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

Guidance for healthcare providers May 2023

Recently, various novel agents have become 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) and an anti-spike protein monoclonal antibody (mAb) sotrovimab (Xevudy)

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 the treatment currently being considered for?

Refer to: Practice Tool #1- Assessment Steps and **Practice Tool #2- CEV Definitions**

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 who are immunocompromised or have high-risk conditions identified as Clinically Extremely Vulnerable (CEV) regardless of vaccine status or previous infection *(Not all children ages 12-17 who are CEV will benefit from treatment. Those with multiple co-morbidities would have the highest potential benefit)*
- Individuals with TWO of the following three risk factors:
  - ≥70 years (≥60 years if they are Indigenous)
  - Are unvaccinated or under-vaccinated as per Strong Recommendations by NACI^
  - Have at least one serious chronic medical condition*

^ National Advisory Committee on Immunization: i.e., lack of a primary two-dose series PLUS a “Fall Booster” (or a booster in the last year), which may be delayed up to 6 months post COVID-19 infection

*Serious chronic medical conditions may include stroke, heart failure, heart disease, diabetes, kidney or liver disease, chronic lung disease like COPD or interstitial lung disease, neurological conditions. Some discretion can be used

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). People on oral contraceptives should use a back-up method when taking nirmatrelvir/ritonavir due to drug interactions leading to lower plasma levels of estrogen.

COVID-19 Treatment
Health Care Provider Information

BC Centre for Disease Control
Provincial Health Services Authority

Pediatrics: Nirmatrelvir/ritonavir (Paxlovid) is not currently approved for children under 18 years. For pediatric cases for which remdesivir or sotrovimab is being considered, prescribers are encouraged to discuss cases with the Pediatric Infectious Diseases physician on call at BC Children's hospital.

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

When to start: PO BID x 5 days is recommended within **5 days of symptom onset***

Refer to the following resource for guidance on drug-drug interactions or contraindications: Practice Tool 3 – 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
• **Severe renal disease (eGFR < 30ml/min)** • **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 3: 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.**

COVID-19 Treatment

Health Care Provider Information

BC Centre for Disease Control
Provincial Health Services Authority

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.**

THERAPY: sotrovimab (Xevudy) - monoclonal antibody administered by intravenous injection

When to start: IV x 1 dose within **7 days of symptom onset** in extenuating circumstances when remdesivir cannot be given. Sotrovimab has demonstrated reduced neutralization against the BA.2 variant although it may retain some activity. If sotrovimab is used as a last line agent where potential of benefit outweighs the risk, disclosure to patients of risks and benefits in consideration of individual circumstances (clinical status, patient values, logistics) is necessary. Sotrovimab should not be chosen solely for convenience reasons.

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

Contraindications and Cautions	Drug-to-Drug Interactions
Hypersensitivity reactions and infusion **reactions are rare**. If reactions develop during the 1-hour infusion, the infusion should be stopped.	Possesses **no significant drug-drug interactions.**