Abemaciclib

Indication

For the treatment of women with hormone receptor (HR) positive, human epidermal growth factor receptor 2 (HER2) negative locally advanced or metastatic breast cancer in combination with an aromatase inhibitor or fulvestrant as initial endocrine-based therapy, or in women who have received prior endocrine therapy.

For the adjuvant treatment of adult patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, node-positive early breast cancer at high risk of recurrence, given with standard endocrine therapy

In pre- or perimenopausal women, the endocrine therapy should be combined with a luteinising hormone-releasing hormone (LHRH) agonist

Regimen details

Abemaciclib 150mg twice daily orally

Cycle frequency

Continuous treatment, dispense monthly

Number of cycles

Metastatic disease: given until disease progression
Adjuvant treatment: 26 cycles (2 years)

Administration

If the patient vomits or misses a dose, an additional dose should not be taken. The next prescribed dose should be taken at the usual time

Tablets should be swallowed whole with or without food

Pre-medication

None

Emetogenicity

Low

Additional supportive medication

Supply metoclopramide and loperamide with first cycle

Investigations – pre first cycle

Investigation	Validity period
FBC	14 days
U+E (including creatinine)	14 days
LFT (including AST)	14 days

Investigations –pre subsequent cycles

FBC and LFT baseline and every 2 weeks for the first 2 months, monthly for the next 2 months, then as clinically indicated.
Clinical toxicity assessment for infection, bleeding, thromboembolism, fatigue, GI effects (diarrhoea) and skin toxicity.

Standard limits for administration to go ahead

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

Do not retreat until ANC ≥ 1 x 10^9/L, platelets ≥ 50 x 10^9/L and non-hematologic toxicities have returned to baseline or ≤ grade 1 (or at physician discretion, ≤ grade 2, if not considered a patient safety risk

See "Dose modifications" below

Dose modifications

Dose Level	Abemaciclib dose (mg twice daily)
0	150
-1	100
-2	50

Toxicity	Grade	Abemaciclib dose
Haematological	1 or 2	No change
	3	Suspend abemaciclib until toxicity resolves to grade 2 or less. Dose reduction is not required.
	3 (recurrent)	Suspend abemaciclib until toxicity resolves to grade 2 or less. Resume at next lower dose.
	4	Suspend abemaciclib until toxicity resolves to grade 2 or less. Resume at next lower dose
Diarrhoea	1 or 2	Dose reduction is not required. If grade 2 toxicity does not resolve to grade 1 or less within 24 hours, suspend abemaciclib until resolution.
	2 that persists or recurs despite supportive measures or grade 3 or 4	Suspend abemaciclib until toxicity resolves to grade 1 or less. Resume at next lower dose
Hepatic (transaminases)	Grade 1 (>ULN-3.0 x ULN) or 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.

ANC: Grade 1: ANC < LLN - 1500/mm^3; Grade 2: ANC 1000 - <1500/mm^3; Grade 3: ANC 500 - <1000/mm^3; Grade 4: ANC <500/mm^3

Renal impairment

No dose adjustments are necessary in patients with mild or moderate renal impairment. There are no data regarding abemaciclib administration 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

Adverse effects –

for full details consult product literature/ reference texts

Infection, myelosuppression (anaemia, neutropenia, lymphopenia and thrombocytopenia), fatigue, mucositis, diarrhoea, nausea, vomiting, alopecia, skin rash, pruritus, muscular weakness, elevated transaminases

Neutropenia grade 3 or 4 was reported in 28%. Febrile neutropenia was reported in 0.9%.
The most common adverse reaction is diarrhoea, mainly during the first month of treatment. Patients should start treatment with anti-diarrhoeal agents (loperamide) at the first sign of loose stools.
Venous Thromboembolism was reported in 5% of cases.

Significant drug interactions

– for full details consult product literature/ reference texts

Drug interactions are possible with strong CYP3A inducers (e.g. phenytoin, rifampicin, dexamethasone, and carbamazepine) and inhibitors (e.g. ketoconazole, clarithromycin, grapefruit juice)
If patients must be co-administered a strong CYP3A inhibitor, reduce the abemaciclib dose to 100mg twice daily

Additional comments

References

Verzenios SPC – accessed 15/09/2020 https://www.medicines.org.uk/emc/product/11047/smpc

THIS PROTOCOL HAS BEEN DIRECTED BY DR BEZECNY, CONSULTANT ONCOLOGIST

RESPONSIBILITY FOR THIS PROTOCOL LIES WITH THE HEAD OF SERVICE

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