

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

## CARFDEXA Regimen

Carfilzomib-Dexamethasone

## CARFDEXA(W) Regimen

Carfilzomib (weekly)-Dexamethasone

**Disease Site** Hematologic  
Multiple Myeloma

**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 the treatment of patients with relapsed multiple myeloma and good performance status, who have received 1 to 3 prior treatments

**Supplementary Public Funding** [carfilzomib](#)  
New Drug Funding Program (Carfilzomib (Doublet Therapy) - In Combination with Dexamethasone for Relapsed Multiple Myeloma)

**dexamethasone**

ODB - General Benefit (dexamethasone) ([ODB Formulary](#))

[back to top](#)

**B - Drug Regimen**

**Once Weekly Carfilzomib Dosing:**

**Cycle 1:**

<a href="#">carfilzomib</a> <sup>†</sup>	20 mg /m <sup>2</sup>	IV	Day 1
<a href="#">carfilzomib</a> <sup>†</sup>	70 mg /m <sup>2</sup>	IV	Days 8, 15
dexamethasone <sup>^</sup>	40 mg	IV / PO	Days 1, 8, 15, 22

**Cycles 2 and beyond:**

<a href="#">carfilzomib</a> <sup>†</sup>	70 mg /m <sup>2</sup>	IV	Days 1, 8, 15
dexamethasone <sup>^</sup>	40 mg	IV / PO	Days 1, 8, 15, 22*

<sup>†</sup>Patients with BSA > 2.2 m<sup>2</sup> should be dosed based on a maximum BSA of 2.2 m<sup>2</sup>.

<sup>^</sup>The dexamethasone dose should be reduced in elderly patients (e.g. ≥ 75 years of age).

\*In the ARROW study, dexamethasone was given on Days 1, 8, and 15 for Cycle 10 onwards

**Twice Weekly Carfilzomib Dosing:**

<a href="#">carfilzomib</a> <sup>†</sup>	20 mg /m <sup>2</sup>	IV	Days 1, 2
<a href="#">carfilzomib</a> <sup>†</sup>	56 mg /m <sup>2</sup>	IV	Days 8, 9, 15, 16
dexamethasone <sup>^</sup>	20 mg /day	IV / PO	Days 1, 2, 8, 9, 15, 16, 22, 23

---

**Cycle 2 and beyond:**

<a href="#">carfilzomib</a> <sup>†</sup>	56 mg /m <sup>2</sup>	IV	Days 1, 2, 8, 9, 15, 16
<b>dexamethasone</b> <sup>^</sup>	20 mg /day	IV / PO	Days 1, 2, 8, 9, 15, 16, 22, 23

<sup>†</sup>Patients with BSA > 2.2 m<sup>2</sup> should be dosed based on a maximum BSA of 2.2 m<sup>2</sup>.

<sup>^</sup>The dexamethasone dose should be reduced in elderly patients (e.g. ≥ 75 years of age).

[back to top](#)

### C - Cycle Frequency

**REPEAT EVERY 28 DAYS**

Until disease progression or unacceptable toxicity

[back to top](#)

## D - Premedication and Supportive Measures

**Antiemetic Regimen:** Low

- Also refer to [CCO Antiemetic Summary](#)

**Screen for hepatitis B virus in all cancer patients starting systemic treatment.** Refer to the [hepatitis B virus screening and management](#) guideline.

### Other Supportive Care:

#### Carfilzomib:

- Consider the use of antiviral prophylaxis during carfilzomib therapy to decrease the risk of herpes zoster and HBV reactivation.
- Consider thromboprophylaxis in patients being treated with carfilzomib. The choice of agent should be based on patient risk factors and clinical status.
- Patients at risk of tumour lysis syndrome (i.e. high tumour burden) should have appropriate prophylaxis and be monitored closely.
- Adequate hydration is required prior to dosing in cycle 1, especially in patients at high risk for tumour lysis syndrome or renal toxicity. The total fluid volume may be adjusted as clinically indicated in patients with baseline or at high risk of cardiac failure.
  - Cycle 1:
    - Oral fluids (30 mL/kg/day for 48 hours before start of cycle), and
    - IV fluids: 250-500 mL before each dose, and if needed after each dose
  - Subsequent cycles:
    - Continue oral and/or IV hydration as needed
- On carfilzomib treatment days, dexamethasone IV/PO should be given at least 30 minutes, but no more than 4 hours before carfilzomib.

[back to top](#)

**E - Dose Modifications**

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

Hypertension should be well-controlled prior to initiation of treatment with carfilzomib.

Carfilzomib doses do not need to be re-calculated for weight changes  $\leq 20\%$ .

**Dosage with toxicity**

Dose Level	CARFDEXA(W)		CARFDEXA	
	Carfilzomib Dose (mg/m <sup>2</sup> ) ONCE weekly	Dexamethasone Dose (mg) ONCE weekly	Carfilzomib Dose (mg/m <sup>2</sup> ) TWICE weekly	Dexamethasone Dose (mg) TWICE weekly
0	70	40	56	20
-1	56	20	45	12
-2	45	12	36	8
-3	36	Discontinue	27	Discontinue
-4	Discontinue	N/A	Discontinue	N/A

**Dexamethasone** doses may be held or reduced for dexamethasone-related adverse events (e.g. hyperglycemia, fluid retention) to improve tolerability. Also refer to the ENDEAVOR and ARROW trials for dexamethasone dose modifications.

Toxicity	Carfilzomib Dose
ANC $< 0.5 \times 10^9/L$ , febrile neutropenia or platelets $< 10 \times 10^9/L$ ; thrombocytopenic bleeding	<p><u>1<sup>st</sup> occurrence</u>: Hold* until recovery (and fever resolves, bleeding is controlled), and then restart at the same dose level.</p> <p><u>Subsequent occurrences</u>: Hold* until recovery (and fever resolves, bleeding is controlled); consider restarting at 1 dose level ↓.</p>
Serum creatinine $\geq 2 \times$ baseline, or CrCl $< 15$ mL/min (or CrCl decreases to $\leq 50\%$ of baseline) or need for dialysis	<p>Hold:</p> <ul style="list-style-type: none"> <li>If attributable to carfilzomib, resume at 1 dose level ↓ when renal function has recovered to within 25% of baseline.</li> </ul>

CARFDEXA  
CARFDEXA(W)

	<ul style="list-style-type: none"> <li>If not attributable to carfilzomib, may resume at physician's discretion.</li> </ul> <p>If tolerated, the reduced dose may be increased to the previous dose.</p>
Grade 3 or 4 cardiac events	Hold until resolved. Consider risk vs. benefit of restarting; resume at 1 dose level ↓.
Hypertensive crisis/emergency	Hold until resolved or under control.  Consider the risk vs. benefit of restarting; consider restarting at 1 dose level ↓.
Tumour lysis syndrome	Hold until resolved. Manage promptly.
ARDS, ILD, pneumonitis, pulmonary hypertension, Grade 3 or 4 dyspnea	Hold until resolved. Consider the risk vs. benefit of restarting.
Thrombotic microangiopathy (including TTP/HUS)	Hold and evaluate. Discontinue if confirmed.
PRES	Hold and evaluate. Discontinue if confirmed.
PML	Hold and evaluate. Discontinue if confirmed.
Other drug related Grade 3 or 4 non-hematological toxicities	Hold until resolved or at baseline. Then, if appropriate to reinitiate, consider restarting at 1 dose level ↓  If tolerated, the reduced dose may be increased to the previous dose.

\*Do not restart until ANC  $\geq 0.5 \times 10^9/L$  (or baseline values for febrile neutropenia) and platelets  $\geq 10 \times 10^9/L$  with resolution of fever and bleeding.

**Hepatic Impairment**

In a pharmacokinetic study, carfilzomib AUC increased by 50% in patients with baseline mild or moderate hepatic impairment compared to those with normal hepatic function. The incidence of serious adverse events was higher in patients with hepatic impairment as well.

<b>Hepatic Impairment</b>	<b>Carfilzomib Starting Dose</b>	<b>Dexamethasone Starting Dose</b>
Mild (bilirubin >1 - 1.5 x ULN or AST > ULN) or  Moderate (bilirubin >1.5 - 3 x ULN)	Reduce dose by 25%.	No dosage adjustment necessary.
Severe (bilirubin > 3 x ULN)	No data.	

**Renal Impairment**

No dosage adjustment required for dexamethasone.

No starting dose adjustment is required for carfilzomib in patients with baseline renal impairment. For patients on dialysis receiving carfilzomib, administer dose after dialysis.

**Dosage in the Elderly**

There were no differences in effectiveness of carfilzomib, when given in combination with dexamethasone, in any of the studied age groups. There was a higher incidence of certain adverse effects (including cardiac failure) observed in patients  $\geq 65$  years of age, especially in those  $\geq 75$  years of age.

The dexamethasone dose should be reduced in elderly patients.

[back to top](#)

---

**F - Adverse Effects**

Refer to [carfilzomib](#) drug monograph(s) for additional details of adverse effects.

Common (25-49%)	Less common (10-24%)	Uncommon (< 10%), but may be severe or life-threatening
<ul style="list-style-type: none"> <li>• Diarrhea (may be severe)</li> <li>• Infusion related reaction (may be severe)</li> <li>• Hypertension (may be severe)</li> <li>• Fatigue (may be severe)</li> <li>• Cough, dyspnea</li> <li>• Myelosuppression ± infection, bleeding (including viral reactivation) (may be severe)</li> <li>• Insomnia</li> <li>• Edema</li> </ul>	<ul style="list-style-type: none"> <li>• Nausea, vomiting</li> <li>• Musculoskeletal pain, weakness</li> <li>• Headache</li> <li>• Constipation</li> <li>• Peripheral neuropathy</li> <li>• Abnormal electrolyte(s) (↓ K, ↓ Ca, ↓ PO4)</li> <li>• Venous thromboembolism</li> <li>• Hyperglycemia</li> <li>• Abdominal pain</li> <li>• Creatinine increased (may be severe)</li> </ul>	<ul style="list-style-type: none"> <li>• Cardiotoxicity</li> <li>• Arterial thromboembolism</li> <li>• QT interval prolonged</li> <li>• Pericarditis</li> <li>• Adult respiratory distress syndrome (ARDS)</li> <li>• Pneumonitis</li> <li>• Pulmonary hypertension</li> <li>• Cataract</li> <li>• Tumour lysis syndrome</li> <li>• GI perforation</li> <li>• GI obstruction</li> <li>• Pancreatitis</li> <li>• Hepatic failure</li> <li>• Thrombotic microangiopathy (including TTP, HUS)</li> <li>• RPLS / PRES</li> <li>• PML</li> </ul>

[back to top](#)

**G - Interactions**

Refer to [carfilzomib](#) drug monograph(s) for additional details.

- Caution with P-glycoprotein substrates (i.e. verapamil, digoxin, morphine, ondansetron) and monitor digoxin levels when given with carfilzomib.
- Caution and consider non-hormonal method(s) of contraception as use of oral contraceptives



---

or other hormonal methods of contraception may have reduced efficacy and may increase the risk of blood clots.

[back to top](#)

## H - Drug Administration and Special Precautions

Refer to [carfilzomib](#) drug monograph(s) for additional details.

### Administration: carfilzomib

- Reconstitute vials with Sterile Water for Injection. Volume for reconstitution depends on vial size; refer to product monograph for instructions.
- After reconstitution, gently swirl and/or invert the vial slowly for 1 minute. Do not shake.
- If foaming occurs, allow the solution to settle in the vial until foaming subsides (approximately 5 minutes) and the solution is clear, colourless and free of visible particulates.
- May further dilute dose in 50-100 mL D5W. Do not dilute in NS for IV administration.
- DO NOT administer as an IV bolus. May be administered directly by IV infusion or in an IV bag.
- Do not mix with or administer as an infusion with other medications.
- Infuse over 30 minutes. Keep infusion time consistent during treatment regardless of any dose modifications.
- Flush line with NS or D5W before and after carfilzomib administration.
- If a dose is missed, a minimum of 5 days between doses is required for once weekly dosing.
- Store unopened vials refrigerated at 2–8°C in original package and protected from light. Reconstituted or diluted drug do not require protection from light during administration.

### Administration: dexamethasone

- Oral self-administration or may be given by IV route on carfilzomib clinic days.
- Dexamethasone IV/PO should be given at least 30 minutes, but no more than 4 hours before carfilzomib.
- Give tablets with food, preferably in the morning.

### Contraindications

- Patients who have a hypersensitivity to these drugs or any of their components

### Warnings/Precautions

- Use carfilzomib with caution in patients on a controlled sodium diet. Each mL of the reconstituted carfilzomib solution contains 0.3 mmols (7 mg) of sodium.
- The risk of heart failure is increased in elderly patients ( $\geq 75$  years). Patients with NYHA Class III/IV heart failure, recent MI, conduction abnormalities, angina or arrhythmias uncontrolled by medications were not eligible for carfilzomib-based clinical trials. These patients may be at greater risk of cardiac complications and should have their medical management optimized, including hypertension, prior to starting treatment with carfilzomib and monitored closely throughout.
- Patients should use caution when driving or using machinery as fatigue, dizziness and a drop in blood pressure may occur with carfilzomib treatment.

### 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.
- Consider non-hormonal method(s) of contraception as use of oral contraceptives or other hormonal methods of contraception may have reduced efficacy and may increase the risk of blood clots.
- 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 effects:
  - Carfilzomib: Unknown

[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 with differential; Baseline and before each cycle; more frequently as clinically indicated
- Liver function tests; Baseline and before each cycle
- Renal function tests; Baseline and before each cycle
- Electrolytes, including potassium; Baseline and before each cycle
- Blood pressure; Baseline and before each treatment
- Blood glucose levels; Baseline and as clinically indicated
- Clinical toxicity assessment for infusion reactions, bleeding, infection, TLS, thromboembolism, GI, skin, respiratory, ophthalmic, cardiovascular and neurological effects; At each visit
- Grade toxicity using the current [NCI-CTCAE \(Common Terminology Criteria for Adverse Events\) version](#)

### Suggested Clinical Monitoring

- ECG; Baseline and as clinically indicated
- LVEF assessment (especially in patients  $\geq 75$  years, or those at greater risk for cardiac complications); Baseline and as clinically indicated

[back to top](#)

## J - Administrative Information

Dexamethasone PO - Outpatient prescription for home administration

### Approximate Patient Visit

CARFDEXA 1 to 2 hours

CARFDEXA(W) 1 to 2 hours

### Pharmacy Workload (average time per visit)

CARFDEXA 19.850 minutes

### Nursing Workload (average time per visit)

CARFDEXA 42.417 minutes

[back to top](#)

## K - References

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

Dimopoulos MA, Moreau P, Palumbo A, et al. Carfilzomib and dexamethasone versus bortezomib and dexamethasone for patients with relapsed or refractory multiple myeloma (ENDEAVOR): a randomised, phase 3, open-label, multicentre study. *Lancet Oncol* 2016;17:27-38.

Moreau P, Mateos MV, Berenson JR, et al. Once weekly versus twice weekly carfilzomib dosing in patients with relapsed and refractory multiple myeloma (A.R.R.O.W.): interim analysis results of a randomised, phase 3 study. *Lancet Oncol*. 2018 Jul;19(7):953-64.

### **PEBC Advice Documents or Guidelines**

- [Treatment of Multiple Myeloma: ASCO and CCO Joint Clinical Practice Guideline](#)

**June 2024** Added carfilzomib weekly option in Drug Regimen; Updated Dose Modifications and Administration sections

[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.*

*The information set out in the drug monographs, regimen monographs, appendices and symptom management information (for health professionals) contained in the Drug Formulary (the “Formulary”) is intended for healthcare providers and is to be used for informational purposes only. The information is not intended to cover all possible uses, directions, precautions, drug interactions or adverse effects of a particular drug, nor should it be construed to indicate that use of a particular drug is safe, appropriate or effective for a given condition. The information in the Formulary is not intended to constitute or be a substitute for medical advice and should not be relied upon in any such regard. All uses of the Formulary are subject to clinical judgment and actual prescribing patterns may not follow the information provided in the Formulary.*

*The format and content of the drug monographs, regimen monographs, appendices and symptom management information contained in the Formulary will change as they are reviewed and revised on a periodic basis. The date of last revision will be visible on each page of the monograph and regimen. Since standards of usage are constantly evolving, it is advised that the Formulary not be used as the sole source of information. It is strongly recommended that original references or product monograph be consulted prior to using a chemotherapy regimen for the first time.*

*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.*

*While care has been taken in the preparation of the information contained in the Formulary, 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.*

*CCO and the Formulary’s content providers shall have no liability, whether direct, indirect, consequential, contingent, special, or incidental, related to or arising from the information in the Formulary or its use thereof, whether based on breach of contract or tort (including negligence), and even if advised of the possibility thereof. Anyone using the information in the Formulary does so at his or her own risk, and by using such information, agrees to indemnify CCO and its content providers from any and all liability, loss, damages, costs and expenses (including legal fees and expenses) arising from such person’s use of the information in the Formulary.*

[back to top](#)