

## CAPIVASERTIB (Truqap) FULVESTRANT

### INDICATION (ICD10) C50

Check the most recent *Blueteq* eligibility criteria before prescribing. *Blueteq* registration required. ([www.england.nhs.uk/publication/national-cancer-drugs-fund-list/](http://www.england.nhs.uk/publication/national-cancer-drugs-fund-list/)) (CAP1)

1. Capiwasertib in combination with fulvestrant only for hormone receptor-positive, HER2-negative, locally advanced or metastatic breast cancer with a PIK3CA or an AKT1 or a PTEN genomic alteration in patients previously treated with a CDK4/6 inhibitor and an aromatase inhibitor, and progressive disease after previous endocrine-based treatment, which is not amenable to curative treatment. Has had no prior treatment with fulvestrant for any indication. PS 0 or 1. (TA1063)

### REGIMEN

Days 1 to 4, 8 to 11, 15 to 18 and 22 to 25 CAPIVASERTIB 400mg tablet oral twice daily  
Day 1 (and day 15 cycle 1 only) FULVESTRANT 500mg IM

### CYCLE FREQUENCY AND NUMBER OF CYCLES

Every 28 days until disease progression

### ADMINISTRATION

Available as 160mg and 200mg tablets  
Swallow whole with or without food.

Fulvestrant each 500mg dose is administered as two consecutive 250mg (5 ml) injections by slow intramuscular injection (1-2 minutes/injection), one in each buttock (gluteal area).

### ANTI-EMETICS

Low risk

### CONCURRENT MEDICATION REQUIRED

If the patient is female and pre- or peri-menopausal, the patient has undergone ovarian ablation or suppression with LHRH agonist treatment, and if the patient is male consideration has been given to administration of LHRH agonist therapy.

### EXTRAVASATION AND TYPE OF LINE / FILTERS

Not applicable

### INVESTIGATIONS

Blood results required before capivasertib administration

FBC, U&Es and LFTs baseline, every cycle

Platelets x 10<sup>9</sup>/L >50

Fasting plasma glucose and HbA1C pre-initiation, and then fasting plasma glucose every cycle.

Blood creatinine

### MAIN TOXICITIES AND ADVERSE REACTIONS

Capiwasertib	Anaemia Cutaneous reactions Diarrhoea, nausea, vomiting Hyperglycaemia Stomatitis UTI
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**INTERACTIONS WHICH MAY REQUIRE DOSE MODIFICATIONS  
(not exhaustive list check SPC/BNF/Stockleys)**

Capivasertib	Strong CYP3A4 inhibitors increase capivasertib concentration, which may increase the risk of capivasertib toxicity. Reduce the dose of capivasertib. Moderate CYP3A4 inhibitors is predicted to increase capivasertib concentration. UGTB27 inhibitors has potential to increase capivasertib concentration.
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**DOSE MODIFICATIONS**

Capivasertib

Recommended dose	400mg twice daily for 4 days, followed by 3 days off treatment
First dose reduction	320mg twice daily for 4 days, followed by 3 days off treatment
Second dose reduction	200mg twice daily for 4 days, followed by 3 days off treatment

Continue fulvestrant during capivasertib treatment breaks for toxicity

**Non-haematological**

Capivasertib

Cutaneous reactions

Grade 1	No capivasertib dose adjustment required. Initiate emollients and consider adding oral non -sedating antihistamine treatment as clinically indicated to manage symptoms.
Grade 2	Withhold capivasertib until recovery to ≤grade 1. Initiate or intensify topical steroid treatment and consider non-sedating oral antihistamines. If recovery occurs in ≤28 days, resume capivasertib at the same dose level. If persistent or recurrent: restart capivasertib by one dose level.
Grade 3	Withhold capivasertib until recovery to ≤grade 1. Initiate appropriate dermatological treatment with topical steroid of moderate/higher strength, non-sedating oral antihistamines and/or systemic steroids. If recovery occurs in ≤28 days, restart capivasertib on one lower dose level. If the symptoms do not improve to ≤grade 1 within 28 days discontinue capivasertib. In patients with reoccurrence of intolerable grade 3 rash, permanently discontinue capivasertib.
Grade 4	Permanently discontinue capivasertib.

Diarrhoea

Grade 1	No capivasertib dose adjustment required. Initiate appropriate anti-diarrhoeal therapy, maximise supportive care and monitor as clinically indicated.
Grade 2	Initiate or intensify appropriate anti-diarrhoeal treatment and monitor as clinically indicated. Withhold capivasertib dose for up to 28 days until recovery to $\leq$ grade 1 and resume capivasertib dosing at same dose or one lower dose level as clinically indicated. If grade 2 diarrhoea is persistent or recurring, maintain appropriate medical therapy and restart capivasertib at one lower dose level, as clinically indicated.
Grade 3	Withhold capivasertib until recovery to $\leq$ grade 1. Initiate or intensify appropriate anti-diarrhoeal treatment and monitor as clinically indicated. If recovery occurs in $\leq$ 28 days, resume capivasertib at one lower dose level. If recovery to $\leq$ grade 1 in >28 days, permanently discontinue capivasertib.
Grade 4	Permanently discontinue capivasertib.

### Hyperglycaemia

<p>Grade 1 &gt;ULN-160mg/dL or &gt;ULN-8.9mmol/L or HbA1C &gt;7%</p>	<p>No capivasertib dose adjustment required. Consider initiation or intensification of oral anti-diabetic treatment.</p>
<p>Grade 2 &gt;160-250mg/dL or &gt;8.9-13.9mmol/L</p>	<p>Initiate or intensify oral anti-diabetic treatment. Withhold capivasertib until fasting glucose (FG) level decrease to <math>\leq 160</math>mg/dl (or <math>\leq 8.9</math>mmol/L). If recovery occurs in <math>\leq 28</math> days, resume capivasertib at the same dose and maintain initiated or intensified anti-diabetic treatment. If improvement to <math>\leq 160</math>mg/dL (or <math>\leq 8.9</math>mmol/L) is reached in more than 28 days restart at one lower dose level and maintain initiated or intensified anti-diabetic treatment.</p>
<p>Grade 3 &gt;250-500mg/dL or &gt;13.9-27.8mmol/L</p>	<p>Withhold capivasertib until fasting glucose (FG) level decrease to <math>\leq 160</math>mg/dl (or <math>\leq 8.9</math>mmol/L) and consult a diabetologist. Initiate or intensify oral anti-diabetic treatment. Consider additional anti-diabetic medicinal products such as insulin, as clinically indicated. Consider intravenous hydration and provide appropriate clinical management as per local guidelines. If FG decreases to <math>\leq 160</math>mg/dL (or <math>\leq 8.9</math>mmol/L) within 28 days, restart capivasertib at one lower dose level and maintain initiated or intensified anti-diabetic treatment. If FG does not decrease to <math>\leq 160</math>mg/dL (or <math>\leq 8.9</math>mmol/L) within 28 days following appropriate treatment permanently discontinue capivasertib.</p>
<p>Grade 4 &gt;500mg/dL or &gt;27.8mmol/L)</p>	<p>Withhold capivasertib and consult with a diabetologist. Initiate or intensify appropriate anti-diabetic treatment. Consider insulin, (dosing and duration as clinically indicated), intravenous hydration and provide appropriate clinical management as per local guidelines. If FG decreases to <math>\leq 500</math>mg/dl (or <math>\leq 27.8</math>mmol/l) within 24 hours, then follow the guidance in the table for the relevant grade. If FG is confirmed at <math>&gt; 500</math>mg/dl (or <math>\geq 27.8</math>mmol/l) after 24 hours, permanently discontinue capivasertib treatment.</p>

Other toxicities

Grade 1	No capivasertib dose adjustment required, initiate appropriate medical therapy and monitor as clinically indicated.
Grade 2	Withhold capivasertib until symptoms improve to $\leq$ grade 1.
Grade 3	Withhold capivasertib until symptoms improve to $\leq$ grade 1. If symptoms improve, restart capivasertib at same dose or one lower dose level as clinically appropriate.
Grade 4	Permanently discontinue capivasertib.

**Hepatic impairment**

Capivasertib

Mild hepatic impairment (bilirubin $\leq$ ULN and AST $>$ ULN or bilirubin $>1.0x-1.5x$ ULN).	No dose adjustment is required
Moderate hepatic impairment (bilirubin $>1.5x-3.0x$ ULN);	Limited data are available. Capivasertib should be administered to patients with moderate hepatic impairment only if the benefit outweighs the risk and these patients should be monitored closely for adverse effects due to potential increase in capivasertib exposure.
Severe hepatic impairment (bilirubin $>3.0x$ ULN),	Capivasertib is not recommended as safety and pharmacokinetics have not been studied in these patients.

**Renal impairment**

Capivasertib

Mild (CrCl 60 to 89mL/min) or moderate (creatinine clearance 30 to 59mL/min) renal impairment	No dose adjustment is required
Severe renal impairment (CrCl $<30$ mL/min),	Capivasertib is not recommended as safety and pharmacokinetics have not been studied in these patients

Fulvestrant

No data for fulvestrant – use with caution

**REFERENCES**

1. SPC
2. CDF list