

Summary of Product Characteristics

Telfast[®] 120 mg

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QUALITATIVE AND QUANTITATIVE COMPOSITION

Active ingredient: fexofenadine base 112 mg (as fexofenadine hydrochloride 120 mg).

PHARMACEUTICAL FORM

Peach, capsule-shaped, film-coated tablets.

CLINICAL PARTICULARS

Therapeutic indications

Relief of symptoms associated with seasonal allergic rhinitis.

Posology and method of administration

Adults and children aged 12 years and over

The recommended dose of fexofenadine hydrochloride for adults and children aged 12 years and over is 120 mg once daily.

Fexofenadine is a pharmacologically active metabolite of terfenadine.

Children under 12 years of age

The efficacy and safety of fexofenadine hydrochloride has not been studied in children under 12 years of age, therefore, it is not recommended for children of this age group.

Special risk groups

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

A dose of 60 mg tablet is recommended as the starting dose in patients with decreased renal function.

Contraindications

The product is contraindicated in patients with known hypersensitivity to any of its ingredients.

Special warnings and special precautions for use

There is no need for any special precautions in the elderly or hepatically impaired patients.

Interaction with other medicaments and other forms of interaction

Fexofenadine does not undergo hepatic biotransformation. Coadministration of fexofenadine hydrochloride 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.

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 of fexofenadine hydrochloride and aluminium and magnesium hydroxide containing antacids.

Pregnancy and lactation

No animal reproduction studies have been performed with fexofenadine hydrochloride. Supportive pharmacokinetic studies with terfenadine have been performed and show adequate extent of exposure to fexofenadine at the high dose level in animal reproduction studies performed with terfenadine. In these studies no evidence of teratogenicity was observed.

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; these doses produced plasma AUC values of fexofenadine that were equal to or greater than three times the human therapeutic value (based on a 60-mg twice-daily fexofenadine hydrochloride dose).

There is no experience with fexofenadine hydrochloride in pregnant women. As with other medications fexofenadine hydrochloride should not be used during pregnancy unless the expected benefit to the patient outweighs any possible risk to the foetus.

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. Therefore fexofenadine hydrochloride is not recommended for mothers breast feeding their babies.

Geriatric use

Adverse events were similar in this group to patients under age 60 years.

Renally impaired

In patients with mild (creatinine clearance 41-80 mL/min) to severe (creatinine clearance 11-40 mL/min) renal impairment, peak plasma levels of fexofenadine were 87% and 111% greater, respectively, and mean elimination half-lives were 59% and 72% longer, respectively, than observed in normal volunteers. Peak plasma levels in patients on dialysis (creatinine clearance \leq 10 mL/min) were 82% greater and half-life was 31% longer than observed in normal volunteers. Based on increases in bioavailability and half-life, a dose of 60 mg once daily is recommended as the starting dose in patients with decreased renal function.

Effects on ability to drive and use machines

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.

Undesirable effects

In controlled clinical trials the most commonly reported adverse events (>1%) were headache, drowsiness, dysmenorrhea, dyspepsia, nausea, dizziness, fatigue, back pain and throat irritation. The incidence of these events observed with fexofenadine was similar to that observed with placebo. Except for headache and throat irritation and back pain which were more common with fexofenadine than placebo.

Events that have been reported during controlled trials with incidences less than 1% and similar to placebo have been reported rarely during postmarketing surveillance include: 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.

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 or 240mg once daily for 1 year have been administered to healthy subjects without the development of clinically significant adverse events as compared with placebo. The maximum tolerated dose of fexofenadine hydrochloride has not been established.

Standard measures should be considered to remove any unabsorbed drug. Symptomatic and supportive treatment is recommended. Haemodialysis does not effectively remove fexofenadine hydrochloride from blood.

PHARMACOLOGICAL PROPERTIES

Pharmacodynamic properties

Fexofenadine hydrochloride is a non-sedating, selective, peripheral H₁ antihistamine. Fexofenadine is a pharmacologically active metabolite of terfenadine.

Human histamine wheal and flare studies following single and twice daily doses of 20 and 40 mg fexofenadine hydrochloride demonstrate that the drug exhibits an antihistaminic effect beginning within one hour, achieving maximum of 2-3 hours and lasting minimum 12 hours. There was no evidence of tolerance to these effects after 28 days of dosing. Using reflective symptom score assessments as the primary endpoint, clinical studies conducted in seasonal allergic rhinitis have shown that a dose of 120 mg is sufficient for 24 hours efficacy. A positive dose-response relationship between doses of 10 mg to 130 mg taken orally was found to exist. In this model of antihistaminic activity, it was found that doses of at least 130 mg were required to achieve a consistent effect that was maintained over a 24 hour period. Maximum inhibition in skin wheal and flare areas were greater than 80%.

No significant differences in QT_c intervals were observed in seasonal allergic rhinitis patients given fexofenadine hydrochloride up to 240 mg twice daily for 2 weeks when compared to placebo

Fexofenadine hydrochloride (5-10 mg/kg p.o.) inhibited antigen induced bronchospasm in sensitised guinea pigs and inhibited histamine release at supratherapeutic conditions (10-100 µM) from peritoneal mast cells.

Pharmacokinetic properties

Fexofenadine hydrochloride is rapidly absorbed into the body following oral administration, with T_{max} occurring at approximately 1-3 hours post dose. The mean C_{max} value was approximately 289 ng/ml following the administration of a 120 mg dose once daily.

Fexofenadine is 60-70% plasma protein bound. Fexofenadine undergoes negligible metabolism, as it was the only major compound identified in urine and faeces of animals and man. The plasma concentration profiles of fexofenadine follow a bi-exponential decline with a terminal elimination half-life ranging from 11 to 15 hours after multiple dosing. The single and multiple dose pharmacokinetics of fexofenadine are linear between 40 mg and 240 mg taken daily. The major route of elimination is believed to be via biliary excretion while up to 10% of ingested dose is excreted unchanged through the urine.

Preclinical safety data

Dogs tolerated 450 mg/kg administered twice daily for 6 months and showed no toxicity other than occasional emesis. Also, in single dose dog and rodent studies, no treatment-related gross findings were observed following necropsy.

Radiolabelled fexofenadine hydrochloride in tissue distribution studies of the rat indicated that fexofenadine did not cross the blood brain barrier.

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

The carcinogenic potential of fexofenadine hydrochloride was assessed using terfenadine studies with supporting pharmacokinetic studies showing fexofenadine hydrochloride exposure (via plasma AUC values). No evidence of carcinogenicity was observed in rats and mice given terfenadine (up to 150 mg/kg/day).

PHARMACEUTICAL PARTICULARS

List of excipients

Tablet core

Microcrystalline Cellulose, Pregelatinised Maize Starch, Croscarmellose Sodium, Magnesium Stearate

Film coat

Hydroxypropyl Methylcellulose, Povidone, Titanium Dioxide (E171), Colloidal Anhydrous Silica, Macrogol 400, Iron Oxide (E172)

Incompatibilities

None

Shelf life

24 months

Special precautions for storage

Controlled room temperature

Nature and contents of container

Blue or white opaque polyvinylchloride blisters (pharmaceutical grade) 200 µm thick with a polyvinylidene chloride coating of 90 g/m² on the internal surface of the blister. The PVC/PE/PVDC is sealed to hard tempered aluminium foil 20 µm thick with a vinyl heat seal coating. The blisters are packaged into cardboard boxes.

Instructions for use/handling

No special instructions

Manufacturer

Marion Merrell Bourgoin SA, France.

Manufacturer's agent

Aventis Pharma Ltd., P.O.Box 8090, Netanya 42170, Israel.

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