Truqap

Procedural steps taken and scientific information after the authorisation

Application number	Scope	Opinion/ Notification[1] issued on	Commission Decision Issued[2] / amended on	Product Information affected[3]	Summary
II/0001	Update of sections 4.2, 4.4 and 4.8 of the SmPC in order to update the posology recommendation and the warning regarding Diabetic Ketoacidosis (DKA) and to add it to the list of adverse drug reactions (ADRs) with a frequency "uncommon", based on a safety review. The Package Leaflet is updated	30/01/2025	28/02/2025	SmPC, Annex II and PL	Hyperglycaemia […] Severe hyperglycaemia, associated with diabetic ketoacidosis (DKA) and with fatal outcomes occurred in patients treated with TRUQAP (see section 4.8). DKA can occur at any time during TRUQAP treatment. In some

[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).

	accordingly. The RMP version 2 has also been submitted. In addition, the MAH also took the opportunity to remove post authorisation measures (PAMs) which were incorrectly added to Annex II.D at time of granting of the Marketing Authorisation, to update the list of local representatives in the Package Leaflet and to bring the PI in line with the latest QRD template version 10.4. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				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. Before initiating treatment with TRUQAP, patients should be informed about TRUQAP's potential to cause hyperglycaemia (see section 4.8) and requested to immediately contact their healthcare professional if hyperglycaemia symptoms (e.g. excessive thirst, urinating more often than usual or greater amount of urine than usual, or increased appetite with weight loss) occur. In a setting of additional co morbidities and treatments (e.g. dehydration, malnourishment, concurrent chemotherapy/steroids, sepsis), the risk of hyperglycaemia progressing to diabetic ketoacidosis may be higher. DKA should be considered as one of the differential diagnoses in the event of additional nonspecific symptoms such as nausea, vomiting, abdominal pain, difficulty breathing, fruity odour on breath, confusion, unusual fatigue, or sleepiness. In patients where DKA is suspected, TRUQAP treatment should be interrupted immediately. If DKA is confirmed, then TRUQAP should be permanently discontinued. Patients must be tested for fasting blood glucose (FG) levels and HbA1C prior to start of treatment with TRUQAP and in accordance with the intervals stated in Table 7. Based on the severity of hyperglycaemia, TRUQAP dosing may be interrupted, reduced, or permanently discontinued (see section 4.2, Table 3). More frequent blood glucose monitoring is recommended in

					patients that develop hyperglycaemia during treatment, those with baseline risk factors for DKA (including but not exclusive to diabetes mellitus, pre diabetes, those receiving regular oral steroids) and in those that develop risk factors for DKA during treatment (e.g. infection, sepsis, raised HbA1c) (see Table 7). In addition to FG, monitoring of ketones (preferably in blood) and other metabolic parameters (as indicated) is recommended when a patient experiences hyperglycaemia. In addition to the recommended management of hyperglycaemia described in Section 4.2 Table 3, counselling on lifestyle changes is recommended for patients with baseline risk factors and those that develop hyperglycaemia during treatment with TRUQAP. For more information, please refer to the Summary of Product Characteristics.
II/0002	Update of section 5.1 of the SmPC in order to update the clinical efficacy information to reflect a new overall survival (OS) interim analysis pertaining to study D3615C00001 (CAPItello-291) in order to fulfil REC 004; this is a phase III 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. In addition, the MAH took the opportunity to introduce minor formatting changes to the PI and to update the list of local representatives	23/01/2025	28/02/2025	SmPC and PL	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 a 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 alteration. PFS results by investigator assessment were supported by consistent results from a

	in the Package Leaflet. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				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. A prespecified interim analysis of OS (DCO 15 April 2024, 59% of patients had died) showed a HR of 0.88 (95% CI: 0.65, 1.19) in the PIK3CA/AKT1/PTEN-altered subgroup.