Regimen Monograph

Regimen Name | Drug Regimen | Cycle Frequency | Premedication and Supportive Measures | Dose Modifications | Adverse Effects | Interactions | Drug Administration and Special Precautions | Recommended Clinical Monitoring | Administrative Information | References | Other Notes | Disclaimer

A - Regimen Name

ABEM Regimen

Abemaciclib

Disease Site	Breast
Intent	Palliative
Regimen Category	**Evidence-Informed :** Regimen is considered appropriate as part of the standard care of patients; meaningfully improves outcomes (survival, quality of life), tolerability or costs compared to alternatives (recommended by the Disease Site Team and national consensus body e.g. pan-Canadian Oncology Drug Review, pCODR). Recommendation is based on an appropriately conducted phase III clinical trial relevant to the Canadian context OR (where phase III trials are not feasible) an appropriately sized phase II trial. Regimens where one or more drugs are not approved by Health Canada for any indication will be identified under Rationale and Use.
Rationale and Uses	For treatment of refractory HR+/HER2- metastatic breast cancer

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B - Drug Regimen

abemaciclib	200 mg	PO	BID

(This drug is not currently publicly funded for this regimen and intent)

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C - Cycle Frequency

CONTINUOUS TREATMENT

Until disease progression or unacceptable toxicity

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D - Premedication and Supportive Measures

Antiemetic Regimen: Minimal – No routine prophylaxis; PRN recommended

- Also refer to CCO Antiemetic Recommendations.

Screen for hepatitis B virus in all cancer patients starting systemic treatment. Refer to the hepatitis B virus screening and management guideline.

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E - Dose Modifications

Doses should be modified according to the protocol by which the patient is being treated.

Dosage with toxicity

Dose Level	Abemaciclib Dose (mg BID)
0	200
-1	150
-2	100
-3	50
-4	Discontinue

Toxicity	Grade	Action
Hematologic*	Grade 3	Hold until ≤ grade 2; resume at same dose.
	Grade 4 or recurrent grade 3	Hold until ≤ grade 2; resume at 1 dose level ↓.
Diarrhea**	Grade 2	If no resolution to ≤ grade 1 within 24 hours, hold until resolution; resume at same dose.
	Grade 2 that persists/recurs after resumption at the same dose (despite maximal supportive measures)	Hold until ≤ grade 1; resume at 1 dose level ↓.
	≥ Grade 3 or requires hospitalization	
Interstitial lung disease (ILD)/ Pneumonitis	Persistent or recurrent grade 2 toxicity that does not resolve to baseline or grade 1 within 7 days (despite maximal supportive measures)	Hold until recovery to baseline or ≤ grade 1; resume at 1 dose level ↓.
	Grade 3 or 4	Discontinue
Hepatotoxicity	Persistent or recurrent grade 2, or grade 3 (ALT, AST >5 to 20 times ULN), WITHOUT increase in total bilirubin >2 times ULN	Hold until recovery to baseline or grade 1; resume at 1 dose level ↓.
	AST and/or ALT >3 times ULN with total bilirubin >2 times ULN (in the absence of cholestasis)	Discontinue
	Grade 4 (ALT, AST >20 times ULN)	Discontinue
Venous thromboembolism	Grade 3 or 4	Hold; restart when patient is stable and if clinically appropriate
All other non-hematologic toxicities	Persistent or recurrent grade 2 toxicity that does not resolve to baseline or grade 1 within 7 days (despite maximal supportive measures)	Hold until recovery to baseline or ≤ grade 1; resume at 1 dose level ↓.
	Grade 3 or 4	

*If blood cell growth factors are required, hold abemaciclib for at least 48 hours after the last growth factor dose and until toxicity resolves to ≤ grade 2; resume at the next lower dose (unless already reduced due to the toxicity that required the growth factor). Growth factor use is as per current local guidelines.

**At the first sign of loose stools, begin management with antidiarrheal agents (i.e. loperamide) and increase oral fluid intake.

Hepatic Impairment

Hepatic Impairment	Abemaciclib Dose
Mild or moderate impairment (Child-Pugh class A or B)	No dosage adjustment necessary.
Severe impairment (Child-Pugh class C)	Reduce the abemaciclib frequency to once daily.

Renal Impairment

Renal Impairment	Abemaciclib Dose
Mild or Moderate (CrCl ≥ 30 mL/min)	No dosage adjustment necessary.
Severe (CrCl < 30 mL/min); ESRD	Has not been studied.

Dosage in the Elderly

No dosage adjustment is required. No overall differences in safety or efficacy between patients ≥ 65 years of age and younger. Patients ≥65 years of age reported more hematologic adverse events, hypokalemia (including grade 3), hypocalcemia, grade ≥3 infections, decreased appetite, and increased blood creatinine compared to younger patients in a subgroup analysis from clinical studies.

Dosage based on Ethnicity

No dose adjustment based on race is required. Higher incidences of increased ALT and AST and neutropenia have been reported in East Asian patients compared to Caucasian patients in clinical trials.

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F - Adverse Effects

Refer to abemaciclib drug monograph(s) for additional details of adverse effects.

Very common (≥ 50%)	Common (25-49%)	Less common (10-24%)	Uncommon (< 10%), but may be severe or life-threatening
• Diarrhea (may be severe)	• Infection (may be severe) • Myelosuppression (may be severe) • Fatigue • Nausea, vomiting (generally mild)	• Creatinine increased • Musculoskeletal pain • Headache • Cough, dyspnea • Mucositis • Flu-like symptoms • Anorexia, weight loss • ↑ LFTs (may be severe) • Rash, pruritus, dry skin • Alopecia • Peripheral edema • Constipation • Dizziness	• Cardiotoxicity • Arterial / Venous thromboembolism • Hypersensitivity • Pneumonitis • Nephrotoxicity

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G - Interactions

Refer to abemaciclib drug monograph(s) for additional details.

- Avoid co-administration with strong CYP3A inhibitors. Use caution when co-administered with moderate or weak CYP3A inhibitors.
    - If co-administration with a strong or moderate CYP3A inhibitor is unavoidable, reduce abemaciclib dose to 50 mg twice daily.
        - When combined with ketoconazole, abemaciclib dose should be reduced to 50 mg once daily.
        - When combined with clarithromycin, diltiazem or verapamil, abemaciclib dose should be reduced to 100 mg twice daily.
    - If co-administration with a weak CYP3A inhibitor is unavoidable, reduce abemaciclib dose to 100 mg twice daily.
    - If the CYP3A inhibitor is discontinued, increase the abemaciclib dose (after 3-5 half-lives of the inhibitor) to the dose used before starting the inhibitor.
- Avoid co-administration with strong CYP3A inducers. Consider alternative agents with less CYP3A induction. Use with caution when co-administered with moderate or weak CYP3A inducers.

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H - Drug Administration and Special Precautions

Refer to abemaciclib drug monograph(s) for additional details.

Administration

- Abemaciclib tablets should be swallowed whole (do not chew, crush, or split tablets before swallowing). Tablets should not be ingested if they are not intact.
- Abemaciclib doses may be taken with or without food and should be administered at approximately the same times every day.
- Avoid fruit or juice from grapefruit, Seville oranges or starfruit.
- Abemaciclib tablets contain lactose. Use with caution in patients with lactose intolerance.
- If a dose is missed or vomited, the next dose should be taken at the scheduled time. The patient should not take 2 doses at the same time to make up for the missed dose.
- Store at room temperature (15°C to 30°C).

Contraindications

- Patients who are hypersensitive to this drug or to any ingredient in the formulation or component of the container.

Other Warnings/Precautions

- There are no data regarding abemaciclib safety or efficacy in patients with prior exposure to other CDK 4/6 inhibitors.

Pregnancy/Lactation

- This regimen is not recommended for use in pregnancy. Adequate contraception should be used by patients and their partners while on treatment and after the last treatment dose. Recommended methods and duration of contraception may differ depending on the treatment. Refer to the drug monograph(s) for more information.
- Breastfeeding is not recommended during this treatment and after the last treatment dose. Refer to the drug monograph(s) for recommendations after the last treatment dose (if available).
- Fertility: Probable
  Abemaciclib may impair fertility in males.

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I - Recommended Clinical Monitoring

Treating physicians may decide to monitor more or less frequently for individual patients but should always consider recommendations from the product monograph.

Refer to the hepatitis B virus screening and management guideline for monitoring during and after treatment.

Recommended Clinical Monitoring

- CBC; Baseline, every two weeks for the first 2 months, monthly for the next 2 months, and as clinically indicated.
- Liver function tests; Baseline, every 2 weeks for the first 2 months, monthly for the next 2 months, and as clinically indicated.
- Renal function tests*; Baseline and as clinically indicated
- Clinical toxicity assessment for signs and symptoms of venous thrombosis, infections, gastrointestinal, respiratory, dermatologic effects and fatigue; At each visit
- Grade toxicity using the current NCI-CTCAE (Common Terminology Criteria for Adverse Events) version

  *Abemaciclib may increase serum creatinine, without affecting glomerular function, by inhibiting renal tubular secretion transporters. Consider alternative markers that are not based on creatinine (e.g. BUN) for determining renal function.

Suggested Clinical Monitoring

- Electrolytes, including calcium; Baseline and as clinically indicated

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K - References

Abemaciclib drug monograph, Ontario Health (Cancer Care Ontario).

Dickler MN, Tolaney SM, Rugo HS, et al. MONARCH 1, a phase 2 study of abemaciclib, a CDK4 and CDK6 inhibitor, as a single agent, in patients with refractory HR+/HER2- metastatic breast cancer. Clin Cancer Res. 2017;23(17):5218-24.

April 2024 Updated pregnancy/breastfeeding section

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M - Disclaimer

Regimen Abstracts

A Regimen Abstract is an abbreviated version of a Regimen Monograph and contains only top level information on usage, dosing, schedule, cycle length and special notes (if available). It is intended for healthcare providers and is to be used for informational purposes only. It is not intended to constitute or be a substitute for medical advice, and all uses of the Regimen Abstract are subject to clinical judgment. Such information is provided on an "as-is" basis, without any representation, warranty, or condition, whether express, or implied, statutory or otherwise, as to the information's quality, accuracy, currency, completeness, or reliability, and Cancer Care Ontario disclaims all liability for the use of this information, and for any claims, actions, demands or suits that arise from such use.

Information in regimen abstracts is accurate to the extent of the ST-QBP regimen master listings, and has not undergone the full review process of a regimen monograph. Full regimen monographs will be published for each ST-QBP regimen as they are developed.

Regimen Monographs

Refer to the New Drug Funding Program or Ontario Public Drug Programs websites for the most up-to-date public funding information.

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Some Formulary documents, such as the medication information sheets, regimen information sheets and symptom management information (for patients), are intended for patients. Patients should always consult with their healthcare provider if they have questions regarding any information set out in the Formulary documents.

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