Palbociclib

Indication

Treatment of hormone receptor positive, Her2 negative locally advanced or metastatic breast cancer

- In combination with an aromatase inhibitor
- In combination with fulvestrant in women who have received prior endocrine therapy

In pre or perimenopausal women, the endocrine therapy should be combined with a LHRH agonist

Regimen details

Palbociclib 125mg orally once daily for 21 days

Cycle frequency

Every 28 days (i.e. three weeks on treatment with a week off)

For patients who experience a maximum of grade 1 or 2 neutropenia in the previous 6 cycles, patients may be changed to the 3-monthly regimen. Patients will be supplied with a pack of 63 capsules and instructed to take them in a "three weeks on, one week off" cycle.

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

3-monthly supply:
For patients who experience a maximum of grade 1 or 2 neutropenia in the previous 6 cycles, patients may be changed to the 3-monthly regimen. Patients will be supplied with a pack of 63 capsules and instructed to take them in a "three weeks on, one week off" cycle. These patients only need to have their bloods checked every 3 months (i.e. prior to each supply)

Pre-medication

None

Emetogenicity

Mild

Additional supportive medication

Supply metoclopramide and loperamide with first cycle

Extravasation

N/A

Investigations – pre first cycle

Investigation	Validity period
FBC	14 days
U+E (including creatinine)	14 days
LFT (including AST)	14 days

Investigations –pre subsequent cycles

FBC, U+E (including creatinine), LFT (including AST)
Clinical toxicity assessment for infection, bleeding, thromboembolism, fatigue, GI effects and neuropathy

Patients who are receiving 3-monthly supplies only need to have their bloods checked every 3 months (i.e. prior to each supply)

Standard limits for administration to go ahead

If blood results not within range, authorisation to administer **must** be given by prescriber/ consultant.

Investigation	Limit
Neutrophil count	≥ 1.0 x 10^9/L
Platelet count	≥ 50 x 10^9/L
Creatinine clearance	≥ 30 mL/min
Bilirubin	≤ 1.5 x ULN
AST	≤ 3 x ULN

Dose modifications

Dose reductions should follow the table below:

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

Haematological Toxicity Grades

Neutropenia	
Grade	**Neutrophils (x 10^9/L)**
1	≥ 1.5-2
2	≥ 1-1.5
3	≥ 0.5-1
4	<0.5

Thrombocytopenia	
Grade	**Platelets (x 10^9/L)**
1	≥ 75-150
2	≥ 50-75
3	≥ 25 – 50
4	< 25

Haematological Toxicity:

Grade	Dose
1-2	No dose modification required
3	Withhold and repeat FBC. When recovered to ≤ grade 2 start next cycle at the same dose Consider dose reduction if not recovered within 7 days or recurrent neutropenia
3 with fever +/- infection	Withhold until recovered to ≤ grade 2 Resume with one dose level reduction
4	Withhold until recovered to ≤ grade 2 Resume with one dose level reduction

Non-haematological Toxicity

Grade	Dose
1 or 2	No change
3 or 4	Delay until recovery to ≤ grade 2. Restart at next lower dose level

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

Hepatic impairment
No dose adjustment of palbociclib is required for patients with mild or moderate hepatic impairment (Child-Pugh classes A and B). For patients with severe hepatic impairment (Child-Pugh class C), the recommended dose of palbociclib is 75 mg once daily

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, rifampicin, 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

Ibrance SPC - https://www.medicines.org.uk/emc/product/7945/smpc

SWCN protocols - http://www.swscn.org.uk/guidance-protocols/cancer-protocols/

THIS PROTOCOL HAS BEEN DIRECTED BY DR EATON, CONSULTANT ONCOLOGIST

RESPONSIBILITY FOR THIS PROTOCOL LIES WITH THE HEAD OF SERVICE

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