How to Use this Guide

This guide is a step-by-step clinical assessment tool for clinicians such as nurses or physicians who are directly involved in assessment and management of patients with mild-moderate COVID-19. Additional materials have been developed to accompany this tool, and include:

- The Clinical Practice Guide, a comprehensive guide with recommendations and supporting evidence
- Practice Tool #2 – Definitions of Clinically Extremely Vulnerable criteria
- Practice Tool #3 – Drug-drug Interaction and Contraindication management tool

Please consult these resources in addition to this Assessment Guide for more comprehensive information. *Therapy roll-out is gradual; consult leadership for details (e.g., availability in your region, use in-hospital or LTC)*

This guide is intended to be practical and was developed clinicians who routinely care for patients with COVID-19. It should not replace clinical judgement.

### STEP-by-STEP ASSESSMENT

#### 1. Verify Treatment Eligibility Criteria:

- **Immunocompromised individuals** identified as Clinically Extremely Vulnerable Group 1 and Group 2 (CEV 1 and CEV 2), regardless of vaccine status or previous infection. *(See Practice Tool 2 – CEV Definitions)*. Generally, these are patients who:
  - Have received a solid organ transplant and are taking immunosuppressive treatment
  - Had a bone marrow or stem cell transplant
  - Are currently being treated for cancer, including haematological malignancies
  - Diagnosed with a moderate to severe primary immunodeficiency
  - Have untreated or advanced HIV (CD4 ≤ 200 cells/mm$^3$)
  - Are taking immunosuppressive treatment, such as high dose of steroids, biologics (e.g., adalimumab, etanercept, infliximab, interferon products), anti-CD20 agents (e.g., rituximab, ocrelizumab, ofatumumab, obinutuzumab, ibritumomab, tositumomab), B-cell depleting agents (e.g., epratuzumab, belimumab, atacicept, anti-BR3, alemtuzumab), or immune-suppressing agents (e.g. cyclophosphamide, cisplatin, methotrexate)
  - Patients who are on dialysis or have severe kidney disease who are also receiving any immunosuppressants

- **Unvaccinated or partially vaccinated individuals with high-risk conditions** identified as Clinically Extremely Vulnerable Group 3 (CEV 3) *(See Practice Tool 2 – CEV Definitions)*. Generally, these are patients who:
- Have Cystic fibrosis
- Have severe COPD or asthma requiring hospitalization in the last year
- Are on long-term home oxygen; assessment for a lung transplant; severe pulmonary arterial hypertension; severe pulmonary fibrosis/interstitial lung disease
- Diagnosed with a rare blood disorder: urea cycle defects; methylmalonic aciduria; propionic aciduria; glutaric aciduria; maple syrup urine disease
- Have had a splenectomy or have functional asplenia
- Have Insulin-dependent diabetes
- Have significant developmental disabilities: Down Syndrome, or Cerebral Palsy, or Intellectual Developmental Disability (IDD), or receiving supports from: Community Supports for Independent Living (CSIL) or Community Living British Columbia (CLBC)
- Are pregnant and have a serious heart disease, congenital or acquired, that requires observation by a cardiologist throughout pregnancy
- Have neurological or other conditions causing significant muscle weakness around lungs requiring the use of a ventilator of continuous Bi-level positive airway pressure (Bi-PAP)
- Are on dialysis or have stage 5 chronic kidney disease (eGFR ≤ 15ml/min)

*Note: Patients on dialysis are in the CEV 2 category for vaccination but are regarded as CEV 3 for treatment*

- **Unvaccinated or partially vaccinated individuals aged ≥70 years with one or more chronic condition/co-morbidity** (e.g., obesity, diabetes, heart failure, stroke, neurological conditions)

- **Unvaccinated or partially vaccinated individuals ≥ 60 years with three or more chronic conditions/co-morbidities** (e.g., obesity, diabetes, heart failure, stroke, neurological conditions)

- **Unvaccinated or partially vaccinated individuals ≥ 60 years who are Indigenous**

*Note: For this group, unvaccinated or partially vaccinated refers to the receipt of 0, 1 or 2 vaccine doses. Previous infection alone is equivalent to 2-dose vaccination without a booster*

**CEV Criteria:**
- Patients who are classified as CEV have received a letter from Dr. Bonnie Henry and usually know who they are
- CEV status *may* make them eligible but consult Practice Guide #2 – CEV Definitions to make sure the patient is still vulnerable. For example, if the patient’s cancer treatment ended or if some time has passed since the receipt of their immunosuppression drugs, they are no longer at risk. Pay attention to dates in the guide. They still qualify for vaccine boosters and their CEV status is not revoked; their risk has simply decreased to the point where treatment may not be needed
- Use additional judgement if such CEV patient is unvaccinated or partially vaccinated
- Pediatric patients and pregnant patients who are in the CEV category require consultation with a BCCH or BCWH specialist; use the on-call contact information and refer to the pregnancy and pediatric sections below

**Indigenous Status:**
- Patients can self-identify
- Patients do not need to provide any documentation or justification of their Indigenous identity
Indigenous individuals face social determinants of health (e.g., remote location, lack of access to culturally appropriate care, housing and food insecurity) that increase their risk of hospitalization and death from COVID-19 similarly to age-matched non-Indigenous individuals with multiple chronic health conditions.

**Chronic Conditions/Co-morbidities**

- A large cohort study in BC showed that many conditions put patients at risk for hospitalization from COVID-19 and disease progression.
- Conditions should be chronic, and generally require medical treatment or follow-up.
- Some at-risk conditions are not related to the respiratory or immune system and may be surprising.
- Co-morbidities/chronic conditions that were shown to increase risk of hospitalization included:
  - Neurological conditions such as epilepsy, dementia, multiple sclerosis, neuropathy
  - Psychiatric conditions such as schizophrenia, bipolar disorder, mania
  - Substance use disorders like opioid addiction, alcoholism
  - Disabilities such as intellectual developmental disability
  - Liver and kidney disease
  - Cardiovascular conditions such as arrhythmia, congestive heart failure, hypertension, stroke
  - Diabetes treated with medication
  - Rheumatic diseases such as rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, lupus
  - Ulcerative colitis or Crohn’s
  - Asthma, COPD, bronchiectasis
  - Smoking, obesity, and frailty also qualify and may not be apparent from medical records
  - Pregnancy
- Conditions that are likely not serious enough to qualify may include:
  - Hypothyroidism
  - Gout
  - Osteoarthritis
  - Vitamin deficiencies such as low iron or vitamin D levels
  - Skin conditions such as eczema or acne, or those treated with topical medication only
  - Anxiety and depression, while serious, have not been linked to increased risk of hospitalization; use judgement, assessment depends on severity and other risk factors.
- This list is a guide only, use clinical judgement and assess the risk in a comprehensive manner, using age, vaccine status and co-existing condition.

**Expected Benefit**

In trials of therapies for mildly-moderately ill patients, the risk of hospitalization decreased from about 6% to about 1%. This is an ~85% relative reduction and a 5% absolute reduction in risk. This was consistent in trials of nirmatrelvir/ritonavir, sotrovimab and remdesivir. These trials were conducted before the identification of Omicron, which carries a much lower risk of hospitalization. In BC, the average hospitalization rate from Omicron is only 1.2%.

Giving a patient who has a 1.2% risk of hospitalization such therapies would decrease their absolute risk very minimally. As such, high-risk patients were selected as initial therapy candidates. Patients who meet the treatment eligibility criteria in this guide have a range of hospitalization risk of approximately 15-25%, with the CEV 1 population being at highest risk. These patients can expect their absolute risk decreasing very significantly, to <5%. In a sub-group analysis of the nirmatrelvir/ritonavir study, 200 highest risk
patients were analysed. Their risk of hospitalization decreased with drug therapy from 16.3% to 1.1%.

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.** Even within the highest-risk priority group, a wide range of risk exists; risk increases by age, number of comorbidities and incomplete vaccination status. In the setting of resource scarcity, expert consultation can assist with additional risk assessment and prioritization. Patients should be informed of these nuances and reassured that if treatment is not being prescribed, that their risk was deemed to be low, and informed of the rationale for the decision. Inversely, a patient may not directly be represented in the eligibility criteria; use the thermal map to conduct treatment eligibility assessment. Use your judgement and ensure that treatment is justifiable (i.e., that the patient has a combination of risk factors that equate to a risk of hospitalization of approximately ≥ 15%).

Use thermal chart to assist further with risk assessment:
2. Ensure Patient has Confirmed COVID-19 Infection

Patients who are eligible for treatment are those who test positive for COVID-19 via a Polymerase Chain Reaction (PCR) or Rapid Antigen Test (RAT) test. During early days of symptom onset, PCR is the preferred diagnostic test due to its increased sensitivity (standard PCR or rapid molecular tests). RAT sensitivity improves on day 3 of symptoms and beyond.

New testing guidelines issued by the BCCDC prioritize patients who may be candidates for treatment. Such patients should be encouraged to get tested if they are symptomatic. In cases of limited access to timely PCR results, if a RAT is provided at the testing centre or if a patient performs a RAT from their own purchased supply, positive results will be accepted for treatment considerations. A positive RAT test does not require confirmation by PCR to proceed with treatment; however, in some settings patients may be asked to also get a PCR test for other reasons (e.g., to facilitate documentation of treatment outcomes in medical records).

Practical Considerations:
- Ensure the test was done recently and that it is positive
- For patients who test positive via a RAT, verify how the test was done and how did the positive result present. Patients can be asked to show a photo or the test itself to ensure therapy is not provided with the intention of diversion or medication stockpiling
- Patients given a gargle test will have a QR code to register the positive test; encourage that they follow the steps outlined on the testing package if they have not already done so
- Epidemiologically linked cases (e.g., household contacts of those who test positive) who have not been confirmed via COVID-19 testing should not be offered treatment. Encourage such patients to make an appointment for testing if they qualify

3. Verify Vaccination Status

Unvaccinated or partially vaccinated refers to the receipt of 0, 1 or 2 vaccine doses. Previous infection alone is equivalent to 2-dose vaccination without a booster. Immunosuppressed patients (CEV 1 and 2) can be offered treatment regardless of vaccine status.

Practical Considerations:
- The last vaccine dose should have been given 14 days ago or longer to be counted
- Although the “AstraZeneca”, “Pfizer” and “Moderna” vaccines are the most common vaccines, many patients in BC received other vaccinations and know them under different names.
- One Janssen vaccine dose necessitated one mRNA vaccine dose to complete the 3-dose immunization
- Verity is a name of the Canadian distributor of the AstraZeneca vaccine, it shows up as “Verity”
- Some patients were immunized outside of Canada; those vaccines are clinically acceptable and count towards their immunization status
Examples of vaccine and infection combinations

<table>
<thead>
<tr>
<th>Dose 1</th>
<th>Dose 2</th>
<th>Dose 3</th>
<th>Vaccination status for treatment assessment of highest-risk individuals</th>
</tr>
</thead>
<tbody>
<tr>
<td>mRNA</td>
<td>mRNA</td>
<td>mRNA</td>
<td>Fully Vaccinated</td>
</tr>
<tr>
<td>AstraZeneca</td>
<td>AstraZeneca</td>
<td>mRNA</td>
<td>Fully Vaccinated</td>
</tr>
<tr>
<td>Janssen</td>
<td>mRNA</td>
<td>Fully Vaccinated</td>
<td></td>
</tr>
<tr>
<td>Verity</td>
<td>AstraZeneca</td>
<td>mRNA</td>
<td>Fully Vaccinated</td>
</tr>
<tr>
<td>Verity</td>
<td>mRNA</td>
<td>mRNA</td>
<td>Fully Vaccinated</td>
</tr>
<tr>
<td>Janssen</td>
<td>mRNA</td>
<td>Not fully vaccinated – 2 doses</td>
<td></td>
</tr>
<tr>
<td>Janssen</td>
<td>AstraZeneca</td>
<td>Not fully vaccinated – 2 doses</td>
<td></td>
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<tr>
<td>AstraZeneca</td>
<td>AstraZeneca</td>
<td>Not fully vaccinated – 2 doses</td>
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</tr>
<tr>
<td>mRNA</td>
<td>mRNA</td>
<td>Not fully vaccinated – 2 doses</td>
<td></td>
</tr>
<tr>
<td>Verity</td>
<td>AstraZeneca</td>
<td>Not fully vaccinated – 2 doses</td>
<td></td>
</tr>
<tr>
<td>mRNA</td>
<td>mRNA</td>
<td>Not fully vaccinated – 1 dose</td>
<td></td>
</tr>
<tr>
<td>AstraZeneca</td>
<td>mRNA</td>
<td>Not fully vaccinated – 1 dose</td>
<td></td>
</tr>
<tr>
<td>Verity</td>
<td>mRNA</td>
<td>Not fully vaccinated – 1 dose</td>
<td></td>
</tr>
<tr>
<td>Infection</td>
<td>mRNA</td>
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</tr>
<tr>
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<td>Infection</td>
<td>Fully vaccinated</td>
<td></td>
</tr>
<tr>
<td>Vitamins</td>
<td>Unvaccinated</td>
<td>Unvaccinated</td>
<td></td>
</tr>
</tbody>
</table>

**Previous infection alone is equivalent to 2-dose vaccination.**

Previous infection with other variants (e.g., Delta) has shown to be insufficiently protective from *re-infection* with Omicron. Vaccination is recommended in those with previous infection history by Public Health and National Advisory Committee on Immunizations.

However, the risk of hospitalization or ICU admission has been observed to be low in those with previous infection in BC. For example, a study in the NEJM published February 2022 showed that effectiveness of previous infection against Omicron with any variant was 90.2%. Furthermore, epidemiological data from South Africa showed that the hospitalization risk went down significantly in the Omicron wave, despite that only ~40% of the population was vaccinated. The low hospitalization rate was attributed in part to a large proportion of patients being previously infected, and very small numbers of re-infected patients developed severe disease.

Precise data on the severity of disease with reinfection in BC is forthcoming. As a 3-dose series is considered fully immunized for the purposes of treatment eligibility assessment, previous infection alone in this highest-risk group is still considered inadequate protection from hospitalization. Patients who have a history of previous infection without any vaccination meet the under-vaccinated definition in this guide. Previous infection plus one vaccine dose, either before or after infection, is considered as if fully vaccinated (see Vaccination).

4. **Establish Symptoms and Symptom Progression**
COVID-19 Mild and Moderate illness categories were developed by the WHO and focus on lower respiratory symptoms and oxygenation status of the patient. Patients offered treatment should be appreciably symptomatic from COVID 19.

Asymptomatic or no longer symptomatic patients should not be offered treatment. This includes patients who were symptomatic at the time of testing but have improved, or those who tested positive as part of screening (e.g., during travel, in the case of an outbreak or at the time of hospitalization). Vague or non-specific symptoms require a great deal of clinical judgement, especially in vulnerable patients (e.g., confusion, a fall, gastrointestinal symptoms) Prophylactic or pre-emptive treatment should NOT be offered. Follow-up is reasonable in patients who would qualify for treatment if otherwise symptomatic. Patients in whom the diagnosis of COVID-19 is not clear from their symptomatology should be referred appropriately.

Mild illness refers to individuals who have any of the various signs and symptoms of COVID-19 (e.g., fever, cough, sore throat, malaise, headache, muscle pain, nausea, vomiting, diarrhea, loss of taste and smell) but who do not have increased work of breathing, dyspnea, reduced oxygen saturations or abnormal chest imaging. These patients can still progress to severe illness, especially if those symptoms are profound, or exist in combination, but the chance is lower than in moderate illness. Flu-like symptoms such as fever and diffuse myalgia are indicative of systemic illness and have been shown to be associated with higher risk of illness progression. Great deal of case-by-case clinical judgement is required to discern whether mild symptoms warrant treatment. In equivocal cases, a 24–48-hour follow-up period is reasonable, if still within the treatment window.

Moderate illness refers to evidence of lower respiratory disease during clinical assessment or imaging but who still have an oxygen saturation (SpO2) ≥94% on room air. Oxygen saturation of <94% usually necessitates supplemental oxygen support and is classified as severe illness. Patients with moderate illness are more likely to progress to severe illness and can be offered therapy.

Illness trajectory is a useful in establishing progression of COVID-19. Patients who are visibly deteriorating are more likely to become severely ill. Treatment is unlikely to benefit those who are mildly ill who are clearly improving on their own. Treatment should not be given to asymptomatic or minimally symptomatic patients.

5. Calculate the Time since Symptom Onset

Symptom windows vary with each therapeutic agent and generally follow study inclusion criteria. Sotrovimab and remdesivir should be given within 7 days of symptom onset whereas for oral antivirals should be given within 5 days. It is appropriate to allow the addition of adequate time for drug delivery for those living in remote and rural communities.

Many patients do not recall when the first developed symptoms. Questions such as “How did you feel when you got tested?”, “What made you call for your test appointment” can be useful.

If patients have passed their symptom window, they can be reassured that in most cases, they would have already cleared the virus from their nasopharynx and have mounted an antibody response. Therapies like
antivirals and antibodies have no additional impact. There is little clinical rationale for extending the treatment window in practice and such practice cannot be routinely recommended in a general guide.

Patients who have had prolonged symptoms or more or protracted illness despite recently testing positive for COVID-19 require a clinical assessment of the illness trajectory to rule out other causes responsible for their symptoms. Patients are encouraged to get tested as soon as possible after COVID symptoms appear to avoid conflating persistent symptoms with COVID-19 infection.

6. Note on Patient Location

This guide refers to patients on the basis of their symptoms and not their physical location.

While mildly-moderately ill patients are usually outpatients recovering at home, patients can reside in Long-Term Care, present to the emergency department, or be hospitalized. Hospitalized patients who are mildly-moderately ill may be hospitalized for other reasons and incidentally diagnosed, be part of nosocomial outbreaks, or be hospitalized for COVID-related complications (e.g. a fall or dehydration), but still be mildly-moderately ill on the basis of their respiratory status. The receipt of systemic corticosteroids or baricitinib for the treatment of COVID-19 means that the patient’s severity of symptoms is beyond mild-moderate and antiviral or monoclonal antibody treatment should not be offered.

Hospitalized patients, if they meet treatment criteria, can more easily receive intravenous therapy than outpatients. Remdesivir, due to its multiple-day IV dosing, is only feasible in this setting and has been added to nirmatrelvir/ritonavir and sotrovimab as an option in this population. These three drugs are similar in their efficacy but differ in safety and administration considerations. The ultimate choice of therapeutic agent in-hospital depends on drug scarcity, drug-drug interactions and contraindications and needs to be determined on a case-by-case basis at the time of treatment selection.

Nirmatrelvir/ritonavir roll-out is gradual; consult leadership for drug/prescribing availability in your location (e.g., ED, in-hospital, in LTC).

7. Assess Contraindications

Nirmatrelvir/ritonavir has an extensive list of contraindications. Consult the accompanying Practice Tool #3 – Drug Interactions and Contraindications.

Most common contraindications with nirmatrelvir/ritonavir include:

- Severe renal disease (eGFR < 30ml/min or dialysis) – sotrovimab is an option for these patients
- End-stage liver disease (Child-Pugh C or cirrhosis)
- In patients with hepatitis B and C, or HIV infection regardless of treatment status, Specialist Consultation (ID, HIV GP or GI) is recommended.
- Patients with hypersensitivity to ritonavir or other protease inhibitors should not be prescribed nirmatrelvir/ritonavir.
- Many drug-drug interactions contraindicate the use of nirmatrelvir-ritonavir. The most common ones include:
  - **Novel anticoagulants rivaroxaban and apixaban**: switching the patient to dabigatran is
recommended in some circumstances. A Special Authority coverage category has been arranged for this indication for 10 days while taking nirmatrelvir/ritonavir. Patient should be provided with a prescription. The dose of dabigatran depends on their renal function and if not known, age. (see Practice Tool #3 – Drug Interaction and Contraindications) (The 10-day dosing regimen of dabigatran has been simplified in consultation with thrombosis experts)

<table>
<thead>
<tr>
<th>If eGFR or renal function available:</th>
<th>If eGFR or renal function unknown:</th>
</tr>
</thead>
<tbody>
<tr>
<td>eGFR ≥50</td>
<td>age &lt; 75</td>
</tr>
<tr>
<td>dabigatran 150 mg BID.</td>
<td>dabigatran 150 mg BID.</td>
</tr>
<tr>
<td>eGFR 30-49</td>
<td>age ≥75</td>
</tr>
<tr>
<td>dabigatran 110 mg BID.</td>
<td>dabigatran 110 mg BID.</td>
</tr>
<tr>
<td>eGFR &lt;30</td>
<td></td>
</tr>
<tr>
<td>do not use dabigatran.</td>
<td></td>
</tr>
</tbody>
</table>

1. Start first dose when patient would normally take next dose of rivaroxaban or apixaban.
2. If patient already on reduced dose rivaroxaban (10 or 15 mg once daily) or apixaban (2.5 mg twice daily), switch to dabigatran 110 mg BID.
3. DO NOT take with ASA, NSAIDs or other anticoagulants.

- **Antiarrhythmics** like amiodarone and dronedarone: Holding the medication may be considered due to prolonged half-lives and restarted 3 days after nirmatrelvir/ritonavir treatment finishes
- **Statins** like lovastatin or simvastatin: Lipid lowering agents can be held for 5 days during treatment with nirmatrelvir/ritonavir and restarted 3 days after treatment finishes
- **Antipsychotics** like lurasidone and quetiapine. Dose adjustments with oral forms may be possible
- **Inhaled salmeterol**
- **Antiepileptics** such as valproic acid, carbamazepine and phenytoin are contraindicated and due to prolonged enzyme induction, there are no modification options
- **Opioids especially fentanyl**: patients who use drugs need to be very carefully selected, counselled and monitored

Sotrovimab is known to cause hypersensitivity reactions and infusion reactions, although they are rare. Sotrovimab is contraindicated in those who are hypersensitive to this drug or to any ingredient in the formulation: if reactions develop during the 1-hour infusion, the infusion should be stopped.

Remdesivir is contraindicated in those with demonstrated hypersensitivity to the product or any of its ingredients, eGFR < 30ml/min (due to the cyclodextrin component) and pregnancy (due to lack of data). Remdesivir should not be used in patients with ALT ≥5 times the ULN. The pharmacokinetics and safety of remdesivir in hepatic impairment have not been evaluated; expert consultation is recommended.

8. Assess and Manage Drug-Drug Interactions (pertains to nirmatrelvir/ritonavir)

Nirmatrelvir and ritonavir have significant drug-drug interactions. Some drug-drug interactions can be managed. Clinicians must take a Best-Possible Medication History and review drug-drug interactions and provide patient counselling see Practice Tool 3 – Drug Interactions and Contraindications. Please note that some medications may not be on PharmaNet (e.g., anti-cancer drugs).

The most comprehensive resource for DDI assessment with nirmatrelvir/ritonavir is available from the
University of Liverpool at [https://www.covid19-druginteractions.org/checker](https://www.covid19-druginteractions.org/checker). No resource contains 100% of the drug-drug interactions. Check an additional resource (e.g., LexiComp) for drug-drug interactions not listed on the University of Liverpool website.

Most common drug-drug interactions in addition to those listed in contraindications include:

- Opioids such as fentanyl and methadone: Patients with substance use disorder who routinely use opioids should cautioned due to potential for overdose. Methamphetamine levels also increase; use caution.
- Transplant medications such as tacrolimus and cyclosporine: Transplant specialist consultation is recommended.
- Other statins such as atorvastatin: lipid lowering agents can be held for 5 days during co-administration with nirmatrelvir/ritonavir and restarted 3 days after treatment ends.
- Certain anticancer drugs, especially tyrosine kinase inhibitors (end in “-nib”): consult the BC Cancer Agency if an interacting anti-cancer drug is on the list or if the cancer medication is not on PharmaNet (IV medications).
- Some systemic and inhaled corticosteroids: Management depends on indication and type of steroid.
- Some antidepressants: Most can be co-administered, but patients need to be counselled about increase risk of adverse effects like sedation or dizziness.
- Calcium channel blockers like amiodipine, diltiazem or verapamil: lower doses can be co-administered with increased patient self-monitoring.
- HIV medications: Infectious Diseases consultation is recommended; the overall recommendation from BCCfE is to continue the regimen unaltered.
- Hormonal birth control: Back-up contraception methods should be used due to decreased levels of estrogen in estrogen-containing contraceptives.

9. Special Step for Pregnancy, Breastfeeding and Pediatrics

Currently available therapies have not been evaluated in pregnancy or breastfeeding. Most BC reproductive experts agree that sotrovimab may be used, and also support nirmatrelvir/ritonavir use due to lack of harm in animal studies and experience with other protease inhibitors in pregnant or breastfeeding women. Clinicians who are managing women who are candidates for treatment can connect with the Reproductive ID physician at BC Women’s Hospital (604-875-2161) for guidance and assistance.

Most patients who are candidates for treatment are over the age of 60, and very few pregnant patients are expected to present for treatment. Such patients usually have other risk factors such as significant immunosuppression or cardiac issues and are followed by a specialist.

Patient 12-17 will only be offered treatment if they are significantly immunocompromised (i.e., CEV) and have additional risk factors as determined by consensus from their group. Such patients should be managed in collaboration with the BC Children’s Hospital Pediatric Infectious Diseases Specialist on-call. Sotrovimab is the only approved therapeutic in this age group.

10. Select Appropriate Therapy

The COVID Therapeutics Committee has issued the following recommendations for eligible patients:

**Nirmatrelvir/ritonavir 300/100mg PO BID x 5 days is recommended** within 5 days of symptom onset.
The dose of nirmatrelvir/ritonavir is nirmatrelvir/ritonavir 300/100mg PO BID x 5 days for those with eGFR > 60 ml/min. It is supplied as a pre-packaged kit containing both products: 2 tablets of nirmatrelvir 150mg and 1 tablet of ritonavir 100mg per dose. The patient takes 3 tablets per dose, for a total of 30 tablets during the treatment course.

Patients with an eGFR of 30-60 ml/min should take nirmatrelvir/ritonavir 150/100mg PO BID x 5 days, or one nirmatrelvir 150mg tablet and one ritonavir 100mg tablet per dose. The second nirmatrelvir tablet should be removed from the kit from each dose by the dispensing pharmacist for the patient to avoid confusion and diversion.

OR, if drug-drug interactions or contraindications prohibit administration (See Practice Tool 3 – Drug Interactions and Contraindications)

Sotrovimab 500mg IV x 1 dose is recommended within 7 days of symptom onset as an alternative to nirmatrelvir, in cases where IV administration is feasible

Patients need to be referred to their individual health authority for a sotrovimab infusion.

OR, in mildly-moderately ill hospitalized patients admitted for non-COVID reasons only

Remdesivir 200mg IV on day 1, followed by 100mg IV on days 2 and 3 can be considered within 7 days of symptom onset as an alternative to nirmatrelvir/r or sotrovimab

THERE IS NO INDICATION TO COMBINE THESE THERAPIES: Due to high efficacy with monotherapy and limited additional absolute benefit, patients should receive ONE COVID-19-specific therapy.

Inhaled budesonide 800 μg twice daily for 14 days may be considered on a case-by-case basis in patients who have significant lower respiratory tract symptoms (cough, shortness of breath) for symptom relief in addition to other therapies or as monotherapy. There is no evidence of additional benefit of inhaled steroids to antivirals or antibody therapy. Use clinical judgement and symptom type, severity and progression.

Colchicine is not recommended due to low certainty of benefit and potential risk of adverse events and additional immunosuppression in this population.

Fluvoxamine is not recommended due to low certain of benefit and potential risk of adverse events associated with the dose evaluated (100mg PO BID) especially in vulnerable populations and elderly.

11. Provide Patient Information and Counselling

Use patient-specific materials to provide drug information.

Patient information considerations:
• Patient-facing materials are located on the BCCDC website
• Provide clear drug-drug interaction management strategies. Ask patients to repeat instructions back. Call the patient's pharmacy if significantly amending the patient’s medications. Follow-up by the dispensing pharmacist at the end of treatment may be useful if significant medication changes were made
• Provide any follow-up instructions, particularly lab work like INR monitoring
• Caution patients of common side effects. For nirmatrelvir/ritonavir these can include:
  o Gastrointestinal upset, nausea, and diarrhea
  o Taste disturbance or altered taste sensation
  o Headache
  o Hypertension
  o Muscle aches
• Patients should be encouraged to call if they develop significant or unexpected adverse effects of these therapeutics. These are novel agents and real-world data on their use is currently lacking. Adverse event reporting can be done through the Health Canada Adverse Drug reporting tool on their website.
• Use Practice Tool #4 – Counselling Checklist to ensure all patient information has been provided