Abemaciclib

Indication

In combination with an aromatase inhibitor:
Abemaciclib with an aromatase inhibitor is recommended as an option for treating locally advanced or metastatic, hormone receptor-positive, human epidermal growth factor receptor 2 (HER2)-negative breast cancer as first endocrine-based therapy.

(NICE TA563)

In combination with fulvestrant:
Abemaciclib with fulvestrant is recommended as an option for treating hormone receptor-positive, HER2-negative locally advanced or metastatic breast cancer in people who have had endocrine therapy only if exemestane plus everolimus would be the most appropriate alternative.

(NICE TA579)

ICD-10 codes

Codes with a pre fix C50.

Regimen details

Day	Drug	Dose	Route
1-28 (continuous)	Abemaciclib	150mg BD	PO

Cycle frequency

28 days.

Number of cycles

Until disease progression or unacceptable toxicity.

Administration

Abemaciclib is available as 50mg, 100mg and 150mg tablets. The tablets should be swallowed whole and not chewed, crushed or split. The dose may be taken with or without food. Doses should be taken at approximately the same times each day.

Grapefruit and grapefruit juice should be **avoided** whilst taking abemaciclib.

If a patient vomits or misses a dose an additional dose should not be taken but the next prescribed dose should be taken as planned.

Pre-medication

Nil

Emetogenicity

This regimen has mild emetic potential.

Additional supportive medication

Loperamide as required.

Extravasation

N/A

Investigations – pre first cycle

Investigation	Validity period
FBC	14 days
U+Es (including creatinine)	14 days
LFTs	14 days

Investigations – pre subsequent cycles

Investigation	Validity period
FBC	2 weekly for the first 2 cycles then monthly for next 2 months, then as clinically indicated.
U+Es (including creatinine)	Monthly or as clinically indicated
LFTs	2 weekly for the first 2 cycles then monthly for next 2 months, then as clinically indicated.

Standard limits for administration to go ahead

If blood results not within range, authorisation to administer **must** be given by prescriber/ consultant

Investigation	Limit
Neutrophils	≥ 1.5 x 10^9/L
Platelets	≥ 100 x 10^9/L
Haemoglobin	≥ 8g/dL
CrCl	≥ 30mL/min
Bilirubin	< 1.5 x ULN
AST/ALT	< 3 x ULN

Dose modifications

Dose reductions should follow the table below:

Dose level	Dose
Full dose	150mg BD
First reduction	100mg BD
Second reduction	50mg BD

- **Haematological toxicity**

Before treatment initiation it is recommended that neutrophils ≥1.5 x 10^9/L, platelets ≥100 x 10^9/L, and haemoglobin ≥8 g/dL.

Dose interruption, dose reduction, or delay in starting treatment cycles is recommended for patients who develop grade 3 or 4 neutropenia.

Haematological toxicity	Dose
Grade 1-2 (neutrophils ≥ 1.0 x 10^9/L)	No dose modification required.
Grade 3 (neutrophils 0.5- 1.0 x 10^9/L)	Withhold until recovered to ≤ grade 2. Dose reduction is not required.
Recurrent grade 3 (neutrophils 0.5- 1.0 x 10^9/L) or grade 4 (neutrophils < 0.5 x 10^9/L)	Withhold until recovered to ≤ grade 2. Resume with one dose level reduction.
Patient requiring blood cell growth factors	Withhold until recovered to ≤ grade 2 and for at least 48 hours after last dose of blood cell growth factors. Resume with one dose level reduction (unless the dose was already reduced).

- **Renal impairment**

No dose adjustments are necessary in patients with mild or moderate renal impairment. There are no data regarding use in patients with severe renal impairment, end stage renal disease, or in patients on dialysis. Abemaciclib should be administered with caution in patients with severe renal impairment, with close monitoring for signs of toxicity.

- **Hepatic impairment**

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. See below for management of raised transaminases during treatment.

- **Other toxicities**

Diarrhoea:

Antidiarrhoeal agents, such as loperamide, should be started at the first sign of loose stools.

Grade of toxicity	Dose
Grade 1	No dose modification required.
Grade 2	If within 24 hours diarrhoea has not recovered to ≤ grade 1 withhold until resolution. Dose reduction is not required.
Recurrent grade 2 (recurs despite supportive measures)	Withhold until recovered to ≤ grade 1. Resume with one dose level reduction.
Grade 3 or 4 or diarrhoea requiring hospitalisation	

Raised transaminases:

ALT/AST should be monitored prior to commencing treatment, every two weeks for the first two months, monthly for the next two months, and then as clinically indicated.

Grade of toxicity	Dose
Grade 1 (>ULN-3.0 x ULN)	No dose modification required.
Grade 2 (>3.0-5.0 x ULN)	
Persistent grade 2 or grade 3 (>5.0-20.0 x ULN)	Withhold until recovered to ≤ grade 1 or baseline. Resume with one dose level reduction
Grade 4 (>20.0 x ULN)	Discontinue treatment

Other non haematological toxicity (except diarrhoea or raised transaminases):

Grade of toxicity	Dose
Grade 1 or 2	No dose modification required.
Persistent grade 2 that does not resolve to grade 1 or baselines with supportive measures within 7 days.	Withhold until recovered to ≤ grade 1 or baseline. Resume with one dose level reduction
Grade 3 or 4	

Adverse effects - for full details consult product literature/ reference texts

- **Serious side effects**

Neutropenia, anaemia, leukopenia.
Infections
Venous thromboembolism

- **Frequently occurring side effects**

Neutropenia, anaemia, leukopenia.
Thrombocytopenia
Infections
Fatigue
Nausea and vomiting
Stomatitis
Rash, dry skin
Alopecia
Diarrhoea

- **Other side effects**

Reduced appetite
Dysgeusia
Dizziness
Muscle weakness
Increased transaminases

Significant drug interactions – for full details consult product literature/ reference texts

CYP3A4 inhibitors (e.g. clarithromycin, itraconazole, ketoconazole, lopinavir/ritonavir, posaconazole, voriconazole, grapefruit): Concomitant use of strong inhibitors should be avoided due to increased risk of toxicity. If co-administrated is deemed essential the dose of Abemaciclib should be reduced and patients closely monitored for signs of toxicity. No dose modification is required for moderate or weak CYP3A4 inhibitors but patients should be closely monitored.

Strong CYP3A4 inducers (e.g. carbamazepine, phenytoin, rifampin, and St. John's Wort)**:** Concomitant use may reduce the exposure of abemaciclib and should therefore be avoided.

P-glycoprotein (P-gp) substrates: Co-administration of abemaciclib and P-gp substrates may result in an increase in P-gp substrate plasma exposure. This may be clinically relevant for those agents with a narrow therapeutic window.

Hormonal contraceptives: It is currently unknown whether abemaciclib may reduce the effectiveness of systemically acting hormonal contraceptives, and therefore women using systemically acting hormonal contraceptives are advised to add a barrier method.

Additional comments

Women of childbearing potential or their male partners must use a highly effective method of contraception.

References

- National Institute for Clinical Excellence (TA563) accessed 7 June 2019 via www.nice.org.uk
- National Institute for Clinical Excellence (TA579) accessed 7 June 2019 via www.nice.org.uk
- Summary of Product Characteristics Abemaciclib (Lilly) accessed 7 June 2019 via www.medicines.org.uk
- Goetz, MP et al ; MONARCH 3: Abemaciclib As Initial Therapy for Advanced Breast Cancer JCO 2017 ; 35 (32) : 3638 - 3646
- Sledge, G et al ; MONARCH 2: Abemaciclib in Combination With Fulvestrant in Women With HR+/HER2- Advanced Breast Cancer Who Had Progressed While Receiving Endocrine Therapy.JCO 2017 ; 35 (25) : 2875 – 2884

Written/reviewed by: Professor M Beresford (Consultant Oncologist, RUH Bath NHS Trust), Dr R Bowen (Consultant Oncologist, RUH Bath NHS Trust)

Checked by: Sarah Murdoch (Oncology/Haematology Pharmacist, SW Clinical Network)

Authorised by: Dr J Braybrooke (Consultant Oncologist, UHBristol NHS Trust, SW Clinical Network)

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