PALBOCICLIB (Ibrance) (with aromatase inhibitor)

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/) (PAL1)

1. The treatment of previously untreated, histologically or cytologically documented, hormone receptor-positive, HER2-negative, without prior CDK 4/6 treatment locally advanced or metastatic breast cancer amenable to curative treatment, without previous hormone therapy for locally advanced or metastatic disease (previous hormone therapy with anastrazole or letrozole whether as adjuvant therapy or as neoadjuvant treatment is allowed as long as the patient has had a disease-free interval of 12 months or more since completing treatment with neoadjuvant or adjuvant anastrazole or letrozole). PS 0, 1 or 2. (TA495)

REGIMEN

Days 1 to 21 PALBOCICLIB 125mg PO once daily oral (then 7 days off)
Aromatase inhibitor (prescribe appropriate support regimen)

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

ANTI-EMETICS

Low risk days 1 to 21

CONCURRENT MEDICATION REQUIRED

Aromatase inhibitor (letrozole or anastrazole (or exemestane but exemestane would make patients ineligible for 2nd line everolimus)) must be prescribed (may be by GP)

EXTRAVASATION AND TYPE OF LINE / FILTERS

Not applicable

INVESTIGATIONS

Blood results required 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 10^9/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 TOXICITES AND ADVERSE REACTIONS

Palbociclib	Neutropenia, infections, fatigue, diarrhoea, nausea,; mucositis, alopecia

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

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

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

REFERENCES

1. CDF
2. SPC Dec 2019
3. Finn, R et al ; NEJM 2016; 375: 1925-1936