Indication	The treatment of hormone receptor-positive, HER2-negative, locally advanced or metastatic breast cancer in people who have had previous endocrine therapy. 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 **or** • 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 **or** • progressive disease on 1st line endocrine therapy for advanced/metastatic breast cancer with no subsequent endocrine therapy received following disease progression. The patient should have had no prior treatment with a CDK 4/6 inhibitor unless either ribociclib (in combination with fulvestrant) or palbociclib (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	Every 28 days Until disease progression or excessive toxicity or patient choice to discontinue.
Monitoring parameters pre-treatment	• **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 U&Es, LFTs and FBC prior to the start of treatment, day 15 of cycle 1 and 2, then at each cycle for 4 months and then as clinically indicated thereafter. • If neuts <1.5 and/or PLT<100 and/ or Hb<80g/L prior to initiation of treatment d/w consultant. • For subsequent cycles if PLT >/=100 and neuts >/=1proceed with treatment. • If PLT 50-99 and neuts >/=1 proceed with fulvestrant, withhold abemaciclib and alert consultant. • If PLT >/=100 and neuts <1 proceed with fulvestrant, withhold abemaciclib and alert consultant. • If PLT <50 and neuts <1 delay both drugs for 1 week. • If neuts <1, see below for dose adjustments. • Pre- or peri-menopausal women should have undergone ovarian ablation or be treated with LHRH agonists. • **Renal impairment:** No dose adjustment of abemaciclib or 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 or those requiring haemodialysis to provide any dose adjustment recommendation, administer with caution. • **Hepatic impairment:** No dose adjustment of abemaciclib or fulvestrant is required for patients with mild or moderate hepatic impairment (Child-Pugh classes A and B), although use fulvestrant with caution. For patients with severe hepatic impairment (Child-Pugh class C), the dose frequency of abemaciclib should be reduced to once daily. D/W consultant if bilirubin >2 x ULN. • **Interstitial lung disease/pneumonitis:** Monitor patients for pulmonary symptoms indicative of ILD/pneumonitis (e.g. hypoxia, cough, dyspneoa). See table 3 below for dose modification and

	guidance in patients who have new or worsening respiratory symptoms and are suspected to have developed ILD/pneumonitis. • **Venous thromboembolism:** Patients should be monitored for signs and symptoms of deep vein thrombosis and pulmonary embolism and treated as medically appropriate. Based on the grade of VTE, abemaciclib may require dose modification, see table 4 below. • **Dose adjustments** • Dose reductions: 1st dose reduction to 100mg bd, 2nd dose reduction to 50mg bd • 1st occurrence of grade 3 haematological toxicity, excluding thrombocytopenia (e.g. neuts 0.5 – 0.99) suspend dose until toxicity resolves to Grade 2 or less (neuts >/=1), then resume at the same dose. Recurrence of grade 3 haematological toxicity excluding thrombocytopenia, suspend dose until toxicity resolves to Grade 2 or less, then resume at next lower dose level. • Grade 4 haematological toxicity excluding thrombocytopenia (neuts <0.5), suspend dose until toxicity resolves to Grade 2 or less (neuts >/=1), then resume at next lower dose level. • If platelets <100 discuss dose modification of abemaciclib with consultant. • NB: Platelets should be >/=50 for intramuscular injection with fulvestrant. • If patient requires administration of blood cell growth factors, suspend abemaciclib dose for at least 48 hours after the last dose of blood cell growth factors was administered and until toxicity resolves to Grade 2 or less then resume at next lower dose unless the dose was already reduced for the toxicity that led to the use of the growth factor. • **Management of diarrhoea:** Treat with loperamide. If grade 2 and toxicity does not resolve within 24 hours to grade 1 or less, suspend until resolution and restart at the same dose. For Grade 2 that persists or recurs after resuming the same dose or Grade 3 or 4 (or requires hospitalisation), suspend dose until toxicity resolves to Grade 1 or less and resume at next lower dose. • See tables 1 and 2 for management of increased aminotransferases and other non-haematological toxicities. • If a patient vomits or misses a dose of abemaciclib, the patient should be instructed to take the next dose at its scheduled time; an additional dose should not be taken. • **Drug interactions:** • Concomitant use of strong CYP3A4 inhibitors (eg ketoconazole, itraconazole, clarithromycin) should be avoided. If strong CYP3A4 inhibitors cannot be avoided, the abemaciclib dose should be reduced to 100 mg twice daily. In patients who have had their dose reduced to 100 mg abemaciclib twice daily and in whom co-administration of a strong CYP3A4 inhibitor cannot be avoided, the abemaciclib dose should be further reduced to 50 mg twice daily. In patients who have had their dose reduced to 50 mg abemaciclib twice daily and in whom co-administration of a strong CYP3A4 inhibitor cannot be avoided, the abemaciclib dose may be continued with close monitoring of signs of toxicity. Alternatively, the abemaciclib dose may be reduced to 50 mg once daily or discontinued. If the CYP3A4 inhibitor is discontinued, the abemaciclib dose should be increased to the dose used prior to the initiation of the CYP3A4 inhibitor (after 3 to 5 half-lives of the CYP3A4 inhibitor). • Concomitant use of abemaciclib with strong CYP3A4 inducers (carbamazepine, phenytoin, rifampicin, St Johns Wort) should be avoided as it may lead to reduced exposure. • Caution with narrow therapeutic index substrates of P-gp and BCRP, such as digoxin or dabigatran etexilate. • **Missed Dose:** If a patient vomits or misses a dose of abemaciclib, the patient should be instructed to take the next dose at its scheduled time; an additional dose should not be taken. • **Driving:** Patients should be advised to be cautious when driving or using machines in case they experience fatigue or dizziness during treatment with abemaciclib.

	• For oral self-administration: refer to local Trust policy on oral anti-cancer medicines and supply Patient Information Leaflet and Macmillan information sheet.
Reference(s)	SPC accessed on line 23.06.2022 CDF V1.344 accessed online 28.01.2025 KMCC protocol BRE-068 V2

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

Table 1. Management of increased aminotransferases

Toxicity	Management recommendations
Grade 1 (>ULN-3.0 x ULN) Grade 2 (>3.0-5.0 x ULN)	No dose adjustment required.
Persistent or Recurrent Grade 2, or Grade 3 (>5.0-20.0 x ULN)	Suspend dose until toxicity resolves to baseline or Grade 1. Resume at next lower dose.
Elevation in AST and/or ALT >3 x ULN WITH total bilirubin >2 x ULN, in the absence of cholestasis	Discontinue abemaciclib.
Grade 4 (>20.0 x ULN)	Discontinue abemaciclib.

Table 2. Management recommendations for non-haematological toxicities (excluding diarrhoea, increased aminotransferases, VTEs and interstitial lung disease (ILD)/pneumonitis)

Toxicity	Management recommendations
Grade 1 or 2.	No dose adjustment required.
Persistent or recurrent Grade 2 toxicity that does not resolve with maximal supportive measures to baseline or Grade 1 within 7 days	Suspend dose until toxicity resolves to Grade 1 or less. Resume at next lower dose.
Grade 3 or 4	

Table 3. Management recommendations for interstitial lung disease (ILD)/pneumonitis

Toxicity	Management recommendations
Grade 1 or 2	No dose adjustment required.
Persistent or recurrent Grade 2 toxicity that does not resolve with maximal supportive measures within 7 days to baseline or Grade 1	Suspend dose until toxicity resolves to baseline or Grade 1. Resume at next lower dose.
Grade 3 or 4	Discontinue abemaciclib.

Table 4: Management recommendations for venous thromboembolic events (VTEs)

Toxicity	Management recommendations
Advanced or metastatic breast cancer	
Grade 1 or 2	No dose modification is required.
Grade 3 or 4	Suspend dose and treat as clinically indicated. Abemaciclib may be resumed when the patient is clinically stable.

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	
1	**ABEMACICLIB**	**150mg**	PO	Twice DAILY for 28 days with or without food Swallow whole, do not chew or crush. Take the dose at approximately the same times each day. Do not take with grapefruit or grapefruit juice. This medicine may make you sleepy. If this happens, do not drive or use tools or machines. Available as 50mg, 100mg or 150mg tablets.	
	Loperamide	2-4mg	PO	Take 4mg (2 capsules) initially, then 2mg (1 capsule) after each loose stool when required. Maximum 16mg (8 capsules) a day. Dispense 30 capsules on cycle 1 then only if specified.	

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	**ABEMACICLIB**	**150mg**	PO	Twice DAILY for 28 days with or without food Swallow whole, do not chew or crush. Take the dose at approximately the same times each day. Do not take with grapefruit or grapefruit juice. This medicine may make you sleepy. If this happens, do not drive or use tools or machines. Available as 50mg, 100mg or 150mg tablets	