"This Prescriber Guide, format and content has been checked and approved by the Ministry of Health in Sep 2024"

HCP guide

TRUQAP (Capivasertib): Important Safety Information about hyperglycaemiaRisk Minimisation Guide for Healthcare professionals

For ordering additional HCP guide please call:

073-222 6099

or email to:

Safety.Israel@astrazeneca.com

About this guide

This guide

- Is a condition of the marketing authorisation and has been approved by Israel health authority.
- Provides important information for healthcare professionals related to hyperglycaemia associated with capivasertib
- Only explains specific side effects. It does not replace the IL approve physician label which contains the full prescribing information.

This guide will help you to

- Understand the risk of hyperglycaemia with capivasertib
- Know what to do before initiating treatment
- Know what to do during treatment
- Manage hyperglycaemia
- Educate patients on hyperglycaemia
- Report adverse events

1. The Risk of Hyperglycaemia with capivasertib

Hyperglycaemia has been observed in clinical studies with Capvasertib. In the CAPItello-291 study in patients receiving capivasertib plus fulvestrant:

Hyperglycemia[a] occurred in 18% of patients treated with TRUQAP. Grade 3 (insulin therapy initiated; hospitalization indicated) or Grade 4 (life-threatening consequences; urgent intervention indicated) hyperglycemia occurred in 2.8% of patients.

Diabetic ketoacidosis occurred in 0.3% of patients and diabetic metabolic decompensation in 0.6% of patients.

Dose reduction for hyperglycemia was required in 0.6% of patients and permanent discontinuation was required in 0.6% of patients. The median time to first occurrence of hyperglycemia was 15 days (range: 1 to 367).

[a] Hyperglycemia includes hyperglycemia, blood glucose increased, glycosylated hemoglobin increased, glucose tolerance impaired and diabetes mellitus.

In the case of poor blood sugar control in high-risk patients, hyperglycaemia can potentially lead to acute complications

Patients with Type 1 diabetes and Type 2 diabetes requiring insulin and/or patients with HbA1C > 8.0% (63.9 mmol/mol), were excluded from CAPItello-291 study therefore the safety of capivasertib in these patients is unknown.

Patients with a history of diabetes mellitus may require intensified diabetic treatment and should be closely monitored (see section 3).

2. What to do before initiating treatment

- Inform patient of the risk of hyperglycaemia (see section 5), the possible symptoms and how these might be managed
- Test patients' fasting blood glucose (FG) and HbA1C levels to ensure optimal glucose control prior to starting , capivasertib

3. What to do during treatment

I. Monitor patients' fasting blood glucose (FG) and HbA1C levels at regular intervals prior to dosing as indicated below. Note the recommended schedule for monitoring is more intensive for patients with risk factors.

Minimum monitoring requirements for **all patients**

- Test FG at least every two weeks during the first month of treatment
- Test FG at least once a month after the first month of treatment
- Test HbA1C every three months

In addition to the recommended management of hyperglycaemia counselling on lifestyle changes is recommended for patients with baseline risk factors and those that develop hyperglycaemia during treatment with TRUQAPAdditional monitoring guidance for **patients with risk factors***:

- Test FG more frequently
- Test HbA1C, ketones (preferably in blood) and other metabolic parameters (as indicated)

*Risk factors include:

- medical history of diabetes mellitus
- FG of > ULN-160 mg/dl (> ULN-8.9 mmol/L) during treatment
- intercurrent infections or other conditions which may require intensified glycaemia management to prevent worsening of impaired glucose metabolism and potential complications
- use of concomitant medication with a known risk of increase in blood glucose e.g. corticosteroids
- High values of BMI
- High values of HbA1C

II. Consider interrupting, reducing or permanently discontinuing capivasertib depending on the severity of the event (see section 4)

4. How to manage hyperglycaemia

The table below provides the recommended dose modifications and treatments in the event a patient suffers hyperglycaemia. Consultation with diabetologist should be considered when selecting an antidiabetic medicinal product, a potential for hypoglycaemia with antidiabetic medicinal product administration on non-capivasertib dosing days should be considered.

Severity*	TRUQAP Dosage Modification
FG > ULN-160 mg/dL or FG > ULN-8.9 mmol/L or HbA1C > 7%	Consider initiation or intensification of oral anti-diabetic treatment
FG 161-250 mg/dL or FG 9-13.9 mmol/L	Withhold TRUQAP until FG decrease ≤ 160 mg/dL (or < 8.9 mmol/L) If recovery occurs in ≤ 28 days, resume TRUQAP at same dose. If recovery occurs in > 28 days, resume TRUQAP at one lower dose.
FG 251-500 mg/dL or > 14-27.8 mmol/L	Withhold TRUQAP until FG decrease ≤ 160 mg/dL (or < 8.9 mmol/L) If recovery occurs in ≤ 28 days, resume TRUQAP at one lower dose. If recovery occurs in > 28 days, permanently discontinue TRUQAP.
FFG > 500 mg/dL or > 27.8 mmol/L or life-threatening sequelae of hyperglycemia at any FG level	For life-threatening sequelae of hyperglycemia or if FG persists at ≥ 500 mg/dL after 24 hours, permanently discontinue TRUQAP. If FG ≤ 500 mg/dL (or ≤ 27.8 mmol/L) within 24 hours, then follow the guidance in the table for the relevant grade.

*Severity grading according to Common Terminology Criteria for Adverse Events (CTCAE) Version 5.0.

5. How to educate patients on the risk hyperglycaemia

Counsel your patients about the risk of hyperglycaemia and inform them that:

I. They may experience increased blood sugar levels (hyperglycaemia)
II. They should tell you immediately if they experience any of the following symptoms of potential hyperglycaemia and its complications such as:
   - excessive thirst
   - dry mouth
   - passing urine more often, or a greater amount of urine, than usual
   - increased appetite with weight loss

- They will be asked to provide a blood sample regularly to check for hyperglycaemia
- You may need to treat these symptoms or alter the patients' treatment with capivasertib
- Advise the patient how lifestyle changes may reduce the risk of hyperglycaemia; examples are shown in the figure below:

Counsel patients on how to reduce the risk of hyperglycemia by making lifestyle changes. Along with pharmceutical management, the following tipes are advised for patients:

- Oncrease physican activity
- Maintaining a healthy diet (low in sugar and fat) and weight
- Limiting use of alchol, tabacoo and/or other substances
- Reducing stress

6. Reporting adverse events

Reporting suspected adverse reactions after authorisation of a medicine is important. It allows continual monitoring of the benefit and risk balance of the medicine to patients. When reporting adverse reactions, please provide as much information as possible including:

- information about the patient's medical history
- any other medicines they are taking, and all other information known.

Adverse drug reactions can be reported at https://aereporting.astrazeneca.com or you can send an email to: Safety.Israel@astrazeneca.com

You can also call us on phone number: 073-2226099

You may also report side effects directly to the Israeli ministry of health by pressing "Report side effects of drug treatment" on the Ministry of Health (www.health.gov.il) linking to the portal or by the link: https://sideeffects.health.gov.il

Referances

- Israel Truqap SPC 06.2024
- Ref 1. Hammer M, et al. *ONF.* 2019;46(4):459-472
- TRUQAP Israel approve physician label – July 2023

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Truqap™
capivasertib
160 mg • 200 mg tablets

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ת.ד 8044 כפר סבא, 4464301 טל: 073-2226099