ELACIN 80
(Febuxostat Tablets 80 mg)
SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT:

ELACIN 80 (Febuxostat Tablets 80 mg)

2 QUALITATIVE AND QUANTITATIVE COMPOSITION:

Batch size : 1,00,000 Tablets

Sr. No.	Ingredients	Spec	Label claim (mg)	Overages (%)	Qty/ Tablet (mg)	Qty/ batch (kg)	Function
	DRY MIXING						
1.	Febuxostat	IH	80.00	3	8.24	82.40	Xanthine Oxidase Inhibitor
2.	Starch	BP	--	--	1.70	17.00	binder
3.	Cross Carmellose sodium	BP	--	--	1.00	10.00	binder
4.	Micro Crystalline Cellulose	BP	--	--	4.00	40.00	binder
BINDING							
5.	PVPK-30	BP	--	--	0.45	4.50	Lubricant
6.	Iso Propyl Alcohol	BP	--	--	q.s	q.s	binder
	LUBRICATION						
7.	Talcum Powder	BP	--	--	0.36	3.60	binder
8.	Magnesium Stearate	BP	--	--	0.25	2.50	binder
9.	Cross Povidone	BP	--	--	0.40	4.00	binder
10.	Colloidal Silicon Dioxide	BP	--	--	0.10	1.00	Lubricant
11.	Cros Carmellose Sodium	BP	--	--	1.50	15.00	Lubricant
	Total				180.0	18.0	
	COATING						
12.	Fine coat	BP			0.3	3.00	Coating Material
13.	Iso Propyl Alcohol	BP			q.s	q.s	Solvent
14.	Methylene Dichloride	BP			q.s	q.s	Solvent
15.	Titanium Dixide	BP			0.04	0.40	Opacifier
16.	Talcum Powder	BP			0.02	0.20	Colouring Agent
17.	Poly Ethylene Glycol-6000	BP			0.04	0.40	Glident
	Total				184.00 mg	18.4 kg	

BP: British Pharmacopoeia 2017 edition
IH : In _House

3 PHARMACEUTICAL FORM

Description : White coloured, round shaped, biconvex, film coated tablets.

Pharmaceutical class: Xanthine Oxidase Inhibitor

4 CLINICAL PARTICULARS

4.1 Therapeutic indications:

ELACIN is a xanthine oxidase (XO) inhibitor indicated for the chronic management of hyperuricemia in patients with gout.
ELACIN is not recommended for the treatment of asymptomatic hyperuricemia.

4.2 Posology and method of administration:

Posology:

ELACIN is recommended at 40 mg or 80 mg once daily. The recommended starting dose of ELACIN is 40 mg once daily. For patients who do not achieve a serum uric acid (sUA) less than 6 mg/dL after 2 weeks with 40 mg, ELACIN 80 mg is recommended.
ELACIN can be administered without regard to food or antacid use.
No dose adjustment is necessary when administering ELACIN to patients with mild to moderate renal or hepatic impairment

Method of administration: Tablets for oral administration.

4.3 Contraindications:

ELACIN is contraindicated in patients being treated with azathioprine or mercaptopurine.

4.4 Special warnings and precautions for use:

Gout Flare: After initiation of ELACIN, an increase in gout flares is frequently observed. This is due to reduction in serum uric acid levels, resulting in mobilization of urate from tissue deposits. To prevent gout flares, ELACIN is recommended along with an NSAID or colchicine.

Cardiovascular Events: In the randomized controlled studies, there was a higher rate of cardiovascular thromboembolic events (cardiovascular deaths, non-fatal myocardial infarctions, and non-fatal strokes) in patients treated with Febuxostat. A causal relationship with ELACIN has not been established.

Hepatic Effects: Postmarketing reports indicates fatal and non-fatal hepatic failure in patients taking ELACIN, although the reports contain insufficient information necessary to establish the probable cause. During randomized controlled studies, transaminase elevations greater than three times the upper limit of normal (ULN) were observed. No dose-effect relationship for these transaminase elevations was obtain. 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.

4.5 Interaction with other medicinal products and other forms of interaction

ELACIN is an XO inhibitor. Based on a drug interaction study in healthy subjects, febuxostat altered the metabolism of theophylline in humans. Therefore, ELACIN is used with caution when

coadministering with theophylline. Drug interaction studies of ELACIN with other drugs that are metabolized by XO (e.g., mercaptopurine and azathioprine) have not been conducted. Inhibition of XO by ELACIN may cause increased plasma concentrations of these drugs leading to toxicity. ELACIN is contraindicated in patients being treated with azathioprine or mercaptopurine.
No data are available regarding the safety of ELACIN during cytotoxic chemotherapy.
ELACIN does not have clinically significant interactions with colchicine, naproxen, indomethacin, hydrochlorothiazide, warfarin or desipramine. Therefore, ELACIN may be used concomitantly with these medications.

4.6 Pregnancy and lactation

Pregnancy Category C: There are no adequate and well-controlled studies in pregnant women. ELACIN should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Febuxostat was not teratogenic in rats and rabbits at oral doses up to 48 mg/kg. However, increased neonatal mortality and a reduction in the neonatal body weight gain were observed when pregnant rats were treated with oral doses up to 48 mg/kg (40 times the human plasma exposure at 80 mg/day) during organogenesis and through lactation period.
Nursing Mothers: Febuxostat is excreted in the milk of rats. It is not known whether this drug is excreted in human milk. Caution should be exercised when ELACIN is administered to a nursing woman.

4.7 Effects on ability to drive and use machines

Somnolence, dizziness, paraesthesia and blurred vision have been reported with the use of Febuxostat. Patients should exercise caution before driving, using machinery or participating in dangerous activities until they are reasonably certain that ELACIN 80 does not adversely affect performance.

4.8 Undesirable effects

Heart problems. A small number of heart attacks, strokes and heart-related deaths were seen in clinical studies. It is not certain that ELACIN caused these events. The most common side effects of ELACIN include: liver problems, nausea, gout flares, joint pain, rash.

4.9 Overdose:

ELACIN was studied in healthy subjects in doses up to 300 mg daily for seven days without evidence of dose-limiting toxicities. No overdose of ELACIN was reported in clinical studies. Patients should be managed by symptomatic and supportive care should there be an overdose.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamics properties ATC classification

ATC classification

Pharmacotherapeutic group: Xanthine Oxidase Inhibitor

ATC code: M04AA03
M **Musculo-Skeletal System**
M04 **Antigout Preparations**
M04A **Antigout Preparations**
M04AA **Preparations Inhibiting Uric Acid Production**
M04AA03 febuxostat

Mode of action

Febuxostat is a non-purine-selective inhibitor of xanthine oxidase. It works by non-competitively blocking the molybdenum pterin center which is the active site on xanthine oxidase. Xanthine oxidase is needed to successively oxidize both hypoxanthine and xanthine to uric acid. Hence, febuxostat inhibits xanthine oxidase, therefore reducing production of uric acid. Febuxostat inhibits both oxidized as well as reduced form of xanthine oxidase because of which febuxostat cannot be easily displaced from the molybdenum pterin site.

5.2 Pharmacokinetic properties

Absorption: Maximum plasma concentrations of febuxostat occurred between 1 and 1.5 hours post-dose. After multiple oral 40 mg and 80 mg once daily doses, Cmax is approximately 1.6 ± 0.6 mcg/mL (N=30), and 2.6 ± 1.7 mcg/mL (N=227), respectively. Absolute bioavailability of the febuxostat tablet has not been studied.
No clinically significant change in the %decrease in serum uric acid concentration was observed with food. (58% fed vs. 51% fasting). Thus, ELACIN may be taken without regard to food.
Concomitant ingestion of an antacid containing magnesium hydroxide and aluminum hydroxide with an 80 mg single dose of ELACIN has been shown to delay absorption of febuxostat (approximately one hour) with antacid. Therefore, ELACIN may be taken without regard to antacid use.
Distribution: The mean apparent steady state volume of distribution (Vss/F) of febuxostat was approximately 50 L (CV ~40%). 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.
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.
Elimination: Febuxostat is eliminated by both hepatic and renal pathways. The apparent mean terminal elimination half-life (t½) of febuxostat was approximately 5 to 8 hours.

5.3 Preclinical safety data

Effects in non-clinical studies were generally observed at exposures in excess of the maximum human exposure.

Pharmacokinetic modelling and simulation of rat data suggests that, when co-administered with febuxostat, the clinical dose of mercaptopurine/azathioprine should be reduced to 20% or less of the previously prescribed dose in order to avoid possible haematological effects.

Carcinogenesis, mutagenesis, impairment of fertility

In male rats, a statistically significant increase in urinary bladder tumours (transitional cell papilloma and carcinoma) was found only in association with xanthine calculi in the high dose group, at approximately 11 times human exposure. There was no significant increase in any other tumour type in either male or female mice or rats. These findings are considered a consequence of species specific purine metabolism and urine composition and of no relevance to clinical use.

A standard battery of test for genotoxicity did not reveal any biologically relevant genotoxic effects for febuxostat.

Febuxostat at oral doses up to 48 mg/kg/day was found to have no effect on fertility and reproductive performance of male and female rats.

There was no evidence of impaired fertility, teratogenic effects, or harm to the foetus due to febuxostat. There was high dose maternal toxicity accompanied by a reduction in weaning index and reduced development of offspring in rats at approximately 4.3 times human exposure. Teratology studies, performed in pregnant rats at approximately 4.3 times and pregnant rabbits at approximately 13 times human exposure did not reveal any teratogenic effects.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Starch, Cross Carmellose sodium, Micro Crystalline Cellulose, PVPK-30, Iso Propyl Alcohol, Talcum Powder, Magnesium Stearate, Cross Povidone, Colloidal Silicon Dioxide, Fine coat, Methylene Dichloride, Titanium Dioxide, Poly Ethylene Glycol-6000

6.2 Incompatibilities

None known

6.3 Shelf life

24 months from the date of packing

6.4 Special precautions for storage

Store below 30°C. protect from light.

6.5 The nature of the primary packaging

10 tablets are packed in ALU-ALU blister pack. 3 such ALU- ALU blister is packed in a printed carton with a printed insert.

Presentation:

Alu-Alu blister of 10 Tablets each.

6.6 Special precautions for disposal.

-Not special requirement.

7.APPLICANT/MANUFACTURER

APPLICANT
INTERMAC PHARMACEUTICAL PTE LTD,
Address: P.O. Box 235, Singapore 911508.
Email: reshma@intermacpharmaceutical.com

ELACIN 80
(Febuxostat Tablets 80 mg)
SUMMARY OF PRODUCT CHARACTERISTICS

MANUFACTURER
TRUGEN PHARMACEUTICAL PVT. LTD
Address: Tejjupur , Roorkee, Dist. Haridwar, Uttarakhand , India.
E-mail: trugenpharma@gmail.com