AUSTRALIAN PRODUCT INFORMATION – TELFAST DECONGESTANT (FEXOFENADINE AND PSEUDOEPHEDRINE)

1 NAME OF THE MEDICINE

Fexofenadine hydrochloride and pseudoephedrine hydrochloride.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each Telfast Decongestant tablet contains 60mg of fexofenadine hydrochloride in an immediate release formulation and 120mg of pseudoephedrine hydrochloride in a wax matrix for sustained release.

For the full list of excipients, see Section 6.1 List of excipients.

3 PHARMACEUTICAL FORM

Telfast Decongestant tablets are bilayer, capsule shaped, film coated tablets with one half (lengthwise) white to off-white and the other half tan. The white half of the tablet is debossed with “06/012D”.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

For the relief of the symptoms of allergic rhinitis with nasal congestion when both the antiallergic properties of fexofenadine hydrochloride and the decongestant activity of pseudoephedrine hydrochloride are required.

4.2 DOSE AND METHOD OF ADMINISTRATION

For adults and children over the age of 12 years, the recommended dosage of Telfast Decongestant is one tablet 12 hourly. The tablet should be swallowed whole and administration with or after a high fat meal should be avoided.

The safety and efficacy of Telfast Decongestant in patients under the age of 12 years has not been established.

Dosage adjustment is not required in the elderly or in patients with hepatic impairment. However, for renally impaired patients, a dose of one tablet once daily is recommended as a starting dose (see Section 4.4 Special Warnings and Precautions for Use).

The maximum tolerated dose of Telfast Decongestant has not been established.

4.3 CONTRAINDICATIONS

Telfast Decongestant is contraindicated in patients with a known hypersensitivity to fexofenadine, pseudoephedrine, terfenadine or any excipient.

Pseudoephedrine and thus Telfast Decongestant is contraindicated in the following patients:

- Patients with severe hypertension or severe coronary artery disease, narrow angle glaucoma, urinary retention or those who have shown sensitivity to adrenergic events (manifestations include insomnia, dizziness, weakness, tremor or arrhythmia).
- Patients with urinary retention related to urethroprostatic disorders.
- Patients receiving monoamine oxidase (MAO) inhibitors or patients who have received MAO inhibitors in the previous 14 days (see Section 4.4 Special Warnings and precautions for use).
- Patients with a history of seizures.
- Patients using other vasoconstrictor agents used as nasal decongestants, whether administered orally or nasally (see Section 4.4 Special Warnings and precautions for use).

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Sympathomimetics, such as pseudoephedrine, should be used with caution in patients with diabetes mellitus, hypertension, heart disease, increased intraocular pressure, hyperthyroidism, prostatic hypertrophy, renal disease and hyperreactivity to ephedrine, stroke and psychosis.

Like some sympathomimetics amines, pseudoephedrine may produce CNS stimulation with convulsions or cardiovascular collapse. Patients should be informed that the inactive ingredients of Telfast Decongestant may be eliminated in the faeces in a form that may resemble the original tablet.

Treatment should be discontinued if patients develop:

- Hypertension
- Tachycardia, palpitations, cardiac arrhythmias
- Any neurological symptoms such as onset or worsening of headache

Neurological and psychiatric symptoms and irregular heartbeat have been reported after systemic administration of vasoconstrictors, especially with overdose (see Section 4.9 Overdose).

Use in renal impairment

Pseudoephedrine should be used with caution in patients with renal disease as up to 90% of pseudoephedrine is excreted unchanged in the urine.

Use in the elderly

Elderly patients may be more sensitive to the effects on the CNS.

Paediatric use

Safety and effectiveness of Telfast Decongestant in children below the age of 12 years have not been established.

Effects on laboratory tests

Related to Pseudoephedrine component

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.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

As fexofenadine undergoes negligible hepatic biotransformation, it is unlikely to interact with other drugs through hepatic metabolism.

The pharmacokinetics of fexofenadine HCl and pseudoephedrine are not altered when both drugs are co-administered.

Co-administration of fexofenadine 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 events compared to the drugs given singly. Fexofenadine had no effect on the pharmacokinetics of erythromycin or ketoconazole.

Animal studies have shown that the increase in plasma levels of fexofenadine observed after co-administration of erythromycin or ketoconazole appears to be due to an increase in gastrointestinal absorption and either a decrease in biliary excretion or gastrointestinal secretion respectively.

A clinical drug-drug interaction study showed that co-administration of apalutamide (a weak inducer of P-glycoprotein) and a single oral dose of 30 mg fexofenadine resulted in a 30 % decrease in AUC of fexofenadine.

Concomitant use of pseudoephedrine with antihypertensive drugs which interfere with sympathetic activity, such as methyldopa or reserpine, may reduce their antihypertensive effects.

Concomitant use of pseudoephedrine with sympathomimetic or vasoconstrictor agents may have an additive cardiovascular effect (see Section 4.4 Special Warnings and precautions for use).

The use of pseudoephedrine within 14 days of use or after discontinuation of use of a monoamine oxidase (MAO) inhibitor is contraindicated. Concomitant use of

pseudoephedrine with monoamine oxidase inhibitors (MAOI) may lead to paroxysmal hypertension and hyperthermia, which can be fatal. (see Section 4.4 Special Warnings and Precautions for Use).

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.

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on fertility

In rat fertility studies, dose-related reductions in implants and increases in post implantation losses were observed at oral doses equal to or greater than 150mg/kg of terfenadine respectively; these doses produced plasma AUC values of fexofenadine that were equal to or greater than three times the human therapeutic value respectively (based on a 60mg twice daily fexofenadine HCl dose).

Use in pregnancy – Category B2

Telfast Decongestant should not be used in pregnancy unless, in the physician's judgement, the potential benefits outweigh the potential risk to the fetus.

Reproductive toxicity of fexofenadine in animals was assessed through terfenadine exposure. No evidence of teratogenicity was observed in animal reproduction studies (rat and rabbit) when terfenadine was given at oral doses of up to 300 mg/kg/day throughout organogenesis, which corresponds to levels of systemic fexofenadine exposure 4- and 32-fold higher, respectively, than those anticipated in clinical use. Decreased pup weight and survival occurred in rats when terfenadine was given at oral doses of 150 mg/kg/day and above throughout pregnancy and lactation.

There are no studies in pregnant women exposed to fexofenadine alone or through the administration of terfenadine.

Use in lactation

Pseudoephedrine is excreted in breast milk.

Fexofenadine 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. There are no data on the content of human milk after administering fexofenadine. However, when terfenadine was administered to nursing mothers, fexofenadine was found to cross into human breast milk.

Exposure of rats to fexofenadine and terfenadine through the administration of terfenadine at dietary doses of 150 and 300 mg/kg/day throughout pregnancy and lactation (corresponding to systemic exposure at levels (AUC) approximately 3- and 6-fold higher than those anticipated in clinical use) caused decreased pup weight gain and survival. The relative risks

of these effects from terfenadine or fexofenadine are unknown. Effects on pups exposed to fexofenadine only during lactation are unknown.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

No data available.

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

CLINICAL TRIALS

Telfast Decongestant is generally well tolerated. In clinical pharmacokinetic trials, adverse events reported were similar to experience with fexofenadine in placebo controlled clinical trials and similar to effects attributable to pseudoephedrine hydrochloride.

In placebo controlled clinical trials with fexofenadine alone, the incidence of reported adverse events was similar to that observed with placebo. No apparent dose trends were revealed in adverse events.

Headache, fatigue, drowsiness, dizziness and nausea were reported commonly.

Events that have been reported during controlled trials with incidences less than 1% and similar to placebo and have been reported rarely during postmarketing surveillance include: nervousness, insomnia, sleep disorders or paroniria. In rare case, rash, urticaria, pruritus and hypersensitivity reactions with manifestations such as angioedema, chest tightness, dyspnoea, flushing and systemic anaphylaxis have been reported.

Common reactions reported with pseudoephedrine include insomnia, dry mouth, nervousness, nausea, anorexia and palpitations. Headaches, drowsiness, excitability, restlessness, dizziness, weakness may occur. Tachycardia, pressor activity/hypertension, cardiac arrhythmias, acute generalized exanthematous pustulosis (AGEP), urinary retention and ischemic colitis have been reported. Sympathomimetic drugs have also been associated with untoward effects such as fear, anxiety, tenseness, tremor, hallucinations, seizures, pallor, respiratory difficulty, difficulty in micturition and cardiovascular collapse. Manic symptoms such as insomnia, high or irritable mood, inflated self-esteem, increased activity or restlessness, racing thoughts, rapid speech, and distractibility have been reported.

POST MARKETING

Psychiatric disorders

Frequency 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

Frequency not known: Stroke, headache, seizures, dizziness, somnolence, tremor

Cardiac disorders

Frequency not known: Palpitations, arrhythmia, tachycardia

Vascular disorders

Frequency not known: Hypertension

Gastrointestinal disorders

Frequency not known: Nausea, vomiting, dry mouth, decreased appetite, Ischemic colitis

Immune system disorders

Frequency not known: Hypersensitivity reactions

Respiratory, thoracic and mediastinal disorders

Frequency not known: Dyspnea

Skin and subcutaneous tissue disorders

Frequency not known: Rash, urticaria, pruritus, hyperhidrosis, Acute generalized exanthematous pustulosis (AGEP)

Renal and urinary disorders

Frequency not known: Dysuria, Urinary retention

General disorders and administration site

Frequency not known: Thirst, fatigue, asthenia, chest pain

Reporting suspected adverse effects

Reporting suspected adverse reactions after registration of the medicinal product is important. It allows continued monitoring of the benefit-risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions at www.tga.gov.au/reporting-problems (Australia) or https://nzphvc.otago.ac.nz/reporting/ (New Zealand).

4.9 OVERDOSE

In the case of an overdose, standard measures to remove any unabsorbed drug should be considered. Haemodialysis is not an effective means of removing fexofenadine from blood. Excretion of pseudoephedrine is increased by lowering the pH of the urine. Symptomatic and supportive treatment is recommended. If sympathomimetic amines are necessary, caution should be used in the presence of pseudoephedrine.

Fexofenadine

Most reports of overdose with fexofenadine hydrochloride have provided limited information. However, dizziness, drowsiness and dry mouth have been observed.

Single doses of fexofenadine of up to 800mg, twice daily doses of up to 690mg for one month and four times daily doses of 240mg for one year were studied in healthy subjects without the development of clinically significant adverse events as compared to placebo. The maximum tolerated dose of fexofenadine 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.

For the pseudoephedrine component of Telfast Decongestant, information on acute overdose is limited to the marketing history of pseudoephedrine hydrochloride.

In very large doses, sympathomimetics may give rise to giddiness, headache, nausea, vomiting, sweating, thirst, tachycardia, precordial pain, irritability, convulsions, palpitations, hypertension, difficulty with micturition, muscular weakness and tenseness, anxiety, restlessness and insomnia. Many patients can present a toxic psychosis with delusions and hallucinations. Some may develop cardiac arrhythmias, circulatory collapse, coma and respiratory failure. Necessary measures should be taken to maintain and support respiration and circulation. Gastric lavage should be performed if indicated. Convulsions should be controlled with an anticonvulsant. Catheterisation of the bladder may be necessary. Alpha-Adrenergic blockade may be required to treat hypertensive crises and beta-adrenergic blockade for the control of supraventricular dysrhythmias. The elimination of pseudoephedrine can be accelerated by acid diuresis or by dialysis.

For information on the management of overdose, contact the Poisons Information Centre on 131126 (Australia) or the National Poisons Centre on 0800 POISON or 0800 764 766 (New Zealand).

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Mechanism of action

The antihistaminic effects of fexofenadine have been demonstrated in animal systems *in vitro* and *in vivo*. Oral administration of fexofenadine to guinea pigs indicated that fexofenadine antagonised histamine-induced skin wheals in a dose-dependent manner. Fexofenadine and terfenadine antagonised the contractile effects of histamine in the guinea pig ileum in vitro. In this model fexofenadine was found to be a more selective histamine antagonist than terfenadine.

Fexofenadine inhibited antigen-induced bronchospasm in sensitised guinea pigs and, at high doses (>100-fold higher than those required for antihistaminic activity), inhibited histamine release from peritoneal mast cells of the rat. In laboratory animals, no anticholinergic or alpha-1-adrenergic receptor blocking effects were observed. Radiolabelled tissue distribution studies in rat indicated that fexofenadine does not cross the blood-brain barrier.

Fexofenadine is not associated with significant ECG abnormalities. Studies have shown that fexofenadine does not affect the action potential or ion channel currents (I_K, I_{Ca}, I_{Na}) in either guinea pig or neonatal rat myocytes. Fexofenadine was 583 times less potent than terfenadine in blocking a delayed rectifier potassium channel cloned from human heart. Additionally, doses of fexofenadine ten times greater than the dose of terfenadine that produces prolongation of QT_C intervals do not prolong QT_C intervals in anaesthetised rabbits and conscious dogs.

Pseudoephedrine is an orally active sympathomimetic amine which exerts a decongestant action on the nasal mucosa and is an effective agent for the relief of nasal congestion. 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 effects in normotensive adults.

Clinical trials

Administration of the combination tablet for approximately 2 weeks to 215 seasonal allergic rhinitis patients demonstrated no statistically significant increase in the mean QT_C interval compared to the monotherapies administered alone.

5.2 PHARMACOKINETIC PROPERTIES

Fexofenadine HCl is rapidly absorbed into the body following oral administration, with T_{max} occurring approximately 1-3 hours post-dose. Following administration of a single 60mg oral dose to healthy volunteers, fexofenadine HCl was rapidly absorbed, with a mean C_{max} of 209ng/mL. Following the administration of single oral doses of 120mg and 180mg fexofenadine HCl, the mean C_{max} values were approximately 427ng/mL and 494ng/mL, respectively.

The absolute bioavailability following fexofenadine HCl administration was estimated to be 33%. Coadministration with food has no clinically significant effect on the absorption of fexofenadine HCl.

The single and multiple dose pharmacokinetics of fexofenadine are linear for oral doses up to 120mg bd. A dose of 240mg bd produced a slightly greater than proportional increase (8.8%) in steady state area under the curve, indicating that fexofenadine pharmacokinetics are practically linear at daily doses between 40mg and 240mg. Fexofenadine is 60% to 70% bound to plasma proteins.

Fexofenadine undergoes negligible metabolism. Following a single radiolabelled 60mg oral dose, approximately 80% and 11% of the total [14C]-fexofenadine dose was excreted in faeces and urine respectively.

The plasma concentration vs time profiles of fexofenadine follow a bi-exponential decline with a mean terminal elimination half-life ranging from 14 to 15 hours following multiple dosing.

The pharmacokinetics of fexofenadine in seasonal allergic rhinitis patients are similar to those in healthy subjects.

Studies indicated that females may be exposed to higher plasma levels than males, however, there was no indication of any difference in efficacy or in the frequency of adverse events reported. Elderly patients, patients with hepatic impairment and patients with cardiac disease exposed to fexofenadine by administration of terfenadine showed no statistically significant differences in pharmacokinetic parameters for fexofenadine compared to healthy individuals. Although peak plasma level and half-life were increased 68% and 15% respectively in elderly patients and 54% and 19% respectively in patients with renal disease, regardless of disease severity, these levels are within the range of plasma levels shown to be tolerated in short term dose ranging trials.

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 metabolised by the liver.

The pharmacokinetics of fexofenadine hydrochloride and pseudoephedrine hydrochloride are not altered when they are administered together.

Fexofenadine hydrochloride was rapidly absorbed with T_{max} occurring at 2.1 hours and 1.7 hours post dose after multiple and single doses of Telfast Decongestant, respectively, in healthy volunteers. In the same studies, the T_{max} after multiple and single dosing of pseudoephedrine hydrochloride was determined to be 4.8 hours and 5.5 hours respectively.

5.3 PRECLINICAL SAFETY DATA

Genotoxicity

Fexofenadine showed no genotoxic activity in a series of assays for gene mutations and chromosomal damage.

Carcinogenicity

There are no studies evaluating the carcinogenic or mutagenic potential of Telfast Decongestant.

The carcinogenic potential and reproductive toxicity of fexofenadine HCl were assessed using terfenadine studies. No evidence of carcinogenicity was observed when mice and rats were given daily oral doses of 50 and 150mg/kg of terfenadine for 18 and 24 months, respectively; these doses resulted in plasma AUC values of fexofenadine that were two to four times the human therapeutic value (based on a 60mg twice daily fexofenadine HCl dose).

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Telfast Decongestant tablets also contain microcrystalline cellulose, pregelatinised maize starch, croscarmellose sodium, magnesium stearate, carnauba wax, stearic acid, colloidal anhydrous silica and Opadry-YS-1-7006 Clear.

6.2 INCOMPATIBILITIES

No data available.

6.3 SHELF LIFE

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store below 25°C.

6.5 NATURE AND CONTENTS OF CONTAINER

Telfast Decongestant tablets are available in PVC/PE/PVDC aluminium blister packs of 2, 6 and 10.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

In Australia, any unused medicine or waste material should be disposed of by taking to your local pharmacy.

6.7 PHYSICOCHEMICAL PROPERTIES

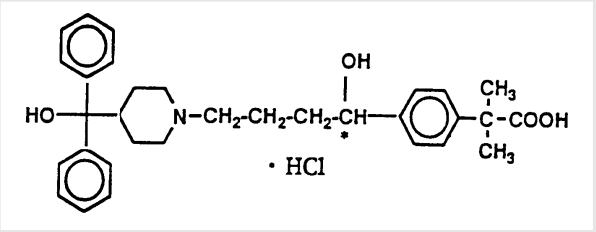
Fexofenadine is the carboxylic acid metabolite of terfenadine. It is an orally-active non-sedating histamine H1-receptor antagonist that is administered as the hydrochloride salt in Telfast Decongestant. The chemical name is benzeneacetic acid, 4-[1-hydroxy-4-[4-(hydroxydiphenylmethyl)-1-piperidinyl]butyl]-α,α-dimethyl-, hydrochloride.

Fexofenadine occurs as a fine white to off-white powder. It is freely soluble in methanol, soluble in ethanol, slightly soluble in water (3.6mg/mL) and only very slightly soluble in chloroform and hexane.

Pseudoephedrine hydrochloride is a white or off-white crystal or powder and is an orally active sympathomimetic amine which exerts a decongestant action on the nasal mucosa.

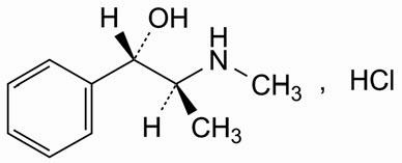
Chemical structure

Fexofenadine HCl is an equimolar mixture of two enantiomers. It has the following structure:



The molecular formula is C32H39NO4.HCl and the molecular weight is 538.13.

Pseudoephedrine HCl has the following structure



The molecular formula is $C_{10}H_{16}ClNO$ and the molecular weight is 201.69.

CAS number

Fexofenadine hydrochloride: 153439-40-8

Pseudoephedrine hydrochloride: 345-78-8

7 MEDICINE SCHEDULE (POISONS STANDARD)

Pharmacist Only Medicine (Schedule 3)

8 SPONSOR

Sanofi Consumer Healthcare
87 Yarraman Place, Virginia
Qld 4014 Australia

Toll Free Number (medical information): 1800 818 806
Email: medinfo.australia@sanofi.com

9 DATE OF FIRST APPROVAL

20 January 2000

10 DATE OF REVISION

03 March 2025

SUMMARY TABLE OF CHANGES

Section Changed	Summary of new information
4.5	Addition of interactions with P-gp inducers
4.8	Amendment to spelling of tremor.
4.9	Addition of text regarding maximum tolerated dose of fexofenadine.
5.1	Amendment to spelling of excitatory
-	Editorial amendment to PI header
6.3	Editorial amendments to shelf-life section
6.5	Addition of the nature of the container
6.7	Addition of pseudoephedrine HCl chemical structure