EDA Assessment Report for human medicinal product

(Scientific Discussion)

Moxiboard 400mg Film Coated Tablet (FCT)

(Moxifloxacin Hydrochloride)

Date: July, 2025

I. Introduction

-Based on the review of the quality, safety and efficacy data, the Egyptian Drug Authority have granted marketing authorization for Moxiboard film coated tablet from Averroes Pharma for Pharmaceutical Industries.

-The product is indicated for the treatment of sinus and lung infections such as sinusitis, pneumonia, and secondary infections in chronic bronchitis. Additionally, it's used for the treatment of bacterial conjunctivitis (pinkeye).

II. Quality Aspects

Drug Substance

- An APIMF (Applicant/ restricted part) has been submitted for evaluation.
- The drug substance is slightly yellow to yellow crystalline powder, slightly hygroscopic. Moxifloxacin HCl is soluble in 0.1N sodium hydroxide, sparingly soluble in Water and Methanol, slightly soluble in 0.1 N Hydrochloric acid, Dimethylformamide and Alcohol, practically insoluble in Methylene chloride, Acetone, Ethyl acetate and Toluene and insoluble in Tert-butyl methyl ether and n-Heptane. There are two chiral centres in the molecule. Moxifloxacin HCl exhibits polymorphism.
- The synthesis of drug substance includes two stages with the formation of one intermediate. All starting materials, reagents, solvents are well controlled.
- The drug substance is elucidated via IR spectrometry, UV spectroscopy, ^{1}H-NMR, ^{13}C-NMR, Mass spectroscopy, Elemental Analysis and X-ray powder diffraction (XRPD). The structure is well characterized.
- The drug substance specifications are description, solubility, identification by (IR & HPLC & chemical), Enantiomeric purity, pH, Residue on ignition, Chloride and Sulfate, Water content, Organic impurities by (HPLC), Assay (HPLC), Residual solvents (GC) and Microbial enumeration tests. All limits are acceptable
- Analytical methods were adequately described and validated.
- The applicant provided batch analysis results of of 3 drug substance batches demonstrating compliance with the current drug substance specification.
- The drug substance is packed in a transparent LDPE Bag of virgin material. The mouth of the bag is tied with a special type of PVC tie strip with grooves. The first LDPE bag is then inserted in the second black colored LDPE bag and similarly the mouth of the bag is closed as in the first case then further placed in HDPE drum. The Container closure system is suitable to store the drug substance and comply with food grade packaging material and the specifications are acceptable.
- Stability of API is submitted in (accelerated 40°C±2°C /75% ± 5% RH and long-term storage conditions 30°C ±2°C /75% ± 5% RH) conclude the conformity of specifications during the retest period and storage conditions.

Medicinal Product

- **Product Description**

-The 400 mg tablet is presented as rose to brick red oblong biconvex film coated tablet Plain from both sides.

-The drug product is packed in an opaque triplex (PVC/PE/PVDC) /Aluminium foil blister (s) which is further placed in a carton box with inner leaflet.

-The excipients used in core tablets are Microcrystalline cellulose (Avicel PH 102), Lactose monohydrate, Croscarmellose sodium, Colloidal silicon dioxide (Aerosil 200) & Magnesium Stearate. The coating ingredient are Hypromellose (HPMC E5), Polyethylene glycol (PEG 6000), Talc, Titanium Dioxide, Iron oxide red (C.I.N 77491), Purified water &Ethanol 95%.

- **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 a product equivalent to the reference product.

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

- **Manufacturing process**

-The manufacturing process consists of mixing, dry granulation, compression, coating and blistering.

-The manufacturing process was adequately validated according to relevant guidelines. It has been demonstrated that the manufacturing process is capable of producing the finished product of intended quality in a reproducible manner. The in-process controls are adequate for this type of manufacturing process.

- **Control of excipients**

-All excipients comply with USP except for iron oxide red which comply with in-house specifications.

- **Control of Drug Product**

-Product specification includes description, uniformity of mass, water content, disintegration time, dissolution (HPLC), uniformity of dosage units (weight variation), identification (HPLC), assay (HPLC), Organic impurities (HPLC), residual solvent (GC) & microbiological tests.

-Analytical methods were revised and found to be suitable for the required testing.

-Batch Analysis from the proposed production site were provided for 3 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 opaque triplex (PVC/PE/PVDC)/Aluminium foil blister (primary packaging material) then further placed in carton box with inner leaflet (secondary packaging materials).

- **Stability**

-Stability of finished pharmaceutical product is submitted in accelerated (40°C ± 2 °C /75% ± 5% RH) and long-term (30°C ± 2 °C /65% RH ± 5% RH) storage conditions. Detailed review was carried out for all stability indicating parameters and all found in line with their acceptance criteria throughout all time intervals. The finished pharmaceutical product is stable for 24 months if stored below 30°C in dry place.

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

-A certificate of TSE/BSE free is provided for lactose monohydrate used in the manufacture of Moxiboard FCT.

Summary basis of opinion:
From Chemistry, Manufacture and Control perspective, the main concerns found during the evaluation process were as follow:
For the Drug substance:
-The specifications of the intermediate of the manufacturing process should be submitted.
-Justification for the absence of palladium, which is an intentionally added element in the manufacturing process of Moxifloxacin HCl, from the risk assessment of elemental impurities should be provided.
For the Drug product:
-Discussion of the Quality Target Product Profile (QTPP) of the generic product compared to the reference product should be provided.
-Discussion of the Critical Quality Attributes (CQAs) of the drug product and how those attributes are affected by the Critical Material Attributes (CMAs) of the raw materials and Critical Process Parameters of the manufacturing process should be provided. Moreover, the control strategies adopted to mitigate the risks of the Critical Material Attributes (CMAs) of the raw materials and Critical Process Parameters of the manufacturing process should be clarified.
-The acceptance criteria of water content test should be revised considering the trend results in batch analysis and stability data.
The Quality of the drug product has been found satisfactory after:
-The API supplier submitted the specifications of the intermediate of the manufacturing process.
-The API supplier has revised the risk assessment of elemental impurities to include Pd as required.
-The FPP manufacturer has submitted the discussion of the QTPP of the generic product compared to the reference product as requested.
-The FPP manufacturer discussed the CQAs of the drug product and the control strategy adopted to mitigate the risks that could arise from the CMAs of the raw materials and the CPPs of the manufacturing process.
-The FPP manufacturer has revised the acceptance criteria of water content as requested.

III. Non-Clinical

No new preclinical data have been submitted with this application. As such, no pre-clinical assessment has been made on the application. This is acceptable for this type of application. An Environmental Risk Assessment has not been performed as this product is intended for generic substitution and therefore will not result in an increase of risk to the environment during use, storage and disposal.

IV. Clinical Aspects

Introduction

Moxifloxacin Hydrochloride is a well-known active substance with established efficacy and tolerability. A clinical overview has been provided, which is based on scientific literature.

Moxifloxacin Hydrochloride is indicated for the treatment of sinus and lung infections such as sinusitis, pneumonia, and secondary infections in chronic bronchitis. Additionally, it's used for the treatment of bacterial conjunctivitis (pinkeye).

Bioequivalence Study

The bioequivalence study was conducted for Moxiboard Film Coated Tablet (Moxifloxacin Hydrochloride 400 mg) Manufactured by Averroes Pharma for Pharmaceutical Industries relative to Avelox Film Coated Tablet (Moxifloxacin Hydrochloride 400mg) by: Bayer HealthCare Manufacturing- Italy, administered to healthy participants.

Design

The Study was an open-label, balanced, randomized, two-treatment, two-sequence two period crossover study with a Washout Period of one week between periods in 34 healthy participants.

- Sampling time schedule as the following:

Zero time (predose), 10min, 20min, 30min, 40min, 50min, 1hr, 1:15hr, 1:30hr, 1:45hr, 2hr, 2:15hr, 2:30hr, 2:45hr, 3hr, 3:15hr, 3:30hr, 4hr, 5hr, 6hr, 7hr, 9hr, 11hr, 24hr, 48hr, & 72hr after administration of each of the products. All plasma samples were stored at -20º C ±5ºC.

Analytical Methods

All procedures used to perform the bio-analyses of Moxifloxacin Hydrochloride in subject samples were executed according to international guidelines and official publications.

CRO developed an adequately validated method to ensure data integrity, Accuracy and Precision of data generated during sampling, sample treatment and bioanalyses. The bioequivalence study accordance with acceptable standards of Good Clinical Practice (GCP) and Good Laboratory Practice (GLP).

Results

Table 1. Pharmacokinetic parameters (non-transformed values; arithmetic mean ± SD, t_{max} (median, range) of Product name and strength under fast.

Treatment N=34	AUC_{0-t} ng.h/ml	$AUC_{0-\infty}$ ng.h/ml	C_{max} ng/ml	t_{max} h	$t_{1/2}$ h
Test	37707.64	40540.17	3778.16	2.2	5.13
Reference	36915.66	39752.86	3587.23	1.8	5.46
***Ratio (90%) CI**	101.481 (95.583 -107.743)	101.292 (95.484 -107.454)	105.024 (95.880 -115.041)	-----	--------
CV (%)	14.412 %	14.213 %	22.077%	----------	--------

*ln-transformed values

Vol.no 11 withdrawn before phase II due to personal reason

Conclusion

Based on this study demonstrated that Moxifloxacin Hydrochloride of Moxiboard 400 mg Film Coated Tablet Manufactured by: Averroes Pharma for Pharmaceutical Industries relative to Avelox Film Coated Tablet Bayer HealthCare Manufacturing- Italy are Bioequivalent after a single oral dose of test and reference administration under Fasting on 33 participants.

The 90% confidence intervals calculated for AUC_{0-t} and C_{max} are within the bioequivalence acceptance range of 80-125%.