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: The patient either has: • progressive disease whilst still receiving adjuvant or neoadjuvant endocrine therapy for early breast cancer with no subsequent endocrine therapy received following disease progression. • 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. • progressive disease on 1st line endocrine therapy for advanced/metastatic breast cancer with no subsequent endocrine therapy received following disease progression. 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 within 6 months of its start 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 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. • 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. • If neuts >/= 1 and PLT >/= 100 proceed with treatment. • If neuts >/= 1 and PLT 76 to 99 give one month's supply of palbociclib and inform consultant, proceed with fulvestrant. • If neuts >/= 1 and PLT 50 to 75 withhold palbociclib and discuss with consultant, proceed with fulvestrant. • If PLT >/=100 and neuts <1 proceed with fulvestrant, withhold palbociclib and alert consultant • NB SPC recommendation; patients can receive palbociclib if neuts >/=1 and PLT >/=50 • **NB**: Platelets should be >/=50 for intramuscular injection with fulvestrant. • The most common Grade >/= 3 adverse reactions of palbociclib were neutropenia, leukopenia, anaemia, fatigue, and infections. • If patient is pre or peri-menopausal they must have undergone ovarian ablation or suppression with LHRH agonist treatment. • **Dose Modifications**: • **Palbociclib:** First dose reduction to 100mg/day, second dose reduction to 75mg/day. If further dose reduction required, discontinue treatment. • For haematological toxicities see table 1 and guidance above, for non-haematological toxicities see table 2.

	• **Hepatic impairment:** • **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. • **Fulvestrant:** no dose adjustment in mild or moderate impairment, use with caution. No data for the use of fulvestrant in severe hepatic impairment. • **Renal impairment:** • **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. • **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. • **Interstitial lung disease/pneumonitis** 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. • **Venous thromboembolic events:** Monitor patients for clinical signs and symptoms of venous thrombosis and pulmonary embolism and treat as medically appropriate. • **<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. Concomitant use of palbociclib with strong CYP3A4 inducers (carbamazepine, phenytoin, rifampicin) should be avoided as it may lead to reduced palbociclib exposure. Use with St John's Wort is contraindicated. 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. • **Driving and machinery:** Palbociclib may cause fatigue and patients should exercise caution when driving or using machines. • For oral self-administration: refer to local Trust policy on oral anti-cancer medicines and supply Patient Information Leaflet and Macmillan information sheet.
References	SPC accessed online 19.03.2026 KMCC protocol BRE-073 V3

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**: 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*. **Day 15 of cycle 1:** If Grade 3 on Day 15, continue palbociclib at the *current dose* to complete cycle and repeat complete blood count on Day 22. If Grade 4 on Day 22, see Grade 4 dose modification guidelines below. 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] (< 1 to 0.5) + Fever ≥ 38.5 °C and/or infection	At any time: Withhold palbociclib until recovery to Grade ≤ 2 Resume at next lower dose.
Grade 4	At any time: Withhold palbociclib until recovery to Grade ≤ 2. Resume at next lower dose.
Grading according to CTCAE 4.0. ANC=absolute neutrophil counts; CTCAE=Common Terminology Criteria for Adverse Events; LLN=lower limit of normal. [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: • Grade ≤1; • Grade ≤2 (if not considered a safety risk for the patient) Resume at the next lower dose.

Cycle 1: Cycle length- 28 days

Day	Drug	Dose	Route	Infusion 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. Swallow whole, do not chew, crush or split tablets. Take the dose at approximately the same time each day. If a dose is missed or vomiting occurs, an additional dose should not be taken that day. Do not take with grapefruit or grapefruit juice. Available as 125mg, 100mg or 75mg tablets.	
	Metoclopramide	10mg	PO	10mg TDS PRN. Do not take for more than 5 days continuously. Dispense with cycle 1 and then only if required.	

Cycle 2 onwards: repeat every 28 days

Day	Drug	Dose	Route	Infusion 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. Swallow whole, do not chew, crush or split tablets. Take the dose at approximately the same time each day. If a dose is missed or vomiting occurs, an additional dose should not be taken that day. Do not take with grapefruit or grapefruit juice. Available as 125mg, 100mg or 75mg tablets.	
	Metoclopramide	10mg	PO	10mg TDS PRN. Do not take for more than 5 days continuously. Only supply if required.	