# EDA Assessment Report for human medicinal product

(Scientific Discussion)

**Truqap 160mg & 200 mg Film Coated Tablet.**

**Capivasertib**

**Date: March, 2026.**

# I. Introduction

-Based on the review of the quality, safety and efficacy data, the Egyptian Drug Authority have granted marketing authorization for **Truqap 160mg & 200mg Film Coated Tablet** from Astrazeneca scientific office.

-The product is indicated in combination with fulvestrant for the treatment of adult patients with estrogen receptor (ER)-positive, HER2-negative locally advanced or metastatic breast cancer with one or more PIK3CA/AKT1/PTEN-alterations following recurrence or progression on or after an endocrine-based regimen.

# II. Quality Aspect

**Drug Substance**

- Full details of the S part have been submitted for evaluation.
- The drug substance is white to off-white crystalline powder. Capivasertib exhibits pH dependent solubility in aqueous media across the physiological pH range. Capivasertib has one chiral center and is manufactured as the S enantiomer. Capivasertib exhibits polymorphism, the manufacturing process adopted by the manufacturer yields the thermodynamically stable form.
- The synthesis of the drug substance was revised and found to comply with ICH Q11 guideline. (Development and Manufacture of Drug Substances). The starting materials, reagents and intermediate products were adequately controlled.
- A combination of mass spectrometry (MS), $^{1}H$ and $^{13}C$ nuclear magnetic resonance (NMR) spectroscopy, infrared spectroscopy (IR), elemental analysis and ultraviolet spectroscopy were used to confirm the structure of capivasertib. The absolute configuration of capivasertib has been confirmed by single crystal X-ray diffraction (SXRD).
- The drug substance specifications include Description (Visual), Identification (FT-IR), Assay (LC), Organic Impurities (LC), Chiral Impurity (LC), Residual Solvents (HS-GC), Water Content (Karl Fisher) and Particle Size Distribution (Laser Diffraction).
- Analytical methods were adequately described and validated. They were revised and found to be suitable for the required testing.
- The applicant provided batch analysis results of several batches. The results of all tests were well within the specification limits and batch data was found acceptable.

- The drug substance is packed in Double LDPE bags with a rigid outer container. The specifications of the primary packaging component are provided including appropriate identification test for the primary packaging in contact with the drug substance. All these specifications are revised and found to be satisfactory.
- Stability of API is submitted in accelerated 40°C±2°C /75% ± 5% RH and long-term storage conditions (25°C ±2°C /60% ± 5% RH & 30°C ±2°C /75% RH ± 5% RH) and conclude the conformity of specifications during the shelf life and storage conditions. The retest period of the API is 48 months when stored below 30°C in the proposed container.

**Medicinal Product**

- **Product Description & Composition:**

**-160 mg Tablets:** beige, round, biconvex, film-coated tablets, approximately 10 mm in diameter and marked with 'CAV' above '160' on one side and plain on the reverse

**-200 mg Tablets:** beige, capsule-shaped, biconvex, film-coated tablets, approximately 14.5 x 7.25 mm and marked with 'CAV200' on one side and plain on the reverse

-The product is packed in aluminium/aluminium blister.

-The excipients in core tablets are microcrystalline cellulose, calcium hydrogen phosphate, croscarmellose sodium and magnesium stearate.

-The excipients in the tablet coating are hypromellose, copovidone, macrogols 3350, polydextrose, medium-chain triglycerides, Titanium dioxide, iron oxide yellow, iron oxide red, iron oxide black and purified water.

- **Pharmaceutical development**

- The development of the product has been described, the choice of excipients is justified and their functions explained. The formulation design focused on the development of an immediate release solid oral dosage form containing Capivasertib.

-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, lubrication, Compression, Coating and Packing.

-The manufacturing process was adequately validated according to relevant guidelines. The Validation included three full production scale batches per strength.

- **Control of excipients**

-All excipients comply with European Pharmacopeia and European standard for coloring agents.

- **Control of Drug Product**

-Product specifications include Description (Visual), Identification (NIR/LC-UV), Assay (NIR/LC), Degradation products (LC), Dissolution (UV) and Uniformity of dosage units.

-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 of both strengths from the proposed production site were provided. 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 aluminium/aluminium blister pack.

- **Stability**

-Stability of FPP is submitted in accelerated (40°C/75% RH) and long- term (25°C/60% RH & 30°C/75% 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 provided stability study supports the proposed shelf life of 48 months.

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

-There are no substances of ruminant animal origin present in the product nor have any been used in the manufacturing of this product, so a theoretical risk of transmitting TSE can be excluded.

**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 Spectra of the elucidation techniques should be submitted.

**For the Drug product:**

-Risk assessment of elemental impurities according to ICH Q3D guideline should be submitted.

**The Quality of the drug product has been found satisfactory after:**

-The drug substance manufacturer has submitted the full characterization data of the API including the spectra.

- The drug product manufacturer has submitted results of elemental impurities in 3 commercial batches of each strength and the results were far below the control threshold according to ICH Q3D guideline.

## III. Non-Clinical & Clinical Aspects

- **Introduction**

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

-Capivasertib is an AKT kinase inhibitor used to treat hormone receptor-positive, HER2-negative, locally advanced or metastatic breast cancer.

-Capivasertib is indicated in combination with fulvestrant for the treatment of adult patients with estrogen receptor (ER)-positive, HER2-negative locally advanced or metastatic breast cancer with one or more *PIK3CA/AKT1/PTEN*-alterations following recurrence or progression on or after an endocrine-based regimen

- **Pharmacokinetics**

-Absorption: capivasertib steady-state AUC is 8,069 h·ng/mL (37%) and Cmax is 1,371 ng/mL (30%). Steady-state concentrations are predicted to be attained on the 3rd and 4th dosing day of each week, starting week 2
-Capivasertib plasma concentrations are approximately 0.5% to 15% of the steady-state Cmax during the off-dosing days.
-Capivasertib AUC and Cmax are proportional with doses over a range of 80 to 800 mg (0.2 to 2 times the approved recommended dosage).
-Tmax is approximately 1-2 hours. The absolute bioavailability is 29%.
-The half-life of capivasertib is 8.3 hours.

- **Summary List of clinical studies:**

**- Pivotal Efficacy, Safety, And PK Study:** Phase III double-blind, placebo-controlled, parallel-group, randomised study assessing the efficacy and safety of capivasertib + fulvestrant (N = 355 treated) versus placebo + fulvestrant (N = 350 treated).

**-Efficacy and Safety Study:** Phase Ib/II randomised placebo-controlled study of fulvestrant ± capivasertib. Safety run-in (N = 8 treated) followed by randomised Phase II study of capivasertib + fulvestrant (N = 69 treated) versus placebo + fulvestrant (N = 71 treated).

- **PK DATA:** ADME study" Phase I, open-label study to investigate the absolute bioavailability, absorption, metabolism, distribution and excretion of 14C-capivasertib. (N = 6 treated).

***Based on the clinical studies of Truqap 160mg & 200 mg Film Coated Tablet submitted to EDA, found to recommend the approval of the marketing authorization of product.**