Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Fexofenadine Hydrochloride 120 mg Film-coated tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 120 mg of fexofenadine hydrochloride, which is equivalent to 112 mg of fexofenadine.

Excipient(s) with known effect: Each tablet contains 152.42 mg lactose.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Film-coated tablet
Peach-coloured capsule-shaped film-coated tablet of 16.00 mm x 6.20 mm x 4.90 mm, debossed as '120' on one side and 'FX' on other side.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Fexofenadine Hydrochloride 120 mg is 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

Posology

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 one daily taken before a meal.

- Children under 12 years of age

The efficacy and safety of fexofenadine hydrochloride 120 mg has not been studied in children under 12.

In children from 6 to 11 years of age: fexofenadine hydrochloride 30 mg tablet is the appropriate formulation for administration and dosing in this population.

Special populations
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.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

There is limited data in the elderly and renally or hepatically impaired patients. Fexofenadine hydrochloride should be administered with care in these special groups (see section 4.2).

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).

This medicinal product contains lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

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.

Fexofenadine is a P-glycoprotein (P-gp) and organic-anion-transporting polypeptide (OATP) substrate. Concomitant use of fexofenadine with P-gp inhibitors or inducers can affect the exposure to fexofenadine. Coadministration of fexofenadine hydrochloride with P-gp inhibitors 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.

A clinical drug-drug interaction study showed that co-administration of apalutamide (a weak inducer of P-gp) and a single oral dose of 30 mg fexofenadine resulted in a 30% decrease in AUC of fexofenadine.

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.

4.6 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 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, 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 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 ≥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 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
Uncommon: fatigue

In adults, the following undesirable effects have been reported in postmarketing 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

Eye disorders
Vision blurred

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. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system: HPRA Pharmacovigilance
Website: www.hpra.ie

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: R06A X26.

Mechanism of action
Fexofenadine hydrochloride is a non-sedating H1 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.

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

Absorption
Fexofenadine hydrochloride is rapidly absorbed into the body following oral administration, with Tmax occurring at approximately 1-3 hours post dose. The mean Cmax value was approximately 427 ng/ml following the administration of a 120 mg 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.

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

Tablet core:
Lactose monohydrate
Low-substituted hydroxypropylcellulose
Pregelatinised starch
Colloidal anhydrous silica
Microcrystalline cellulose
Croscarmellose sodium
Magnesium stearate

Film-coating:
Hypromellose,
Povidone,
Titanium dioxide,
Iron oxide Red,
Iron oxide Yellow
Macrogol 400.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months.

6.4 Special precautions for storage

This medicinal product does not require any special storage condition.

6.5 Nature and contents of container

Fexofenadine hydrochloride 120 mg film-coated tablets are available in Alu-PVC/PVdC, Alu /PVC/PE/ACLAR blisters of 10 and 30 tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Azure Pharmaceuticals Ltd.
12 Hamilton Drive
The Rock Road
Blackrock
Co. Louth
A91 T997
Ireland

8 MARKETING AUTHORISATION NUMBER

PA22871/004/002

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 26th June 2020
Date of last authorisatin 25th June 2025

10 DATE OF REVISION OF THE TEXT

October 2024