SAFETY DATA SHEET
Febuxostat Tablets

Strength: 40,80mg

Pack Size: 30's 90's 100's 500's and 1000's Tablets per bottle, 10x10 Unit dose Tablets per carton

Revision No.: 00

EMERGENCY OVERVIEW

Each **FEBUXOSTAT TABLETS, USP 40mg,80mg** intended for oral administration contains Febuxostat and excipients generally considered to be non-toxic and non-hazardous in small amounts under conditions of normal occupational exposure.

Section 1. IDENTIFICATION OF THE PRODUCT

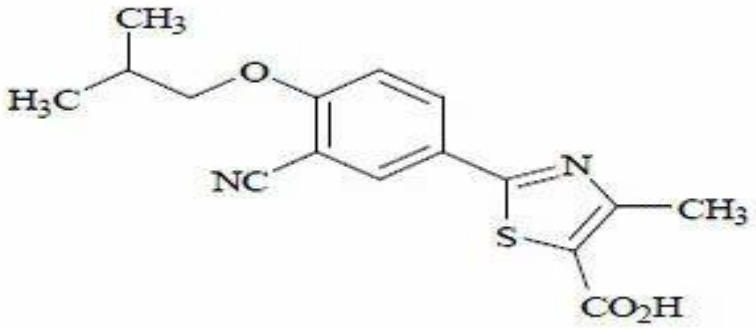
Product Name: **FEBUXOSTAT TABLETS, USP 40mg 80mg**

Active Pharmaceutical Ingredient: **FEBUXOSTAT**

Formula: C16H16N2 O3 S

Chemical Name: 2-[3-cyano-4-(2-methylpropoxy) phenyl]-4- methylthiazole-5-carboxylic acid.

Structure:



Manufacturer / supplier identification

Company: Zydus Lifesciences Limited

Address: Survey No. 417, 419 & 420,
Sarkhej – Bavla National Highway No. 8A, Village – Moraiya, Taluka – Sanand, Dist.- Ahmedabad - 382 210, Gujarat State, India.

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Therapeutic Category: Xanthine Oxidase Inhibitors

Mechanism of Action: Febuxostat, a xanthine oxidase inhibitor, achieves its therapeutic effect by decreasing serum uric acid. Febuxostat is not expected to inhibit other enzymes involved in purine and pyrimidine synthesis and metabolism at therapeutic concentrations.

Indications: Febuxostat tablets are xanthine oxidase (XO) inhibitor indicated for the chronic management of hyperuricemia in adult patients with gout who have an inadequate response to a maximally titrated dose of allopurinol, who are intolerant to allopurinol, or for whom treatment with allopurinol is not advisable.

Recommended usage:	The recommended febuxostat dosage is 40 mg or 80 mg once daily. The recommended starting dosage of febuxostat tablet is 40 mg once daily. For patients who do not achieve a serum uric acid (sUA) less than 6 mg/dL after two weeks, the recommended febuxostat dosage is 80 mg once daily. Febuxostat tablets can be taken without regard to food or antacid use. The recommended dosage of febuxostat is limited to 40 mg once daily in patients with severe renal impairment. Testing for the target serum uric acid level of less than 6 mg/dL may be performed as early as two weeks after initiating febuxostat therapy.
Restriction on Use / Contraindications:	Febuxostat is contraindicated in patients being treated with azathioprine or mercaptopurine..

Section 2. HAZARDS IDENTIFICATION

DOSAGE AND ADMINISTRATION:	Recommended febuxostat dosage is 40 mg or 80 mg once daily. The recommended starting dose 40 mg once daily. For patients who do not achieve a serum uric acid (sUA) less than 6 mg/dL after 2 weeks, the recommended dosage is 80 mg once daily. • Can be administered without regard to food or antacid use. • Limit the dosage of febuxostat tablets to 40 mg once daily in patients with severe renal impairment.
ADVERSE EFFECTS:	The following serious adverse reactions are described elsewhere in the prescribing information: • Cardiovascular Death • Hepatic • Serious Skin Reactions
OVER DOSE EFFECT:	Febuxostat tablets were studied in healthy patients in doses up to 300 mg daily for seven days without evidence of dose-limiting toxicities. No overdose of febuxostat tablet was reported in clinical studies. Patients should be managed by symptomatic and supportive care should there be an overdose.
PREGNANCY COMMENTS:	Limited available data with febuxostat use in pregnant women are insufficient to inform a drug associated risk of adverse developmental outcomes. No adverse developmental effects were observed in embryo-fetal development studies with oral administration of febuxostat to pregnant rats and rabbits during organogenesis at doses that produced maternal exposures up to 40 and 51 times, respectively, the exposure at the maximum recommended human dose (MRHD). No adverse developmental effects were observed in a pre-and

postnatal development study with administration of febuxostat to pregnant rats from organogenesis through lactation at an exposure approximately 11 times the MRHD (see Data). The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the US general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2 to 4% and 15 to 20%, respectively.

WARNINGS & PRECAUTIONS:

CARDIOVASCULAR DEATH

Gout patients with established cardiovascular (CV) disease treated with febuxostat had a higher rate of CV death compared to those treated with allopurinol in a CV outcomes study.

Consider the risks and benefits of febuxostat when deciding to prescribe or continue patients on febuxostat. Febuxostat should only be used in patients who have an inadequate response to a maximally titrated dose of allopurinol, who are intolerant to allopurinol, or for whom treatment with allopurinol is not advisable.

Drug Interactions:

Concomitant administration of febuxostat with XO substrate drugs, azathioprine or mercaptopurine could increase plasma concentrations of these drugs resulting in severe toxicity.

Section 3. COMPOSITION / INFORMATION ON INGREDIENTS

Component	Exposure	CAS No.
Principle Component :		
Febuxostat	Not Found	144060-53-7
Inactive ingredients :		
colloidal silicon dioxide	Not Found	112926-00-8
croscarmellose sodium	Not Found	74811-65-7
lactose monohydrate	Not Found	10039-26-6
hypromellose	Not Found	9004-65-3
povidone	Not Found	25655-41-8
microcrystalline cellulose	Not Found	9004-34-6
polyethylene glycol	Not Found	25322-68-3
sodium stearyl fumarate	Not Found	4070-80-8
talc	Not Found	14807-96-6
titanium dioxide	Not Found	13463-67-7

Section 4. FIRST - AID MEASURES

Description of First Aid Measures

Eye Contact:	Flush with water while holding eyelids open for at least 15 minutes. Seek medical attention immediately.
Skin Contact:	Remove contaminated clothing. Flush area with large amounts of water. Use soap. Seek medical attention.
Ingestion:	Never give anything by mouth to an unconscious person. Wash out mouth with water. Do not induce vomiting unless directed by medical personnel. Seek medical attention immediately.
Inhalation:	Remove to fresh air and keep patient at rest. Seek medical attention immediately.

Section 5. FIRE FIGHTING MEASURES

Extinguishing Media:	Use carbon dioxide, dry chemical, or water spray.
Hazardous Combustion Products:	Formation of toxic gases is possible during heating or fire.
Fire Fighting Procedures:	During all firefighting activities, wear appropriate protective equipment, including self contained breathing apparatus.
Fire / Explosion Hazards:	Not applicable

Section 6. ACCIDENTAL RELEASE MEASURES

Health and Safety Precautions:	Personnel involved in clean-up should wear appropriate personal protective equipment. Minimize exposure.
Measures for Cleaning / Collecting:	Contain the source of spill if it is safe to do so. Collect spilled material by a method that controls dust generation. A damp cloth or a filtered vacuum should be used to clean spills of dry solids. Clean spill area thoroughly.
Measures for Environmental Protections:	Place waste in an appropriately labelled, sealed container for disposal. Care should be taken to avoid environmental release.
Additional Consideration for Large Spills:	Non-essential personnel should be evacuated from affected area. Report emergency situations immediately. Clean up operations should only be undertaken by trained personnel.

Section 7. HANDLING AND STORAGE

Storage	Store at 20°C to 25°C (68°F to 77°F) [See USP Controlled Room Temperature]. Protect from light.
Specific end use	Pharmaceutical drug product
Precautions for safe handling	If Tablets are crushed and/or broken, avoid breathing dust and avoid contact with eyes, skin, and clothing. Use appropriate ventilation. Avoid generating

airborne dust. When handling, use appropriate personal protective equipment. Wash thoroughly after handling. Releases to the environment should be avoided. Review and implement appropriate technical and procedural waste water and waste disposal measures to prevent occupational exposure or environmental releases. Potential points of process emissions of this material to the atmosphere should be controlled with dust collectors, HEPA filtration systems or other equivalent controls.

Section 8. EXPOSURE CONTROLS / PERSONAL PROTECTION

Engineering Controls:	Engineering controls should be used as the primary means to control exposures. General room ventilation is adequate unless the process generates dust, mist or fumes. Keep airborne contamination levels below the exposure limits listed above in this section.
Environmental Exposure Controls:	Refer to specific Member State legislation for requirements under Community environmental legislation.
Personal Protective Equipment:	Refer to applicable national standards and regulations in the selection and use of personal protective equipment (PPE).
Hands:	Impervious gloves are recommended if skin contact with drug product is possible and for bulk processing operations.
Eyes:	Wear safety glasses or goggles if eye contact is possible.
Skin:	Impervious protective clothing is recommended if skin contact with drug product is possible and for bulk processing operations.
Respiratory protection:	If the applicable Occupational Exposure Limit (OEL) is exceeded, wear an appropriate respirator with a protection factor sufficient to control exposures to below the OEL.

Section 9. PHYSICAL AND CHEMICAL PROPERTIES

Appearance

Physical state	Tablet
Description	Febuxostat Tablets, 40 mg are white to off-white, beveled-edge, oval-shaped tablets debossed with "401" on one side and plain on the other side and are supplied as follows: NDC 72578-136-06 in bottle of 30 tablets with child-resistant closure. NDC 72578-136-16 in bottle of 90 tablets with child-resistant closure. NDC 72578-136-01 in bottle of 100 tablets NDC 72578-136-05 in bottle of 500 tablets NDC 72578-136-10 in bottle of 1,000 tablets NDC 72578-136-77 in unit-dose blister cartons of 100 (10 x 10) unit-dose tablets. Febuxostat Tablets, 80 mg are white to off-white, beveled-edge, round-shaped tablets debossed with "402" on one side and plain on the other side and are supplied as follows:

	NDC 72578-137-06 in bottle of 30 tablets with child-resistant closure. NDC 72578-137-16 in bottle of 90 tablets with child-resistant closure. NDC 72578-137-01 in bottle of 100 tablets NDC 72578-137-05 in bottle of 500 tablets NDC 72578-137-10 in bottle of 1,000 tablets NDC 72578-137-77 in unit-dose blister cartons of 100 (10 x 10) unit-dose tablets
Pure/Mixture	Mixture

Section 10. STABILITY AND REACTIVITY

The product is stable

Section 11. TOXICOLOGICAL INFORMATION

Carcinogenesis, Mutagenesis, Impairment of Fertility	**Carcinogenesis, Mutagenesis, and Impairment of Fertility** Two year carcinogenicity studies were conducted in F344 rats and B6C3F1 mice. Increased transitional cell papilloma and carcinoma of the urinary bladder was observed at 24 mg/kg (25 times the MRHD on an AUC basis) and 18.75 mg/kg (12.5 times the MRHD on an AUC basis) in male rats and female mice, respectively. The urinary bladder neoplasms were secondary to calculus formation in the kidney and urinary bladder. Febuxostat showed a positive clastogenic response in a chromosomal aberration assay in a Chinese hamster lung fibroblast cell line with and without metabolic activation in vitro. Febuxostat was negative in the following genotoxicity assays: the in vitro Ames assay, in vitro chromosomal aberration assay in human peripheral lymphocytes, the L5178Y mouse lymphoma cell line assay, the in vivo mouse micronucleus assay, and the rat unscheduled DNA synthesis assay. Fertility and reproductive performance were unaffected in male or female rats that received febuxostat at oral doses up to 48 mg/kg/day (approximately 31 and 40 times the MRHD on an AUC basis in males and females respectively).

Section 12. ECOLOGICAL INFORMATION

Environmental Overview:	Environmental properties have not been investigated. Releases to the environment should be avoided.

Section 13. DISPOSAL CONSIDERATION

Disposal Recommendations	Dispose of waste in accordance with all applicable laws and regulations. Member State specific and Community specific provisions must be considered. Considering the relevant known environmental and human health hazards of the material, review and implement appropriate technical and procedural waste water and waste disposal measures to prevent occupational exposure and environmental release. It is recommended that waste minimization be practiced. The best available technology should be utilized to prevent environmental releases. This may include destructive techniques for waste and wastewater.

Section 14. TRANSPORT INFORMATION

Not regulated for transport under USDOT, EUADR, IATA, or IMDG regulations.

Section 15. REGULATORY INFORMATION

Generic Medicine, 205443
ANDA Number

Section 16. OTHER INFORMATION

Refer Product Packing Insert for more details

Date of issue: 27th May, 2023 **Supersedes edition:** 00

The information presented in the safety data sheet is, to the best of our knowledge, accurate and reliable. It characterizes the product with regard to the appropriate safety precautions. It does not represent a guarantee of the properties of the product.