1.4.1 Prescribing Information (Summary of Product Characteristics)

1. NAME OF THE MEDICINAL PRODUCT

1.1 Product Name

Brand Name: FEXOGLOB 120

Generic Name: Fexofenadine Hydrochloride Tablets USP 120 mg

1.2 Dosage Strength

Each film coated tablet contains:

Fexofenadine Hydrochloride USP..... 120 mg

Excipients .....Q.S.

Colour: Titanium Dioxide BP

1.3 Dosage Form

Oral solid dosage form (Film Coated Tablet)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

2.1 Qualitative Declaration

Each film coated tablet contains:

Fexofenadine Hydrochloride USP..... 120 mg

Excipients .....Q.S.

Colour: Titanium Dioxide BP

2.2 Quantitative Declaration

Batch size: 10,000 bottles

Sr. No:	Ingredients	Spec.	Label Claim (mg)	Qty./Tab (mg)	Qty./ Batch 1 Lac Tab (kg)	Function
SHIFTING/MIXING						
1.	Fexofenadine Hydrochloride	USP	120	120.00	12.00	Active
2.	Microcrystalline Cellulose (Avicel)	BP	---	43.800	4.380	diluent
3.	CrosCarmellose Sodium (Vivasol)	BP	---	32.000	3.200	Super-disintegrant
4.	Lactose Monohydrate	BP		64.700	6.470	Diluents
PASTE PREPARATION						
5.	Anhydrous Citric Acid	BP	---	4.500	0.450	Antioxidant
6.	Povidone (PVPK-30)	BP	---	8.000	0.800	Binder
7.	Iso Propyl Alcohol*	BP	---	Q.S	Q.S	Binding Solvent
LUBRICATION						
8.	Sodium Starch Glycolate (Type-A)	BP	---	14.000	1.400	Glident/ Disintegrant
9.	Colloidal Anhydrous Silica (Light)	BP	---	8.000	0.800	Adsorbent
10.	Microcrystalline Cellulose (Avicel)	BP	---	10.000	1.000	Disintegrant
11.	Magnesium Stearate	BP	---	5.000	0.500	Lubricant
Average Wt. of Uncoated Tablet				**310 mg**	**Limit: 310 ± 5%**	
COATING						
12.	Iso Propyl Alcohol*	BP	---	80.000	8.000	Coating Solvent
13.	Methylene Chloride DCM*	BP	---	120.00	12.000	Coating Solvent
14.	Macrogol (PEG 6000)	BP	---	1.000	0.100	Plasticizer
15.	Titanium Dioxide	BP	---	1.000	0.100	Opacifier
16.	Purified Talc (Talcum)	BP	---	1.000	0.100	Glidant
17.	Hyperomellose (H.P.M.C. E 15)	BP	---	7.000	0.700	Film forming agent
Average wt. of Film Coated Tablet				**320 mg**	**Limit: 320 ± 5%**	

Note: Active material was calculated on assay or Potency Basis.
USP = United states Pharmacopoeia
BP = British Pharmacopoeia
*Does not found in finished product

3. PHARMACEUTICAL FORM

FEXOGLOB 120, Fexofenadine Hydrochloride Tablets USP 120 mg available as White colour round shaped film coated tablet having both side plain.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Fexofenadine hydrochloride 120 mg tablet 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

Adolescents aged 12 years and over

The recommended dose of fexofenadine hydrochloride for adolescents 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 120 mg has not been studied in children under 12.

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.

Method of administration

Fexofenadine hydrochloride tablet is for oral use.

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.

Excipient

This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium-free.'

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. 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 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 was observed. However, the administration of 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. Fexofenadine hydrochloride should not be used during pregnancy unless clearly necessary.

Breast-feeding

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

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 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 to <1/10;

Uncommon ≥1/1,000 to <1/100;

Rare ≥1/10,000 to <1/1,000;

Very rare <1/10,000;

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 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

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

General properties

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 products 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 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 was 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 per orally) inhibited antigen induced bronchospasm in sensitised guinea pigs and inhibited histamine release at supra-therapeutic 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 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.

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

Microcrystalline Cellulose (Avicel)

CrosCarmellose Sodium (Vivasol)

Lactose Monohydrate

Anhydrous Citric Acid

Povidone (PVPK-30)

Iso Propyl Alcohol

Sodium Starch Glycolate (Type-A)

Colloidal Anhydrous Silica (Light)

Magnesium Stearate

Methylene Chloride DCM

Macrogol (PEG 6000)

Titanium Dioxide

Purified Talc (Talcum)

Hyperomellose (H.P.M.C. E 15)

6.2 Incompatibilities

None Known

6.3 Shelf life

36 months from the date of manufacture.

6.4 Special precautions for storage: Store below 25°C, Protect from light.

6.5 Nature and contents of container

10 Tablets packed in one Alu-PVC Blister. Such 1 Alu-PVC Blisters packed in unit printed duplex board carton along with its package insert. Such cartons packed in export worthy shipper.

Multipack style: : 3 X 10, 10 X 10 Alu-PVC/Alu- Alu/ Strip-Blister

Note: All pack style may not be marketed

6.6 Special precautions for disposal and other handling

No special requirements

7. Marketing Authorization Holder: GLOBELA PHARMA PVT. LTD.

8. Marketing Authorization Number(S): G/25/1749

9. Date of First Authorization / Renewal of Authorization: 13/10/2016