

PALBOCICLIB (Ibrance) 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/) (PAL2)

1. Hormone receptor-positive, HER2-negative, locally advanced or metastatic, histologically or cytologically documented oestrogen receptor positive and her-2 negative breast cancer, without prior CDK 4/6 or everolimus treatment, breast cancer. PS 0, 1 or 2.

REGIMEN

Days 1 to 21 PALBOCICLIB 125mg once daily orally (then 7 days off)
Day 1 FULVESTRANT 500mg IM (and day 15 cycle 1 only)

CYCLE FREQUENCY AND NUMBER OF CYCLES

Every 28 days until disease progression or unacceptable toxicity.

ADMINISTRATION

Available as 75mg, 100mg and 125mg tablets

Swallow whole do not chew. Take at approximately the same time each day with food.

Grapefruit and grapefruit juice should be avoided while on Palbociclib

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 days 1 to 21

CONCURRENT MEDICATION REQUIRED

None required

EXTRAVASATION AND TYPE OF LINE / FILTERS

Not applicable

INVESTIGATIONS

Blood results before palbociclib administration

FBC baseline, every 2 weeks for 2 cycles, then every 4 weeks for 4 cycles, then may be reduced to every 2–3 months in patients with stable disease.

Platelets x 10⁹/L >50

LFTs baseline, every 2 weeks for 2 cycles, then every 4 weeks for 4 cycles, then as indicated

U&Es every 4 weeks, then may be reduced in line with FBC monitoring

MAIN TOXICITIES AND ADVERSE REACTIONS

Palbociclib	Neutropenia, infections, fatigue, diarrhoea, nausea, mucositis, alopecia
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INTERACTIONS WHICH MAY REQUIRE DOSE MODIFICATIONS

(not exhaustive list check SPC/BNF/Stockleys)

Palbociclib	Strong CYP3A4 inhibitors (eg clarithromycin, itraconazole, posaconazole, voriconazole) should be avoided. CYP3A4 inducers (eg carbamazepine, phenytoin) should be avoided. Grapefruit and grapefruit juice should be avoided
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DOSE MODIFICATIONS

Palbociclib

Doses may be held as needed for toxicity resolution during a 4-week cycle.

Doses omitted for toxicity are not replaced or restored within the same cycle. Patients should instead resume Palbociclib at the next planned treatment cycle.

Patients requiring more than 2 dose reductions should be considered for discontinuation from Palbociclib treatment.

Dose Level Palbociclib for 3 out of 4 weeks

Starting dose 125mg / day

-1 100mg / day

-2 75mg / day

Palbociclib dose reduction below 75mg / day is not allowed.

Haematological

Continue fulvestrant during palbociclib treatment breaks for toxicity

Palbociclib

Neutrophils 0.5–0.99x10 ⁹ /l	Day 1 of each cycle Delay starting the next cycle until neutrophils ≥1.0x10 ⁹ /l then re-start at the same dose Day 15 of cycles 1 & 2 If neutrophils 0.5-1.0 x10 ⁹ /l continue at same dose to complete cycle, but repeat FBC on day 22. Consider a dose reduction for subsequent cycles if neutrophils take >1 week to return to ≥1.0x10 ⁹ /l, or if 2nd occurrence of neutrophils 0.5–0.99x10 ⁹ /l on day 1 of subsequent cycles.
Neutrophils 0.5-1.0x10 ⁹ /l and fever ≥38.5°C and/or infection (0.5-0.9x10 ⁹ /l)	At any time withhold treatment until neutrophils ≥1.0x10 ⁹ /l then re-start at next lower dose
Neutrophils <0.5x10 ⁹ /l.	At any time withhold treatment until neutrophils ≥1.0x10 ⁹ /l then re-start at next lower dose

Non-haematological

Palbociclib

Grade 1-2 toxicity	No dose adjustment required
Grade 3-4 toxicity, persisting despite medical treatment	Withhold palbociclib until symptoms resolve to grade ≤1 (or grade ≤2 if not considered a safety risk for the patient), then resume at the next lower dose

Hepatic impairment

Palbociclib

Child-Pugh scores are based on ascites, encephalopathy, INR, albumin, total bilirubin

Mild hepatic impairment (Child-Pugh A)	No dose adjustment is required
Moderate hepatic impairment (Child-Pugh B)	No dose adjustment is required
Severe hepatic impairment (Child-Pugh C)	the recommended dose is 75mg.

Renal impairment

Palbociclib

CrCl \geq 15ml/min	No dose adjustment required
Requiring haemodialysis	Insufficient data are available to provide any dose adjustment recommendation.

REFERENCES

1. CDF November 2017
2. SPC Dec 2019
3. Turner, N et al; NEJM 2018; 379: 1926-1936