Palbociclib (in combination with an aromatase inhibitor)

Indication

First line endocrine therapy for hormone receptor positive, HER2 negative, locally advanced or metastatic breast cancer.

Patients should not have received previous hormone therapy for locally advanced/metastatic breast cancer. Previous hormone therapy with anastrozole or letrozole 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 anastrozole or letrozole.

Patients should be post-menopausal. If pre- or peri- menopausal, prior to starting treatment patients should have undergone ovarian suppression with LHRH agonist treatment or had bilateral oophorectomy.

(NICE TA495)

ICD-10 codes

Codes with a pre fix C50.

Regimen details

Day	Drug	Dose	Route
1-21	Palbociclib	125mg OD	PO

This should be prescribed in combination with an aromatase inhibitor.

Cycle frequency

28 days.

Palbociclib should be taken for 21 days followed by a 7 day break. The aromatase inhibitor should be taken continuously.

Number of cycles

Until disease progression or unacceptable toxicity.

Administration

Palbociclib is available as 125mg, 100mg and 75mg capsules. The capsules should be swallowed whole and not chewed, crushed or opened. The dose should be taken with food, preferably a meal.

Grapefruit and grapefruit juice should be **avoided** whilst taking palbociclib.

Patients should be advised to take the dose at approximately the same time each day. If a patient vomits or misses a dose an additional dose should not be taken that day but the next prescribed dose should be taken as planned.

Pre-medication

Nil

Emetogenicity

This regimen has mild emetic potential.

Additional supportive medication
Nil

Extravasation
N/A

Investigations – pre first cycle

Investigation	Validity period
FBC	14 days
U+Es (including creatinine)	14 days
LFTs	14 days

Investigations – pre subsequent cycles

Investigation	Validity period
FBC	72 hours and on day 14 for the first 2 cycles*
U+Es (including creatinine)	72 hours
LFTs	72 hours

*If neutrophils <1.0 x 10^9/L or platelets < 50 x 10^9/L where possible repeat on day 1 of planned cycle

Standard limits for administration to go ahead
If blood results not within range, authorisation to administer **must** be given by prescriber/ consultant

Investigation	Limit
Neutrophils	≥ 1.0 x 10^9/L
Platelets	≥ 50 x 10^9/L
CrCl	≥ 30mL/min
Bilirubin	< 1.5 x ULN
AST/ALT	< ULN

Dose modifications
Dose reductions should follow the table below:

Dose level	Dose
Full dose	125mg OD
First reduction	100mg OD
Second reduction	75mg OD

Dose reductions below 75mg OD are not recommended and if required treatment should be discontinued.

- **Haematological toxicity**

On day 1 neutrophils ≥ 1.0 x 10^9/L and platelets ≥ 50 x 10^9/L.
Dose interruption, dose reduction, or delay in starting treatment cycles is recommended for patients who develop grade 3 or 4 neutropenia.

Haematological toxicity	Dose
Grade 1-2 (neutrophils ≥ 1.0 x 10^9/L)	No dose modification required.
Grade 3 (neutrophils 0.5- 1.0 x 10^9/L)	**Day 1:** Withhold and repeat FBC. When recovered to ≤ grade 2 start next cycle at the same dose). **Day 14:** Continue to complete cycle and repeat FBC on day 21. Consider dose reduction if not recovered within 7 days or recurrent neutropenia.
Grade 3 (neutrophils 0.5- 1.0 x 10^9/L) with fever +/- infection	Withhold until recovered to ≤ grade 2. Resume with one dose level reduction.

Grade 4 (neutrophils < 0.5 x 10^9/L)	Withhold until recovered to ≤ grade 2. Resume with one dose level reduction.

- **Renal impairment**

Palbociclib should be administered with caution and close monitoring for signs of toxicity in severe renal impairment (CrCl <30mL/min).

- **Hepatic impairment**

Palbociclib should be administered with caution in moderate to severe hepatic impairment (bilirubin > 1.5 x ULN and/or AST/ALT > ULN). The risk and benefits should be carefully considered and patients should be closely monitored for signs of toxicity.

- **Other toxicities**

For any other non-haematological toxicity ≥ Grade 3; withhold until ≤ Grade 1 (≤ Grade 2 if not considered safety risk) then resume with one dose level reduction.

Adverse effects - for full details consult product literature/ reference texts

- **Serious side effects**

Neutropenia, anaemia, leukopenia.
Infections

- **Frequently occurring side effects**

Neutropenia, anaemia, leukopenia.
Thrombocytopenia
Infections
Fatigue
Nausea and vomiting
Stomatitis
Rash, dry skin
Alopecia
Diarrhoea

- **Other side effects**

Reduced appetite
Dysgeusia
Blurred vision
Dry eyes
Increased transaminases

Significant drug interactions – for full details consult product literature/ reference texts

Strong CYP3A4 inhibitors (e.g. clarithromycin, indinavir, itraconazole, ketoconazole, lopinavir/ritonavir, nefazodone, nelfinavir, posaconazole, saquinavir, telaprevir, telithromycin, voriconazole, grapefruit): Concomitant use of strong inhibitors should be avoided due to increased risk of toxicity. If co-administrated is deemed essential the dose of palbociclib should be reduced to 75mg daily and patients closely monitored.

Strong CYP3A4 inducers (e.g. carbamazepine, enzalutamide, phenytoin, rifampin, and St. John's Wort)**:** Concomitant use may reduce the exposure of palbociclib and should therefore be avoided.

Additional comments

Women of childbearing potential or their male partners must use a highly effective method of contraception.

This medicinal product contains lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp

lactase deficiency, or glucose-galactose malabsorption should not take this medicine.

References

- National Institute for Clinical Excellence (TA495) accessed 24 January 2018 via www.nice.org.uk
- Summary of Product Characteristics Palbociclib (Pfizer) accessed 24 January 2018 via www.medicines.org.uk
- Finn, R et al; The cyclin-dependent kinase 4/6 inhibitor palbociclib in combination with letrozole versus letrozole alone as first-line treatment of oestrogen receptor-positive, HER2-negative, advanced breast cancer (PALOMA-1/TRIO-18): a randomised phase 2 study. The Lancet Oncology. 2015. Volume 16:1 p25-35.
- Finn, R et al; Palbociclib and letrozole in advanced breast cancer. NEJM 2016 ; 375 : 1925 – 1936.

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