feces as the unchanged febuxostat (12%), the acyl glucuronide of the drug (1%), its known oxidative metabolites and their conjugates (25%), and other unknown metabolites (7%). The apparent mean terminal elimination half-life (t½) of febuxostat was approximately 5 to 8 hours.

Special Populations

Pediatric Use: The pharmacokinetics of febuxostat in patients under the age of 18 years have not been studied.

Geriatric Use: The Cmax and AUC of febuxostat and its metabolites following multiple oral doses of febuxostat in geriatric subjects (≥ 65 years) were similar to those in younger subjects (18-40 years). In addition, the percent decrease in serum uric acid concentration was similar between elderly and younger subjects. No dose adjustment is necessary in geriatric patients.

Renal Impairment: Following multiple 80 mg doses of febuxostat in healthy subjects with mild (Clcr 50-80 mL/min), moderate (Clcr 30-49 mL/min) or severe renal impairment (Clcr 10-29 mL/min), the Cmax of febuxostat did not change relative to subjects with normal renal function (Clcr greater than 80 mL/min). AUC and half-life of febuxostat increased in subjects with renal impairment in comparison to subjects with normal renal function, but values were

similar among three renal impairment groups. Mean febuxostat AUC values were up to 1.8 times higher in subjects with renal impairment compared to those with normal renal function. Mean Cmax and AUC values for 3 active metabolites increased up to 2- and 4-fold, respectively. However, the percent decrease in serum uric acid concentration for subjects with renal impairment was comparable to those with normal renal function (58% in normal renal function group and 55% in the severe renal function group).

No dose adjustment is necessary in patients with mild to moderate renal impairment.

The recommended starting dose of febuxostat is 40 mg once daily. For patients who do not achieve a sUA less than 6 mg per dL after 2 weeks with 40 mg, febuxostat 80 mg is recommended. There is insufficient data in patients with severe renal impairment; caution should be exercised in those patients. Febuxostat has not been studied in end stage renal impairment patients who are on dialysis.

Hepatic Impairment: Following multiple 80 mg doses of febuxostat in patients with mild (Child-Pugh Class A) or moderate (Child-Pugh Class B) hepatic impairment, an average of 20-30% increase was observed for both Cmax and AUC24 (total and unbound) in hepatic impairment groups compared to subjects with normal hepatic function. In addition, the percent decrease in sUA concentration was comparable between different hepatic groups (62% in healthy group, 49% in mild hepatic impairment group, and 48% in moderate hepatic impairment group). No dose adjustment is necessary in patients with mild or moderate hepatic impairment. Caution should be exercised in subjects with severe hepatic impairment (Child-Pugh Class C) as there are no studies available for those subjects.

Gender: Following multiple oral doses of febuxostat, the Cmax and AUC24 of febuxostat were 30% and 14% higher in females than in males, respectively. However, weight-corrected Cmax and AUC were similar between the genders. In addition, the percent decrease in sUA concentrations was similar between genders. No dose adjustment is necessary based on gender.

6. Nonclinical properties

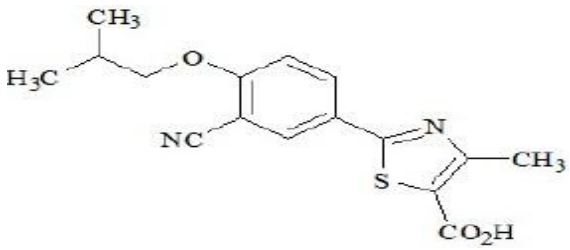
6.1. Animal Toxicology or Pharmacology

Not Available

7. Description

Febuxostat is a xanthine oxidase inhibitor. The Chemical name of febuxostat is 2-[3-cyano-4-(2-methylpropoxy) phenyl]-4-methylthiazole-5-carboxylic acid, with a molecular weight of 316.38. The empirical formula is $C_{16}H_{16}N_2O_3S$.

The chemical structure is:



Febugood 40 is Yellow coloured, round shaped, biconvex, plain on both sides, film coated tablets. The excipients used are Maize starch, Polyvinyl pyrrolidone K30, Microcrystalline cellulose, Crospovidone, Isopropyl alcohol, Croscarmellose sodium, Aerosil, Magnesium stearate, Hypromellose, Polyethylene Glycol 6000, purified Talc, Titanium dioxide, Yellow Oxide of Iron, Dichloromethane.

Febugood 80 is Orange coloured, round shaped, biconvex, plain on both sides, film coated tablets. The excipients used are Maize starch, Polyvinyl pyrrolidone K30, Microcrystalline cellulose, Crospovidone, Isopropyl alcohol, Croscarmellose sodium, Aerosil, Magnesium stearate, Hypromellose, Polyethylene Glycol 6000, purified Talc, Titanium dioxide, Sunset yellow FCF Lake, Dichloromethane.

8. Pharmaceutical particulars

8.1. Incompatibilities

Not applicable

8.2. Shelf-life

Do not use later than the date of expiry.

8.3. Packaging information

FEBUGOOD 40 and 80 mg are available as blister strip of 10 tablets.

8.4. Storage and handing instructions

Store below 30°C. Protect from light and moisture.

Keep out of reach of children.

9. Patient Counselling Information

Ask the patients to inform the treating physicians in case of any of the below:

- Have any allergies
- Have kidney or liver problems
- Are pregnant or plan to become pregnant
- Are breastfeeding or plan to breastfeed
- Have any serious illness
- Are taking any medicines (prescription, over-the-counter, vitamins, or herbal products)

10. Details of manufacturer

Theon Pharmaceuticals Ltd.

Vill. Saini Majra, Tehsil Nalagarh,

Dist. Solan, HP-174 101

11. Details of permission or licence number with date

Licence No. MNB/06/409 issued on date 09.12.2016

12. Date of revision

MAR 2026

MARKETED BY

TORRENT PHARMA

TORRENT PHARMACEUTICALS LTD.

IN/FEBUGOOD 40 and 80 mg/MAR-2026/03/PI