Aw. No.: 200010901

Fexofen Leaflet

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200010901

FEXOFEN 120/FEXOFEN 180

FEXOFENADINE HYDROCHLORIDE TABLETS USP

COMPOSITION:
Fexofen 120 (Fexofenadine Hydrochloride Tablets USP)
Each film coated tablet contains: Fexofenadine Hydrochloride USP 120mg

Fexofen 180 (Fexofenadine Hydrochloride Tablets USP)
Each film coated tablet contains: Fexofenadine Hydrochloride USP 180mg

List of Excipients of Fexofen 120/180 (Fexofenadine Hydrochloride Tablets USP) Tablet Core
Spray dried Lactose, Croscarmellose Sodium, Pregelatinized Maize Starch, Colloidal Anhydrous Silica, Povidone, Purified Water and Magnesium Stearate

Film Coating
Opadry Pink 03B54819 consists of: HPMC 2910/Hypromellose, Titanium Dioxide, Macrogol/PEG 400, Iron Oxide Yellow and Iron Oxide Red Purified Water
Not all dosage strengths may be available locally

DOSAGE FORM:
Film Coated Tablets

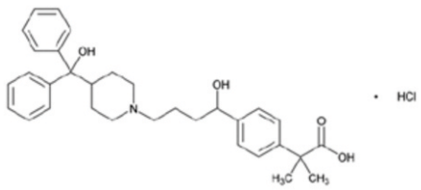
PRESENTATION:
Fexofen 120 (Fexofenadine Hydrochloride Tablets USP):
- Blister pack of 10 tablets, 10 blister packs in a carton along with insert
- Blister pack of 10 tablets, 100 blister packs per box

Fexofen 180 (Fexofenadine Hydrochloride Tablets USP):
- Blister pack of 10 tablets, 10 blister packs in a carton along with insert
- Blister pack of 10 tablets, 100 blister packs per box

PRODUCT DESCRIPTION:
Fexofen 120 (Fexofenadine Hydrochloride Tablets USP): Peach coloured, oblong shaped, biconvex film coated tablet with both sides plain
Fexofen 180 (Fexofenadine Hydrochloride Tablets USP): Peach coloured, oblong shaped, biconvex film coated tablet with both sides plain

PROPERTIES:
Fexofenadine is a pharmacologically active metabolite of Terfenadine. Fexofenadine Hydrochloride is a non-sedating antihistamine with selective peripheral H1 receptor antagonist with the chemical name (±)-4-[1 hydroxy-4-[4-(hydroxydiphenylmethyl)-1-piperidinyl]-butyl]-α, α-dimethyl benzeneacetic acid hydrochloride. The molecular formula is $C_{32}H_{39}NO_4HCl$ and its molecular weight is 538.12.

Structural formula is as shown:



CLINICAL PHARMACOLOGY:
Pharmacodynamics:
Pharmacotherapeutic group: Antihistamines for systemic use, ATC code: R06A X26
Mechanism of action
Fexofenadine hydrochloride is a non-sedating H_1 antihistamine. Fexofenadine is a pharmacologically active metabolite of terfenadine.
Clinical efficacy and safety
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.
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 240 mg 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 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.

Pharmacokinetics and drug metabolism:
Absorption
Fexofenadine hydrochloride is rapidly absorbed into the body following oral administration, with Tmax occurring at approximately max 1-3 hours post dose. The mean Cmax value was approximately 289 ng/ml following the administration of a 120mg dose once daily and 494 ng/ml following the administration of a 180mg dose once daily.
Distribution
Fexofenadine is 60-70% plasma protein bound.
Biotransformation and elimination
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.

INDICATIONS & USAGE:
Fexofenadine Hydrochloride Tablets USP is indicated in adults and children 12 years and older for followings:
- Relief of symptoms associated with seasonal allergic rhinitis.
- Relief of symptoms associated with chronic idiopathic urticaria.

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DOSAGE & 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.

SIDE EFFECTS:
The following frequency rating has been used, when applicable:
Very common ≥1/10; Common ≥1/100 and <1/10; Uncommon ≥1/1,000 and <1/100;
Rare ≥1/10,000 and <1/1,000; Very rare <1/10,000 and not known (frequency cannot be estimated from the available data).
Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.
In adults, the following undesirable effects have been reported with an incidence similar to that observed.
Nervous system disorders:
Common: headache, drowsiness, dizziness
Gastrointestinal disorder:
Common: nausea
General disorders and administration site conditions:
Uncommon: fatigue
In adults, the following undesirable effects have been reported in post-marketing surveillance. The frequency with which they occur is not known (can not be estimated from available data):
Immune system disorders: hypersensitivity reactions with manifestations such as angioedema, chest tightness, dyspnoea, flushing and systemic anaphylaxis
Psychiatric disorders: insomnia, nervousness, sleep disorders or nightmares/excessive dreaming (paroniria)
Cardiac disorders: tachycardia, palpitations
Gastrointestinal disorders: diarrhoea
Skin and subcutaneous tissue disorders: rash, urticaria, pruritus
Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product.

DRUG INTERACTIONS:
Fexofenadine Hydrochloride does not undergo hepatic biotransformation and therefore will not interact with other medicinal products 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 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.
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.

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.
Excipients
The tablets contain lactose and should not be given to patients with rare hereditary problems of galactose intolerance, LAPP lactase deficiency or glucose-galactose malabsorption.

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. Fexofenadine hydrochloride should not be used during pregnancy unless clearly necessary.
Lactation: 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 who 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.
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).

OVERDOSAGE:
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.

CONTRAINDICATION:
Hypersensitivity to the active substance or to any of the excipients listed.

SHELF LIFE: 48 months

STORAGE CONDITIONS: Store below 30°C.

KEEP ALL MEDICINES OUT OF REACH OF CHILDREN.

Product Registration No.: SIN16296P

Manufactured by:
Ind-Swift Limited
Off. NH-21, Village Jawaharpur,
Tehsil Derabassi, Distt. SAS Nagar (Mohali)
Punjab-140507, India.

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Dimension: 160 x 250mm
Paper should be Maplitho 60GSM

Pharmacode	No.
Front	3980
Back	3981

Item Code No.	200010901		Revision No.:	00	
			Prev. Aw. No.:	NA	
Packaging Development	Marketing	Regulatory Affairs	Production	Quality Control	Quality Assurance