EDA Assessment Report for human medicinal product

(Scientific Discussion)

Dapagliflozin-Chemipharm 5 mg & 10 mg Film Coated Tablets.

Dapagliflozin (as Propanediol Monohydrate).

Date: July , 2026.

I. Introduction

Based on the review of the quality, safety and efficacy data, the Egyptian Drug Authority have granted marketing authorization for for Dapagliflozin-Chemipharm 5mg & 10 mg Film Coated Tablets from Chemipharm Pharmaceutical Industries, Egypt.

The product is indicated for:

-To reduce the risk of sustained eGFR decline, end-stage kidney disease, cardiovascular death, and hospitalization for heart failure in adults with chronic kidney disease at risk of progression.

-To reduce the risk of cardiovascular death, hospitalization for heart failure, and urgent heart failure visit in adults with heart failure.

-To reduce the risk of hospitalization for heart failure in adults with type 2 diabetes mellitus and either established cardiovascular disease or multiple cardiovascular risk factors.

-As an adjunct to diet and exercise to improve glycemic control in adults and pediatric patients aged 10 years and older with type 2 diabetes mellitus.

II. Quality Aspect

Drug Substance

- An APIMF (Applicant/ restricted part) has been submitted for evaluation.
- The drug substance is White to off-white powder, Soluble in N,N-dimethylformamide, dimethylsulfoxide, ethanol and insoluble in cyclohexane and water. Dapagliflozin has five chiral centers. Dapagliflozin exhibits polymorphism, the crystalline form resulting from the manufacturing process adopted by the supplier is crystalline form CS-3 (i.e.: form I a).

- The synthesis of drug substance includes one single step with no formation of intermediates was revised. Synthesis of the starting material is presented in section 3.2.S.2.3 and found to comply with ICH Q11.

- The drug substance is elucidated via Infrared Spectroscopy (IR), Mass Spectroscopy (MS), Proton Nuclear Magnetic Resonance, Carbon Nuclear Magnetic Resonance (NMR), X-ray diffraction technique (XRD), Differential scanning colorimetry (DSC), Elemental analysis (C,H,N,S), and Ultra violet spectroscopy (UV).

- The drug substance specifications include Description, Solubility, Identification (IR, HPLC), Water content (KF), Specific optical rotation, Residue on ignition, Heavy metals, Assay (HPLC), Acetic acid and N,N-dimethyl formamide (HPLC), Related substances (HPLC), Residual solvents (GC), 1,2-Propanediol content (GC) and Microbial Test.
- Analytical methods were adequately described and validated.
- The applicant provided batch analysis results of 3 drug substance batches demonstrating compliance with the current drug substance specification.
- The drug substance is packed in LDPE clear, colorless polyethylene bag, which is sealed with irreversible yellow plastic strip seal. This bag is placed in outer clear colourless LDPE polyethylene bag containing desiccant (dried silica bag) and the inner product label is kept in between the two polyethylene bags. The sealed bags are then placed in HDPE drums.
- Stability of API is submitted on (accelerated at 40°C ± 2°C, RH 75% ± 5%) and (long term at 30°C ± 2°C, RH 65% ±5%) storage conditions. The retest period of the API is confirmed for 12 months when stored at a temperature not exceeding 30 °C in tightly closed container and protected from light and moisture.

Medicinal Product

- **Product Description:**

-For both strengths: Yellow, round biconvex film coated tablets, plain on both sides with white to off-white tablet core.

-The product is packed in ALU/ALU Strips each of 10 Film Coated Tablets further placed in a carton box

-The excipients are: Microcrystalline Cellulose, Lactose Monohydrate, Crospovidone, Colloidal Silicon Dioxide, Magnesium Stearate, Kollicoat IR, Talc, Titanium Dioxide, Purified water and Yellow Iron Oxide.

- **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 blending, compression, coating and packaging.

-The applicant submitted the process validation protocol of the manufacturing process in line with relevant guidelines and committed to provide the process validation report for the first three production batches.

- **Control of excipients:**

-All excipients comply with USP except Kollicoat IR and Yellow Iron Oxide which are controlled according to in-house specifications.

- **Control of Drug Product**

-Product specifications include Appearance, Uniformity of Mass, Disintegration time, Dissolution (HPLC), Water Content (by KF), Identification (HPLC, UV), Assay (HPLC), Uniformity of dosage units (Content Uniformity), Related Substances (HPLC) and Microbiological Parameters.

-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 3 batches of each strength. The results of all tests were well within specification limits and batch data was found acceptable.

- **Container closure system**

-The drug product is packed in OPA/ALU/PVC/ALU blister contains 10 film coated tablets in each then placed in a Carton box with an insert.

- **Stability**

-Stability of finished pharmaceutical product is submitted in accelerated (40°C ± 2 °C /75% RH ± 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 a dry place.

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

-A declaration/certificate of TSE/BSE free is submitted for lactose monohydrate.

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:

-Specifications of the API on applicant letterhead including the test particle size distribution should be submitted.

For the Drug product:

-Process validation protocol for the production batches should be submitted as well as a commitment to perform process validation on the first three commercial batches.

-The limit for total impurities should be revised based on the trend results at release and during the stability study.

The Quality of the drug product has been found satisfactory after

-The applicant has submitted the specifications of the API including the test for particle size distribution.

-The applicant has submitted the process validation protocol for the commercial batches and committed to submit the first three production batches to the process validation protocol.

-The applicant has revised the limit of the total impurities as required.

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

-Dapagliflozin 10 mg is a well-known active substance with established efficacy and tolerability. A clinical overview has been provided, which is based on scientific literature.

Dapagliflozin 10 mg is indicated for:

- Reduce the risk of sustained eGFR decline, end-stage kidney disease, cardiovascular death, and hospitalization for heart failure in adults with chronic kidney disease at risk of progression.

- Reduce the risk of cardiovascular death, hospitalization for heart failure, and urgent heart failure visit in adults with heart failure.

- Reduce the risk of cardiovascular death, hospitalization for heart failure, and urgent heart failure visit in adults with heart failure.

- Reduce the risk of hospitalization for heart failure in adults with type 2 diabetes mellitus and either established cardiovascular disease or multiple cardiovascular risk factors.

*As an adjunct to diet and exercise to improve glycemic control in adults and pediatric patients aged 10 years and older with type 2 diabetes mellitus.

Pharmacokinetics

Bioequivalence Study

-The bioequivalence study of Dapagliflozin Chemipharm 10mg FCT from Chemipharm Pharmaceutical Industries, Egypt. relative to Forxiga 10 mg F.C.Tablets form License Holder: AstraZeneca UK Limited, UK, Man. by: AstraZeneca Pharmaceuticals, USA, Packed and Released by: AstraZeneca UK Ltd, UK administered to healthy participants.

Biowaiver

-The EDA was granted a biowaiver for the lower strength Dapagliflozin Chemipharm 5mg FCT
based on the following arguments:
-Both tablet strengths have comparable dissolution profiles according to the provided in vitro dissolution data.

Design

-Open-label, randomized, single dose, two-sequence two-periods crossover study, separated by 7 days washout interval from the first Study Drug Administration, in healthy participants.

Analytical Methods

-All procedures used to perform the bio-analyses of Dapagliflozin 10mg 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 Dapagliflozin Chemipharm 10mg FCT under fast conditions.

Treatment N=26	AUC0-t ng.h/ml	AUC0-∞ ng.h/ml	Cmax ng/ml	tmax h	t1/2 h
Test	359.77± 96.52	380.63± 100.93	88.80± 31.70	1.32± 0.54	11.95± 2.42
Reference	348.33± 85.93	368.49± 89.40	95.07± 30.22	1.33± 0.85	11.37± 3.18
***Ratio**	102.62	102.50	92.32	--------	----------
(90%) CI	97.99- 107.47	97.76- 107.46	82.23- 103.64	--------	----------

*ln-transformed values

Conclusion

The 90% confidence intervals calculated for AUC $_{0\text{-}t}$ and C $_{max}$ are within the bioequivalence acceptance range of 0.80 – 1.25.

Based on this study demonstrated that the of Dapagliflozin 10mg in Dapagliflozin Chemipharm 10mg FCT & reference product, Forxiga 10 mg F.C.Tablets form License Holder: AstraZeneca UK Limited, UK, Man. by: AstraZeneca Pharmaceuticals, USA, Packed and Released by: AstraZeneca UK Ltd, UK are Bioequivalent after a single oral dose of test and reference administration under Fasting conditions on 26 participants.