

Which B.C. residents with mild-moderate COVID-19 are recommended to be treated with Paxlovid[™] (nirmatrelvir/ritonavir)?

Conclusion: People who test positive for SARS-COV-2, who have moderate to severe immunosuppression or who are 60 years of age or older with serious medical conditions are recommended to receive treatment to reduce the risk of progression to severe disease.¹ Consider dose adjustments for renal disease and drug-drug interactions prior to initiating treatment.

The BC Provincial Academic Detailing (PAD) Service delivered the topic "PAD Special Edition: Intro to Paxlovid[™] (nirmatrelvir/ritonavir)" in 2022.² <u>Treatment recommendations</u> for mild-moderate COVID-19 with nirmatrelvir/ritonavir have since been updated by the BC COVID-19 Therapeutics Committee (CTC) (Table 1).¹

- a) Evidence:^{1,3,4} In a 2023 observational study of adult patients in B.C., nirmatrelvir/ritonavir reduced the composite outcome of hospitalization or death in those who were severely (absolute reduction 2.5%) and moderately (absolute reduction 1.7%) immunocompromised. Those with high risk conditions such as end stage lung disease or diabetes treated with insulin also benefited from treatment, but nearly all events occurred in those over 60 years and older. Other individuals, including elderly with less severe comorbidities, did not experience a reduction in hospitalization or mortality when treated with nirmatrelvir/ritonavir. In April 2024, <u>Canada's Drug Agency</u> (formerly CADTH) recommended limiting the use of nirmatrelvir/ritonavir to only those who are severely or moderately immunocompromised.
- b) **Dosing:**⁵ Dose reductions are required for patients with an eGFR < 60 ml/min and those on dialysis. The <u>BC CTC</u> <u>Practice Tool-Drug Interactions and Contraindications</u> provides updated guidance for dosing in renal disease.
- c) Drug interactions:^{5,6} CYP-3A4 related drug-drug interactions are common with nirmatrelvir/ritonavir, some of which may contraindicate its use or result in toxicity. Drug interaction resources such as the <u>BC CTC Practice Tool-Drug</u> <u>Interactions and Contraindications</u>, and <u>Liverpool Interaction Checker</u> should be consulted for management strategies.
- d) Cost and coverage: A 5-day treatment course costs ~\$1400 wholesale and is fully covered by BC PharmaCare.

Table 1: Patients at increased risk for hospitalization or progression to severe COVID-19

Treatment recommended if SARS-COV-2 positive + appreciable symptoms and a non-reassuring presentation and trajectory if:

Moderate to severe immunosuppression

- Solid organ transplant
- Bone marrow or stem cell transplant
- Treatment for a hematological malignancy
- Receiving anti-CD-20 or B-cell depleting agents
- Moderate-severe primary immunodeficiency
- Receiving moderate immunosuppressive agents*
- Cancer treatment for solid tumors
- Advanced or untreated HIV

Aged ≥ 60 years who have serious medical conditions

- End-stage renal disease (eGFR < 30 ml/min or dialysis)
- Diabetes treated with insulin
- Severe or end-stage lung conditions such as COPD, asthma, interstitial lung disease, cystic fibrosis, or neurological conditions requiring Bi-Pap or ventilation
- Severe intellectual or developmental disabilities
- Rare blood and genetic disorders such as sickle cell disease, thalassemia, urea cycle defects

*Refer to the <u>BC CTC Clinical Practice Guide for the Use of Therapeutics in Mild-Moderate COVID-19</u> for examples of moderately and severely immunosuppressive agents.

¹BC COVID Therapeutics Committee (CTC). Clinical Practice Guide for the Use of Therapeutics in Mild-Moderate COVID-19; ²BC PAD Service PAD Special Edition: Intro to Paxlovid[™] (nirmatrelvir/ritonavir); ³Dormuth CR, JAMA Network Open 2023;6(10); ⁴CADTH Reimbursement Recommendation Nirmatrelvir-Ritonavir (Paxlovid[™]). Canadian Journal of Health Technologies Apr 2024, Vol 4, Issue 4; ⁵BC COVID Therapeutics Committee (CTC): Practice Tool – Drug-Drug Interactions and Contraindications; ⁶University of Liverpool COVID-19 Drug Interactions

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