EDA Assessment Report for human medicinal product

(Scientific Discussion)

Bilaxten Faes 10mg and Oro-dispersible Tablets

(Bilastine)

Date: June, 2025.

I. Introduction

-Based on the review of the quality, safety and efficacy data, the Egyptian Drug Authority have granted marketing authorization for Bilaxten Faes 10mg Oro-dispersible Tablets from RX Healthcare.

-The product is indicated as antihistamine that is used to relieve the symptoms of allergic rhino conjunctivitis (sneezing, itchy nose, nasal secretion, nasal congestion and red, streaming eyes) and other forms of allergic rhinitis.

II. Quality Aspect

Drug Substance

- Two APIMFs (Applicant/ restricted part) has been submitted for evaluation from two suppliers.
- The drug substance is white to off white crystalline powder. Bilastine is BCS class II active substance (high permeability and low solubility). Bilastine exhibit polymorphism. The crystalline form resulting from the manufacturing process adopted by both API supplies is polymorph I. Bilastine is not hygroscopic. Bilastine does not exhibit isomerism, due to absence of chiral centers.
- The synthesis of drug substance as per the first API supplier includes four stages with the formation of three intermediates.
- The synthesis of drug substance as per the second API supplier includes four stages with the formation of three intermediates.
- The drug substance from the first API supplier is elucidated via ^{1}H-NMR, ^{13}C-NMR, UV-spectroscopy, Mass spectrometry (MS), IR-spectrometry, X-ray powder diffraction, Elemental analysis and Differential Scanning Calorimetry (DSC).
- The drug substance from the second API supplier is elucidated via ^{1}H-NMR, ^{13}C-NMR, UV-spectroscopy, Mass spectrometry (MS), IR-spectrometry, X-ray powder diffraction, Elemental analysis and Differential Scanning Calorimetry (DSC).
- The specifications used to control the API from the first supplier are Appearance, Identification by (IR, UPLC and DSC), Assay (UPLC), Impurities (UPLC), Sulfated ash, Water Content (KF) and Residual Solvents (GC).
- The specifications used to control the API from the second supplier are Appearance, Identification by (IR, HPLC or UPLC and DSC), Assay (UPLC or HPLC), Impurities (UPLC or HPLC), Residue on ignition, Water Content (KF) and Residual Solvents (GC).
- Analytical methods from both API suppliers were adequately described and validated. They were revised and found to be suitable for the required testing.

- The first supplier has provided batch analysis results of 3 batches. The results of all tests were well within the specification limits and batch data was found acceptable.
- The second supplier has provided batch analysis results of 3 batches. The results of all tests were well within the specification limits and batch data was found acceptable.
- The API from the first API supplier is packaged in an immediate Low-density polyethylene bag packaged inside a second polyethylene black bag closed with a hasp. Both bags are placed within a drum, Drums are made of HDPE.
- The API from the second API supplier is packaged in Low-density polyethylene bag packaged inside a second polyethylene bag then further placed within a drum.
- Stability of API from the first supplier is submitted in accelerated 40°C±2°C /75% ± 5% RH and long-term storage conditions 25°C ±2°C /60% ± 5% and 30°C ±2°C /65% ± 5% RH and also submitted both stress testing and photostability studies and conclude the conformity of specifications during the shelf life and storage conditions. The retest period of the API is 48 months when stored in the proposed container.
- Stability of API from the second supplier is submitted in accelerated 40°C±2°C /75% ± 5% RH and long-term storage conditions 25°C ±2°C /60% ± 5% and 30°C ±2°C /65% ± 5% RH and also submitted both stress testing and photostability studies and conclude the conformity of specifications during the shelf life and storage conditions. The retest period of the API is 60 months when stored in the proposed container.

Medicinal Product

- **Product Description**

-White round slightly biconvex uncoated tablets that are rapidly disperse in the mouth before being swallowed alternatively the Oro dispersible tablets can be dispersed in water before administration.

-The product is packed in (Al / Al) blister then placed in a cardboard box.

-The excipients are: Mannitol, Croscarmellose sodium, Sodium stearyl fumarate, Sucralose and Red grape flavour.

- **Pharmaceutical development:**

-The development of the product has been described, the choice of excipients is justified and their functions explained. It was aimed to develop product containing Bilastine that meet the established Quality Target Product Profile (QTPP).

-Overall, the choices of the packaging, manufacturing process, physicochemical properties and microbiological attributes are justified.

- **Manufacturing process**

-The manufacturing process consists of sieving, blending, sieving, lubrication, compression and packaging.

-The manufacturing process was adequately validated according to relevant guidelines.

- **Control of excipients**

-All excipients comply with European pharmacopeia except for the flavouring material which complies with in-house specifications.

- **Control of Drug Product**

-Product specification includes description, identification (UPLC/UV), odour, water content, uniformity of dosage units by uniformity of content, dissolution (UPLC or UV or HPLC), disintegration, assay (UPLC), organic impurities (UPLC), and microbiological quality.

-The Analytical methods used in testing the finished pharmaceutical product were presented in the dossier. They were reviewed and found to be suitable for the required testing

-Batch Analysis from the proposed production site were provided for 6 batches. The results of all tests are well within specification limits and batch data is acceptable

- **Container closure system**

-The Drug Product is packed in cardboard box containing (Al/Al) blisters.

-Stability data of 6 batches was submitted in (accelerated at 40°C ± 2°C, RH 75% ± 5%) and (long term at 30°C ± 2°C, RH 75% ±5%, 30°C ± 2°C, RH 65% ±5% and 25°C ± 2°C, RH 60% ±5%,) and conclude the conformity of specifications during the shelf life and storage conditions. The finished pharmaceutical product is stable for 60 months if stored below 30°C.

- **Specific measures concerning the prevention of the transmission of animal spongiform encephalopathies**

-A declaration/certificate of TSE/BSE free is submitted for excipients used in the manufacture of Bilaxten Faes 10mg Oro-dispersible Tablets.

Summary basis of opinion:
-Information on development, manufacture and control of the active substance and finished product has been presented in a satisfactory manner. The results of tests carried out indicate consistency and uniformity of important product quality characteristics.

III. Non-Clinical& Clinical Aspects

Introduction
Bilastine is a well-known active substance with established efficacy and tolerability. A clinical overview has been provided, which is based on scientific literature.
Bilastine is a peripheral histamine H1-antagonist used to treat seasonal allergic rhinitis and chronic spontaneous urticaria.
Bilastine is a novel new-generation antihistamine that is highly selective for the H1 histamine receptor, has a rapid onset and prolonged duration of action.

Bilastine is indicated for the used to treat a runny nose due to seasonal allergies and chronic immune reactions of the skin.

Mechanism of action

Bilastine is a selective histamine H1 receptor antagonist (. During allergic response mast cells undergo degranulation which releases histamine and other subastances. By binding to and preventing activation of the H1 receptor, bilastine reduces the development of allergic symptoms due to the release of histamine from mast cells

*Summary of Listing of Clinical Studies:

- Study Title:

***Bioavailability (BA) Study Reports:**

-Open label, fed vs fasted, randomized, Capsule 20 mg, Oral, single dose in Healthy Subjects.

* **Absolute Bioavailability (BA) Study Reports:**

-Open label, oral vs i.v., randomized, crossover Tablet 20 mg, oral, single dose Intravenous solution, 10 mg, single dose in Healthy Subjects.

***Bioequivalence Study**

-Open label, 4 treatment arms, randomized, crossover Bilastine 10 mg orodispersible tablet (ODT1), Bilastine 10 mg orodispersible tablet (ODT2) Bilastine 2.5 mg/mL oral solution Oral, single dose in Healthy Subjects.

***Based on the clinical study Bilaxten Faes 10mg Oro-dispersible Tablets submitted to EDA, found to recommend the approval of the marketing authorization of product.**