Fexet® D

(Fexofenadine HCl + Pseudoephedrine HCl)

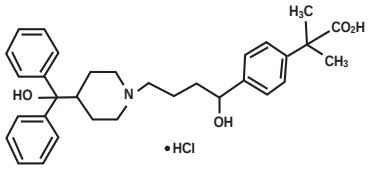
فیکسٹ-ڈی

60mg + 120mg Tablets

DESCRIPTION

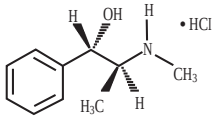
Fexet-D is a combination product containing fexofenadine hydrochloride (HCl), which has antihistaminic properties, and pseudoephedrine hydrochloride, an adrenergic (Vasoconstrictor) agent.

Fexofenadine hydrochloride (HCl) is a histamine H_1 - receptor antagonist with the chemical name (±)-4-[1-hydroxy-4-[4-(hydroxydiphenylmethyl)-1-piperidinyl]-butyl]-α,α-dimethyl benzeneacetic acid hydrochloride. Its molecular formula is $C_{32}H_{39}NO_4$•HCl and the structural formula is:



Fexofenadine HCl

Pseudoephedrine HCl is an orally active sympathomimetic amine having a chemical name of [S-(R*,R*)]-α-[1-(methylamino)ethyl]-benzenemethanol hydrochloride. Its molecular formula is $C_{10}H_{15}NO$•HCl and the structural formula is:



Pseudoephedrine HCl

QUALITATIVE & QUANTITATIVE COMPOSITION

Fexet-D (Fexofenadine HCl + Pseudoephedrine HCl) is available for oral administration as:

Fexet-D Tablets 60mg + 120mg
Each film-coated tablet contains:
Fexofenadine HCl BP… 60mg
Pseudoephedrine HCl USP…120mg

CLINICAL PHARMACOLOGY

Mechanism of Action

Fexofenadine HCl

Fexofenadine HCl is an active non-sedating antihistamine with selective H_1-receptor activity. It does not possess significant sedative or antimuscarinic actions.

Pseudoephedrine HCl

Pseudoephedrine HCl exerts a decongestant action on the nasal mucosa. Pseudoephedrine produces peripheral effects similar to those of ephedrine and central effects similar to, but less intense than, amphetamines.

Pharmacokinetics

Absorption:

Fexofenadine HCl was rapidly absorbed following single-dose administration of the 60mg fexofenadine HCl + 120mg pseudoephedrine HCl tablet with median time to mean maximum fexofenadine plasma concentration of 191ng/ml occurring 2 hours post-dose. Pseudoephedrine HCl produced a mean single-dose pseudoephedrine peak plasma concentration of 206ng/ml, which occurred 6 hours post-dose. Administration with a high fat meal decreased the bioavailability of fexofenadine by approximately 50% (AUC 42% and C_{max} 46%). Time to maximum concentration (T_{max}) was delayed by 50%. The rate or extent of pseudoephedrine absorption was not affected by food.

Distribution:

Fexofenadine is 60% to 70% bound to plasma proteins, primarily albumin and α_1-acid glycoprotein.The protein binding of pseudoephedrine in humans is not known. Pseudoephedrine HCl is extensively distributed into extravascular sites (apparent volume of distribution between 2.6 and 3.5L/kg).

Metabolism:

Approximately 5% of the total dose of fexofenadine HCl and less than 1% of the total oral dose of pseudoephedrine HCl were eliminated by hepatic metabolism.

Elimination:

Elimination half-life, of fexofenadine HCl, is of about 14 hours, although this may be prolonged in patients with renal impairment. Excretion is mainly in the feces (approx 80%) with only 10% being present in the urine.

Pseudoephedrine has been shown to have a mean elimination half-life of 4-6 hours, which is dependent on urine pH. The elimination half-life is decreased at urine pH lower than 6 and may be increased at urine pH higher than 8.

Special Populations

Geriatric Patients:

In older subjects (>65 years old), peak plasma levels of fexofenadine were 99% greater than those observed in younger subjects (<65 years old). Mean fexofenadine elimination half-lives were similar to those observed in younger subjects.

Renal Impairment:

In subjects with mild (creatinine clearance 41-80ml/min) to severe (creatinine clearance 11-40ml/min) renal impairment, peak plasma levels of fexofenadine were 87% and 111% greater, respectively, and mean elimination half-lives were 59% and 72% longer, respectively, than observed in healthy volunteers. Peak plasma levels in subjects on dialysis (creatinine clearance <10ml/min) were 82% greater and half-life was 31% longer than observed in healthy volunteers.

No data are available on the pharmacokinetics of pseudoephedrine in renally impaired subjects. However, most of the oral dose of pseudoephedrine HCl (43%-96%) is excreted unchanged in the urine and the remainder is apparently metabolized in the liver. A decrease in renal function is, therefore, likely to decrease the clearance of pseudoephedrine significantly, thus prolonging the half-life and resulting in accumulation.

THERAPEUTIC INDICATIONS

Fexet-D (Fexofenadine HCl + Pseudoephedrine HCl) Tablets are indicated for the relief of symptoms of allergic rhinitis with nasal congestion, in adults and children 12 years of age and older, when both the anti-allergic properties of fexofenadine HCl and the decongestant activity of pseudoephedrine HCl are required.

DOSAGE AND ADMINISTRATION

The recommended dose of Fexet-D (Fexofenadine HCl + Pseudoephedrine HCl) is one tablet twice daily administered on an empty stomach with water for adults and children 12 years of age and older. It is recommended that the administration of Fexet-D (Fexofenadine HCl + Pseudoephedrine HCl) tablets with food should be avoided.

Renal Impaired Patients
A dose of one Fexet-D (Fexofenadine HCl + Pseudoephedrine HCl) tablet once daily is recommended as the starting dose in patients with decreased renal function.

ADVERSE REACTIONS
Fexofenadine HCl + Pseudoephedrine HCl combination is generally well tolerated. It was observed that patients with seasonal allergic rhinitis receiving combination therapy of Fexofenadine & Pseudoephedrine twice daily for two weeks, were reported to have adverse effects similar to those patients receiving fexofenadine 60mg alone or pseudoephedrine 120mg alone. The adverse reactions commonly reported were: headache, insomnia, nausea, dry mouth, dyspepsia, throat irritation, dizziness, agitation, back pain, palpitation, nervousness, anxiety, upper respiratory infection and abdominal pain.

CONTRAINDICATIONS
Fexofenadine HCl + Pseudoephedrine HCl combination is contraindicated in patients with known hypersensitivity to any of its ingredient.

Due to its pseudoephedrine component, this product is contraindicated
- in patients with narrow-angle glaucoma or urinary retention.
- in patients receiving monoamine oxidase (MAO) inhibitor therapy or within fourteen (14) days of stopping such treatment.
- in patients with severe hypertension or severe coronary artery disease, and in those who have shown idiosyncrasy to its components, to adrenergic agents or to other drugs of similar chemical structures.

WARNINGS
Sympathomimetic amines (like pseudoephedrine) should be used with caution in patients with hypertension, diabetes mellitus, ischemic heart disease, increased intraocular pressure, hyperthyroidism, renal impairment, or prostatic hypertrophy. Sympathomimetic amines may produce central nervous system stimulation with convulsions or cardiovascular collapse with accompanying hypotension.

PRECAUTIONS
Pediatric Use
Safety and effectiveness in children below the age of 12 years have not been established. Fexofenadine HCl + Pseudoephedrine HCl combination is not recommended for pediatric patients under 12 years of age.

Pregnancy
There are no adequate and well-controlled studies in pregnant women with Fexofenadine HCl + Pseudoephedrine HCl combination. Therefore, it should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers
Caution should be exercised when Fexofenadine HCl + Pseudoephedrine HCl combination is administered to nursing women, as pseudoephedrine is excreted in human breast milk.

Drug Interactions
- The concurrent use of Fexofenadine HCl + Pseudoephedrine HCl combination with over-the-counter antihistamines and decongestants should be avoided.

- Fexofenadine HCl + Pseudoephedrine HCl combination should not be taken closely in time with aluminum and magnesium containing antacids.

OVERDOSAGE
Fexofenadine HCl:
Dizziness, drowsiness, fatigue and dry mouth have been reported with overdose of fexofenadine HCl.

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

Pseudoephedrine HCl:
The symptoms of overdose include irritability, nervousness, tremor, palpitations, convulsions, urinary retention and hypertension.
Overdose should be treated by general supportive measures. In the event of gross overdose, the stomach should be emptied using airways protective gastric lavage. Respiratory and circulatory function should be maintained by supportive measures. Convulsions should be controlled using anti-convulsant therapy. Catheterisation of the bladder may be required.

STORAGE
Store at 25°C (Excursions permitted between 15°C to 30°C).
Protect from sunlight & moisture.
The expiration date refers to the product correctly stored at the required conditions.

HOW SUPPLIED
Fexet-D (Fexofenadine HCl + Pseudoephedrine HCl) Tablets 60mg+120mg are available in blister pack of 10 tablets.

Keep out of reach of children.

To be sold on prescription of a registered medical practitioner only.

Please read the contents carefully before use.
This package insert is continually updated from time to time.

Manufactured by:
Getz pharma (PVT) LIMITED
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