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

Recently, various novel agents have become available in BC for the treatment of COVID-19 in mild-moderately ill patients. These therapies include an anti-spike protein monoclonal antibody (mAB) sotrovimab (Xevudy) and a direct-acting oral combination antiviral nirmatrelvir/ritonavir (Paxlovid).

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:
- Immunocompromised individuals identified as Clinically Extremely Vulnerable (CEV) Group 1 and Group 2 (CEV 1 and CEV 2), regardless of vaccine status or previous infection
  - Not all children ages 12-17 who are CEV 1 or 2 will benefit from treatment. Those with multiple co-morbidities would have the highest benefit
- Unvaccinated or partially vaccinated individuals with high-risk conditions identified as CEV 3
- Unvaccinated or partially vaccinated individuals:
  - aged ≥70 years with one or more chronic condition/co-morbidity
  - aged ≥ 60 years with three or more chronic conditions/co-morbidities
  - aged ≥ 60 years who are Indigenous

Unvaccinated or partially vaccinated refers to the receipt of 0, 1 or 2 vaccine doses. Two doses of vaccine is considered partially vaccinated for these treatments.

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

Interactions with oral contraceptives: Patients are encouraged to use additional protection while taking 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.

Pediatrics: Nirmatrelvir/ritonavir (Paxlovid) is not currently available for children under 18 years. For pediatric cases for which 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* (CONDITIONAL RECOMMENDATION pending peer-reviewed publication)

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

- 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.

Drug-to-Drug Interactions

Significant drug-drug interactions: (See Practice Tool 3: Drug Interactions and Contraindications for more details).

- Most common contraindications include amiodarone, rivaroxaban, lurasidone, clozapine, midazolam and triazolam
- 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: sotrovimab (Xevudy) - monoclonal antibody administered by intravenous injection

When to start: IV x 1 dose is recommended within 7 days of symptom onset as an alternative to nirmatrelvir/ritonavir in cases where IV administration is feasible.

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

Contraindications and Cautions

Hypersensitivity reactions and infusion reactions are rare. If reactions develop during the 1-hour infusion, the infusion should be stopped.

Drug-to-Drug Interactions

Possesses no significant drug-drug interactions. COVID-19 vaccination after sotrovimab infusion should be delayed by at least 90 days.

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.