ABEMACICLIB (Verzenios) (with endocrine therapy)

INDICATION (ICD10) C50

Check the most recent Blueteq eligibility criteria before prescribing. Blueteq registration required. (www.england.nhs.uk/publication/national-cancer-drugs-fund-list/) (ABEM3)

1. As adjuvant treatment in combination with endocrine therapy (following locoregional therapy surgery with or without surgery and completion of any neoadjuvant or adjuvant chemo, and no more than 12 weeks of adjuvant endocrine therapy after completion of the last non-endocrine therapy (surgery or chemotherapy or radiotherapy)) for high risk (high risk as specified in Blueteq criteria) hormone receptor-positive and HER2-negative early breast cancer. PS 0 or 1. (TA810)

REGIMEN

ABEMACICLIB 150mg tablet oral twice daily continuously
Endocrine therapy (prescribe appropriate support regimen)

CYCLE FREQUENCY AND NUMBER OF CYCLES

Every 28 days up to maximum 2 calendar years from date of first dose of a CDK4/6 inhibitor.

ADMINISTRATION

Abemaciclib is available as 50mg, 100mg and 150mg tablets.
Abemaciclib tablets should be taken at approximately the same time each day, ideally 12 hours apart.
Swallow whole with or without food.
Contains lactose
Grapefruit and grapefruit juice should be avoided while on abemaciclib.

ANTI-EMETICS

Low risk all days

CONCURRENT MEDICATION REQUIRED

Abemaciclib	Loperamide for diarrhoea Endocrine therapy (Aromatase inhibitor (letrozole, anastrazole, exemestane) or tamoxifen must be prescribed (may be by GP). Premenopausal and receiving aromatase inhibitor need ovarian suppression prescribed.

EXTRAVASATION AND TYPE OF LINE / FILTERS

Not applicable

INVESTIGATIONS

Blood results required before SACT administration
FBC, U&Es & LFTs every 2 weeks for first 8 weeks, Then every four weeks for eight weeks and then as indicated (patients should be assessed every 12 weeks).
Baseline cycle 1 day 1 neutrophils should be ≥1.5x10^9/l and platelets ≥100x10^9/l
An initial rise in creatinine is expected, usually within the first month, and then stabilises at elevated level, it is not an indication of impaired renal function. Continuously rising creatinine requires further investigation.

MAIN TOXICITES AND ADVERSE REACTIONS

Abemaciclib	Diarrhoea Interstitial lung disease (ILD) and pneumonitis Nausea Raised LFTs Neutropenia Infection VTE

INTERACTIONS WHICH MAY REQUIRE DOSE MODIFICATIONS
(not exhaustive list check SPC/BNF/Stockleys)

Abemaciclib	Strong CYP3A4 inhibitors (eg clarithromycin, itraconazole, posaconazole, voriconazole) should be avoided. CYP3A4 inducers (eg carbamazepine, phenytoin) should be avoided. Grapefruit and grapefruit juice should be avoided

DOSE MODIFICATIONS

Abemaciclib dose combination therapy

Recommended dose	150mg twice daily
First dose adjustment	100mg twice daily
Second dose adjustment	50mg twice daily

Haematological

Continue endocrine therapy

Abemaciclib

Grade 3 (neutrophils 0.5–0.99x10^9/l)	Interrupt abemaciclib until neutrophils ≥1.0x10^9/l. Dose reduction is not required.
Recurrent grade 3 (neutrophils 0.5–0.99x10^9/l) or grade 4 (neutrophils <0.5x10^9/l)	Interrupt abemaciclib until neutrophils ≥1.0x10^9/l, then re-start with one dose reduction

Non-haematological

Diarrhoea - grade 1	No dose adjustment required, consider loperamide
Diarrhoea - grade 2	If toxicity does not resolve within 24 hours to ≤grade 1, with loperamide, suspend dose until resolution. Dose reduction is not required.
Diarrhoea - persistent or recurrent grade 2 after resuming the same dose despite maximal supportive measures. Diarrhoea - grade 3 or 4 or requires hospitalisation.	Withhold abemaciclib until symptoms resolve to grade ≤1, then resume at the next lower dose
Interstitial lung disease / pneumonitis - grade 1 or 2	No dose adjustment required.
ILD / pneumonitis - persistent or recurrent grade 2 toxicity that does not resolve with maximal supportive measures within 7 days to baseline or grade 1	Withhold abemaciclib until symptoms resolve to grade ≤1, then resume at the next lower dose
ILD/ pneumonitis - grade 3 or 4	Discontinue abemaciclib

Venous thromboembolic events - 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 than diarrhoea or raised transaminases or ILD / pneumonitis - grade 1-2	No dose adjustment required
Other non-haematological toxicities than diarrhoea or raised transaminases or ILD / pneumonitis - persistent or recurrent grade 2 toxicity that does not resolve with maximal supportive measures to baseline or grade 1 within 7 days. Grade 3–4 toxicity	Withhold abemaciclib until symptoms resolve to grade ≤1, then resume at next lower dose.

Hepatic impairment

Abemaciclib

Grade 2 or 3 (ALT / AST >ULN to 5xULN)	No dose adjustment required
Persistent or recurrent grade 2 or grade 3 (ALT / AST >5 to 20xULN)	Withhold abemaciclib until symptoms resolve to grade ≤1, then resume at the next lower dose
Elevation in AST and/or ALT >3xULN WITH total bilirubin >2xULN, in the absence of cholestasis. Grade 4 (ALT / AST >20xULN)	Discontinue abemaciclib

Renal impairment

Abemaciclib

An initial rise in creatinine is expected, usually within the first month, and then stabilises at elevated level, it is not an indication of impaired renal function. Continuously rising creatinine requires further investigation.

CrCl ≥30ml/min after 1st month abemaciclib	No abemaciclib dose adjustments are necessary.
CrCl <30ml/min after 1st month abemaciclib	There are no data regarding abemaciclib administration in patients with CrCl <30ml/min, or in patients on dialysis. Administer with caution with close monitoring for signs of toxicity.

REFERENCES

1. SPC
2. CDF list www.england.nhs.uk/publication/national-cancer-drugs-fund-list/