Telfast® **180mg**

Fexofenadine HCl

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Composition

Telfast 180mg: Each tablet contains 180mg of the active ingredient fexofenadine hydrochloride (as 168 mg fexofenadine).

Each tablet also contains microcrystalline cellulose, pregelatinised maize starch, croscarmellose sodium, magnesium stearate, hypromellose, povidone, titanium dioxide (E 171), colloidal anhydrous silica, macrogol 400 and iron oxide (E172).

Properties

Pharmacodynamic

Fexofenadine hydrochloride is a non-sedating H_1 antihistamine (ATC-code: R06A X26). Fexofenadine is a pharmacologically active metabolite of terfenadine.

Human histamine wheal and flare studies following single and twice daily doses of fexofenadine hydrochloride demonstrate that the drug exhibits an antihistaminic effect beginning within one hour, achieving maximum at 6 hours and lasting 24 hours. There was no evidence of tolerance to these effects after 28 days of dosing. A positive dose-response relationship between doses of 10mg to 130mg taken orally was found to exist. In this model of antihistaminic activity, it was found that doses of at least 130mg 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 that 80%. Clinical studies conducted in allergic rhinitis have shown that a dose of 120mg is sufficient for 24 hours efficacy. In children aged 6 to 11 years, the suppressive effects of fexofenadine hydrochloride on histamine-induced wheal and flare to were comparable to that in adults at similar exposure.

In an integrated analysis of placebo controlled double-blind phase III studies, involving 1369 children with seasonal allergic rhinitis aged 6 to 11 years, fexofenadine hydrochloride at 30mg twice daily was significantly better than placebo in reducing total symptom score ($p=0.0001$). All individual component symptoms including rhinorrea, sneezing, itchy nose/palate and throat, and nasal congestion were significantly ($p=0.0334$ to $p=0.0001$) improved by fexofenadine hydrochloride.

In a double-blind, placebo-controlled clinical efficacy study involving 821 patients with seasonal allergic rhinitis (SAR), fexofenadine HCL 120mg and 180mg once daily were found to be significantly superior to placebo in relieving symptoms of SAR, including sneezing, rhinorrea, 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 randomized to receive either 120mg fexofenadine or 180mg 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 ($p<0.05$) improvement in symptoms of SAR, compared to placebo. While there was no statistically significant difference in efficacy between the two doses, the 180mg dose showed a trend toward greater reduction in the average total symptom score.

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

Also, no significant change in QTc intervals was observed in healthy subjects given fexofenadine hydrochloride up to 60mg twice daily for 6 months, 400mg twice daily for 6.5 days and 240mg once daily for 1 year, when compared to placebo. In children aged 6 to 11 years, no significant difference in QTc were observed following up to 60mg fexofenadine hydrochloride twice daily for two weeks. Fexofenadine at concentrations 32 times greater than the therapeutic concentration in man had no effect on the delayed rectifier K+ channel cloned from human heart.

Fexofenadine hydrochloride (5-10 mg/kg po) inhibited antigen induced bronchospasm in sensitized guinea pigs and inhibited histamine release at supratherapeutic concentrations (10-100µm) from peritoneal mast cells.

Pharmacokinetic

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} was approximately 142 ng/ml following the administration of a single 60 mg dose, approximately 289 ng/ml following a single 120 mg dose and approximately 494 ng/ml following a single 180 mg dose.

The exposures produced by single doses of 15, 30 and 60mg in children aged 6 to 11 years are dose proportional and comparable to those produced by corresponding single doses of 30, 60 and 120mg in adults respectively. A dose of 30 mg BID was determined to provide plasma levels (AUC and C_{max}) in pediatric patients which were comparable to plasma levels achieved in adults following 120 mg once daily.

Fexofenadine is 60-70% plasma protein bound. Fexofenadine undergoes negligible metabolism, (hepatic or non-hepatic) as it was the only major compound identified in urine and faeces of the animals and man. The plasma concentration profiles of fexofenadine follow a big 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 for oral doses up to 120mg BD. A dose of 240mg BD produced slightly greater than proportional increase (8.8%) in steady state area under the curve, indicating that fexofenadine pharmacokinetics are practically linear at these doses. 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 450mg/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 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 150mg/kg/day).

In a reproductive toxicity study in mice, fexofenadine hydrochloride did not impair fertility, was not teratogenic and did not impair pre- or postnatal development.

Indications

Telfast 180mg is indicated for the relief of symptoms associated with Seasonal Allergic Rhinitis (SAR) and Chronic Idiopathic Urticaria (CIU) in adults and children 12 years of age and older.

Contraindications

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

Precautions

As with most new drug 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.

Fertility, pregnancy and lactation

Pregnancy

There are no adequate data from the use of fexofenadine hydrochloride in pregnant women. Limited animal studies do not indicate direct or indirect harmful effects with respect to effects on pregnancy, embryonal/foetal development, parturition or postnatal development (see Preclinical safety data).

Fexofenadine hydrochloride should not be used during pregnancy unless clearly necessary.

Breast-feeding

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.

Fertility

No human data on the effect of fexofenadine hydrochloride on fertility are available. In mice, there was no effect on fertility with fexofenadine hydrochloride treatment (see Preclinical safety data).

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 180mg have been shown to have no significant effects on central nervous system function. This means patients may drive or perform tasks that require concentration. However, in order to identify sensitive people who have unusual reaction to drugs, it is

advisable to check the individual response before driving or performing complicated tasks.

Adverse effects
In controlled clinical trials the most commonly reported adverse events were headache, drowsiness, nausea, dizziness and fatigue. The incidence of these events observed with fexofenadine was similar to that observed with placebo.
In rare cases, rash, urticaria, pruritus and hypersensitivity reactions have been reported.

Interactions
Fexofenadine does not undergone hepatic biotransformation and therefore will not interact with other drugs through hepatic mechanisms. Co-administration 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.
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 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.

Dosage and method of administration
Adults and children aged 12 years and older
The recommended dose is one tablet once daily.

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.

Overdosage
Most reports of fexofenadine hydrochloride overdose contain limited information. However, dizziness, drowsiness and dry mouth have been reported. The maximum tolerated dose of fexofenadine was not established.
Standard measures should be considered to remove any unabsorbed drug. Haemodialysis does not effectively remove fexofenadine hydrochloride from blood.

Storage
Store below 30°C.

Presentation
Box contains 10 film coated tablets.
Box contains 20 film coated tablets.
Box contains 30 film coated tablets.
Box contains 50 film coated tablets.
Box contains 100 film coated tablets.
Not all pack size are marketed

Manufactured by
PT Kalventis Sinergi Farma, Jakarta, Indonesia.

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