MEDLEY PHARMACEUTICALS

Mexo*120mg CAPSULES*

(Fexofenadine)

COMPOSITION

Each Capsule Contains

Fexofenadine hydrochloride…….120mg (USP SPECS.)

PHARMACODYNAMIC PROPERTIES

Pharmacotherapeutic Group:

Fexofenadine hydrochloride is a non-sedating H_1antihistamine. Fexofenadine is a pharmacologically active metabolite of terfenadine.

PHARMACOKINETIC PROPERTIES

Absorption

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/rnl following the administration of a 120mg 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 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 pharmacokinetics are practically linear at these doses between 40-mg 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.

CLINICAL EFFICACY AND SAFETY

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 is 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 QT_c, intervals were observed in adult and adolescent patients with seasonal allergic rhinitis, when 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 adult subjects

Manufactured by:
ISO 9001-2008 Certified Company
Medley Pharmaceuticals
41-A, P.S.I.E. Jhang Bahtar Road,
Wah Cantt- Rawalpindi

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

THERAPEUTIC INDICATIONS

Fexofenadine Hydrochloride is indicated in adults and children 12 years and older for the relief of symptoms associated with seasonal allergic rhinitis.

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.
Pediatrics 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 120mg has not been studied in children under 12.
In children from 6 to 11 years of age: fexofenadine hydrochloride 30mg tablet is the appropriate formulation for administration and dosing in this population.

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.

CONTRAINDICATIONS

In patients with known hypersensitivity to the active substance or to any of the excipients (listed in section 6.1).

Special warnings and precautions for use

As with most new drugs 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 drug class have been associated with the adverse events, tachycardia and palpitations (see section 4.8).

Interaction with other medicinal products and other forms of interaction

Fexofenadine does not undergo 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 co administration 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 has been 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.

UNDESIRABLE EFFECTS

In adults, the following undesirable effects have been reported in clinical trials, 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*
- *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 (paranoia)
- *Cardiac disorders*
- Tachycardia, palpitations
- *Gastrointestinal disorders*
- Diarrhea
- *Skin and subcutaneous tissue disorders*
- Rash, urticaria, pruritus

PRESENTATION:

Each Unit carton contains ALU-PVC blisters of 2 × 10's Capsules.

Manufactured by:
ISO 9001-2008 Certified Company
Medley Pharmaceuticals
41-A, P.S.I.E. Jhang Bahtar Road,
Wah Cantt- Rawalpindi