PROTOCOL

Systemic Anti Cancer Therapy Protocol

Abemaciclib
EARLY BREAST CANCER

PROTOCOL REF:
(Version No. _MPHAAEBC___)

Approved for use in:

ER positive, HER2 negative, node-positive early breast cancer (EBC) at high risk of recurrence.

High risk of recurrence is defined as patients with either:

- 4+ positive axillary lymph nodes OR
- 1-3 positive axillary lymph nodes and a primary tumour size greater than or equal to 5 cm and/or histological Grade 3 disease

**** BLUETEQ REQUIRED ** see blueteq for full eligibility criteria**

Dosage:

Drug	Dose	Route	Frequency
Abemaciclib	**150 mg**	Oral	Twice Daily continuously, issued every 28 days

To continue until there is progressive disease or excessive toxicity or until the patient chooses to discontinue treatment or for a maximum of 2 calendar years (26 cycles if no delays), whichever is the sooner.

Administration and Counselling Points:

- Abemaciclib is available as 50mg, 100mg and 150mg tablet.
- Abemaciclib tablets should be taken at approximately the same time each day, ideally 12 hours apart.
- The tablets can be taken with or without food and swallowed whole.
- Please note the tablets **contain lactose**.
- Abemaciclib should not be taken with grapefruit or grapefruit juice.

- Diarrhoea is a common side effect and average time to onset is 8 days, ensure patients understand loperamide dosing and contact triage team if ineffective

Emetogenic risk:

Mildly emetogenic.

Supportive treatments:

Loperamide 2mg – TWO capsules to be taken initially followed by 1 capsule after each loose stool (maximum daily dose 16mg) – to be taken when required

Extravasation risk: Not Applicable

Dosing in renal and hepatic impairment:

Renal	**Abemaciclib:** No dose adjustments are required for mild to moderate impairment (CrCl ≥ 30mL/min) Insufficient data for patients with severe impairment or receiving dialysis.

Hepatic	**Abemaciclib:** No dose adjustments are necessary in patients with mild (Child Pugh A) or moderate (Child Pugh B) hepatic impairment. In patients with severe (Child Pugh C) hepatic impairment, a decrease in dosing frequency to ONCE daily is recommended.

Interactions:

Abemaciclib is metabolized by the cytochrome CYP3A4 pathway

INDUCERS (lowers abemaciclib levels): Carbamazepine, phenobarbital, phenytoin, dexamethasone, rifabutin, rifampicin, St John's Wort, troglitazone, pioglitazone

INHIBITORS (increases abemaciclib levels): Indinavir, nelfinavir, ritonavir, clarithromycin, erythromycin, itraconazole, ketoconazole, nefazodone, grapefruit juice, verapamil, diltiazem, cimetidine, amiodarone, fluvoxamine, mibefradil

Abemaciclib may also interact with medicines via the P-glycoprotein mechanism, in particular those medicines with narrow therapeutic index such as digoxin or dabigatran.

For more detailed interactions please refer to the SPC:

https://www.medicines.org.uk/emc/product/9532/smpc#gref

Main toxicities:

Abemaciclib: Neutropenia, anaemia, thrombocytopenia, diarrhea, infection, fatigue, nausea, stomatitis, alopecia, thrombosis and raised transaminases.

Investigations and treatment plan:

	Pre	Cycle 1	Cycle 1, Day 14	Cycle 2	Cycle 2, Day 14	Cycle 3	Ongoing
Informed Consent	X						
Clinical Assessment	X					X	As clinically indicated or at the end of treatment
SACT Assessment (to include PS and toxicities)		X	X	X	X	X	Every cycle
FBC	X		X	X	X	X	Every 2 weeks for the first 2 cycles then every cycle
U&E, Renal profile & Magnesium	X			X		X	Every Cycle
LFTs (AST and ALT)	X		X	X	X	X	Every 2 weeks for the first 2 cycles then every cycle
CrCl (Cockcroft and Gault)	X			X		X	Every cycle
ECG							If clinically indicated
Blood pressure measurement	X						Repeat if clinically indicated
Respiratory Rate							If clinically indicated
Weight recorded	X	X		X		X	Every cycle

Dose Modifications and Toxicity Management:

Dose Level	Dose
Recommended dose	150mg TWICE daily
First dose reduction	100mg TWICE daily
Second dose reduction	50mg TWICE daily

If 50mg twice daily is not tolerated then treatment should be discontinued.

Haematological toxicity:

Administer abemaciclib on day 1 of each cycle if –

ANC ≥ 1.0 x 10^9/L	Platelets ≥ 100 x 10^9/L

These haematological guidelines assume that patients are well with good performance status, that other acute toxicities have resolved and the patient has not had a previous episode of neutropenic sepsis.

If abemaciclib cycle is deferred due to toxicity whilst the patient is also receiving concurrent goserelin, then it is important for patients receiving aromatase inhibitors (anastrazole/letrozole/exemestane) to continue with **goserelin every 4 weeks** even if this does lead to additional appointments

Non- Haematological toxicity

FBC and LFTs should be monitored on day 14 of cycle 1 and cycle 2 – see table above

CTC grade	Dose modifications - abemaciclib
Grade 1 or 2 (ANC ≥ 1.0 x 10^9/L)	No dose adjustment is required
Uncomplicated Grade 3 (ANC 0.5 to 0.9 x 10^9/L) All other grade 3 haematological toxicities except lymphopenia (unless associated with clinical events, e.g., opportunistic infections).	**Day 1 of cycle:** Withhold, repeat complete blood count monitoring within 1 week. When recovered to Grade ≤2, start the next cycle at the same dose. **Day 14 of first 2 cycles:** Continue at current dose to complete cycle. Repeat complete blood count on Day 21. Consider dose reduction in cases of prolonged (>1 week) recovery from Grade 3 neutropenia or

	recurrent Grade 3 neutropenia in subsequent cycles
Grade 3 neutropenia associated with a documented infection and/or fever ≥ 38.5°C. Or recurrent grade 3 neutropenia.	Withhold abemaciclib until recovery to grade ≤2 Reduce by one dose level
All grade 4 haematological toxicities (ANC < 0.5 x 10^9/L) except lymphopenia (unless associated with clinical events, e.g., opportunistic infections).	Withhold abemaciclib until recovery to grade ≤2 Reduce by one dose level

Non-haematological toxicities

DIARRHOEA

CTC grade	Dose modifications - abemaciclib
Grade 1	No dose adjustment is required
Grade 2	If does not resolve within 24 hours to grade 1, suspend treatment until improved, then can resume on current dose.
Grade 2 persistent or recurring Grade ≥ 3	Withhold until symptoms resolved to grade 1 Resume at the next lower dose.

Interstitial lung disease (ILD)/pneumonitis

CTC grade	Dose modifications - abemaciclib
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.

Venous thromboembolic events (VTEs)

CTC grade	Dose modifications - abemaciclib
Early Breast Cancer	

All Grades (1, 2, 3, or 4)	Suspend dose and treat as clinically indicated. Abemaciclib may be resumed when the patient is clinically stable.

Other non-haematological toxicities

CTC grade	Dose modifications - abemaciclib
Grade 1 or 2	No dose adjustment is required
Grade ≥ 3	Withhold until symptoms resolved to grade 1 or grade 2 (if not considered a safety risk for the patient) Resume at the next lower dose.

Hepatic impairment – ALT and AST

CTC grade	Dose modifications – abemaciclib
Grade 1 (less than 3 x ULN) Grade 2 (between 3 and 5 x ULN)	No dose adjustment is required
Grade 2 persistent or recurring Grade 3 (between 5 and 20 x ULN)	Stop abemaciclib until returned to grade 1 Resume at next lower dose For grade 3 also withhold fulvestrant until returned to grade 1
Grade 4 (above 20 x ULN)	Discontinue

References:

1. Summary of Product Characteristics, Verzenios®, Abemeciclib, Eli Lilly, last updated 17th May 2022, http://www.medicines.org.uk [accessed 29th June 2022]
2. Krens S D, Lassche, Jansman G F G A, et al. Dose recommendations for anticancer drugs in patients with renal or hepatic impairment. Lancet Oncol 2019; 20: e201–08.
3. BNF available via: https://bnf.nice.org.uk/
4. Johnston SRD, Harbeck N, Hegg R, et al. Abemaciclib combined with endocrine therapy for the adjuvant treatment of HR+, HER2-, node-positive, high-risk, early breast cancer (monarchE). *J Clin Oncol.* 2020;38(34):3987-3998

Circulation/Dissemination

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Version History

		Author name and designation	Summary of main changes
		Gabriella Langton	New protocol