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| **Indication** | For the treatment of hormone receptor-positive, HER2 negative, locally advanced or metastatic breast cancer in people who have had previous endocrine therapy only if:<br>The patient either has:<br><br>• progressive disease whilst still receiving adjuvant or neoadjuvant endocrine therapy for early breast cancer with no subsequent endocrine therapy received following disease progression.<br>• progressive disease within 12 or less months of completing adjuvant endocrine therapy for early breast cancer with no subsequent endocrine therapy received following disease progression.<br>• progressive disease on 1st line endocrine therapy for advanced/metastatic breast cancer with no subsequent endocrine therapy received following disease progression.<br><br>NB The patient should have had no prior treatment with a CDK 4/6 inhibitor unless either abemaciclib (in combination with fulvestrant) or ribociclib (in combination with fulvestrant) has had to be stopped solely as a consequence of dose-limiting toxicity and in the clear absence of disease progression or a CDK 4/6 inhibitor has been previously received as adjuvant therapy and treatment was completed without disease progression at least 12 months prior to the first diagnosis of recurrent or metastatic disease. |
| **Treatment Intent** | Palliative |
| **Frequency and number of cycles** | 28 days<br>Until disease progression or excessive toxicity or patient choice to discontinue. |
| **Monitoring Parameters** | • **Virology screening:** All new patients referred for systemic anti-cancer treatment should be screened for hepatitis B and C and the result reviewed prior to the start of treatment. Patients not previously tested who are starting a new line of treatment, should also be screened for hepatitis B and C. Further virology screening will be performed following individual risk assessment and clinician discretion.<br>• Monitor **FBCs**, **U&Es** and **LFTs** at baseline, day 15 of cycle 1 then at the beginning of each cycle for 6 months and then every 3 months thereafter or as clinically indicated.<br>• If neuts >/= 1 and PLT >/= 100 proceed with treatment.<br>• If neuts >/= 1 and PLT 76 to 99 give one month's supply of palbociclib and inform consultant, proceed with fulvestrant.<br>• If neuts >/= 1 and PLT 50 to 75 withhold palbociclib and discuss with consultant, proceed with fulvestrant.<br>• If PLT >/=100 and neuts <1 proceed with fulvestrant, withhold palbociclib and alert consultant<br>• NB SPC recommendation; patients can receive palbociclib if neuts >/=1 and PLT >/=50<br>• **NB**: Platelets should be >/=50 for intramuscular injection with fulvestrant.<br>• The most common Grade >/= 3 adverse reactions of palbociclib were neutropenia, leukopenia, anaemia, fatigue, and infections.<br>• If patient is pre or peri-menopausal they must have undergone ovarian ablation or suppression with LHRH agonist treatment.<br>• **Dose Modifications**:<br>• **Palbociclib:** First dose reduction to 100mg/day, second dose reduction to 75mg/day. If further dose reduction required, discontinue treatment.<br>• For haematological toxicities see table 1 and guidance above, for non-haematological toxicities see table 2. |

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| | • **Hepatic impairment:**<br>• **Palbociclib** 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 for 21 consecutive days followed by 7 days off treatment.<br>• **Fulvestrant:** no dose adjustment in mild or moderate impairment, use with caution. No data for the use of fulvestrant in severe hepatic impairment.<br>• **Renal impairment:**<br>• **Palbociclib** No dose adjustment of palbociclib is required for patients with mild, moderate or severe renal impairment (CrCl ≥15 mL/min). Insufficient data are available in patients requiring haemodialysis to provide any dose adjustment recommendation.<br>• **Fulvestrant** No dose adjustment of fulvestrant is required for patients with mild or moderate renal impairment (CrCl ≥30 mL/min). Insufficient data are available in patients with severe renal impairment to provide any dose adjustment recommendation, administer with caution.<br>• **Interstitial lung disease/pneumonitis**<br>Monitor patients for pulmonary symptoms indicative of ILD/pneumonitis (e.g. hypoxia, cough, dyspneoa). In patients who have new or worsening respiratory symptoms and are suspected to have developed ILD/pneumonitis, interrupt palbociclib immediately and evaluate the patient. Permanently discontinue in patients with severe ILD or pneumonitis. NB: Funding arrangements for continuing single agent fulvestrant should be confirmed.<br>• **Venous thromboembolic events:** Monitor patients for clinical signs and symptoms of venous thrombosis and pulmonary embolism and treat as medically appropriate.<br>• **<u>Common drug interactions</u>: (for comprehensive list refer to BNF/SPC)** Avoid concomitant use of palbociclib with strong CYP3A inhibitors (e.g. ketoconazole, itraconazole, clarithromycin) and consider an alternative medication with no or minimal CYP3A inhibition. If patients must be co-administered a strong CYP3A inhibitor, reduce palbociclib dose to 75mg/day. If the strong inhibitor is discontinued, increase the palbociclib dose (after 3-5 half-lives of the inhibitor) to the dose used prior to the initiation of the strong CYP3A inhibitor.<br>Concomitant use of palbociclib with strong CYP3A4 inducers (carbamazepine, phenytoin, rifampicin) should be avoided as it may lead to reduced palbociclib exposure.<br>Use with St John's Wort is contraindicated.<br>Caution with CYP3A substrates with a narrow therapeutic index (e.g. ciclosporine, fentanyl, tacrolimus); the dose of these may need to be reduced as palbociclib may increase their exposure.<br>• **Driving and machinery:** Palbociclib may cause fatigue and patients should exercise caution when driving or using machines.<br>• For oral self-administration: refer to local Trust policy on oral anti-cancer medicines and supply Patient Information Leaflet and Macmillan information sheet. |
| **References** | CDF list V1.408 accessed online 26.10.2026 KMCC protocol BRE-073 V4 |

NB for funding information, refer to CDF and NICE Drugs Funding List

**Table 1: SPC recommended dose modifications for Haematological Toxicities Table applies to all haematological adverse reactions except Lymphopenia (unless associated with clinical events, e.g., opportunistic infections).**
**NB SPC recommendations are provided for information. Haematological parameters agreed by KMCC breast NOG differ. See monitoring parameters above for NOG guidance.**

| CTCAE grade | Dose modifications |
|---|---|
| Grade 1 or 2 | No dose adjustment is required. |
| Grade 3 | **Day 1 of cycle**:<br>Withhold palbociclib, until recovery to Grade ≤ 2, and repeat complete blood count monitoring within 1 week. When recovered to Grade ≤ 2, start the next cycle at the *same dose*.<br>**Day 15 of cycle 1:**<br>If Grade 3 on Day 15, continue palbociclib at the *current dose* to complete cycle and repeat complete blood count on Day 22.<br>If Grade 4 on Day 22, see Grade 4 dose modification guidelines below.<br>Consider dose reduction in cases of prolonged (> 1 week) recovery from Grade 3 neutropenia or recurrent Grade 3 neutropenia on Day 1 of subsequent cycles. |
| Grade 3 ANC[b]<br>(< 1 to 0.5) + Fever ≥ 38.5 °C and/or infection | At any time:<br>Withhold palbociclib until recovery to Grade ≤ 2<br>Resume at next lower dose. |
| Grade 4 | At any time:<br>Withhold palbociclib until recovery to Grade ≤ 2.<br>Resume at next lower dose. |
| Grading according to CTCAE 4.0.<br>ANC=absolute neutrophil counts; CTCAE=Common Terminology Criteria for Adverse Events; LLN=lower limit of normal.<br>[b] ANC: Grade 1: ANC LLN - < 1.5; Grade 2: ANC 1 - <1.5; Grade 3: ANC 0.5 - < 1; Grade 4: ANC < 0.5 | |

**Table 2 Non-haematological toxicities**

| CTCAE Grade | Dose modifications of palbociclib |
|---|---|
| Grade 1 or 2 | No dose adjustment is required. |
| Grade ≥3 non-haematological toxicity (if persisting despite medical treatment) | Withhold until symptoms resolve to:<br>• Grade ≤1;<br>• Grade ≤2 (if not considered a safety risk for the patient)<br>Resume at the next lower dose. |

**Cycle 1: Cycle length- 28 days**

| Day | Drug | Dose | Route | Injection Duration | Administration |
|---|---|---|---|---|---|
| 1 | **FULVESTRANT** | **500mg** | intramuscular | Each 5ml (250mg) injection over 1-2 minutes | Administered as 2 x 250mg (5ml) injections, one in each buttock. |
| 15 | **FULVESTRANT** | **500mg** | intramuscular | Each 5ml (250mg) injection over 1-2 minutes | Administered as 2 x 250mg (5ml) injections, one in each buttock. |
| TTO | Drug | Dose | Route | Directions | |
| Day 1 | **PALBOCICLIB** | **125mg** | PO | Once DAILY for 21 days followed by a 7 day break.<br>Swallow whole, do not chew, crush or split tablets.<br>Take the dose at approximately the same time each day.<br>If a dose is missed or vomiting occurs, an additional dose should not be taken that day.<br>Do not take with grapefruit or grapefruit juice.<br>Available as 125mg, 100mg or 75mg tablets. | |
| | Metoclopramide | 10mg | PO | 10mg TDS PRN.<br>Do not take for more than 5 days continuously.<br>Dispense with cycle 1 and then only if required. | |

**Cycle 2 onwards: repeat every 28 days**

| Day | Drug | Dose | Route | Injection Duration | Administration |
|---|---|---|---|---|---|
| 1 | **FULVESTRANT** | **500mg** | intramuscular | Each 5ml (250mg) injection over 1-2 minutes | Administered as 2 x 250mg (5ml) injections, one in each buttock. |
| TTO | Drug | Dose | Route | Directions | |
| 1 | **PALBOCICLIB** | **125mg** | PO | Once DAILY for 21 days followed by a 7 day break.<br>Swallow whole, do not chew, crush or split tablets.<br>Take the dose at approximately the same time each day.<br>If a dose is missed or vomiting occurs, an additional dose should not be taken that day.<br>Do not take with grapefruit or grapefruit juice.<br>Available as 125mg, 100mg or 75mg tablets. | |
| | Metoclopramide | 10mg | PO | 10mg TDS PRN.<br>Do not take for more than 5 days continuously.<br>Only supply if required. | |