

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Fexofenadine hydrochloride 180 mg film-coated tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film coated tablet contains 180mg of Fexofenadine Hydrochloride; equivalent to 168mg of Fexofenadine

Excipients:

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Fexofenadine Hydrochloride 180mg film-coated tablets are pink coloured, oval biconvex, embossed "FXF" on one side and "180" on the other side.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Relief of symptoms associated with chronic idiopathic urticaria.

4.2 Posology and method of administration

Adults and children over 12 years of age:

The recommended dose is 180 mg once daily taken before a meal.

Fexofenadine hydrochloride 180mg film-coated tablets are not recommended for children under the age of 12.

In special populations like the elderly, patients with renal or hepatic impairment, the usual adult dose is recommended and no change in dose is required.

4.3 Contraindications

Fexofenadine hydrochloride 180mg film-coated tablets are contraindicated in patients with known hypersensitivity to fexofenadine hydrochloride or any of its components.

4.4 Special warnings and precautions for use

Since there is limited clinical experience with Fexofenadine hydrochloride in adult patients with renal or hepatic impairment, and in elderly patients, Fexofenadine 180mg film-coated tablets should be used with caution in such patients.

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

4.5 Interaction with other medicinal products and other forms of interaction

Fexofenadine hydrochloride does not undergo hepatic metabolism or biotransformation and is excreted unchanged. Thus it will not interact with other drugs which are metabolised by the liver.

When co-administered with erythromycin or ketoconazole, fexofenadine hydrochloride plasma concentrations increased 2-3 fold, but were not associated with effect on QTc intervals or increased incidences of adverse events as compared to the drugs given alone. Animal studies have shown that the increased plasma fexofenadine hydrochloride levels on co-administration with erythromycin or ketoconazole appears to be due to an increase in gastrointestinal absorption and either a decrease in biliary excretion or gastrointestinal secretion, respectively.

Fexofenadine hydrochloride does not show any interaction with Omeprazole. A reduced oral bioavailability of fexofenadine hydrochloride is seen when magnesium or aluminium containing antacids are administered 15 minutes prior to administration of fexofenadine, due to binding in the gastrointestinal tract. Thus administration of aluminium or magnesium containing antacids and fexofenadine hydrochloride tablets must be at least 2 hours apart.

4.6 Pregnancy and lactation

Pregnancy

In limited animal studies Fexofenadine hydrochloride did not impair fertility, was not teratogenic and did not impair pre- or postnatal development (see section 5.3). However, experience with the use of Fexofenadine hydrochloride

in pregnant women is limited and Fexofenadine hydrochloride should not be used during pregnancy unless clearly necessary and the benefit of using fexofenadine hydrochloride clearly outweigh the risk to the mother and foetus.

Lactation

Currently no data are available on whether Fexofenadine hydrochloride passes into breast milk. Terfenadine administration caused fexofenadine (the active metabolite of terfenadine) to appear in breast milk, thus fexofenadine hydrochloride administration is not recommended in mothers who breast feed their babies.

4.7 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, fexofenadine hydrochloride 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 drugs, it is advisable to check the individual response before driving or performing complicated tasks.

4.8 Undesirable effects

Adverse effects are categorised below, according to system organ class and frequency:

| | |
|-------------|---|
| Very common | ($\geq 1/10$) |
| Common | ($\geq 1/100$ to $< 1/10$) |
| Uncommon | ($\geq 1/1,000$ to $< 1/100$) |
| Rare | ($\geq 1/10,000$ to $< 1/1,000$) |
| Very rare | ($< 1/10,000$) |
| Not known | (cannot be estimated from the available data) |

In adults, the following adverse events have been reported with an incidence similar to that observed with placebo:

Nervous system disorders

Common: headache, drowsiness, dizziness.

Gastrointestinal disorders

Common: nausea

General disorders and administration site conditions

Uncommon: fatigue

In adults, the following undesirable effects have been reported in post-marketing surveillance:

Immune system disorders

Not known: hypersensitivity reactions with manifestations such as angioedema, chest tightness, dyspnoea, flushing and systemic anaphylaxis

Psychiatric disorders

Not known: nervousness, sleep disorders, such as insomnia, nightmares/excessive dreaming (paroniria).

Cardiac disorders:

Not known: tachycardia and palpitations

Gastrointestinal disorders

Not known: diarrhoea

Skin and subcutaneous tissue disorders

Not known: rash, urticaria, pruritus

4.9 Overdose

Doses up to 60 mg twice daily for two weeks have been administered to children, and 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 events as compared with placebo but the maximum tolerated dose of fexofenadine hydrochloride is yet to be established. The most commonly associated side effects with overdose of fexofenadine hydrochloride are dizziness, drowsiness, fatigue and dry mouth.

Upon overdose of Fexofenadine hydrochloride, standard measures should be taken to remove unabsorbed drug from the body. Symptomatic and supportive treatment is recommended.

Haemodialysis does not effectively remove fexofenadine hydrochloride from the blood.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic Group: Antihistamines for systemic use, ATC code: R06A X26

Fexofenadine hydrochloride is a non-sedating H1 antihistamine. Fexofenadine hydrochloride 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 was greater than 80%. Clinical studies conducted in seasonal allergic rhinitis have shown that a dose of 120mg is sufficient for 24 hour efficacy.

No significant differences in QTc intervals were observed in seasonal allergic rhinitis patients given fexofenadine hydrochloride up to 240 mg twice daily for 2 weeks when compared to placebo. No significant change in QTc 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 hydrochloride 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 also inhibited antigen induced bronchospasm in sensitised guinea pigs and inhibited histamine release at supratherapeutic concentrations (10-100 μ M) 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 427ng/ml following the administration of a 120mg dose once daily and approximately 494ng/ml following the administration of a 180mg dose once daily. Fexofenadine hydrochloride is 60-70% plasma protein bound. Fexofenadine hydrochloride 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 hydrochloride are linear for oral doses up to 120mg BID. A dose of 240mg BID produced slightly greater than proportional increase (8.8%) in steady state area under the curve, indicating that fexofenadine hydrochloride pharmacokinetics are practically linear at these doses between 40mg and 240mg 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 hydrochloride 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

Tablet core:

Powdered Cellulose

Mannitol

Maize starch

Croscarmellose Sodium

Colloidal anhydrous Silica

Magnesium Stearate

Tablet coating:

Opadry Pink 03B54504 film-coating mixture containing Hypromellose (E464), Titanium dioxide (E171), Macrogol 400, Allura Red AC Lake (FD&C Red #40) (E129), and Iron Oxide, Black (E172)

6.2 Incompatibilities

Not Applicable

6.3 Shelf life

3 years

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

Aluminium/ PVC-PE-PVdC blisters in packs of 20 and 30 tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Dr. Reddy's Laboratories (UK) Ltd

6 Riverview Road

Beverley

HU17 0LD

UK

8 MARKETING AUTHORISATION NUMBER(S)

PL08553/0274

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

16/07/2008

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07/03/2011