Regimen Monograph

A - Regimen Name

ABEMANAS Regimen

Abemaciclib-Anastrozole

Disease Site

Breast

Intent

Adjuvant
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 adjuvant treatment of HR+, HER2-, node-positive early breast cancer, in patients who are at high risk of disease recurrence (refer to EAP for abemaciclib funding details)
- For treatment of HR+/HER2- advanced breast cancer in patients who were previously treated with endocrine therapy (abemaciclib **not funded** by EAP)

Supplementary Public Funding

abemaciclib
Exceptional Access Program (abemaciclib - For the adjuvant treatment, in combination with endocrine therapy, of adult patients with HR-positive, HER2-negative, node-positive early breast cancer at high risk of disease recurrence based on clinicopathological features and a Ki-67 score of at least 20%.)

(EAP Website)

anastrozole
ODB - General Benefit (anastrozole) (ODB Formulary)

back to top

B - Drug Regimen

abemaciclib*	150 mg	PO	BID

*abemaciclib is not currently publicly funded for advanced breast cancer

anastrozole	1 mg	PO	Daily

Note: Pre- or perimenopausal women, and men should also be treated with gonadotropin releasing hormone (GnRH) agonists according to local clinical practice.

back to top

C - Cycle Frequency

CONTINUOUS TREATMENT

Early breast cancer: Up to a total of 2 years of treatment, unless disease progression/ unacceptable toxicity occurs. Anastrozole monotherapy may continue.

Advanced or metastatic breast cancer: Until disease progression or unacceptable toxicity

back to top

D - Premedication and Supportive Measures

Antiemetic Regimen: Minimal – No routine prophylaxis; PRN recommended

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

Assess patient's risk factors for osteoporosis and consider calcium and vitamin D supplements and bisphosphonates where appropriate. Refer patients to the Bone Health During Cancer Treatment

pamphlet for more information.

back to top

E - Dose Modifications

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

Dosage with toxicity

Abemaciclib Dose Levels:

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

Dose Modifications:

Toxicity	Grade	Abemaciclib Action	Anastrozole Action
Hematologic*	Grade 3	Hold until ≤ grade 2; resume at same dose.	No adjustment required
	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.	No adjustment required
	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 ↓.	Not applicable
	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 ↓.	Refer to “hepatic impairment” table below
	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 1 or 2	**Early breast cancer:** Hold; restart when patient is stable and if clinically appropriate **Metastatic breast cancer:** No dose modification required	Not applicable
	Grade 3 or 4	**For early or metastatic breast cancer:** Hold; restart when patient is stable and if clinically appropriate	
Hypercalcemia	≥ Grade 3	Hold until recovery to baseline or ≤ grade 1; resume at 1 dose level ↓.	Hold; discontinue if recurs
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 ↓.	No adjustment required
	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	Anastrozole Dose
Mild or moderate impairment (Child-Pugh class A or B)	No dosage adjustment necessary.	No dosage adjustment necessary.
Severe impairment (Child-Pugh class C)	Reduce the abemaciclib frequency to once daily.	Not studied; consider potential risk/benefit.

Renal Impairment

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

Dosage in the Elderly

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

Dosage based on Ethnicity

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

back to top

F - Adverse Effects

Refer to abemaciclib, anastrozole 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 • Estrogen deprivation symptoms • Musculoskeletal pain • Nausea, vomiting (generally mild)	• Creatinine increased • Mood changes (including depression) • Headache • Cough, dyspnea • Mucositis • Flu-like symptoms • Anorexia, weight loss • Osteoporosis, fracture • ↑ LFTs • Dry skin, rash, pruritus • Alopecia • Peripheral edema • Lymphedema • Constipation • Dizziness	• Cardiotoxicity • Arterial / venous thromboembolism • Hypersensitivity • Erythema multiforme • Stevens-Johnson syndrome • Nephrotoxicity • Hypercalcemia • Endometrial cancer • Pneumonitis • Vasculitis • Osteonecrosis of jaw • Cataract

back to top

G - Interactions

Refer to abemaciclib, anastrozole 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 that was 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.
- Do not co-administer anastrozole with tamoxifen due to ↓ anastrozole concentration and no efficacy or safety benefit.
- Avoid co-administration of anastrozole with estrogen-containing or estrogenic agents due to ↓ estrogen suppression.

back to top

H - Drug Administration and Special Precautions

Refer to abemaciclib, anastrozole drug monograph(s) for additional details

Administration

Abemaciclib

- 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).

Anastrozole

- Administer anastrozole with or without food.
- Tablets should be swallowed whole with a glass of water at the same time each day.
- Missed dose should be taken as soon as possible, but only if there are at least 12 hours before the next dose is due.
- Store at room temperature (15 to 30°C)

Contraindications

- Patients who are hypersensitive to abemaciclib or anastrozole or to any ingredient in the formulation or component of the container.
- Pregnancy/breastfeeding is contraindicated with anastrozole.

Other Warnings/Precautions

- Use of formulations containing lactose should be carefully considered in patients with hereditary galactose intolerance, severe lactase deficiency or glucose-galactose malabsorption.
- There are no data regarding abemaciclib safety or efficacy in patients with prior exposure to other CDK 4/6 inhibitors.
- Use anastrozole with caution in patients with known osteoporosis or risk factors for osteoporosis, in patients with pre-existing cardiovascular disorders, severe liver or renal impairment.
- Anastrozole has not been studied in patients with brain, leptomeningeal or pulmonary lymphangitic disease.

Pregnancy/Lactation

- This treatment is **contraindicated** 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 **contraindicated** 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 Effects:
    - Abemaciclib: Probable; may impair fertility in males
    - Anastrozole: Probable

back to top

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
- Bone mineral density for patients at risk; Baseline and as clinically indicated
- Clinical toxicity assessment for signs and symptoms of venous thrombosis, infections, musculoskeletal, estrogen withdrawal symptoms, mood changes (including depression), dermatological, edema, cardiovascular, gastrointestinal, respiratory and genitourinary 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

- Cholesterol and lipid evaluation; baseline and as clinically indicated
- Electrolytes, including calcium; baseline and as clinically indicated

back to top

K - References

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

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

CADTH reimbursement review: Abemaciclib (Adjuvant treatment of hormone receptor–positive, human epidermal growth factor receptor 2–negative early breast cancer), December 2022.

Goetz MP, Toi M, Campone M, et al. MONARCH 3: abemaciclib as initial therapy for advanced breast cancer. J Clin Oncol. 2017;35:3638-3646.

Johnston SRD, Harbeck N, Hegg R. Abemaciclib combined with endocrine therapy for the adjuvant treatment of HR+, HER2-, node-positive, high-risk, early breast cancer (monarchE). J Clin Oncol. 2020 Dec 1;38(34):3987-98.

October 2023 Modified Rationale/uses and Pregnancy/lactation sections; added abemaciclib funding information

back to top

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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back to top