Truqap

Procedural steps taken and scientific information after the authorisation*

*Due to the Agency`s update of its procedure management systems, an additional document, reflecting the historical lifecycle may be available in the 'Assessment history' section. For the complete product lifecycle procedures, you may need to also refer to **EPAR - Procedural steps taken and scientific information after authorisation (archive)**.

Application number	Scope	Opinion/ Notification [1] issued on	Commission Decision Issued [2] / amended on	Product Information affected [3]	Summary
Variation type IB /	This was an application for a group of	08/04/2026			

[1] Notifications are issued for type I variations and Article 61(3) notifications (unless part of a group including a type II variation or extension application or a worksharing application). Opinions are issued for all other procedures.
[2] A Commission decision (CD) is issued for procedures that affect the terms of the marketing authorisation (e.g. summary of product characteristics, annex II, labelling, package leaflet). The CD is issued within two months of the opinion for variations falling under the scope of Article 23.1a(a) of Regulation (EU) No. 712/2012, or within one year for other procedures.
[3] SmPC (Summary of Product Characteristics), Annex II, Labelling, PL (Package Leaflet).

EMA/VR/0000323856	variations. B.II.b.3 Change in the manufacturing process of the finished product, including an intermediate used in the manufacture of the finished product - B.II.b.3.z Other changes - Accepted B.II.b.3 Change in the manufacturing process of the finished product, including an intermediate used in the manufacture of the finished product - B.II.b.3.z Other changes - Accepted B.II.b.4 Change in the batch size (including batch size ranges) of the finished product - B.II.b.4.a Up to 10-fold compared to the originally approved batch size - Accepted				
Variation type II / EMA/VR/0000320727	C.I HUMAN AND VETERINARY MEDICINAL PRODUCTS - C.I.4 Change(s) in the Summary of Product Characteristics, Labelling or Package Leaflet due to new quality, preclinical, clinical or pharmacovigilance data - Accepted Update of sections 4.2, 4.4, 4.8, and 5.1 of the SmPC in order to change posology recommendations in Table 3, amend an existing warning for Hyperglycaemia, update the summary of safety profile & description of selected adverse reaction, update efficacy based on final results from study CAPItello-	12/03/2026		SmPC	Section 4.4 'Special warnings and precautions for use' of the SmPC Hyperglycaemia The safety and efficacy of TRUQAP in patients with preexisting Type 1 diabetes or Type 2 diabetes requiring insulin and/or in patients with HbA1C > 8.0% (63.9 mmol/mol) has not been studied as these patients were excluded from the phase III clinical study. This study included 21 (5.9%) patients in the TRUQAP plus fulvestrant arm with HbA1C ≥ 6.5%. Hyperglycaemia was more frequently reported in patients with a baseline HbA1C ≥ 6.5% (38.1% of patients) than those with a baseline HbA1C < 6.5% (17.8%). Severe hyperglycaemia, associated with diabetic ketoacidosis (DKA) and with fatal outcomes

	291 listed as a PAM Recommendation PAES; this is a phase 3 double-blind randomised study assessing the efficacy and safety of capivasertib + fulvestrant versus placebo + fulvestrant as treatment for locally advanced (inoperable) or metastatic hormone receptor positive, human epidermal growth factor receptor 2 negative (HR+/HER2−) breast cancer following recurrence or progression on or after treatment with an aromatase inhibitor.				occurred in patients treated with TRUQAP (see section 4.8). DKA can occur at any time during TRUQAP treatment. In some reported cases, DKA developed in less than 10 days. Patients with history of diabetes mellitus may require intensified anti diabetic treatment and should be closely monitored. Consultation with a diabetologist or a healthcare professional experienced in the treatment of hyperglycaemia is recommended for patients with diabetes. Section 4.8 'Undesirable effects' of the SmPC Summary of safety profile The summary of safety profile of TRUQAP is based on data from 355 patients who received TRUQAP plus fulvestrant in the phase III (CAPItello 291) study. The median duration of exposure to capivasertib in CAPItello 291 was 5.4 months, with 28.2% patients exposed ≥ 12 months. The most common adverse reactions were diarrhoea (72.4%), rash (40.6%), nausea (34.6%), fatigue (32.1%), vomiting (21.4%), hyperglycaemia (19.2%), stomatitis (18.6%), , headache (17.2%),decreased appetite (16.9%), and urinary tract infection (16.6%). The most common grade 3 or 4 adverse reactions were rash (12.4%), diarrhoea (10.4%), anaemia (3.4%) hypokalaemia (2.8%), hyperglycaemia (2.5%), and stomatitis (2.3%). Serious adverse reactions were seen in 9% of patients receiving TRUQAP plus fulvestrant. Most common serious adverse reactions reported in patients receiving TRUQAP plus fulvestrant included rash (2.3%), diarrhoea (2.5%) and vomiting (1.1%). Dose reductions due to adverse reactions were reported in 18.9% of

					patients. The most common adverse reactions leading to dose reduction of TRUQAP were diarrhoea (8.7%) and rash (4.5%). Treatment discontinuation due to adverse reactions occurred in 10.4% of patients. The most common adverse reactions leading to treatment discontinuation were rash (4.5%), diarrhoea (2.3%) and vomiting (2%). […] Description of selected adverse reactions Hyperglycaemia Hyperglycaemia of any grade occurred in 68 (19.2%) patients and grade 3 or 4 occurred in 9 (2.5%) patients receiving TRUQAP. The median time to first occurrence of hyperglycaemia was 16 days (range: 1 to 1221). In the study, dose reduction was required in 4 (1.1%) patients and 2 (0.6%) patients discontinued treatment due to hyperglycaemia. In the 68 patients with hyperglycaemia, 35 (51.5%) patients were treated using anti-hyperglycaemic medication (including insulin in 17.6%). See section 4.4. Diarrhoea Diarrhoea occurred in 257 (72.4%) patients receiving TRUQAP. Grade 3 and/or 4 diarrhoea occurred in 37 (10.4%) patients. The median time to first occurrence was 8 days (range 1 to 519). Dose reduction was required in 31 (8.7%) patients and 8 (2.3%) patients discontinued TRUQAP due to diarrhoea. In the 257 patients with diarrhoea, anti-diarrheal medication was required in 59.5% (153/257) of patients to manage diarrhoea symptoms. Rash Rash (including erythema, rash, rash erythematous, rash macular, rash maculo-papular, rash papular, and rash pruritic) was reported in 144 (40.6%) patients. The median time

					to first occurrence of rash was 12 days (range 1 to1529). Grade 3 and/or 4 occurred in 44 (12.4%) of patients who received capivasertib. Erythema multiforme occurred in 6 (1.7%) patients and the highest grade was grade 3 in 3 (0.8%) of the patients. Dermatitis exfoliative generalised occurred in 2 (0.6%) patients, these events were grade 3 in severity. Dose reduction was required in 16 (4.5%) patients and 16 (4.5%) patients discontinued TRUQAP due to rash. Section 5.1 'Pharmacodynamic properties' of the SmPC Clinical efficacy […] At the data cutoff date (DCO) of 15 August 2022, the study showed statistically significant improvement in PFS for patients receiving TRUQAP plus fulvestrant compared to patients receiving placebo plus fulvestrant, in both the overall population and the PIK3CA/AKT1/PTEN-altered subgroup (see table 9). An exploratory analysis of PFS in the 313 (44%) patients whose tumours did not have PIK3CA/AKT1/PTEN alterations showed a HR of 0.79 (95% CI: 0.61, 1.02), indicating that the difference in the overall population was primarily attributed to the results seen in the population of patients whose tumours have PIK3CA/AKT1/PTEN alterations. PFS results by investigator assessment were supported by consistent results from a blinded independent central review (BICR) assessment. The investigator-assessed ORR in patients receiving TRUQAP plus fulvestrant and placebo plus fulvestrant was 22.9% and 12.2%, respectively, in the overall population and 28.8% and 9.7%, respectively, in the altered subgroup. The prespecified final analysis of OS

					(DCO 16 June 2025) showed a HR of 0.83 (95% CI 0.63, 1.10) in the PIK3CA/AKT1/PTEN-altered subgroup, which was not statistically significant. For more information, please refer to the Summary of Product Characteristics.
Variation type IA / EMA/VR/0000323151	This was an application for a group of variations. A. ADMINISTRATIVE CHANGES - A.4 Change in the name and/or address of: a manufacturer (including where relevant quality control testing sites); or an ASMF holder; or a supplier of the active substance, starting material, reagent or intermediate used in the manufacture of the active substance (where specified in the technical dossier) where no Ph. Eur. Certificate of Suitability is part of the approved dossier; or a manufacturer of a novel excipient (where specified in the technical dossier) - Accepted B.I.a.2 Changes in the manufacturing process of the active substance - B.I.a.2.a Minor change in the manufacturing process of the active substance - Accepted	16/01/2026			
Variation type II / EMA/VR/0000284700	C.I HUMAN AND VETERINARY MEDICINAL PRODUCTS - C.I.4 Change(s) in the Summary of Product Characteristics, Labelling or Package Leaflet due to new quality, preclinical, clinical or pharmacovigilance data - Accepted	18/09/2025		SmPC	5.3 Preclinical safety data Non-clinical/Repeat-dose toxicity The major target organs or systems for toxicity were insulin signalling (increased levels of glucose and insulin in rats and dogs), the male reproductive organs (tubular degeneration in rats and dogs), and the renal system in rats (polyuria,

	Update of section 5.3 of the SmPC in order to update non-clinical information, based on results of the 2-Year Oral (Gavage) Carcinogenicity Study in the Rat (Study 8003384).				decreased tubular epithelial cell size, decreased kidney size and weight). The findings present following 1 month of dosing were largely reversible within 1 month of cessation of dosing. Findings occurred at plasma concentrations lower or similar to those in humans (approximately 0.14 to 2 times) at the recommended dose of 400 mg twice daily (based on total AUC). Lens degeneration was observed in male rats in the 2 year rat carcinogenicity study at exposures lower than those in humans (0.1 times) at the recommended dose of 400 mg twice daily (based on total AUC) and may be related to elevated glucose levels. […] Mutagenicity and carcinogenicity Capivasertib showed no mutagenic or genotoxic potential in vitro. When dosed orally to rats, capivasertib induced micronuclei in the bone marrow via an aneugenic mode of action. In a 2 year rat carcinogenicity study there was an increased incidence and/or severity of islet of Langerhans hypertrophy/hyperplasia (males and females) and neoplastic findings in the testis in males. Findings were observed at exposures lower than those in humans (0.2 to 0.5 times) at the recommended dose of 400 mg twice daily (based on total AUC). For more information, please refer to the Summary of Product Characteristics.
Variation type II / EMA/VR/0000272181	C.I HUMAN AND VETERINARY MEDICINAL PRODUCTS - C.I.4 Change(s) in the Summary of Product Characteristics, Labelling or Package Leaflet due to new	24/07/2025		SmPC and PL	Section 4.4 Special warnings and precautions for use Hyperglycaemia The safety and efficacy of TRUQAP in patients with pre existing Type 1 diabetes or Type 2 diabetes requiring insulin and/or

	quality, preclinical, clinical or pharmacovigilance data - Accepted Update of sections 4.4 and 4.8 of the SmPC to amend the current wording pertaining to the adverse drug reaction (ADR) 'hyperglyceamia', update of section 4.8 of the SmPC to add 'Weight Decreased' as a new adverse drug reaction (ADR) with a frequency 'common' as well as to add footnotes in table 8 for the following ADRs: 'Hypokalaemia', 'Diabetic ketoacidosis' and 'Pyrexia', based on the MAH's Core Data Sheet update . The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to introduce minor formatting changes to the PI as well as to update the list of local representatives in the Package Leaflet.				in patients with HbA1C > 8.0% (63.9 mmol/mol) has not been studied as these patients were excluded from the phase III clinical study. This study included 21 (5.9%) patients in the TRUQAP plus fulvestrant arm with HbA1C ≥ 6.5%. Hyperglycaemia was more frequently reported in patients with a baseline HbA1C ≥ 6.5% (33.3% of patients) than those with a baseline HbA1C < 6.5% (16.0%). Section 4.8 Undesirable effects Summary of safety profile […] The most common adverse reactions were diarrhoea (72.4%), rash (40.3%), nausea (34.6%), fatigue (32.1%), vomiting (20.6%), stomatitis (17.2%), hyperglycaemia (17.2%), headache (16.9%) and decreased appetite (16.6%). […] Serious adverse reactions were seen in 7.0% of patients receiving TRUQAP plus fulvestrant. Most common serious adverse reactions reported in patients receiving TRUQAP plus fulvestrant included rash (2.3%), diarrhoea (1.7%) and vomiting (1.1%). […] Treatment discontinuation due to adverse reactions occurred in 9.9% of patients. The most common adverse reactions leading to treatment discontinuation were rash (4.5%), diarrhoea (2%) and vomiting (2%). […] Description of selected adverse reactions Hyperglycaemia Hyperglycaemia of any grade occurred in 61 (17.2%) patients and grade 3 or 4 occurred in 8 (2.3%) patients receiving TRUQAP. The median time to first occurrence of hyperglycaemia was 15 days (range: 1 to 367). In the study, dose reduction was required in 2 (0.60%) patients and 1 (0.30%) patient

					discontinued treatment due to hyperglycaemia. In the 61 patients with hyperglycaemia, 29 (47.5%) patients were treated using anti-hyperglycaemic medication (including insulin in 16.4%). See section 4.4. For more information, please refer to the Summary of Product Characteristics.
PSUR / EMA/PSUR/0000288286					Maintenance
PSUR / EMA/PSUR/0000248507					Based on the PRAC review of data on safety and efficacy, the PRAC considers that the risk-benefit balance of medicinal products containing capivasertib remains unchanged and therefore recommends the maintenance of the marketing authorisation(s).