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NEW ZEALAND DATASHEET

1 PRODUCT NAME

Telfast® 6 – 11 years 30mg film coated tablets#

Telfast® 60mg film coated tablets

Telfast® 120mg film coated tablets

Telfast® 180mg film coated tablets

Telfast® Oral Liquid, 6mg/mL, suspension

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

6 – 11 years 30mg film coated tablets#: Each tablet contains 30mg of fexofenadine hydrochloride equivalent to 28mg of fexofenadine.

60mg film coated tablets: Each tablet contains 60mg of fexofenadine hydrochloride equivalent to 56mg of fexofenadine.

120mg film coated tablets: Each tablet contains 120mg of fexofenadine hydrochloride equivalent to 112mg of fexofenadine.

180mg film coated tablets: Each tablet contains 180mg of fexofenadine hydrochloride equivalent to 168mg of fexofenadine.

Oral liquid, 6mg/mL: Each mL of liquid contains 6mg (30mg/5mL) of fexofenadine hydrochloride equivalent to 5.6mg of fexofenadine.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

6 – 11 years 30mg film coated tablets#: peach, round, standard convex.

60mg film coated tablets: peach, oval, double convex.

120mg film coated tablets: peach, modified capsule shaped (6.1mm x 15.8mm).

180mg film coated tablets: peach, capsule shaped (7.6mm x 17.3mm).

Oral liquid: white uniform aqueous suspension, with a raspberry cream flavour.

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4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Relief of symptoms associated with seasonal allergic rhinitis and allergic rhinitis in adults and children from 2 years of age.

Relief of symptoms of urticaria in adults and children from 6 months of age.

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.

The efficacy and safety of Telfast has not been established in children under 2 years of age for seasonal allergic rhinitis and under 6 months of age for urticaria.

Special risk groups

Studies in special risk groups (elderly, renally or hepatically impaired patients) indicate that it is not necessary to adjust the dose of fexofenadine hydrochloride in these patients.

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4.3 Contraindications

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

4.4 Special warnings and precautions for use

Studies in the elderly, patients with hepatic impairment and patients with cardiac disease exposed to fexofenadine through administration of terfenadine showed no statistically significant differences in pharmacokinetic parameters for fexofenadine when compared to those pharmacokinetic parameters in healthy individuals.

As with most new drugs there is only limited data in the elderly and renally or hepatically impaired patients. Fexofenadine hydrochloride should be administered with care in these special groups.

4.5 Interaction with other medicines and other forms of interaction

Since fexofenadine does not undergo hepatic biotransformation, it is unlikely to interact with drugs that rely upon hepatic metabolism.

Interaction studies with erythromycin and ketoconazole have shown that although the plasma levels of fexofenadine are increased 2–3 fold, there were no changes to QT interval and there were no changes to the incidence of any adverse events. The concentration of fexofenadine experienced by individuals during the interaction studies are well within the range experienced in acute and chronic dose-tolerance studies.

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 gastrointestinal absorption and either a decrease in biliary excretion or gastrointestinal secretion, respectively.

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

4.6 Fertility, pregnancy and lactation

Category B2.

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Reproductive toxicity of fexofenadine in animals was assessed through terfenadine exposure. Data from supporting pharmacokinetic studies, showing the extent of fexofenadine exposure, demonstrate that these studies are relevant to the assessment of fexofenadine hydrochloride. No evidence of teratogenicity was observed in animal reproduction studies (rat and rabbit) when terfenadine was given at oral doses of up to 300mg/kg/day throughout organogenesis which corresponds to levels of systemic fexofenadine exposure 4– and 32–fold higher, respectively, than those anticipated in clinical use. No effects on male or female fertility or perinatal or postnatal development were observed in terfenadine animal studies at non- maternally toxic doses.

There are no studies in pregnant women exposed to fexofenadine hydrochloride alone or through the administration of terfenadine. As with other medications, Telfast should be used during pregnancy only if the potential benefit justifies the potential risk to the foetus.

There are no studies of Telfast in lactating women. Telfast is not recommended for nursing women and should only be used if in the physician's judgement, the potential benefit outweighs the potential risk to the infant. There are no data on the content of human milk after administering fexofenadine hydrochloride. 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 doses of 150 and 300mg/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 in offspring. The relative risks of these effects from terfenadine or fexofenadine are unknown. Effects on pups exposed to fexofenadine only during lactation are not known.

4.7 Effects on ability to drive and use machines

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.

On the basis of the pharmacodynamic profile and reported adverse events it is unlikely that fexofenadine hydrochloride tablets will produce an effect on the ability to drive or use machines. In objective tests, Telfast has been shown to have no significant effects on central nervous system function. This means that patients may drive or perform tasks that require concentration.

4.8 Undesirable effects

Telfast is generally well tolerated. In placebo controlled clinical trials involving seasonal allergic rhinitis and chronic idiopathic urticaria the most commonly reported adverse events were

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headache (>3%), drowsiness, nausea, fatigue and dizziness (1-3%). The incidence of these events observed with fexofenadine hydrochloride was similar to that observed with placebo and no apparent dose trends were revealed in adverse events.

Events that have been reported during controlled clinical 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, pruritis and hypersensitivity reactions such as angiooedema, dyspnoea, chest tightness, flushing and systemic anaphylaxis have been reported.

No notable dose effects on QTc were found.

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 patients (6-11 years of age), adverse events were similar to those observed in trials involving patients 12 years and older, with incidences similar to placebo. 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.

Reporting of suspected adverse reactions:

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions https://nzphvc.otago.ac.nz/reporting/

4.9 Overdose

Most reports of fexofenadine hydrochloride overdose contain limited information. However, dizziness, drowsiness and dry mouth have been reported. Single doses up to 800mg and doses up to 690mg twice daily for 1 month were studied in healthy subjects without the development of clinically significant adverse events.

Clinical signs of toxicity and effects on body weight or food consumption were not observed in acute toxicity studies in several animal species administered fexofenadine by oral lavage at doses of 2,000mg/kg.

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.

There has been no reported case of an acute overdose of fexofenadine hydrochloride.

For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).

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5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: orally active non-sedating H1-receptor antagonist Mechanism of action

Fexofenadine hydrochloride is the synthetic hydrochloride salt of fexofenadine, the carboxylic acid metabolite of terfenadine (Teldane). It is an orally active non-sedating H1-receptor antagonist and is effective for the relief of symptoms associated with seasonal allergic rhinitis (sneezing, rhinorrhea, pruritus and lacrimation).

Fexofenadine is the major metabolite of terfenadine in man and is largely responsible for the antihistaminic effect following the administration of terfenadine.

Clinical efficacy and safety:

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. The antihistaminic

effects of fexofenadine and terfenadine were also assessed in the isolated guinea pig ileum in vitro. Both drugs antagonised the contractile effects of histamine, however, 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 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 did 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 and ion channel currents (IK , ICA , INa) in guinea pig or neonatal rat myocytes. The effect of fexofenadine on blocking a delayed rectifier potassium channel cloned from human heart was 583 times less potent than the same effect with terfenadine.

Doses of fexofenadine, ten times greater than the dose of terfenadine producing prolongation of QTc intervals, do not prolong QTc intervals in anaesthetised rabbits and conscious dogs.

An escalating acute-dose study demonstrated antihistaminic activity via skin wheal and flare inhibition at doses ranging from 10 to 800mg, with maximum inhibition reaching a plateau at a dose of 130mg. An escalating repeat-dose study demonstrated increasing skin flare inhibition at

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twice daily doses ranging from 20 to 690mg. 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 is no evidence of tolerance to these effects after 28 days of dosing.

In dose-ranging studies, fexofenadine hydrochloride was shown to relieve the symptoms of seasonal allergic rhinitis, significantly reducing total symptom scores (including scores for nasal congestion, sneezing, rhinorrhea, itchy nose, palate and/or throat, and itchy, watery, red eyes) over a dosage range of 40 to 240mg twice daily.

The 60mg twice daily dose was determined to be the optimal dose as reduction in symptom severity was similar over the 40–240mg dosage range, however, the 60mg dose had a faster onset of action than the 40mg dose. Significant symptom reduction was observed one hour following a single 60mg dose of fexofenadine hydrochloride. Onset of action was similar for doses of 60–240mg.

In controlled clinical studies, fexofenadine hydrochloride 120mg once daily was shown to relieve the symptoms of seasonal allergic rhinitis, significantly reducing total symptom scores (including scores for nasal congestion, sneezing, rhinorrhea, itchy nose, palate and/or throat, and itchy, watery, red eyes.

The incidence of drowsiness in controlled clinical seasonal allergic rhinitis trials was similar when comparing patients treated with fexofenadine hydrochloride (1.3%) and placebo (0.9%). There was no dose-related increase in drowsiness.

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

Interaction studies involving erythromycin and ketoconazole demonstrated that, although the plasma AUC for fexofenadine increased approximately 2–3 fold, there were no significant effects on ECG, nor were there any effects on the incidence of adverse events. These changes in plasma levels were within the range of plasma levels achieved in adequate and well-controlled clinical trials.

The duration of the clinical studies presented for evaluation was limited to two weeks, however, studies on longer term use are ongoing.

In a phase 3, single-center, sequential and parallel-group, double-blind, randomized study (NCT03664882) that was conducted in 266 allergic rhinitis subjects (251 in the modified-ITT population) to demonstrate the aggravation of allergic rhinitis (AR) symptoms in presence of pollutants [Diesel Exhaust Particulate (DEP)] and to evaluate the efficacy of fexofenadine HCl in AR subjects with symptoms aggravated in presence of DEP.

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The first primary endpoint was the change from baseline in the Area Under the Curve (AUC) for the Total Nasal Symptom Score (TNSS, the sum of rhinorrhea, nasal itching and sneezing scores) from Hours 0-12 between Period 2 and Period 1. Mean TNSS AUC_{0-12} was significantly higher in Period 2 compared to Period 1 (41.22 vs 36.25 respectively). The Least-Square (LS) mean difference (95% CI) between the two periods was 0.13 [95% CI: 0.081; 0.182 ($p<0.0001$)], indicating an aggravation of pollen-induced AR symptoms in the presence of DEP.

The second primary endpoint was the comparison of AUC_{2-12} for TNSS between placebo- and fexofenadine-treated groups during Period 3. AUC_{2-12} for TNSS during Period 3 was significantly lower in the fexofenadine-treated subjects compared to placebo-treated subjects (18.53 vs 26.34 respectively). The LS-mean difference (95% CI) between the two groups was 0.24 (-0.425 to -0.047) [$p=0.0148$)], demonstrating that fexofenadine 180 mg was effective in reducing DEP-aggravated AR symptoms induced by ragweed pollen.

In addition, secondary efficacy endpoints included changes from baseline in Total Symptom Score (TSS) for individual AR symptoms.

The mean (SD) AUC_{2-12} for individual symptom scores was lower in the fexofenadine HCl group vs placebo:

Symptom	**AUC_{2-12} for individual symptom scores***	
	Mean (SD)	
	SE	
	Placebo	Fexofenadine
Rhinorrhea	10.59 (6.50)	7.54 (5.96)
	0.581	0.531
Sneezing	7.01 (6.49)	4.26 (4.75)
	0.580	0.423
Nasal itching	8.74 (6.03)	6.73 (5.63)
	0.539	0.502
Nasal congestion	11.27 (6.98)	8.48 (5.81)
	0.624	0.517
Itchy eyes	5.92 (5.53)	4.56 (4.95)
	0.495	0.441

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Symptom	AUC_{2-12} for individual symptom scores*	
	Mean (SD)	
	SE	
	Placebo	Fexofenadine
Watery eyes	4.44 (5.61)	3.22 (4.00)
	0.501	0.56
Red or burning eyes	5.13 (6.14)	3.86 (5.13)
	0.549	0.457
Ear itching or palate or throat itching	6.13 (5.75)	4.99 (5.88)
	0.515	0.524

Proportional mean symptom reduction with fexofenadine, compared to placebo, was: rhinorrhea (28.8%); sneezing (39.2%); nasal itching (23.0%); nasal congestion (24.8%); itchy eyes (23.0%); watery eyes (27.5%); red or burning eyes (24.8%); and ear, palate, or throat itching (18.6%; all data were cumulative, from treatment intake up to 10 hours post treatment).

* Individual symptom scores are presented for descriptive purposes only as TSS scores were not significantly different between fexofenadine and placebo treatments.

SD: Standard Deviation

SE: Standard Error

5.2 Pharmacokinetic properties

Absorption

Fexofenadine hydrochloride is rapidly absorbed following oral administration. Tmax occurred approximately 1-3 hours postdose. The mean Cmax was approximately 142ng/mL following the administration of a single 60mg dose, approximately 289ng/mL following a single 120mg dose and approximately 494ng/mL following a single 180mg dose.

The absolute bioavailability following fexofenadine hydrochloride administration is calculated to be 33%.

Absorption of fexofenadine is not significantly altered by food.

Distribution

Fexofenadine is 60–75% bound to plasma proteins in healthy subjects.

Biotransformation

Fexofenadine undergoes negligible metabolism.

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Elimination

Following a single 60mg oral dose, 80% and 11.5% of total fexofenadine dose was excreted in the faeces and urine respectively. Following multiple dosing, fexofenadine has a mean terminal elimination half-life of 11-16 hours. The major route of elimination is believed to be biliary excretion while up to 10% of the ingested dose is excreted unchanged through the urine.

Linearity

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

In 7-12 year old allergic rhinitis patients, cross study comparisons indicated that fexofenadine area under the curve following oral administration of a 60mg dose was 56% greater compared to healthy adult subjects given the same dose. Additionally, fexofenadine clearance in paediatric patients has been determined to be approximately 40% lower than in adults. In view of this a dose of 30mg twice daily in paediatric patients will provide plasma fexofenadine concentration that are comparable to those associated with efficacy in adults. Administration of a 15 mg dose of fexofenadine to paediatric subjects aged 6 to 23 months, and of a 30 mg dose to paediatric subjects 2 to 11 years, produced exposures comparable to those seen with a dosage of 60 mg administered to adults.

The pharmacokinetics of fexofenadine in seasonal allergic rhinitis patients are similar to those in healthy subjects. One study indicated that females may be exposed to higher plasma levels than males, however, there was no indication of any difference in safety or efficacy. 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 well tolerated in adequate and well controlled safety and efficacy trials.

5.3 Preclinical safety data

The carcinogenic potential of fexofenadine was assessed using terfenadine studies with supporting pharmacokinetics studies showing fexofenadine exposure (via plasma AUC values). No evidence of carcinogenicity was observed in rats and mice given terfenadine.

Fexofenadine was found not to be mutagenic in various in vitro and in vivo mutagenicity tests.

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6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablets:

Tablet core: Microcrystalline cellulose Pregelatinised maize starch Croscarmellose sodium Magnesium stearate

Film coat: Hypromellose Povidone Titanium Dioxide

Colloidal silicon dioxide Macrogol 400

Pink ferric oxide Yellow iron oxide

Oral Liquid:

Butyl hydroxybenzoate

Dibasic sodium phosphate heptahydrate Disodium edetate

Monobasic sodium phosphate monohydrate Poloxamer

Propyl hydroxybenzoate Propylene glycol Purified water

Sucrose Titanium dioxide Xanthum gum Xylitol

Raspberry flavor

6.2 Incompatibilities

Not applicable

6.3 Shelf life

6 – 11 years 30mg film coated tablets#: 2 years

60mg film coated tablets: 3 years

120mg film coated tablets: 3 years

180mg film coated tablets: 3 years

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Oral liquid 150mL: 2 years

Oral liquid 60mL: 2 years

6.4 Special precautions for storage

6 – 11 years 30mg film coated tablets#: store below 25°C.

60mg film coated tablets: store below 30°C.

120mg film coated tablets: store below 30°C.

180mg film coated tablets: store below 30°C.

Oral liquid 150mL: store below 30°C.

Oral liquid 60mL: store below 30°C.

6.5 Nature and contents of container

Film coated tablets:

Blisters, packaged into cardboard boxes.

6 – 11 years 30mg film coated tablets#: 20 tablets per pack 60mg film coated tablets: 10 and 20 tablets per pack 120mg film coated tablets: 5, 10 and 30 tablets per pack 180mg film coated tablets: 10, 30, 50, 60 and 70 tablets per pack

Oral liquid:

30mL#,60mL, 150mL and 300mL# bottle, plastic bottle, polypropylene child resistant closure, packaged into cardboard boxes.

6.6 Special precautions for disposal and other handling

No special requirements.

Any unused waste should be disposed of in accordance with local requirements

7 MEDICINE SCHEDULE

Pharmacy Only Medicine

6 – 11 years 30mg film coated tablets#: 20 tablets 60mg film coated tablets: 20 tablets

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120mg film coated tablets: 10 and 30 tablets 180mg film coated tablets: 10, 30, 50, 60 and 70 tablets

Telfast Oral Liquid: bottles of 30mL#, 60mL , 150mL and 300mL#

General Sale Medicine

60mg film coated tablets: 10 tablets 120mg film coated tablets: 5 tablets

8 SPONSOR

sanofi-aventis new zealand limited

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9 DATE OF FIRST APPROVAL

Pharmacy Only Medicine

6 – 11 years 30mg film coated tablets#: 20 tablets; 14 October 1999

60mg film coated tablets: 20 tablets; 14 October 1999

120mg film coated tablets: 10 and 30 tablets; 28 May 1998

180mg film coated tablets: 10, 30, 50, 60 and 70 tablets; 28 May 1998

Telfast Oral Liquid: 30mL#, 60mL, 150mL, 300mL#;

4 August 2011 General Sale Medicine

60mg film coated tablets: 10 tablets; 7 October 2010

120mg film coated tablets: 5 tablets; 7 October 2010

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10 DATE OF REVISION OF THE TEXT

10 Sept 2020

#Not marketed

SUMMARY TABLE OF CHANGES

Section changed	Summary of new information
5.1	Update of the Pharmacodynamic properties to include the pollution study for the 180mg.
10	Date changed to 10 September 2020