SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF DRUG PRODUCT

Fexet Tablets 120mg

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains:

Fexofenadine HCl BP ….. 120mg

3. PHARMACEUTICAL FORM

White oblong shaped film-coated tablet, engraved 'GETZ' on one side and bisect line on other side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Seasonal Allergic Rhinitis
FEXET (Fexofenadine HCI) is indicated for the relief of symptoms associated with seasonal allergic rhinitis in adults and children 6 years of age and older.

Chronic Idiopathic Urticaria
FEXET (Fexofenadine HCI) is indicated for the treatment of uncomplicated skin manifestations of chronic idiopathic urticaria in adults and children 6 years of age and older. It significantly reduces pruritis and the number of wheals.

4.2 Posology and method of administration

Seasonal Allergic Rhinitis
Adults and Children 12 Years and Older: The recommended dose of FEXET (Fexofenadine HCI) is 120mg once daily.

Children 6 to 11 Years: The recommended dose of FEXET (Fexofenadine HCI) is 30mg twice daily. A dose of 30mg once daily is recommended as the starting dose in pediatric patients with decreased renal function.

Chronic Idiopathic Urticaria
Adults and Children 12 Years and Older: The recommended dose of FEXET (Fexofenadine HCI) is 180mg once daily.

Children 6 to 11 Years: The recommended dose of FEXET (Fexofenadine HCI) is 30mg twice daily. A dose of 30mg once daily is recommended as the starting dose in pediatric patients with decreased renal function.

Dosage in renal insufficiency:

- *Adults:* In patients with decreased renal function the recommended dose of Fexofenadine HCl is 60mg once daily as the starting dose.
- *Pediatrics:* In pediatric patients with decreased renal function the recommended dose of Fexofenadine HCl is 30mg once daily as the starting dose.

4 .3 Contraindications

Fexofenadine HCI is contraindicated in patients with known hypersensitivity to the drug or any component of the product.

4.4 Special warnings and precautions for use

As with most new medicinal products there is only limited data in the older people and renally or hepatically impaired patients. Fexofenadine hydrochloride should be administered with care in these special groups.

Patients with a history of or ongoing cardiovascular disease should be warned that, antihistamines as a medicine class, have been associated with the adverse reactions, tachycardia and palpitations.

Pediatric Use

The safety and effectiveness of fexofenadine HCI in pediatric patients under 6 years of age have not been established.

Geriatric Use

This drug is known to be substantially excreted by the kidney, and the risk of toxic reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function.

Epilepsy

Seizures or convulsions have been reported with some newer-generation antihistamines including fexofenadine. Patients should be reminded not to exceed the recommended or maximum daily dose.

4.5 Interaction with other medicinal products and other forms of interaction

Fexofenadine does not undergo hepatic biotransformation and therefore will not interact with other medicinal products through hepatic mechanisms. Coadministration of fexofenadine hydrochloride with erythromycin or ketoconazole has been found to result in a 2-3 times increase in the level of fexofenadine in plasma. The changes were not accompanied by any effects on the QT interval and were not associated with any increase in adverse reactions compared to the medicinal products given singly.

No interaction between fexofenadine and omeprazole was observed. However, the administration of an antacid containing aluminium and magnesium hydroxide gels 15 minutes prior to fexofenadine hydrochloride caused a reduction in bioavailability, most likely due to binding in the gastrointestinal tract. It is advisable to leave 2 hours between administration of fexofenadine hydrochloride and aluminium and magnesium hydroxide containing antacids.

4.6 Fertility pregnancy and lactation

Pregnancy

Fexofenadine HCI should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers

Because many drugs are excreted in human milk, caution should be exercised when fexofenadine HCI is administered to a nursing woman.

4.7 Effects on ability to drive and use machines

Although drowsiness is rare, nevertheless patients should be advised that it can occur and may affect performance of skilled tasks (e.g. cycling or driving); alcohol should be avoided.

4.8 Undesirable effects

The following frequency rating has been used, when applicable:

Common:

Headache, drowsiness, dizziness, nausea

Uncommon:

Fatigue, Hypersensitivity reactions, Insomnia, nervousness, sleep disorders or nightmares/excessive dreaming (paroniria), tachycardia, palpitations, diarrhea, rash, urticaria, pruritus.

4.9 Overdose

Dizziness, drowsiness, fatigue and dry mouth have been reported with overdose of fexofenadine hydrochloride. Single doses up to 800 mg and doses up to 690 mg twice daily for 1 month or 240 mg once daily for 1 year have been administered to healthy subjects without the development of clinically significant adverse reactions as compared with placebo. The maximum tolerated dose of fexofenadine hydrochloride has not been established.

Standard measures should be considered to remove any unabsorbed medicinal product. Symptomatic and supportive treatment is recommended. Haemodialysis does not effectively remove fexofenadine hydrochloride from blood.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antihistamines for systemic use
ATC code: R06AX26

Mechanism of action

Fexofenadine hydrochloride is a non-sedating H_1 antihistamine. Fexofenadine is a pharmacologically active metabolite of terfenadine.

Clinical efficacy and safety

Human histamine wheal and flare studies following single and twice daily doses of fexofenadine hydrochloride demonstrate that the medicinal product exhibits an antihistaminic effect beginning

within one hour, achieving maximum at 6 hours and lasting 24 hours. There was no evidence of tolerance to these effects after 28 days of dosing. A positive dose-response relationship between doses of 10 mg to 130 mg taken orally was found to exist. In this model of antihistaminic activity, it was found that doses of at least 130 mg were required to achieve a consistent effect that was maintained over a 24 hour period. Maximum inhibition in skin wheal and flare areas were greater than 80%.
No significant differences in QT_c intervals were observed in seasonal allergic rhinitis patients given fexofenadine hydrochloride up to 240 mg twice daily for 2 weeks when compared to placebo. Also, no significant change in QT_c intervals was observed in healthy subjects given fexofenadine hydrochloride up to 60 mg twice daily for 6 months, 400 mg twice daily for 6.5 days and 240 mg once daily for 1 year, when compared to placebo. Fexofenadine at concentrations 32 times greater than the therapeutic concentration in man had no effect on the delayed rectifier K+ channel cloned from human heart.
Fexofenadine hydrochloride (5-10 mg/kg po) inhibited antigen induced bronchospasm in sensitised guinea pigs and inhibited histamine release at supratherapeutic concentrations (10-100 μM) from peritoneal mast cells.

5.2 Pharmacokinetic properties

Absorption
Fexofenadine hydrochloride is rapidly absorbed into the body following oral administration, with T_{max} occurring at approximately 1-3 hours post dose. The mean C_{max} value was approximately 494 ng/ml following the administration of a 180 mg dose once daily.

Distribution
Fexofenadine is 60-70% plasma protein bound. Primarily albumin and al-acid glycoprotein.

Biotransformation and elimination
Fexofenadine undergoes negligible metabolism (hepatic or non-hepatic), as it was the only major compound identified in urine and faeces of animals and man. The plasma concentration profiles of fexofenadine follow a bi-exponential decline with a terminal elimination half-life ranging from 11 to 15 hours after multiple dosing. The single and multiple dose pharmacokinetics of fexofenadine are linear for oral doses up to 120 mg BID. A dose of 240 mg BID produced slightly greater than proportional increase (8.8%) in steady state area under the curve, indicating that fexofenadine pharmacokinetics are practically linear at these doses between 40 mg and 240 mg taken daily. The major route of elimination is believed to be via biliary excretion while up to 10% of ingested dose is excreted unchanged through the urine.

Excretion
Elimination half-life of about 14 hours has been reported although this may be prolonged in patients with renal impairment. Excretion is mainly in the faeces with only 10% being present in the urine.

5.3 Preclinical safety data

Dogs tolerated 450 mg/kg administered twice daily for 6 months and showed no toxicity other than occasional emesis. Also, in single dose dog and rodent studies, no treatment-related gross findings were observed following necropsy.
Radiolabelled fexofenadine hydrochloride in tissue distribution studies of the rat indicated that fexofenadine did not cross the blood brain barrier.

Fexofenadine hydrochloride was found to be non-mutagenic in various *in vitro* and *in vivo* mutagenicity tests.
The carcinogenic potential of fexofenadine hydrochloride was assessed using terfenadine studies with supporting pharmacokinetic studies showing fexofenadine hydrochloride exposure (via plasma AUC values). No evidence of carcinogenicity was observed in rats and mice given terfenadine (up to 150 mg/kg/day).
In a reproductive toxicity study in mice, fexofenadine hydrochloride did not impair fertility, was not teratogenic and did not impair pre- or postnatal development.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

- Lactose Monohydrate
- Avicel PH-102 (Microcrystalline Cellulose)
- Pregelatinized Starch
- Croscarmellose Sodium
- Magnesium Stearate
- Methocel E-5 (HPMC 5CPs)
- Titanium Dioxide
- P.E.G. 6000 (Macrogol)

6.2 Incompatibilities

None

6.3 Shelf-life

3 Years
The expiration date refers to the product correctly stored in the required conditions.

6.4 Special precautions for storage

- Store below 30°C.
- Protect from sunlight and moisture
- Keep out of reach of children

6.5 Nature and contents of container

Fexet Tablets 120mg are packed in Alu-Alu blister pack of 2x10's along with a package insert in a unit carton.

6.6 Instructions for use/handling

- To be dispensed on medical prescription only.
- Keep out of the reach of children.

7. MARKETING AUTHORISATION HOLDER

Getz Pharma (Private) Limited
29-30/27, Korangi Industrial Area Karachi 74900, Pakistan
Tel: (92-21) 111-111-511
Fax: (92-21) 5057592

8. PRODUCT REGISTRATION NUMBER

007210-EX

9. DATE OF PRODUCT REGISTRATION ISSUED

29 June, 2018