



National Agency for Food & Drug Administration & Control (NAFDAC)

Registration & Regulatory Affairs (R & R) Directorate

SUMMARY OF PRODUCT CHARACTERISTICS (SmPC) TEMPLATE

1. NAME OF THE MEDICINAL PRODUCT

Fexofenadine Tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film coated tablet contains:

Fexofenadine Hydrochloride Ph.Eur.....180 mg

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablet

Peach coloured, circular, biconvex, beveled edged film coated tablets, debossed with 'F' on one side and plain on other side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Fexofenadine hydrochloride 120 mg tablets are indicated in adults and children 12 years and older for the relief of symptoms associated with seasonal allergic rhinitis.

4.2 Posology and method of administration

Adults

The recommended dose of fexofenadine hydrochloride for adults is 120 mg once daily taken before a meal.

Fexofenadine is a pharmacologically active metabolite of terfenadine.

Paediatric population

- *Children aged 12 years and over*

The recommended dose of fexofenadine hydrochloride for children aged 12 years and over is 120 mg once daily taken before a meal.

- *Children under 12 years of age*

The efficacy and safety of fexofenadine hydrochloride has not been studied in children under 12.

Special populations

Only limited data is available regarding the administration in elderly and in patients with renal or hepatic impairment. It is not necessary to adjust the dose of fexofenadine hydrochloride in these patient groups, however, it should be used with caution in these patient groups.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients.

4.4 Special warnings and precautions for use

As with most new medicinal products 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.

Patients with a history of or ongoing cardiovascular disease should be warned that, antihistamines as a medicine class, have been associated with the adverse reactions, tachycardia and palpitations (see section 4.8).

4.5 Interaction with other medicinal products and other forms of interaction

Fexofenadine does not undergo hepatic biotransformation and therefore will not interact with other medicinal products through hepatic mechanisms. 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 reactions compared to the medicinal products 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.

Also single dose of lopinavir and ritonavir combination (400 mg/100 mg) has been found to increase the AUC of fexofenadine 4.0-fold, while the steady-state lopinavir/ritonavir increased the fexofenadine AUC by 2.9-fold. Thus the adverse effects of fexofenadine may increase. No pharmacodynamic interaction is known.

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.

Allergy tests: Use of fexofenadine hydrochloride must be discontinued three days before allergy tests (s.c. pricktest).

4.6 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 section 5.3). Fexofenadine hydrochloride should not be used during pregnancy unless clearly necessary.

Breastfeeding

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 section 5.3).

4.7 Effects on ability to drive and use machines

On the basis of the pharmacodynamic profile and reported adverse reactions 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. However, in order to identify sensitive people who have an unusual reaction to medicinal products, it is advisable to check the individual response before driving or performing complicated tasks.

4.8 Undesirable effects

The following frequency rating has been used, when applicable:

Very common $\geq 1/10$; Common $\geq 1/100$ and $< 1/10$; Uncommon $\geq 1/1,000$ and $< 1/100$; Rare $\geq 1/10,000$ and $< 1/1,000$; Very rare $< 1/10,000$ and not known (frequency cannot be estimated from the available data).

Immune system disorders

Rare: Hypersensitivity reactions with manifestations such as angio-oedema, chest tightness, dyspnoea, flushing and systemic anaphylaxis

Psychiatric disorders

Uncommon: Insomnia, sleep disorders or nightmares/excessive dreaming (paroniria), nervousness

Nervous system disorders

Common: Headache (7.3%), drowsiness (2.3%), dizziness (1.5%)

Uncommon: Fatigue

Gastrointestinal disorders

Common: Nausea (1.5%), dry mouth (3-5%)

Not known: Diarrhoea

Skin and subcutaneous tissue disorders

Rare: Rash, urticaria, pruritus

Cardiovascular disorders

Uncommon: Tachycardia, palpitations

General disorders and administration site conditions

Uncommon: Fatigue

In controlled clinical trials, the incidence of the common adverse events was similar to that observed with placebo.

Events that have been reported with incidences less than 1% and similar to placebo in controlled trials have also been reported rarely during post marketing surveillance.

4.9 Overdose

Dizziness, drowsiness, fatigue and dry mouth have been reported with overdose of fexofenadine hydrochloride. Single doses up to 800 mg and doses up to 690 mg twice daily for 1 month or 240 mg once daily for 1 year have been administered to healthy subjects without the development of clinically significant adverse reactions as compared with placebo. The maximum tolerated dose of fexofenadine hydrochloride has not been established.

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

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antihistamines for systemic use, ATC code: R06AX26

Fexofenadine hydrochloride is a non-sedating H₁ antihistamine. 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 medicinal product 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 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%. Clinical studies conducted in seasonal allergic rhinitis have shown that a dose of 120 mg is sufficient for 24 hour efficacy.

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. Also, no significant change in QT_c intervals was observed in healthy subjects given fexofenadine hydrochloride up to 60 mg twice daily for 6 months, 400 mg twice daily for 6.5 days and 240 mg once daily for 1 year, when compared to placebo. 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 sensitised guinea pigs and inhibited histamine release at supratherapeutic concentrations (10-100 μM) from peritoneal mast cells.

5.2 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 427 ng/ml following the administration of a 120 mg dose 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 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 for oral doses up to 120 mg BID. A dose of 240 mg BID 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 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.

5.3 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).

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

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Microcrystalline Cellulose 101
Lactose Monohydrate
Povidone
Croscarmellose Sodium
Sodium Lauryl Sulphate
Maize Starch (for paste)
Microcrystalline Cellulose 102
Talc
Magnesium Stearate
Opadry II Brown 85G86605
Purified Water

6.2 Incompatibilities

Not applicable

6.3 Shelf life

3 years

6.4 Special precautions for storage

Do not store above 30°C. Protect from light.

6.5 Nature and contents of container

Blister of 10 tablets

6.6 Special precautions for disposal and other handling

No special requirements.

7. MARKETING AUTHORISATION HOLDER

1389, Trasad Road, Dholka – 382225,
District: Ahmedabad,
Gujarat State, India

8. MARKETING AUTHORISATION NUMBER(S)

B4-4521

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

26/03/2015

10. DATE OF REVISION OF THE TEXT

September 2019