AstraZeneca	AZ Swiss Marketing Company

Truqap®

160 mg and 200 mg, film-coated tablets

Summary of the Risk Management Plan (RMP) for Truqap® (Capivasertib)

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Disclaimer:

The Risk Management Plan (RMP) is a comprehensive document submitted as part of the application dossier for market approval of a medicine. The RMP summary contains information on the medicine's safety profile and explains the measures that are taken in order to further investigate and follow the risks as well as to prevent or minimise them.

The RMP summary of Truqap® is a concise document and does not claim to be exhaustive.

As the RMP is an international document, the summary might differ from the “Arzneimittelinformation / Information sur le médicament” approved and published in Switzerland, e.g. by mentioning risks occurring in populations or indications not included in the Swiss authorization.

Please note that the reference document which is valid and relevant for the effective and safe use of “Präparatename” in Switzerland is the “Arzneimittelinformation / Information sur le médicament” (see www.swissmedicinfo.ch) approved and authorized by Swissmedic. “Name of the marketing authorisation holder” is fully responsible for the accuracy and correctness of the content of the published summary RMP of “Präparatename”.

This is a summary of the risk management plan (RMP) for TRUQAP. The RMP details important risks of TRUQAP, how these risks can be minimised, and how more information will be obtained about TRUQAP’s risks and uncertainties (missing information).

TRUQAP's Summary of Product Characteristics (SmPC) and its Package Leaflet (PL) give essential information to healthcare professionals and patients on how TRUQAP should be used.

This summary of the RMP for TRUQAP should be read in the context of all this information including the assessment report of the evaluation and its plain-language summary, all which is part of the Swiss Public Assessment Report (SwissPAR).

Important new concerns or changes to the current ones will be included in updates of the TRUQAP RMP.

1. THE MEDICINE AND WHAT IT IS USED FOR

TRUQAP is authorised in combination with fulvestrant for the treatment of adult female patients with hormone receptor (HR) positive, human epidermal growth factor receptor 2 (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.

It contains capivasertib as the active substance and it is given as two 200 mg tablets taken orally twice daily. The 160 mg tablets can be used to reduce the dose in the event of side effects.

Further information about the evaluation of TRUQAP's benefits can be found in TRUQAP's SwissPAR, including in its plain-language summary, available on the EMA website under the medicine's webpage.

2. RISKS ASSOCIATED WITH THE MEDICINE AND ACTIVITIES TO MINIMISE OR FURTHER CHARACTERISE THE RISKS

Important risks of TRUQAP, together with measures to minimise such risks and the proposed studies for learning more about the risks of TRUQAP, are outlined below.

Measures to minimise the risks identified for medicinal products can be:

- Specific information, such as warnings, precautions, and advice on correct use, in the PL and SmPC addressed to patients and healthcare professionals
- Important advice on the medicine's packaging
- The authorised pack size — the amount of medicine in a pack is chosen so to ensure that the medicine is used correctly
- The medicine's legal status — the way a medicine is supplied to the patient (eg, with or without prescription) can help to minimise its risks.

Together, these measures constitute *routine risk minimisation measures*.

In addition to these measures, information about adverse reactions is collected continuously and regularly analysed, including Periodic Safety Update Report

(PSUR) assessment, so that immediate action can be taken as necessary. These measures constitute *routine pharmacovigilance activities*.

2.1 List of important risks and missing information

Important risks of TRUQAP are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely taken. Important risks can be regarded as identified or potential. Identified risks are concerns for which there is sufficient proof of a link with the use of TRUQAP. Potential risks are concerns for which an association with the use of this medicine is possible based on available data, but this association has not been established yet and needs further evaluation. Missing information refers to information on the safety of the medicinal product that is currently missing and needs to be collected (eg, on the long-term use of the medicine).

Table 2 List of Important Risks and Missing Information

Important identified risks	• Hyperglycaemia
Important potential risks	• Acute Complications of Hyperglycaemia
Missing Information	None

2.2 Summary of important risks

Summaries of the important identified risk of hyperglycaemia and the important potential risk of Acute Complications of Hyperglycaemia are provided in Table 2 and Table 3, respectively.

Table 1 Important Identified Risk: Hyperglycaemia

Evidence for linking the risk to the medicine	Increased levels of glucose and insulin were observed in nonclinical toxicology and safety pharmacology studies in both rats and dogs, following which the effects of capivasertib on glucose homeostasis and insulin signalling was categorised as a risk. In clinical trials, the frequency of hyperglycaemia was greater in patients receiving capivasertib plus fulvestrant than in patients receiving placebo plus fulvestrant, and there is a plausible mechanism of action for how capivasertib may lead to hyperglycaemia.
Risk factors and risk groups	Patients with pre-existing diabetes or patients exposed to medicines impacting the homeostasis or control of blood glucose levels (eg, steroids) may be at greater risk of experiencing capivasertib-induced hyperglycaemia.

Table 1 Important Identified Risk: Hyperglycaemia

Evidence for linking the risk to the medicine	Increased levels of glucose and insulin were observed in nonclinical toxicology and safety pharmacology studies in both rats and dogs, following which the effects of capivasertib on glucose homeostasis and insulin signalling was categorised as a risk. In clinical trials, the frequency of hyperglycaemia was greater in patients receiving capivasertib plus fulvestrant than in patients receiving placebo plus fulvestrant, and there is a plausible mechanism of action for how capivasertib may lead to hyperglycaemia.
Risk minimisation measures	**Routine risk minimisation measures**: • SmPC Sections 4.2, 4.4, and 4.8 • PL Sections 2 and 4 • Prescription-only medicine **Additional risk minimisation measures:** • No additional risk minimisation measures.

Table 2 Important Potential Risk: Acute Complications of Hyperglycaemia

Evidence for linking the risk to the medicine	Very rare occurrences of acute complications due to hyperglycaemia have been reported in the capivasertib clinical development programme.
Risk factors and risk groups	No specific risk factors for the development of acute complications of hyperglycaemia in capivasertib-treated patients have been identified. However, high-risk patients (eg, those with a medical history of type 1 or 2 diabetes, concurrent infections, or other conditions requiring more intensified glycaemia management) may be at greater risk of experiencing hyperglycaemia leading to acute complications.
Risk minimisation measures	**Routine risk minimisation measures**: • SmPC Section 4.4 • PL Section 2 • Prescription-only medicine **Additional risk minimisation measures:** • No additional risk minimisation measures.

3. POST-AUTHORISATION DEVELOPMENT PLAN

3.1 Studies which are conditions of the marketing authorisation

There are no studies which are conditions of the marketing authorisation or specific obligation of capivasertib.

3.2 Other studies in post-authorisation development plan

There are no studies required for TRUQAP.