AUSTRALIAN PRODUCT INFORMATION – TELFAST (FEXOFENADINE)

1 NAME OF THE MEDICINE

Fexofenadine (as hydrochloride)

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Telfast 6 – 11 Years Tablets*
Each tablet contains fexofenadine HCl 30 mg equivalent to 28 mg fexofenadine.

Telfast 60 mg Tablets
Each tablet contains fexofenadine HCl 60 mg equivalent to 56 mg fexofenadine.

Telfast 120 mg Tablets
Each tablet contains fexofenadine HCl 120 mg equivalent to 112 mg fexofenadine.

Telfast 180 mg Tablets
Each tablet contains fexofenadine HCl 180 mg equivalent to 168 mg fexofenadine.

Telfast Oral Liquid- (reformulation)
Each mL of oral liquid contains fexofenadine HCl 6 mg (30 mg/ 5mL) equivalent to 5.6 mg fexofenadine.

Excipients with known effect in Telfast Oral Liquid: potassium sorbate, sucrose.

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

3 PHARMACEUTICAL FORM

Telfast 6 – 11 Years Tablets*
Peach, round, standard convex film-coated tablets engraved with ‘03’ on one side and a scripted ‘*e*’ on the other.

Telfast 60mg Tablets
Peach, oval, double convex, tablets, debossed with ‘06’ on one side and a scripted ‘e’ on the other.

Telfast 120 mg Tablets
Peach, oblong, double convex, tablets debossed with ‘012’ (underlined) on one side and a scripted “e” on the other.

Telfast 180 mg Tablets
Peach oblong, double convex tablets, debossed with ‘018’ (underlined) on one side and a scripted “e” on the other.

Telfast Oral Liquid – (reformulation)
White to beige uniform aqueous suspension, with a raspberry cream flavour.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

Oral Liquid
Relief of symptoms associated with urticaria from 6 months of age. Relief of symptoms associated with seasonal allergic rhinitis and allergic rhinitis from 2 years of age.

6 – 11 Years Tablets*
Relief of symptoms associated with seasonal allergic rhinitis, allergic rhinitis or urticaria in children aged 6 to 11 years.

60 mg Tablets
Relief of symptoms associated with allergic rhinitis in adults and children aged 12 years or older.

120 mg Tablets
Relief of symptoms associated with seasonal allergic rhinitis in adults and children aged 12 years or older.

180 mg Tablets
Relief of symptoms associated with seasonal allergic rhinitis or urticaria in adults and children aged 12 years or older.

4.2 DOSE AND METHOD OF ADMINISTRATION

Paediatrics

Allergic Rhinitis and Seasonal Allergic Rhinitis:

Children aged 2 to 11 years: 30 mg twice daily, when required.

Urticaria:
Children aged 6 to 23 months: 15 mg twice daily, when required.
Children aged 2 to 11 years: 30 mg twice daily, when required.

Adults and Children aged 12 years or older

Allergic Rhinitis:
60 mg twice daily, when required.

Seasonal Allergic Rhinitis:
120 mg or 180 mg once daily, when required.

Urticaria:
180 mg once daily, when required.

Dosage adjustment is not required in the elderly or in patients with hepatic or renal impairment.

4.3 CONTRAINDICATIONS

Telfast is contraindicated in patients with a known hypersensitivity to fexofenadine, terfenadine or any of its excipients.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Use in renal impairment

Dosage adjustment is not required in patients with renal impairment.

Use in hepatic impairment

Dosage adjustment is not required in patients with hepatic impairment.

Use in the elderly

Dosage adjustment is not required in the elderly.

Paediatric use

Safety and effectiveness of Telfast has not been established in children under 2 years of age for allergic rhinitis and under 6 months of age for chronic idiopathic urticaria.

Telfast 6 – 11 Years tablets* is intended for paediatric patients 6 to 11 years of age and Telfast Oral Liquid for children from 6 months.

Effects on laboratory tests

No data available

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.

Coadministration 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 coadministration 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.

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

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on fertility

In rat fertility studies, dose-related reductions in implants and increases in postimplantation losses were observed at oral doses equal to or greater than 150 mg/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 60 mg twice daily fexofenadine HCl dose).

Use in pregnancy

Category B2. 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

Telfast 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

The effects of this medicine on a person's ability to drive and use machines were not assessed as part of its registration.

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

Telfast is generally well tolerated. 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 common adverse events reported in controlled clinical trials were headache, fatigue, dizziness or drowsiness and nausea. No apparent dose trends were revealed in adverse events.

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 postmarketing 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, dyspnoea, flushing and systemic anaphylaxis have been reported.

Adverse events reported in placebo-controlled chronic idiopathic urticaria studies were similar to those reported in placebo-controlled seasonal allergic rhinitis studies. In placebo-controlled trials involving paediatric seasonal allergic rhinitis patients (6-11 years of age), adverse events were similar to those observed in trials involving seasonal allergic rhinitis patients 12 years and older.

In controlled clinical trials involving paediatric patients 6 months to 5 years of age, there were no unexpected adverse events in patients treated with fexofenadine hydrochloride.

As with adults, the incidence of adverse events with fexofenadine in paediatric patients was similar to placebo.

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

There is no clinical experience with a fexofenadine overdose. The maximum single dose tested in clinical trials is 800 mg in six healthy subjects. In a multiple-dose study, doses of 690 mg every 12 hours for 28.5 days were given to three healthy subjects and, in another study with forty subjects, a dose of 400 mg every 12 hours was given for 6.5 days. No clinically significant adverse events were reported in these studies.

In the case of an overdose, standard measures to remove any unabsorbed drug should be employed. Symptomatic and supportive treatment is recommended. Haemodialysis is not an effective means of removing fexofenadine from plasma.

For general advice on management of overdose, contact the Poisons Information Centre, telephone number 13 11 26 (Australia) or the National Poisons Centre, 0800 POISON or 0800 764 766 (New Zealand).

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Pharmacotherapeutic group: Antihistamine for systemic use, ATC code: R06A X26

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 (IK, ICa, INa) 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 QTC intervals do not prolong QTC intervals in anaesthetised rabbits and conscious dogs.

Clinical trials

An escalating acute dose study demonstrated antihistaminic activity via skin wheal and flare inhibition at doses ranging from 40 mg to 800 mg, with maximum inhibition reaching a plateau at a dose of 130 mg. An escalating repeat dose study demonstrated increasing skin flare inhibition at twice daily doses ranging from 20 mg to 690 mg. During both acute dose and repeat dose studies, an antihistaminic effect was observed within one hour, achieving maximum effect within 2 - 4 hours and lasting a minimum of 12 hours. There was no evidence of tolerance to these effects after 28 days of dosing.

In dose ranging studies, fexofenadine HCl was shown to relieve the symptoms of seasonal allergic rhinitis, significantly reducing total symptom scores (including scores for sneezing, rhinorrhoea, itchy nose, palate and/or throat, and itchy, watery, red eyes) over a dosage range of 40 mg to 240 mg twice daily. In a double-blind, placebo-controlled trial of 208 patients with chronic idiopathic urticaria, fexofenadine HCl 180 mg and 240 mg once daily for 6 weeks were found to significantly reduce total symptom scores (number of wheals (hives) and pruritus).

In a double-blind, placebo-controlled clinical efficacy study involving 821 patients with seasonal allergic rhinitis, fexofenadine HCl 120 mg and 180 mg once daily were found to be significantly superior to placebo in relieving symptoms of seasonal allergic rhinitis, including sneezing, rhinorrhoea, itchy nose, palate and/or throat, itchy, red or watery eyes and nasal congestion, after 24 hours. There was no statistically significant difference in efficacy between the two doses of fexofenadine, however the 180mg dose did show a trend toward greater reduction in the mean total symptom score.

In a double blind placebo controlled study, 861 patients aged 12 – 65 years were randomised to receive either 120 mg fexofenadine or 180 mg fexofenadine or placebo, once daily for a 2 week period. The primary efficacy measure was change from baseline of average total symptom score. Both doses provided significant ($p \leq 0.05$) improvement in symptoms of seasonal allergic rhinitis, compared to placebo. While there was no statistically significant difference in efficacy between the two doses, the 180 mg dose showed a trend toward greater reduction in the average total symptom score.

In a double blind placebo controlled study investigating quality-of-life, 845 patients aged 12 65 years were randomised to receive 120 mg fexofenadine or 180 mg fexofenadine or placebo once daily for a 2 week period. The primary efficacy measures were change from baseline in a quality-of-life score and in a work / activity impairment score. Patients receiving either 120 mg or 180 mg dose reported a significant ($p \leq 0.006$) improvement in overall quality-of-life score and a significant ($p \leq 0.004$) reduction in work / activity impairment score, compared to placebo. No statistical comparison was made between the effects of the two doses of fexofenadine.

The incidence of drowsiness in controlled clinical seasonal allergic rhinitis trials was similar when comparing patients treated with fexofenadine and placebo. There was no dose-related increase in drowsiness.

The effects of fexofenadine on the QT_c interval have been investigated in a variety of studies at doses up to 800 mg/day. There were no statistically significant differences in QT_c interval between fexofenadine and placebo treated patients. Similarly, there were no statistically significant differences from placebo or dose-related changes in other ECG parameters as a result of fexofenadine treatment.

Also, no statistically significant change in QT_c intervals was observed in long term studies in healthy subjects given fexofenadine HCl 60 mg twice daily for 6 months and 240 mg once daily for 12 months, when compared to placebo.

Interaction studies in healthy volunteers between fexofenadine and erythromycin or ketoconazole demonstrated that although the plasma AUC for fexofenadine increased approximately 2 - 3 fold, there were no significant effects on mean or maximal QT_c, nor were there any effects on the incidence of adverse events. Although these plasma levels were above those seen with the recommended dose, they were within the range of plasma levels achieved in controlled dose ranging clinical trials. Fexofenadine had no effect on the pharmacokinetics of erythromycin or ketoconazole (see **4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS** for further information).

Across the clinical trials, patients between the ages of 12 to 16 years have received doses ranging from 20 mg to 240 mg twice daily. Adverse events were similar in this group compared to patients above the age of 16 years.

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 60 mg oral dose to healthy volunteers, fexofenadine HCl was rapidly absorbed, with a mean C_{max} of 209 ng/mL. Following the administration of single oral doses of 120 mg and 180 mg fexofenadine HCl, the mean C_{max} values were approximately 427 ng/mL and 494 ng/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 120 mg bd. A dose of 240 mg 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 40 mg and 240 mg. Fexofenadine is 60% to 70% bound to plasma proteins.

Fexofenadine undergoes negligible metabolism. Following a single radiolabelled 60 mg 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 pharmacokinetics of fexofenadine in children and adults are similar, including t_{max}, clearance (corrected for body surface area), $t_{1/2}$ and volume of distribution, because fexofenadine undergoes negligible metabolism, with 80% of the dose being eliminated unchanged in the faeces. In contrast, other H1-receptor antagonists, which are extensively metabolised in the hepatic cytochrome P450 system, usually have shorter half-life values in children than adults.

In children, studies indicate that 30 or 60 mg fexofenadine suppresses the histamine induced wheal and flare within 1 to 2 hours, with both doses producing similar mean maximal suppression.

A dose of 5mL of Telfast Oral Liquid containing 30 mg of fexofenadine HCl is bioequivalent to a 30 mg dose of Telfast tablets. Following oral administration of a 30 mg dose of Telfast Oral Liquid to healthy adult subjects, the mean C_{max} was 118.0 ng/mL and occurred at approximately 1.0 hour.

5.3 PRECLINICAL SAFETY DATA

Genotoxicity

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

Carcinogenicity

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 150 mg/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 60 mg twice daily fexofenadine HCl dose).

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Telfast tablets contain the following excipients: croscarmellose sodium, pregelatinised maize starch, microcrystalline cellulose, magnesium stearate, hypromellose, povidone, titanium dioxide,

colloidal anhydrous silica, macrogol 400, Pigment Blend Pink PB1254 (ARTG PI No.3225) and Pigment Blend Yellow PB1255 (ARTG PI No.3226).

Telfast Oral Liquid – (reformulation) contains 6 mg/mL of fexofenadine HCl. Telfast Oral Liquid – (reformulation) also contains the following excipients: propylene glycol, edetate disodium, xanthan gum, poloxamer 407, titanium dioxide, sodium phosphate monobasic monohydrate, sodium phosphate dibasic heptahydrate, potassium sorbate, artificial raspberry cream flavour (ARTG PI No. 12546), sucrose, xylitol and purified water.

6.2 INCOMPATIBILITIES

Incompatibilities were either not assessed or not identified as part of the registration of this medicine.

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

Telfast 6 – 11 Years Tablets*
Store below 25°C.

Telfast 60mg Tablets
Store below 30°C.

Telfast 120 mg Tablets
Store below 30°C.

Telfast 180 mg Tablets
Store below 30°C.

Telfast Oral Liquid – (reformulation)
Store below 30°C.

6.5 NATURE AND CONTENTS OF CONTAINER

Telfast 6 – 11 Years Tablets*
Available in blister packs of 20 tablets.

Telfast 60mg Tablets
Available in blister packs of 10, 20 tablets.

Telfast 120 mg Tablets
Available in blister packs of 5, 10 and 30 tablets.

Telfast 180 mg Tablets
Available in blister packs of 5, 10, 30, 50, 60, 70, 80, 90 and 100 tablets.

Telfast Oral Liquid – (reformulation)
This product is available in 60mL and 150mL bottle presentations.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

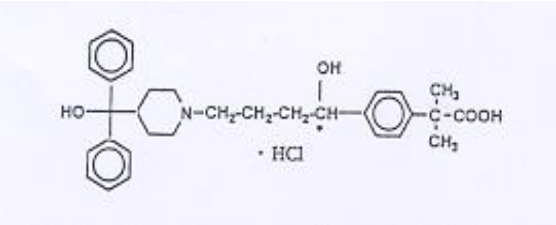
In Australia, any unused medicine or waste material should be disposed of by taking to your local pharmacy.

6.7 PHYSICOCHEMICAL PROPERTIES

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

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. The chemical name is benzeneacetic acid, 4-[1-hydroxy-4-[4-(hydroxydiphenylmethyl)-1-piperidinyl]butyl]- α,α-dimethyl-, hydrochloride.

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



The molecular formula is $C_{32}H_{39}NO_4$.HCl and the molecular weight is 538.13.

CAS number

83799-24-0

7 MEDICINE SCHEDULE (POISONS STANDARD)

Pharmacy Medicine (Schedule 2)

8 SPONSOR

Sanofi Consumer Healthcare,
87 Yarraman Place, Virginia,
Qld 4014 Australia.
Toll-free: 1800 818 806
Email: medinfo.australia@sanofi.com

9 DATE OF FIRST APPROVAL

10 January 1997

10 DATE OF REVISION

03 October 2023

*Not marketed in Australia

SUMMARY TABLE OF CHANGES

Section Changed	Summary of new information
3	Updated description of the Telfast Oral Liquid - (reformulation) to align with the approved 3.2.p.1 Description and Composition of the Drug Product
6.1	Updated the formulation ingredients of the Telfast Oral Liquid - (reformulation) to align with approved 3.2.p.1 Description and Composition of the Drug Product