# PALBOCICLIB

An option for previously untreated, hormone receptor-positive, HER2 -ve, locally advanced or metastatic breast cancer, in combination with an aromatase inhibitor

Female patients must be post-menopausal, whether natural or induced

The patient must have a disease-free interval of ≥ 12 months since completing any neo-adjuvant or adjuvant treatment with anastrazole or letrozole.

***Blueteq registration is required before treatment may start***

*No previous treatment with ribociclib, unless ribociclib has had to be stopped within 3 months of its start solely as a consequence of dose-limiting toxicity and in the clear absence of disease progression*

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| Drug/Dosage: | **Palbociclib** | initiate at 125mg po once daily on Days 1 – 21, then 7 days, rest |
| Other Drugs: | An oral aromatase inhibitor (*letrozole, anastrazole or exemestane)* | |
| Administration: | Palbociclib is available as 75mg, 100mg and 125mg capsules which should be swallowed whole with food, preferably a meal. Grapefruit and grapefruit juice should be avoided while on palbociclib. | |
| Frequency: | Every 28 days (21 days of treatment, then 7 days rest)<br>Toxicity check at Day 14 of Cycle 1 +/- Cycle 2<br>Continue until disease progression or unacceptable adverse events | |
| Main Toxicities: | neutropenia; infections; fatigue; diarrhoea; nausea; mucositis; alopecia | |
| Anti- emetics: | mildly emetogenic | |
| Regular Investigations: | FBC | baseline, Day 1 of each cycle, plus Day 14 of Cycles 1 and 2*<br>May be reduced to every 2 – 3 months, in stable patients |
| | LFTs | Day 1 of each cycle, then may be reduced in line with FBC monitoring |
| | U&Es | Day 1 of each cycle, then may be reduced in line with FBC monitoring |

*may omit Day 14 of Cycle 2, if no previous problems or concerns with FBC

Interactions: Elimination of palbociclib is mainly through hepatic metabolism.

Concomitant use of strong CYP3A inhibitors (e.g. clarithromycin, itraconazole, posaconazole, voriconazole, grapefruit or grapefruit juice) should be avoided, as it may lead to increased toxicity. If co-administration is unavoidable, reduce palbociclib to 75mg once daily.
When the strong inhibitor is discontinued, increase palbociclib back to the previous dose, after 3 to 5 half-lives of the inhibitor drug.
No dose adjustment is required for moderate CYP3A inhibitors (e.g. erythromycin, fluconazole, verapamil).

Concomitant use of strong CYP3A inducers (e.g. carbamazepine, phenytoin, St John's wort) should be avoided as it may result in loss of efficacy.
Moderate CYP3A inducers do not require a dose adjustment of palbociclib.


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| Reason for Update: N/A | Approved by Consultant: Dr T Crook |
| Version: 1 | Approved by Lead Chemotherapy Nurse: S Wills-Percy |
| Supersedes: any compassionate use protocol | Date: 22.11.17 |
| Prepared by: S Taylor | Checked by: C Tucker |

**Dose Modifications** Dose reductions steps are 125mg → 100mg → 75mg
Dose reduction below 75mg/day is not recommended; treatment must instead be discontinued.

Haematological Toxicity:

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| Neutrophils 0.5 – 0.99 x $10^9$/l or Platelets 25 - 49 x $10^9$/l | ***Day 1 of each cycle:*** Delay starting the next cycle until neutrophils ≥ 1.0 x $10^9$/l and platelets ≥ 50 x $10^9$/l; then re-start at the same dose<br>***Day 14 of cycles 1 & 2:*** Continue at same dose to complete cycle, but repeat FBC on Day 21. Consider a dose reduction for subsequent cycles if neutrophils take > 1 week to return to ≥ 1.0 x $10^9$/l, or if 2nd occurrence of neutrophils 0.5 – 0.99 x $10^9$/l. |
| Neutrophils < 0.5 x $10^9$/l or Platelets < 25 x $10^9$/l or Grade 3 febrile neutropenia (neuts 0.5 - 0.9 x $10^9$/l) | Withhold treatment until neutrophils ≥ 1.0 x $10^9$/l and platelets ≥ 50 x $10^9$/l; then re-start at next lower dose |

Non-haematological Toxicities*:

| Non-Haematological Toxicity* | Palbociclib dose adjustment |
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| 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 |

*Also consider toxicity related to the aromatase inhibitor

Hepatic Impairment: Note that palbociclib is extensively hepatically metabolised.

| Degree of hepatic impairment | Palbociclib Dose |
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| Bilirubin ≤ ULN and AST/ALT > ULN or Bilirubin 1 – 1.5 x ULN and any AST/ALT | No dose adjustment required |
| Bilirubin > 1.5 x ULN and any AST/ALT | Insufficient data to recommend a dose reduction. Use only after careful consideration of the risks and benefits, and monitor closely for toxicity |

Renal Impairment: No dose adjustment required if CrCl ≥ 30 ml/min. Insufficient data are available if CrCl < 30ml/min, or if requiring haemodialysis, to provide any dose adjustment recommendation. If CrCl < 30ml/min, consider carefully the potential benefits and risks before starting, and monitor patient closely.

References:
Finn, R et al ; NEJM 2016 ; 375 : 1925 - 1936