

Fexet D™

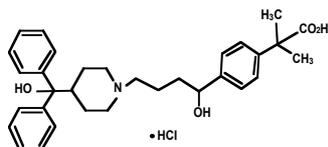
(Fexofenadine HCl + Pseudoephedrine HCl)

60mg + 120mg TABLETS

DESCRIPTION

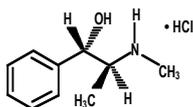
FEXET D is a combination product containing fexofenadine hydrochloride, which has antihistaminic properties, and pseudoephedrine hydrochloride, an adrenergic (Vasoconstrictor) agent.

Fexofenadine HCl is an orally-active non-sedating antihistamine H_1 -receptor antagonist, having a chemical name of (\pm) -4-[1-hydroxy-4-[4-(hydroxydiphenylmethyl)-1-piperidinyl]-butyl]- α,α -dimethyl benzeneacetic acid hydrochloride and a molecular formula of $C_{22}H_{39}NO_4 \cdot HCl$. It has the following chemical structure.



Fexofenadine hydrochloride

Pseudoephedrine HCl is an orally active sympathomimetic having a chemical name of $[S-(R^*,R^*)-\alpha$ -[1-(methylamino)ethyl]-benzenemethanol hydrochloride and its molecular formula is $C_{10}H_{15}NO \cdot HCl$. Pseudoephedrine HCl has the following chemical structure:



Pseudoephedrine hydrochloride

QUALITATIVE & QUANTITATIVE COMPOSITION

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

FEXET D Tablets

Each film-coated tablet contains:
Fexofenadine HCl USP... 60mg
Pseudoephedrine HCl USP... 120mg
(Extended-Release Tablets)

CLINICAL PHARMACOLOGY

Mechanism of Action:

Fexofenadine HCl

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

Pseudoephedrine HCl

Pseudoephedrine hydrochloride 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 hydrochloride was rapidly absorbed following single-dose administration of the 60mg fexofenadine hydrochloride + 120mg pseudoephedrine hydrochloride tablet with median time to mean maximum fexofenadine plasma concentration of 191ng/ml occurring 2 hours post-dose. Pseudoephedrine hydrochloride produced a mean single-dose pseudoephedrine peak plasma concentration of 206ng/ml,

which occurred 6 hours post-dose. The administration of FEXET D 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 hydrochloride 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 hydrochloride and less than 1% of the total oral dose of pseudoephedrine hydrochloride 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 ≤ 10 mL/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 hydrochloride (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) tablets 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

FEXET D (Fexofenadine HCl + Pseudoephedrine HCl) is generally well tolerated. It was observed that patients with seasonal allergic rhinitis receiving combination therapy of fexofenadine and 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, abdominal pain.

CONTRAINDICATIONS

FEXET D (Fexofenadine HCl + Pseudoephedrine HCl) is contraindicated in patients with known hypersensitivity to any of its ingredients.

Due to its pseudoephedrine component, FEXET D (Fexofenadine HCl + Pseudoephedrine HCl) 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 of FEXET D in children below the age of 12 years have not been established. FEXET D is not recommended for pediatric patients under 12 years of age.

Pregnancy

There are no adequate and well-controlled studies in pregnant women with FEXET D, 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 FEXET D is administered to nursing women, as pseudoephedrine is excreted in human breast milk.

Drug Interactions

- The concurrent use of FEXET D tablets with over-the-counter antihistamines and decongestants should be avoided.
- FEXET D should not be taken closely in time with aluminum and magnesium containing antacids.

STORAGE

Store below 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 packs of 10 tablets.

Keep out of reach of children.

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

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