Chemotherapy Protocol

Breast Cancer

Capivasertib- Fulvestrant

Regimen

- Breast Cancer – Capivasertib- Fulvestrant

Indication

- Capivasertib is indicated in combination with Fulvestrant for the treatment of adult 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, where the following criteria have been met:
  - The patient has metastatic or locally advanced breast cancer which is not amenable to curative treatment.
  - 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.
  - The patient has been previously treated with an aromatase inhibitor: solely for early breast cancer or, solely for locally advanced/metastatic breast cancer, or in both early and advanced breast cancer settings.
  - The patient has been previously treated with a CDK4/6 inhibitor.
  - The patient has had no prior treatment with Fulvestrant for any indication unless this patient has either received Capivasertib plus Fulvestrant via the company early access programme.
  - Capivasertib will only be given in combination with Fulvestrant.
  - Treatment will continue until there is progressive disease or excessive toxicity or until the patient chooses to discontinue treatment, whichever is sooner.
  - The patient has a WHO performance status of 0 or 1.

Toxicity

Treatment breaks of up to 6 weeks are allowed.

Drug	Adverse Effect
Capivasertib	Hyperglycaemia, diarrhoea, nausea, vomiting, cutaneous reactions, fatigue, blood creatinine increased, anaemia, urinary tract infections.
Fulvestrant	Headache, hot flushes, elevated hepatic enzymes, hypersensitivity reactions, injection site reactions, nausea, vomiting, diarrhoea, skin rashes, joint and musculoskeletal pain, vaginal haemorrhage

The adverse effects listed are not exhaustive. Please refer to the relevant summary of product characteristics for further details.

Monitoring

Regimen

- FBC, LFTs and U&Es at baseline and then every two weeks for the first eight weeks. NB. A four-week supply may be dispensed on day 1 of each cycle even though monitoring may be every two weeks. After eight weeks, the frequency of monitoring can be reduced to every four weeks.
- Blood glucose monitoring: Prior to initiating treatment with Capivasertib, patients must be tested for fasting blood glucose levels. Levels of blood glucose must be optimised prior to commencing treatment. Fasting glucose should be monitored at weeks 1, 2, 4, 6 and 8 after initiation of treatment and monthly thereafter. A blood glucose monitor should be issued to all patients to monitor glucose at home. Hyperglycaemia should be managed locally and referred to the Trust endocrine team.
- HbA1c monitoring: Monitored at baseline and every three months.

Dose Modifications

Please discuss all dose reductions/delays with the treating consultant if appropriate. The approach may be different depending on the clinical circumstances. The following is a general guide only.

Treatment with Capivasertib may be interrupted to manage adverse reactions and dose reduction can be considered. The dose of Capivasertib can be reduced up to two times.

Dose Reduction Guidelines for Adverse Reactions	
Capivasertib	**Dose and schedule**
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

Haematological

Consider blood transfusion or the use of erythropoietin according to NICE TA323 if patient symptomatic of anaemia or has haemoglobin of less than 8g/dL (80g/L).

Prior to prescribing cycle 1, the following criteria must be met:

Criteria	**Eligible Level**
Neutrophils	≥ 1.5x 10^9/L
Platelets	≥ 100x 10^9/L

Hepatic Impairment

No dose change for fulvestrant is required in patients with mild hepatic impairment. Caution is advised in patients with moderate to severe hepatic impairment.

No dose change for capivasertib is required in patients with mild hepatic impairment. In patients with moderate hepatic impairment, capivasertib should only be administered if the benefits outweigh the risks and monitored closely for adverse events. Capivasertib is not recommended for patients with severe hepatic impairment (Bilirubin >3.0x ULN).

Renal Impairment

No dose change for fulvestrant is required in patients with mild to moderate renal impairment.

No dose change for capivasertib is required in patients with mild (CrCl 60- 89mL/min) or moderate (CrCl 30- 59mL/min) renal impairment. Capivasertib is not recommended for patients with severe renal impairment (CrCl <30mL/min).

Hyperglycaemia

NCI CTC Grade and Fasting Glucose (FG) values prior to Capivasertib dose	Management and Dosing Recommendations for Capivasertib
Grade 1 FG>ULN – 8.9 mmol/L or HbA1c > 53mmol/L	No dose adjustment required. Consider initiation or intensification of oral anti-diabetic medication.
Grade 2 FG> 8.0- 13.9 mmol/L	Initiate or intensify oral anti-diabetic medication. Withold capivasertib until FG resolves to ≤ 8.9 mmol/L. If recovery occurs in ≤ 28 days, resume at the same dose level. If recovery occurs ≥ 28 days restart at one lower dose level. Maintain current anti-diabetic medication.
Grade 3 FG> 13.9- 27.8 mmol/L	Withold capivasertib until FG resolves to ≤ 8.9 mmol/L and consult endocrinology. Initiate or intensify oral anti-diabetic medication (including addition of insulin). Consider intravenous hydration. If FG ≤ 8.9 mmol/L within 28 days, restart capivasertib at one lower dose level and maintain initiated or intensified anti-diabetic treatment. Permanently discontinue capivasertib if FG does not resolve to ≤ 8.9 mmol/L within 28 days following appropriate management.
Grade 4 FG> 27.8 mmol/L	Withold capivasertib and consult endocrinology. Initiate or intensify oral anti-diabetic medication (including addition of insulin). Consider intravenous hydration. If FG recovers ≤ 27.8 mmol/L within 24 hours, then follow the guidance within this table for the relevant grade. If FG is confirmed at ≥ 27.8 mmol/L after 24 hours, permanently discontinue capivasertib treatment.

Diarrhoea

Secondary prophylaxis with antidiarrhoeal agents should be started in patients with recurrent diarrhoea.

Toxicity (NCI CTC)	Management and Dosing Recommendations for Capivasertib
Grade 1	No dose adjustment required.
Grade 2	Initiate or intensify antidiarrhoeal treatment. Withold Capivasertib for up to 4 weeks until recovery ≤ Grade 1 and resume Capivasertib at same dose or one lower dose level. If Grade 2 diarrhoea is persistent or recurring, maintain appropriate antidiarrhoeal management and restart Capivasertib at one lower dose level.
Grade 3	Withold Capivasertib until recovery ≤ Grade 1. Initiate or intensify antidiarrhoeal treatment. If recovery occurs ≤ 4 weeks, resume Capivasertib at one lower dose level. If recovery ≤ Grade 1 takes longer than 4 weeks, permanently discontinue treatment.
Grade 4	Permanently discontinue treatment.

Cutaneous Reactions

In patients with persistent rash and/or previous occurrence of Grade 3 rash, consider secondary prophylaxis by continuing oral antihistamines and/or topical steroids.

Toxicity (NCI CTC)	Management and Dosing Recommendations for Capivasertib
Grade 1	No dose adjustment required. Recommend emollients and consider oral non-sedating antihistamine treatment as clinically indicated to manage symptoms.
Grade 2	Withold capivasertib until recovery ≤ Grade 1. Initiate or intensify topical steroid treatment and consider non-sedating oral antihistamines. If recovery occurs ≤ 28 days, resume capivasertib at the same dose level. If persistent or recurrent: reduce by one dose level.
Grade 3	Withold capivasertib until recovery ≤ Grade 1. Initiate treatment with topical steroid of moderate/higher strength, non-sedating oral antihistamines and/or systemic steroids. If recovery occurs ≤ 28 days, resume capivasertib on one lower dose level. If symptoms do not improve ≤ Grade 1 within 28 days, discontinue capivasertib. In patients with reoccurrence of intolerable Grade 3 rash, permanently discontinue capivasertib.
Grade 4	Permanently discontinue treatment.

Other toxicities, excluding hyperglycaemia, diarrhoea and cutaneous reactions, should be managed as follows:

Toxicity (NCI CTC)	Management and Dosing Recommendations for Capivasertib
Grade 1	No dose adjustment required. Initiate appropriate medical therapy and monitor as clinically indicated.
Grade 2	Withold capivasertib until symptoms resolve to ≤ Grade 1.
Grade 3	Withold capivasertib until symptoms resolve to ≤ Grade 1. If symptoms resolve, restart capivasertib at same dose or one lower dose level as clinically appropriate.
Grade 4	Permanently discontinue treatment.

Regimen

28- day cycle until disease progression or patient intolerance (12 cycles will be set in ARIA)

Cycle 1

Drug	Dose	Days	Route
Capivasertib	400mg TWICE daily	On days 1-4, 8-11, 15-18 and 22-25 of each cycle (i.e. continuous 4 days on / 3 days off)	Oral
Fulvestrant	500mg	1 and 15	Intramuscular

Cycle 2 Onwards

Drug	Dose	Days	Route
Capivasertib	400mg TWICE daily	On days 1-4, 8-11, 15-18 and 22-25 of each cycle (i.e. continuous 4 days on / 3 days off)	Oral
Fulvestrant	500mg	1	Intramuscular

Dose Information

- Capivasertib is available as 160mg and 200mg film-coated tablets.

Administration Information

- If a dose of Capivasertib is missed, it can be taken within 4 hours after the time it is usually taken. If a dose is missed and more than 4 hours have passed, the dose

should be omitted. The next dose of Capivasertib should be taken at the usual time. There should be at least 8 hours between doses.

- If a patient vomits, an additional dose of capivasertib should not be taken. The next dose should be taken at the usual time.
- Fulvestrant should be administered as two consecutive 5mL injections by slow intramuscular injection (1-2 minutes per injection), one in each buttock (gluteal area). Caution should be taken if injection fulvestrant at the dorsogluteal site due to the proximity of the underlying sciatic nerve.

Supportive Therapy

- Loperamide 4mg after the first loose stool and 2mg after each subsequent loose stool (maximum dose 16mg/24 hours).
- Anti-diabetic medication as clinically appropriate (see Dose Modifications- Hyperglycaemia section).
- Emollients, topical and/or systemic steroids as clinically appropriate (see Dose Modifications- Cutaneous Reactions section).

Additional Information

- The National Patient Safety Alert on oral chemotherapy (NPSA/2008/RRR001) must be followed in relation to Capivasertib.
- It must be made to clear to staff, including those in the community, that capivasertib should only be prescribed under the supervision of a consultant oncologist.
- Capivasertib is primarily metabolised by CYP3A4 and UGT2B7 enzymes. Co-administration with strong CYP3A4 inhibitors such as clarithromycin, itraconazole, posaconazole, ritonavir and grapefruit juice, and UGT2B7 inhibitors such as valproic acid, increase capivasertib concentration therefore increasing the risk of capivasertib toxicity. This is not exhaustive. Please refer to the Summary of Product Characteristics (SPC) for a full list of interactions.

References

1. AstraZeneca UK Limited. Truqap (Capivasertib) 200mg film-coated tablets. Updated 15 July 2025. Available at: Truqap 200 mg film-coated tablets - Summary of Product Characteristics (SmPC) - (emc) | 15839. Accessed September 2025.
2. Royal Surrey NHS Trust. St Luke's SACT Protocols and Policies. Breast cancer – Advanced Breast Cancers. Capivasertib. Version 1 (May 2025). Available at: COLORECTAL. Accessed September 2025.

REGIMEN SUMMARY

Capivasertib- Fulvestrant

Cycle One

Day One

1. **Capivasertib 400mg twice a day on days 1-4, 8-11, 15-18 and 22-25 of each cycle(oral) (i.e. continuous 4 days on / 3 days off)**
   Administration instructions
   Oral chemotherapy. Swallow whole with water. Avoid grapefruit/grapefruit juice.

2. **Fulvestrant 500mg intramuscular**
   Administration instructions
   Fulvestrant should be administered as two consecutive 5mL injections by slow intramuscular injection (1-2 minutes/injection), one in each buttock (gluteal area). Caution should be taken if injecting fulvestrant at the dorsogluteal site due to the proximity of the underlying sciatic nerve. Please refer to the package insert for instructions on administering the injection.

Day Fifteen

3. **Fulvestrant 500mg intramuscular**
   Administration instructions
   Fulvestrant should be administered as two consecutive 5mL injections by slow intramuscular injection (1-2 minutes/injection), one in each buttock (gluteal area). Caution should be taken if injecting fulvestrant at the dorsogluteal site due to the proximity of the underlying sciatic nerve. Please refer to the package insert for instructions on administering the injection.

Take Home Medicines (Day One only)

4. **Loperamide 4mg after the first loose stool and 2mg after each subsequent loose stool. Maximum 16mg in 24 hours.**
   Administration instructions
   Take 4mg after the first loose stool and then 2mg after each subsequent loose stool to a maximum of 16mg/24 hours. Please supply one original pack.

Cycle Two

Day One

1. **Capivasertib 400mg twice a day on days 1-4, 8-11, 15-18 and 22-25 of each cycle(oral) (i.e. continuous 4 days on / 3 days off)**
   Administration instructions
   Oral chemotherapy. Swallow whole with water. Avoid grapefruit/grapefruit juice.

2. **Fulvestrant 500mg intramuscular**
   Administration instructions
   Fulvestrant should be administered as two consecutive 5mL injections by slow intramuscular injection (1-2 minutes/injection), one in each buttock (gluteal area). Caution should be taken if injecting fulvestrant at the dorsogluteal site due to the proximity of the underlying sciatic nerve. Please refer to the package insert for instructions on administering the injection.

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1	October 2025	New Document	Amira Atrach Pharmacist	Dr Sanjay Raj Medical Oncologist

This chemotherapy protocol has been developed as part of the chemotherapy electronic prescribing project. This was and remains a collaborative project that originated from the former CSCCN. These documents have been approved on behalf of the following Trusts:

Hampshire Hospitals NHS Foundation Trust
NHS Isle of Wight
Portsmouth Hospitals NHS Trust
Salisbury NHS Foundation Trust
University Hospital Southampton NHS Foundation Trust
Western Sussex Hospitals NHS Foundation Trust

All actions have been taken to ensure these protocols are correct. However, no responsibility can be taken for errors that occur as a result of following these guidelines.