For the use only of a Registered Medical Practitioner, Hospital, Laboratories

This package insert is continually updated: Please read carefully before using a new pack

Fexofenadine HCl and Pseudoephedrine HCl ER Tablets IP
Allegra® D

1. Generic Name

Fexofenadine HCl 60mg + Pseudoephedrine HCl 120mg Extended Release Tablets IP

2. Qualitative and quantitative composition

Each extended release tablet contains:
Fexofenadine Hydrochloride IP …… 60 mg
Pseudoephedrine Hydrochloride IP ……. 120mg

3. Dosage form and strength
Extended release tablets - 60mg/120mg

4. Clinical particulars

4.1 Therapeutic indication

Allegra® D is indicated for the relief of symptoms associated with allergic rhinitis in adults and children 12 years of age and older. Symptoms treated effectively include sneezing, rhinorrhea, itchy nose/palate/ and/or throat, itchy/watery/red eyes, and nasal congestion.

Allegra® D should be administered when both the antihistaminic properties of fexofenadine hydrochloride and the nasal decongestant properties of pseudoephedrine hydrochloride are desired (refer section *Pharmacological properties*).

4.2 Posology and method of administration

The recommended dose of Allegra® D is one tablet twice daily for adults and children 12 years of age and older. It is recommended that the administration of Allegra® D with food should be avoided. The tablet should be swallowed whole.

A dose of one tablet once daily is recommended as the starting dose in-patients with decreased renal function. (refer section *Pharmacological properties and Precautions*).

Patients should be informed that the inactive ingredients of Allegra D may be eliminated in the feces in a form that may resemble the original tablet.

4.3 Contraindications

Allegra® D is contraindicated in-patients with known hypersensitivity to fexofenadine, pseudoephedrine, or any of the excipients in the formulation.

Pseudoephedrine is contraindicated in the following patients:

- Severe or uncontrolled hypertension
- In Patients with severe coronary artery disease
- In patients at risk of angle closure glaucoma
- In patients at risk of urinary retention related to urethroprostatic disorders

- In patients with history of seizures
- Concomitant use of monoamine oxidase (MAO) inhibitor therapy or within 14 days of stopping such treatment (see Drugs interactions)
- Concomitant other vasoconstrictor agents used as nasal decongestants, whether administered orally or nasally (see Drugs interactions)

4.4 Warnings / Precautions

Pseudoephedrine:
- hypertension
- tachycardia, palpitations, cardiac arrhythmias
- any neurological symptoms such as onset or worsening of headache

Allegra® D should be used upon medical advice in patients with:
- diabetes
- hypertension
- heart disease
- stroke
- hyperthyroidism
- psychosis
- concomitant administration of methylphenidate or antimigraine agents, especially ergot alkaloid vasoconstrictors (because of the α-sympathomimetic activity of pseudoephedrine) (see Drugs interactions)

Neurological and psychiatric symptoms and irregular heartbeat have been reported after systemic administration of vasoconstrictors, especially with overdose (see Undesirable Effects and Overdose).

Elderly patients may be more sensitive to the effects on the central nervous system (CNS).

Pseudoephedrine should be used with caution in patients with renal disease (Posology and method of administration).

Risk of abuse:
Pseudoephedrine carries the risk of abuse. Increased doses may ultimately produce toxicity. Continuous use can lead to tolerance resulting in an increased risk of overdosing. The recommended maximum dose and treatment duration should not exceed than 5 days (Posology and Method of Administration).

4.5 Drugs interactions

The coadministration of Allegra® D with erythromycin or ketoconazole resulted in no significant increases in QTc.. No differences in adverse events were reported whether these agents were administered alone or in combination

Administration of an antacid containing aluminum and magnesium hydroxide gels 15 minutes prior to fexofenadine hydrochloride caused a reduction in bioavailability. It is advisable to leave 2 hours between administration of fexofenadine hydrochloride and aluminum and magnesium containing antacids.

No interaction between fexofenadine and omeprazole was observed.

P-gp inducers (such as apalutamide) may reduce the exposure of fexofenadine.
A clinical drug-drug interaction study showed that co-administration of apalutamide and a single oral dose of 30 mg fexofenadine resulted in a 30 % decrease in AUC and 7 % in Cmax of fexofenadine. Clinical impact on the pharmacodynamics and efficacy has not been studied.

Pseudoephedrine:
Concomitant use of pseudoephedrine with monoamine oxidase inhibitors (MAOI) may lead to paroxysmal hypertension and hyperthermia, which can be fatal. Because of the long duration of action of MAOIs, this interaction can occur up to 2 weeks after discontinuation of the MAOI.
Therefore, use of Allegra® D concomitantly with MAOI or within 2 weeks after MAOI treatment discontinuation is contraindicated (see Contraindications)..

Concomitant use of pseudoephedrine with antihypertensive drugs that interfere with sympathetic activity may reduce their anti-hypertensive effects.

Concomitant use of pseudoephedrine with antihypertensive drugs that interfere with sympathetic activity may reduce the decongestive effect of pseudoephedrine.

Concomitant use of pseudoephedrine with sympathomimetic or vasoconstrictor agents may have additive cardiovascular effects (see Contraindications and Warnings / Precautions).

Concomitant use of pseudoephedrine with tricyclic antidepressants may diminish or enhance the effect of pseudoephedrine.

Concomitant use of pseudoephedrine with digitalis, quinidine or tricyclic antidepressants may increase risk of arrhythmia.

Carcinogenicity

The carcinogenic potential of fexofenadine hydrochloride was assessed using terfenadine studies with supporting pharmacokinetics studies showing adequate fexofenadine exposure (viaplasma AUC values). No evidence of carcinogenicity was observed in rats mice given terfenadine (up to 150 mg/kg) resulting in fexofenadine plasma exposure up to four times the human therapeutic value (based on 60 mg twice daily of fexofenadine hydrochloride.

Pregnancy
Allegra® D should be used in pregnancy only if the potential benefit outweighs the potential risk to the fetus. There are no studies of fexofenadine hydrochloride in pregnant women.

Fexofenadine:
In a comprehensive reproductive toxicity study in mice, fexofenadine was not teratogenic and did not impair pre- or postnatal development.
The combination of terfenadine and pseudoephedrine HCl in a ratio of 1:2 by weight was studied in rats and rabbits. In rats, an oral combination dose of 150/300 mg/kg produced reduced fetal weight and delayed ossification with a finding of wavy ribs. The dose of 150 mg/kg of terfenadine in rats produced on AUC value of fexofenadine that was approximately 3 times the human AUC at the maximum recommended daily oral dose in adults. The dose of 300 mg/kg pseudoephedrine HClin rats was approximately 10 times higher than the recommended oral dose in adults on a mg/m² basis. In rabbits, an oral combination dose of 100/200 mg/kg produced decreased fetal weight. By extrapolation, the AUC of fexofenadine for 100 mg/kg orally of terfenadine was approximately 10 times the human AUC at the maximum recommended daily oral dose in adults. The dose of 200 mg/kg of pseudoephedrine HCl was approximately 15 times the maximum recommended daily oral dose in adults on a mg/m² basis.

Lactation
Pseudoephedrine is excreted in breast milk.
Allegra® D is is not recommended for nursing women unless in the physician's judgment the potential benefit to the patient outweighs the potential risk to the infant.

Fertility
Fexofenadine:
In a comprehensive reproductive toxicity study in mice, fexofenadine did not impair fertility.

4.6 Effects on ability to drive and use machines
Not applicable

4.7 Adverse Reactions
The following CIOMS frequency rating is used, when applicable:
Very common ≥ 10%; Common ≥ 1 and < 10%; Uncommon ≥ 0.1 and < 1%; Rare ≥ 0.01 and < 0.1%; Very rare < 0.01%; Not known (cannot be estimated from available data).

Combination Product:
In clinical pharmacokinetic trials, subjects receiving Allegra® D reported adverse events similar to adverse events reported in placebo-controlled clinical trials for fexofenadine and similar to effects attributable to pseudoephedrine hydrochloride.

Fexofenadine Hydrochloride
In placebo-controlled trials involving seasonal allergic rhinitis and chronic idiopathic urticaria patients, adverse events were comparable in fexofenadine- and placebo-treated patients.
The most frequent adverse events reported with fexofenadine include:

>3%: headache.
1-3%: drowsiness, dizziness and nausea.

Events that have been reported during controlled trials involving seasonal allergic rhinitis and chronic idiopathic urticaria patients with incidences less than 1% and similar to placebo and have been reported rarely during post marketing surveillance include: fatigue, insomnia, nervousness, and sleep disorders or paroniria. In rare cases, rash, urticaria, pruritus and hypersensitivity reactions with manifestations such as angioedema, chest tightness, dyspnea, flushing and systemic anaphylaxis have been reported. (In fexofenadine monotherapy studies) adverse events reported in placebo-controlled chronic idiopathic urticaria studies were similar to those reported in placebo-controlled seasonal allergic rhinitis studies.

Pseudoephedrine:

- Psychiatric disorders
  Not known: Anxiety, agitation, hallucination, nervousness, manic symptoms such as insomnia, high or irritable mood, inflated self-esteem, increased activity or restlessness, racing thoughts, talking fast, and distractibility .
- Nervous system disorders
  Not known: Stoke, headache, seizures, dizziness, somnolence, tremor
- Cardiac disorders
  Not known: Palpitations, tachycardia, arrhythmia
- Vascular disorders
  Not known: Hypertension
- Gastrointestinal disorders
  Not known: Nausea, vomiting, dry mouth, decreased appetite, Ischemic colitis
- Immune system disorders
  Not known: Hypersensitivity reactions
- Respiratory, thoracic and mediastinal disorders
  Not known: Dyspnea
- Skin and subcutaneous tissue disorders
  Not known: Rash, urticaria, pruritus, hyperhidrosis, acute generalized exanthematous pustulosis (AGEP)
- Renal and urinary disorders

Not known: Dysuria, Urinary retention

- General disorders and administration site condition
  Not known: Thirst, fatigue, asthenia, chest pain

4.8 Overdose

Human Experience

Fexofenadine:

Most reports of fexofenadine hydrochloride overdose contain limited information. However, dizziness, drowsiness, and dry mouth have been reported.

Single doses up to 800 and doses up to 690 mg BID for 1 month or 240 mg QD for 1 year were studied in healthy subjects without the development of clinically significant adverse events as compared to placebo. The maximum tolerated dose of Allegra® D was not established.

Pseudoephedrine:

The expected pharmacological effects in cases of overdose would be caused by the sympathomimetic properties of pseudoephedrine affecting the nervous, psychiatric, and cardiac systems.

Management

In the event of overdose of Allegra® D, take all appropriate measures immediately.

Hemodialysis did not effectively remove fexofenadine from blood.

Excretion of pseudoephedrine is increased by lowering the pH of the urine.

5. Interferences with Laboratory and Diagnostic Test

Pseudoephedrine:

Athletes should be informed that treatment with pseudoephedrine hydrochloride can lead to positive results in doping tests.

Interference with serological testing

Pseudoephedrine has the potential to reduce iobenguane i-131 uptake in neuroendocrine tumors, thus interfering with scintigraphy.

6. Pharmacology

6.1 Mechanism of action

Fexofenadine:

Fexofenadine is an antihistamine with selective peripheral H1-receptor antagonist activity.

Fexofenadine inhibited antigen-induced bronchospasm in sensitized guinea pigs and histamine release from peritoneal mast cells in rats. In laboratory animals, no anticholinergic or alpha-adrenergic receptor blocking effects were observed. Moreover, no sedative or other central nervous system effects were observed. Radiolabeled tissue distribution studies in rats indicated that fexofenadine does not cross the blood-brain barrier.

Pseudoephedrine:

Pseudoephedrine is an orally active sympathomimetic amine and exerts a decongestant action on the nasal mucosa.

It is an effective agent for the relief of nasal congestion due to allergic rhinitis. Pseudoephedrine produces peripheral effects similar to those of ephedrine and central effects similar to, but less intense than, amphetamines, it has the potential for excitatory side effects. At the recommended oral dose, it has little or no pressor effect in normotensive adults.

Clinical Efficacy/Clinical Studies

Fexofenadine hydrochloride inhibits skin wheal and flare responses produced by histamine injection. Following single and twice daily oral dose administration, antihistaminic effects occurred within 1 hour, achieved a maximum of 2–3 hours, and lasted a minimum of 12 hours. Maximum inhibition in skin wheal and flare areas were greater than 80%. There is no evidence of tolerance to these effects after 28 days of dosing

No effect on QTc intervals was observed in seasonal allergic rhinitis patients given fexofenadine hydrochloride up to 240 mg twice daily for 2 weeks when compared to placebo. Also, no effect on QTc intervals was observed in healthy subjects given fexofenadine hydrochloride up to 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 potassium rectifier K+ channel cloned from human heart.

Combination Product:
Administration of the 60 mg fexofenadine hydrochloride/120 mg pseudoephedrine hydrochloride combination tablet for approximately 2 weeks to seasonal allergic rhinitis patients demonstrated no increase in the mean QTc interval compared to fexofenadine hydrochloride administered alone (60 mg twice daily), or compared to pseudoephedrine hydrochloride (120 mg twice daily) administered alone.

5.3 Pharmacokinetics

Absorption

Combination Product:
The pharmacokinetics of fexofenadine hydrochloride and pseudoephedrine hydrochloride are not altered when both agents are co-administered.
Fexofenadine hydrochloride was rapidly absorbed following multiple dose administration of Allegra® D to healthy volunteers with a mean peak fexofenadine plasma concentration occurring 2.1 hours post dose. Pseudoephedrine hydrochloride, in the same study, produced a mean peak pseudoephedrine plasma concentration at 4.8 hours post dose.

Fexofenadine hydrochloride was rapidly absorbed following single-dose administration of Allegra® D to healthy volunteers with a mean peak fexofenadine plasma concentration occurring 2.1 hours post dose. Pseudoephedrine hydrochloride, in the same study, produced a mean peak pseudoephedrine plasma concentration at 5.2 hours postdose.
Co-administration of Allegra® D with a high fat meal decreased bioavailability; the rate or extent of pseudoephedrine absorption was not affected. The administration of Allegra® D with food should be avoided.

Distribution

Fexofenadine:
Fexofenadine is 60% to 70% bound to plasma proteins.

Metabolism

Fexofenadine:
Fexofenadine undergoes negligible metabolism.

Elimination

Fexofenadine:
Following a single 60 mg oral dose, 80% of the total fexofenadine hydrochloride dose was recovered in the feces and 11% was recovered in the urine. Following multiple dosing, fexofenadine has a mean terminal elimination half-life of 11 to 16 hours. The major route of elimination is believed to be biliary excretion while up to 10% of ingested dose is excreted unchanged through the urine.

The single and multiple dose pharmacokinetics of fexofenadine hydrochloride are linear from 20 mg to 120 mg doses. A dose of 240 BID produced slightly greater than proportional increase (8.8%) in steady state area under the curve.

Pseudoephedrine:
The serum half-life of pseudoephedrine is approximately 4 to 8 hours. The elimination half-life may be decreased at urine pH <6 and may be increased at urine pH >8. About 43% to 96% of an administered dose is excreted unchanged in the urine; the remainder is apparently metabolized in the liver.

6 Nonclinical Safety Data

Combination Product:

There are no studies evaluating the carcinogenic or mutagenic potential of Allegra® D.

No clinical signs of toxicity and no effects on body weight or food consumption were observed in acute toxicity studies in several animal species administered fexofenadine hydrochloride by oral gavage at doses of 2,000 mg/kg. No treatment-related gross findings were observed in rodents following necropsy. Dogs tolerated 450 mg/kg administered twice daily for 6 months and showed no toxicity other than occasional emesis.

Single Dose Toxicity

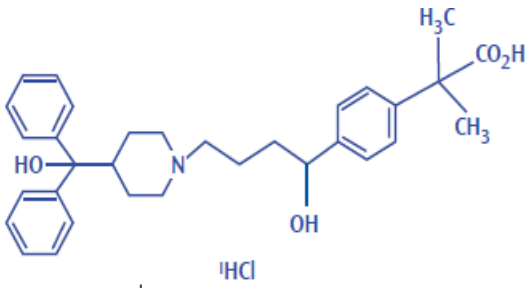
No clinical signs of toxicity and no effects on body weight or food consumption were observed in acute toxicity studies in several animal species administered fexofenadine hydrochloride by oral gavage at doses of 2,000 mg/kg. No treatment-related gross findings were observed in rodents following necropsy. Dogs tolerated 450 mg/kg administered twice daily for 6 months and showed no toxicity other than occasional emesis.

Other Toxicity Studies

Fexofenadine was found to be non-mutagenic in various in vitro and in vivo mutagenicity tests.

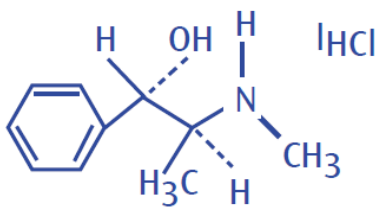
7. Description

Allegra® D (fexofenadine hydrochloride and pseudoephedrine hydrochloride) Extended- Release Tablets for oral administration contain 60 mg fexofenadine hydrochloride for immediate-release and 120 mg pseudoephedrine hydrochloride for extended-release. Tablets also contain as excipients: microcrystalline cellulose, pregelatinized starch, croscarmellose sodium, magnesium stearate, carnauba wax, stearic acid, silicon dioxide, hydroxypropyl methylcellulose and polyethylene glycol. Fexofenadine hydrochloride, one of the active ingredients of Allegra® D, is a histamine H-receptor antagonist with the chemical name (±)–4-[1-hydroxy – 4 - [4 - (hydroxy di phenylmethyl) - 1 - piperidinyl] - butyl] - α , α – dimethyl benzeneacetic acid hydrochloride and the following chemical structure:



The molecular weight is 538.13 and the empirical formula is $C_{32}H_{39}NO_4 \cdot HCl$. Fexofenadine hydrochloride is a white to off-white crystalline powder. It is freely soluble in methanol and ethanol, slightly soluble in chloroform and water, and insoluble in hexane. Fexofenadine hydrochloride is a racemate and exists as a zwitter ion in aqueous media at physiological pH.

Pseudoephedrine hydrochloride, the other active ingredient of Allegra® D, is an adrenergic (vasoconstrictor) agent with the chemical name [S-(R*, R*)]-α-[1-(methyl-amino)ethyl]- benzene-methanol hydrochloride and the following chemical structure:



The molecular weight is 201.70. The molecular formula is $C_{10}H_{15}NO$•HCI. Pseudoephedrine hydrochloride occurs as fine, white to off-white crystals or power, having a faint characteristic odor. It is very soluble in water, freely soluble in alcohol, and sparingly soluble in chloroform.

8. Pharmaceutical particulars
8.1 Incompatibilities
Not Applicable

8.2 Shelf-life
Refer outer carton
8.3 Packaging information
Presentation
Box contains 5 blisters x 10 tablets.

8.4 Storage and handing instructions

STORAGE
Store below 30°C

Expiry date
Do not use later than the date of expiry.
Keep all medicine out of the reach of children.

ON MEDICAL PRECRIPTION ONLY

9. Patient Counselling Information
Patients taking Allegra® D tablets should receive the following information: Allegra® D tablets are prescribed for the relief of symptoms of allergic rhinitis. Patients should be instructed to take Allegra® D tablets only as prescribed.

Do not exceed the recommended dose. If nervousness, dizziness or sleeplessness occur, discontinue use and consult the doctor. Patients should also be advised against the concurrent use of Allegra® D tablets with over-the-counter antihistamines and decongestants.

The product should not be used by patients who are hypersensitive to it or to any of its ingredients. Due to its pseudoephedrine component, this product should not be used by patients with narrow angle glaucoma, urinary retention, or by patients receiving a monoamine oxidase (MAO) inhibitor or within 14 days of stopping use of MAO inhibitor. It also should not be used by patients with severe hypertension or severe coronary artery disease.

Patients should be told that this product should be used in pregnancy or lactation only if the potential benefit justified the potential risk to the fetus or nursing infants.
Patients should be cautioned not to break or chew the tablet. Patients should be directed to swallow the tablet whole. Patients should be instructed not to take the tablet with food. Patients should also be instructed to store the medication in a tightly closed container in a cool, dry place, away from children.

10. Details of manufacturer
Manufactured by:
Opella Healthcare International SAS, 56 Route de Choisy 60200 Compiegne, France.

Packaged by:
PT Kalventis Sinergi Farma, Jl. Jenderal Ahmad Yani No. 2, Pulo Mas, Kelurahan Kayu Putih , Jakarta Timur, DKI Jakarta, (Indonesia) - 13210

Imported and marketed in India By:

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11. Details of permission or licence number with date
New drug permission no.: IMP-42/2021

12. Date of revision
Updated: March 2026

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