COVID-19 Therapies - nirmatrelvir/ritonavir (Paxlovid), remdesivir (Veklury)

Guidance for healthcare providers April 2025

Various agents are available in BC for the **treatment of COVID-19 in mild-moderately ill patients**. These therapies include a direct-acting oral combination antiviral nirmatrelvir/ritonavir (Paxlovid), an IV antiviral remdesivir (Veklury). Monoclonal antibodies such as sotrovimab (Xevudy) are no longer used due to viral resistance.

Please see the full guide developed by the B.C. COVID Therapeutics Committee for more information:
Clinical Practice Guide for the Use of Therapeutics in Mild-Moderate COVID-19

Who is treatment currently recommended for?

Patients who test positive for COVID-19 via a Polymerase Chain Reaction (PCR) or Rapid Antigen Test (RAT) test

AND have been identified as being at increased risk for needing to go to the hospital for COVID-19:

- Individuals with **moderate to severe immunosuppression**, due to:
  - Solid organ transplant
  - Active treatment for a hematological malignancy
  - Allogeneic bone marrow or stem cell transplant in the last year
  - Autologous bone marrow or stem cell transplant in the last 6 months
  - Receipt of chimeric antigen receptor (CAR) T-cell therapy in the last 6 months
  - Receipt of anti-CD-20 or B-cell depleting agents in the last 2 years[1]
  - Receipt of moderately immunosuppressive agents[2]
  - Receipt of systemic treatment for cancer, including for solid tumors, in the last 6 months (3 months for hormonal therapy)
  - Moderate-severe primary immunodeficiency
  - Advanced or untreated HIV

- Individuals **≥60 years** who have **serious medical conditions**, who have been shown to significantly and consistently benefit from antivirals, such as those with:
  - End-stage renal disease (eGFR < 30ml/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

1. **Severely immunosuppressive agents: Anti-CD-20 agents:** rituximab, ocrelizumab, ofatumumab, obinutuzumab, ibritumomab, tositumomab; **B-cell depleting agents**: epratuzumab, MEDI-551, belimumab, BR3-Fc, AMG-623, Atacicept, antiBR3, alemtuzamab
2. **Moderately immunosuppressive agents: Biologics**: abatacept, adalimumab, anakinra, benralizumab, brodalumab, canakinumab, certolizumab, dupilumab, etanercept, golimumab, guselkumab, infliximab, interferon products (alpha, beta, and pegylated forms), ixekizumab, mepolizumab, natalizumab, omalizumab, resilizumab, risankizumab, sarilumab, secukinumab, tildrakizumab, tocilizumab, ustekinumab, or vedolizumab**; Oral immune-suppressing drugs**: azathioprine, baricitinib, cyclophosphamide, cyclosporine, leflunomide, dimethyl fumerate, everolimus, fingolimod, mycophenolate, siponimod, sirolimus, tacrolimus, tofacitinib, upadacitinib, methotrexate, or teriflunomide; **Oral steroids on an ongoing basis**: dexamethasone, hydrocortisone, methylprednisolone, or prednisone; at a dose of 20mg/d of prednisone equivalent; **Immune-suppressing infusions/injections**: cladribine, cyclophosphamide, glatiramer, methotrexate

COVID-19 Treatment

Health Care Provider Information

BC Centre for Disease Control
Provincial Health Services Authority

Therapy recommendations:

Patients offered treatment should be **appreciably symptomatic from COVID 19.**

Pregnancy and Breastfeeding: Currently available therapies have not been evaluated in pregnancy or breastfeeding. Prescribers may consult Reproductive Infectious Disease on call at BC Women's Hospital if prescribing COVID-19 therapy, especially nirmatrelvir/ritonavir (Paxlovid).

Interactions with oral contraceptives: Patients are encouraged to use additional protection while taking nirmatrelvir/ritonavir (Paxlovid) due to drug interactions leading to lower plasma levels of estrogen.

Pediatrics: Nirmatrelvir/ritonavir (Paxlovid) is not currently approved for children under 18 years in Canada. For pediatric cases for which nirmatrelvir/ritonavir or remdesivir is being considered, prescribers are encouraged to discuss cases with the Pediatric Infectious Disease Specialist at BC Children's Hospital.

COVID-19 Treatment

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THERAPY: nirmatrelvir/ritonavir (Paxlovid) - Direct-acting oral antiviral

When to start: PO BID x 5 days is recommended within **5 days of symptom onset*.** Dose adjustments are required for those with renal disease or dialysis.

Refer to the following resource for guidance on drug-drug interactions, contraindications and renal dosing: Practice Tool – Drug Interactions and Contraindications.

**It is appropriate to allow the addition of adequate time for delivery of medication for those living in remote and rural communities.*

Contraindications and Cautions	Drug-to-Drug Interactions
• **Patients with renal disease (eGFR < 60 ml/min or dialysis) require dose adjustments** • **End-stage liver disease** (Child-Pugh C, cirrhosis) • **Hepatitis B and C, or HIV infection** regardless of treatment status- Expert Consultation is suggested but treatment should not be delayed • Nirmatrelvir/ritonavir **increase the levels of fentanyl and risk of fatal overdose.** Persons with opioid use disorder require counselling and/or expert consultation • **Hypersensitivity to ritonavir or other protease inhibitors** should not be prescribed nirmatrelvir/ritonavir • Nirmatrelvir and ritonavir are potent **inhibitors of CYP 3A4** and increase the concentration of many drugs metabolized by this enzyme. • Nirmatrelvir/ritonavir is also contraindicated with drugs that are **potent CYP3A inducers** where significantly reduced nirmatrelvir or ritonavir plasma concentrations may be associated with the potential for loss of virologic response and possible resistance.	**Significant drug-drug interactions:** (See Practice Tool – Drug Interactions and Contraindications for more details). • Most common contraindications include amiodarone, DOACs, some antipsychotics, statins, midazolam and triazolam, fentanyl and antiepileptics • Some drug-drug interactions can be managed • The most comprehensive drug-drug interaction checker with nirmatrelvir/ritonavir was developed by the University of Liverpool and is found here: https://www.covid19-druginteractions.org/checker. This tool should be consulted when considering modifying therapy due to drug-drug interactions. **Use multiple resources (e.g. LexiComp) as some information may be conflicting or incomplete.**

THERAPY: remdesivir (Veklury) - direct acting antiviral administered by intravenous injection

When to start: IV x 3 daily doses is recommended within **7 days of symptom onset** as an alternative to nirmatrelvir/ritonavir in cases where IV administration is feasible. Patients with a risk of hospitalization of ≥ 5% are currently being prioritized and offered treatment with remdesivir.

Remdesivir infusions are currently being delivered through Health Authority based clinics.

Contraindications and Cautions	Drug-to-Drug Interactions
• Hypersensitivity reactions and infusion **reactions are rare**. • ALT > 5X ULN • Patients with an eGFR of < 30ml/min require dose adjustments and monitoring.	Possesses **no significant drug-drug interactions.**

This document provides guidance only; patients defined above are those who may benefit from treatment. Case-by-case assessment is still required, and the totality of risk factors needs to be considered when offering treatment. Expert consultation can assist with additional risk assessments.