

## ALPELISIB (Piqray) 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/)) (ALP1)

1. For treatment of hormone receptor positive, HER2-negative, PIK3CA mutation, locally advanced or metastatic breast cancer in patients previously treated with a CDK4/6 inhibitor and an aromatase inhibitor (but no previous fulvestrant). PS 0 or 1. (TA816)

### REGIMEN

ALPELISIB 300mg tablet oral once daily continuously  
FULVESTRANT 500mg IM day 1 (and day 15 cycle 1 only)

### CYCLE FREQUENCY AND NUMBER OF CYCLES

Every 28 days until disease progression or unacceptable toxicity

### ADMINISTRATION

Alpelisib is available as 50mg, 150mg and 200mg tablets.

Alpelisib tablets should be taken at approximately the same time each day, immediately after food. Fulvestrant each 500mg dose is administered as two consecutive 250mg (5ml) injections by slow intramuscular injection (1-2 minutes/injection), one in each buttock (gluteal area).

### ANTI-EMETICS

Minimal risk all days

### CONCURRENT MEDICATION REQUIRED

Alpelisib	<p>Loperamide for diarrhoea.</p> <p>Oral antihistamine administration may be considered prophylactically, at the initiation of treatment with alpelisib. Additionally, antihistamines are recommended to manage symptoms of rash.</p> <p>Topical corticosteroid treatment should be initiated at the first signs of rash and systemic corticosteroids should be considered for moderate to severe rashes. Based on the severity of rash.</p> <p>Metformin rescue pack (28x500mg) with cycle 1, only to be started and taken when directed by Oncology team. Starting dose one daily with evening meal and increase as instructed. (See dose modifications for further information).</p>
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### EXTRAVASATION AND TYPE OF LINE / FILTERS

Not applicable

### INVESTIGATIONS

Blood results required before SACT administration

FBC, U&Es & LFTs every cycle

Fasting plasma glucose pre-initiation, then at weeks 1, 2, 4, 6 and 8 and then monthly

## MAIN TOXICITIES AND ADVERSE REACTIONS

Alpelisib	Diarrhoea Nausea Hyperglycaemia Hypersensitivity Osteonecrosis of jaw Pneumonitis Severe cutaneous reactions, rash
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## INTERACTIONS WHICH MAY REQUIRE DOSE MODIFICATIONS

(not exhaustive list check SPC/BNF/Stockleys)

Alpelisib	Acid reducing agents, therefore alpelisib must be administered immediately after food. CYP3A4 substrates (eg rifampicin, ribociclib, encorafenib) BRCP inhibitors (eg pantoprazole) may increase alpelisib exposure therefore caution and monitor
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## DOSE MODIFICATIONS

Fulvestrant

Do not delay fulvestrant doses

Alpelisib dose combination therapy

Recommended dose 300mg once daily

First dose adjustment 250mg once daily

Second dose adjustment 200mg once daily

## Non-haematological

Alpelisib

Diarrhoea

Grade 1	No dose adjustment required. Initiate appropriate therapy and monitor as clinically indicated.
Grade 2	Interrupt alpelisib dose. Initiate or intensify appropriate medical therapy and monitor as clinically indicated. If diarrhoea improves to grade $\leq 1$ , then resume alpelisib at same dose level. If diarrhoea recurs as grade $\geq 2$ , interrupt alpelisib dose until improvement to grade $\leq 1$ , then resume alpelisib at the next lower dose level.
Grade 3	Interrupt alpelisib dose. Initiate or intensify appropriate medical therapy and monitor as clinically indicated. If diarrhoea improves to grade $\leq 1$ , then resume alpelisib at the next lower dose level. Patients should additionally be managed according to local standard of care, including electrolyte monitoring, administration of antiemetics and antidiarrhoeal medicinal products and/or fluid replacement and electrolyte supplements, as clinically indicated.
Grade 4	Permanently discontinue alpelisib. Patients should additionally be managed according to local standard of care, including electrolyte monitoring, administration of antiemetics and antidiarrhoeal medicinal products and/or fluid replacement and electrolyte supplements, as clinically indicated.

### Hyperglycaemia

Dose modification and management should only be based on fasting glucose (FG) (plasma/blood) values.

FG >ULN-160mg/dl or >ULN-8.9mmol/l	No alpelisib dose adjustment required. Initiate or intensify oral antidiabetic treatment.
FG >160-250mg/dl or >8.9-13.9mmol/l	No alpelisib dose adjustment required. Initiate or intensify oral antidiabetic treatment. If FG does not decrease to $\leq 160$ mg/dl or 8.9mmol/l within 21 days with appropriate oral antidiabetic treatment, reduce alpelisib dose by 1 dose level and follow FG-value-specific recommendations.
FG >250-500mg/dl or >13.9- 27.8mmol/l	Interrupt alpelisib. Initiate or intensify oral antidiabetic treatment and consider additional antidiabetic medicinal products such as insulin for 1-2 days until hyperglycaemia resolves, as clinically indicated. Administer intravenous hydration and consider appropriate treatment (eg intervention for electrolyte / ketoacidosis / hyperosmolar disturbances). If FG decreases to $\leq 160$ mg/dl or 8.9mmol/l within 3 to 5 days under appropriate antidiabetic treatment, resume alpelisib at next lower dose level. If FG does not decrease to $\leq 160$ mg/dl or 8.9mmol/l within 3 to 5 days under appropriate antidiabetic treatment, consultation with a healthcare professional with expertise in the treatment of hyperglycaemia is recommended. If FG does not decrease to $\leq 160$ mg/dl or 8.9mmol/l within 21 days following appropriate antidiabetic treatment permanently discontinue alpelisib treatment
FG >500mg/dl or $\geq 27.8$ mmol/l	Interrupt alpelisib. Initiate or intensify appropriate antidiabetic treatment (administer intravenous hydration and consider appropriate treatment [eg intervention for electrolyte / ketoacidosis / hyperosmolar disturbances]), re-check within 24 hours and as clinically indicated. If FG decreases to $\leq 500$ mg/dl or $\leq 27.8$ mmol/l, then follow FG-value-specific recommendations for $< 500$ mg/dl. If FG is confirmed at $> 500$ mg/dl or $\geq 27.8$ mmol/l after 24 hours, permanently discontinue alpelisib treatment.

Applicable antidiabetic medicinal products, such as metformin, SGLT2 inhibitors or insulin sensitisers (such as thiazolidinediones or dipeptidyl peptidase-4 inhibitors), should be initiated and the respective prescribing information should be reviewed for dosing and dose titration recommendations, including local diabetic treatment guidelines. Metformin was recommended in the phase III clinical study with the following guidance: Metformin should be initiated at 500mg once daily. Based on tolerability, the metformin dose may be increased to 500mg twice daily, followed by 500mg with breakfast, and 1000mg with the evening meal, followed by further increase to 1000mg twice daily if needed.

As recommended in the phase III clinical study, insulin may be used for 1-2 days until hyperglycaemia resolves. However, this may not be necessary in the majority of cases of alpelisib-induced hyperglycaemia, given the short half-life of alpelisib and the expectation that glucose levels will normalise following interruption of alpelisib.

## Rash

All grades	Consultation with a dermatologist should always be considered
Grade 1 (<10% BSA with active skin toxicity).	No alpelisib dose adjustment required. Initiate topical corticosteroid treatment. Consider adding oral antihistamine treatment to manage symptoms. If active rash is not improved within 28 days of appropriate treatment, add a low dose systemic corticosteroid.
Grade 2 (10-30% BSA with active skin toxicity)	No alpelisib dose adjustment required. Initiate or intensify topical corticosteroid and oral antihistamine treatment. Consider low-dose systemic corticosteroid treatment. If rash improves to grade $\leq 1$ within 10 days, systemic corticosteroid may be discontinued.
Grade 3 (e.g. severe rash not responsive to medical management) (>30% BSA with active skin toxicity)	Interrupt alpelisib until rash improves to grade $\leq 1$ . Initiate or intensify topical/systemic corticosteroid and antihistamine treatment. Once rash improves to grade $\leq 1$ , resume alpelisib at next lower dose level.
Grade 4 (e.g. severe bullous, blistering or exfoliating skin conditions) (any % BSA associated with extensive superinfection, with intravenous antibiotics indicated; life-threatening consequences)	Permanently discontinue alpelisib.

## Other toxicities (excluding diarrhoea, hyperglycaemia and rash)

Grade 1 or 2	No alpelisib dose adjustment required. Initiate appropriate medical therapy and monitor as clinically indicated.
Grade 3	Interrupt alpelisib dose until improvement to grade $\leq 1$ , then resume alpelisib at the next lower dose level.
Grade 4	Permanently discontinue alpelisib.

## Hepatic impairment

### Alpelisib

No dose adjustment is necessary in patients with mild, moderate or severe hepatic impairment (Child-Pugh class A, B or C, respectively).

### Fulvestrant

No dose adjustments are necessary in patients with mild or moderate hepatic impairment. However as fulvestrant exposure may be increased fulvestrant should be used with caution in these patients.

There is no data in patients with severe hepatic impairment.

## Renal impairment

### Alpelisib

Based on population pharmacokinetic analysis, no dose adjustment is necessary in patients with mild or moderate renal impairment.

Caution should be used in patients with severe renal impairment as there is no experience with alpelisib in this population.



## REFERENCES

1. SPC December 2021
2. CDF list [www.england.nhs.uk/publication/national-cancer-drugs-fund-list/](http://www.england.nhs.uk/publication/national-cancer-drugs-fund-list/)