

BC COVID THERAPEUTICS COMMITTEE (CTC)

Practice Tool #1 – Assessment Guide for Clinicians

GENERAL INFORMATION

How to Use this Guide

This guide is a step-by-step clinical assessment tool for clinicians such as physicians, pharmacists and nurse practitioners 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

In this Tool you will find:

1. [Who can prescribe](#) and centralized prescribing through [Service BC](#) (811)
2. [Expanded eligibility criteria](#) including the patient [self-screener](#)
3. How to determine [risk of hospitalization](#)
4. [Recommendations](#) for treatment based on risk – and if treatment is being pursued:
5. Confirming COVID-19 – [Testing](#)
6. [Assessing vaccine](#) or previous infection status
7. Establishing [symptoms and progression](#)
8. Calculating [treatment window](#)
9. Assessing contraindications
10. Assessing and managing [drug-drug interactions](#) (including how to access the [pharmacy support line](#))
11. Peer-peer physician support including for [pregnant women](#), [pediatrics](#) and ID
12. [PAXLOVID Prescription](#) link and [pharmacies that carry PAXLOVID](#)
13. [Referring for remdesivir](#) to the Health Authorities
14. [Patient counselling and resources](#)

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. Who Can Prescribe and Centralized Prescribing

At this time, anyone with a license to prescribe can prescribe nirmatrelvir/ritonavir.

Patients are encouraged to make an appointment with their primary care provider for COVID-19 treatment. There may be cases where patients who have a primary care provider are not be able to get an appointment quickly enough to meet the 5-day treatment window. Furthermore, patients may not have a primary care provider, or the primary care provider may not be comfortable with nirmatrelvir/ritonavir.

In these situations, patients should be advised to call Service BC at 1-888-COVID19

They will be screened by an agent for eligibility and if they qualify, put through to a centralized line staffed by physicians and pharmacists dedicated to COVID assessment and treatment (CATE line). This line is for patients only.

Patients who call the office asking for an appointment for COVID-19 therapy can be first directed to the [Self-Screener](#) to see if they qualify. The patient can be advised to go to www.covidtreatments.gov.bc.ca, google “COVID-19 Therapy Self-Assessment Screen” or call 1-888-COVID19 if they would rather talk to an agent. The Self-Screener will guide the patient in determining if they have received the appropriate testing, verify that they are symptomatic and take them through the basic eligibility criteria.

2. Verify Treatment Eligibility Criteria and/or Self-screener

Current eligibility criteria have been developed using BC data that assesses risk of hospitalization from Omicron based on age, vaccine status and number and type of at-risk conditions. Nirmatlevir/ritonavir eligibility criteria are:

- Immunocompromised individuals^{1,2} and those with high-risk conditions³ identified as Clinically Extremely Vulnerable Group 1¹, Group 2², and Group 3³ (**CEV 1, CEV 2, and CEV 3**), regardless of **vaccine status** or previous infection. (See also [Practice Tool 2 – CEV Definitions](#)).
- Individuals with **TWO of the three** following risk factors:
 - o **≥70 years** (≥ 60 years if Indigenous), AND/OR
 - o **unvaccinated** or **under-vaccinated** as per Strong Recommendations by NACI[^], AND/OR
 - o have a **serious chronic medical condition***
- **Individuals residing in Long Term Care facilities** (see guidance statement below)
- CEV 1: severe immunocompromise due to, e.g., solid organ transplant, bone marrow or stem cell transplant, treatment for hematological malignancy, receiving anti-CD20 or B-cell depleting therapies
- CEV 2: moderate immunocompromise due to e.g., receiving immunosuppressive agents, moderate-severe primary immunodeficiency, cancer treatment for solid tumors, advanced or untreated HIV
- CEV 3: e.g., cystic fibrosis, severe asthma or COPD, diabetes requiring insulin, intellectual and developmental disabilities, rare blood disorders, dialysis, neurological conditions requiring Bi-PAP or chronic ventilation, cancer not captured above

[^] [National Advisory Committee on Immunization](#) strongly recommends a primary two-dose series PLUS a subsequent dose (XBB or bivalent) in the last year for those ≥65 or with serious chronic conditions, which may be delayed 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.

Patients can also access a [self-screener online](#) (or by calling 1-888-COVID19 if they’d rather speak to a Service BC service agent) to see if they meet the eligibility criteria above.

CEV Criteria:

- Patients who are classified as CEV have received a letter from Dr. Bonnie Henry or communication from Public Health 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
- 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
- The age criterion was lowered for Indigenous patients to mirror booster recommendations set by BC

Un- or Under-vaccination

- Optimal COVID-19 vaccine status is based on recommendations from The [National Advisory Committee on Immunizations](#) (NACI)
- Recommendations are presented as “Strong Recommendations” (worded as “should be offered”) and “Discretionary Recommendations” (worded as “may be offered”) – only Strong Recommendations are considered herein
- **Currently, NACI strongly recommends the following immunization strategy, which is used herein to define what is considered fully or optimally vaccinated:**
 - A primary two-dose mRNA vaccine series for all adults.
 - A three-dose primary series for those who are immunocompromised (CEV 1 and 2).
 - A “Fall Booster” for those ≥ 65 years and older or those < 65 who have [serious chronic medical conditions](#)
 - The Fall Booster may be delayed for up to 6 months in case of a COVID-19 infection
 - In the Fall of 2023, an XBB 1.5 vaccine has replaced the previous bivalent vaccine and is no longer referred to as a “booster”
- Patients who are not vaccinated in accordance with NACI’s strong recommendations would be considered under-vaccinated
- As treatment in this assessment guide is directed at older patients or those with chronic conditions, generally, *a lack of a vaccine dose in the last year is a good gauge for under-vaccination*

Chronic Condition/Co-morbidity

- A serious, chronic medical condition should be considered when assessing eligibility criteria
- These conditions have been harmonized with other guidelines that list risk factors for hospitalization and mortality, for example Guidelines by [the National Advisory Committee on Immunizations](#)
- This list does not include CEV-defining conditions as such patients are eligible for treatment irrespective the presence of other risk factors
- Co-morbidities/chronic conditions that should be considered include:
 - Cardiovascular conditions such as congestive heart failure, heart disease (post-MI, angina)

- Diabetes treated with medication
- Liver and kidney disease
- COPD, bronchiectasis, interstitial lung disease
- Neurological conditions such as epilepsy, multiple sclerosis, stroke
- Rheumatic diseases such as rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, lupus
- Ulcerative colitis or Crohn's
- Only one condition is required
- Milder conditions that have not been shown to significantly increase the risk of hospitalization or mortality from Omicron should not qualify. Conditions that are excluded from the eligibility criteria:
 - Hypertension
 - Dyslipidemia
 - Benign prostatic hypertrophy
 - Hypothyroidism
 - Arthritis
 - Conditions that are not managed with medications
- This list is a guide only, **use clinical judgement** and assess the co-morbidity in a comprehensive manner, including the number of conditions, how controlled they are and how they impact the patient's health status

Residing in Long Term Care Facilities

- Private and health-authority operate LTC facilities qualify
- The level of care the resident receives does not matter
- All residents are eligible
- It is important to recognize that there are no data characterizing the benefits and harms of COVID-19 treatment in patients residing in LTC facilities – treatment may be considered depending on clinical presentation, symptom trajectory, risk factors for progression to severe disease, goals of care, presence of drug-drug interactions and tolerance of potential adverse effects

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.**

2. Assess the Risk of Hospitalization from Omicron

Risk assessment can help with clinical decision making and discussions with patients. The CTC collaborated with the BCCDC to create thermal risk maps in the first wave of Omicron (see Practice Guide); while these thermal maps remain informative, the absolute risk is over-estimated by these data.

In the BC population, the general risk of hospitalization and mortality from COVID-19 is approximately 0.3% and 0.1% respectively, making treatment futile for the average individual with COVID-19. However, as age and other risk factors such as under-vaccination and high-risk comorbidities accumulate, the risk increases to a point where treatment is warranted.

Recent BC-specific evidence has suggested published [BC analysis](#) of nirmatrelvir/ritonavir during the Omicron waves showed that untreated patients in the CEV 1, 2 and 3 categories had a risk of hospitalization

and mortality of 3.2%, 3.1% and 3.5%, respectively. Some groups such as immunocompromised elderly had a risk of hospitalization and mortality exceeding 5%.

Furthermore, many BC residents have now been exposed to COVID-19 and have additional protection from natural infection, but about 40% of elderly have not. A [recent BC study](#) showed that adults 80 years and older without hybrid immunity had a hospitalization rate of about 3.5%.

Expected Benefit

Initially, randomized controlled trials of therapies for mildly-moderately ill patients showed a decrease in risk from ~5% to ~1% with treatment, for an NNT of 25 to prevent one hospitalization. However, real-world data have shown that the benefit is likely much smaller, with an average NNT of 100-200 to prevent one hospitalization. As hospitalization rates do not generally drop below 1% even in treated patients, treatment likely has no benefit in individuals with a baseline hospitalization risk of below 1%.

3. Follow Recommendations

Nirmatrelvir/ritonavir 300/100mg PO BID x 5 days (150/100mg PO BID x 5 days in eGFR 30-60 ml/min) **is recommended** within 5 days of symptom onset for patients with a non-reassuring symptom presentation and trajectory who are at an increased risk for hospitalization or progression to severe COVID-19 as defined by the eligibility criteria.

NOTES:

The eligibility criteria above apply to outpatients, patients presenting to the emergency department or hospitalized patients who have COVID-19 of mild-moderate severity. See below for eligibility criteria for residents of long-term care facilities.

Strong clinical judgment assessing symptoms and symptom trajectory is particularly important in immunocompromised patients.

The symptom window for nirmatrelvir/ritonavir can be extended to 7 days in outpatients if they would otherwise be referred for remdesivir solely based on its longer treatment window.

Nirmatrelvir/ritonavir **may be considered** in patients who reside in Long Term Care (LTC) facilities. There are a lack of data supporting the efficacy and safety of nirmatrelvir/ritonavir in patients residing in LTC facilities. Treatment may be given depending on patient’s clinical presentation, symptom trajectory, risk factors for progression to severe disease, goals of care, presence of drug-drug interactions and tolerance of potential adverse effects. Nirmatrelvir/ritonavir should not be used for post-exposure prophylaxis as data for this indication have been negative.

If nirmatrelvir/ritonavir cannot be given to eligible patients due to drug-drug interactions or contraindications ([See Practice Tool 3 – Drug Interactions and Contraindications](#)),

Remdesivir 200mg IV on day 1, followed by 100mg IV on days 2 and 3 (200mg IV on day 1, followed by 100mg IV 48-72 hours later in eGFR less than 30ml/min) **is recommended** within 7 days of symptom onset as an alternative to nirmatrelvir/ritonavir to outpatients at highest risk of progression to severe disease, i.e., in those:

- Immunocompromised individuals identified as Clinically Extremely Vulnerable group 1 (**CEV 1**) regardless of age, vaccine status or previous infection.

- Clinical Extremely Vulnerable patients in groups 2 and 3 (CEV 2/3) aged 60 years or older, or
- Under **extenuating circumstances**, (clinical judgment required), patients who have NOT had a COVID-19 vaccine or COVID-19 infection in the last year who are:
 - CEV 2/3 less than 60 years, or
 - Elderly 70 years or older with 3 or more chronic conditions

NOTES:

Outpatients with the highest risk of hospitalization are currently being prioritized and offered treatment with remdesivir due to operational constraints and unclear benefit in lower risk individuals.

Inpatients with mild-moderate COVID-19 are at higher risk of progression to severe disease than outpatients, and they may be offered remdesivir in accordance with the nirmatrelvir/ritonavir eligibility criteria if drug-drug interactions or contraindications are present.

4. Ensure Patient has Confirmed COVID-19 Infection - Testing

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. Most patients present for treatment as a result of a RAT. RATs are less sensitive in the first 24-48 hours of symptoms, but sensitivity increases on days 3-4, and with repeat testing it parallels that of a PCR test.

Testing guidelines in BC continue to focus on a RAT-based test-to-treat strategy. Patients are encouraged to self-administer a RAT as soon as they have symptoms. A positive RAT test does not require confirmation by PCR to proceed with treatment. A negative RAT should be repeated every 24 hours if it remains negative and symptoms persist, until the end of the 5-day treatment window is reached. Clinicians can also order a PCR at their discretion, for example in high-risk patients (e.g., CEV 1) who remain negative via RAT but the clinical suspicion is very high. Treatment may also be started empirically while awaiting PCR results.

Testing guidance for RAT and PCR (NAAT) use is currently being developed. Check back for an updated link for testing guidance for the 2023/24 respiratory virus season.

Practical Considerations:

- Ensure the test was done recently, was administered correctly and that it is in fact positive
- 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 self-administer a RAT to see if they are positive with COVID-19
- For more information on testing performance, see [Clinical Practice Guide](#)

5. Verify Vaccination Status

“Unvaccinated” refers to the receipt of 0 vaccine doses and no history of previous infection.

“Under-vaccinated” refers to the lack of vaccination as per “Strong Recommendations” by the [National Advisory Committee on Immunizations](#) (NACI) Recommendations are presented as “Strong Recommendations” (worded as “should be offered”) where the evidence of benefit for a vaccine is

convincing, and “Discretionary Recommendations” (worded as “may be offered”) where there is a paucity of data or an unclear clinical benefit.

Currently, NACI strongly recommends the following immunization strategy, which is used herein to define what is considered fully or optimally vaccinated:

- A primary two-dose mRNA vaccine series for all adults.
- A three-dose primary series for those who are immunocompromised (CEV 1 and 2).
- A “Fall Booster” for those ≥ 65 years and older or those < 65 who have [serious chronic medical conditions](#)
- The Fall Booster may be delayed for up to 6 months in case of a COVID-19 infection
 - In the Fall of 2023, an XBB 1.5 vaccine has replaced the previous bivalent vaccine and is no longer referred to as a “booster”

Patients who are not vaccinated in accordance with NACI’s strong recommendations would be considered under-vaccinated. When assessing vaccine status for treatment eligibility, *a lack of a vaccine dose in the last year (and a lack of infection which could delay the dose) is a good gauge of under-vaccination* since the presence of another risk factor (older age or chronic conditions) is required for treatment, which is also a risk factor where a booster would be recommended.

Previous infection is assumed in most patients as over 80% of BC residents have had COVID-19 infection. Previous infection is not considered for eligibility criteria or by NACI guidelines as it is difficult to determine who has been infected, when, and the degree of protection the infection offers.

Practical Considerations:

- Clinicians may wish to access the CareConnect registry to obtain vaccination records as many patient no longer recall their last vaccine dose or know whether they are optimally immunized
- The last vaccine dose should have been given 14 days ago or longer to be counted
- NACI guidelines focus on mRNA vaccines; those who have had other vaccines require an additional mRNA vaccine dose as a part of their primary series
- Bi-valent and monovalent mRNA vaccines count equally
- Waning of vaccine efficacy has been observed; however, waning of immunity is considered in NACI guidelines and hence boosters are recommended
- Currently, high risk individuals (those who are elderly or have chronic conditions) are strongly recommended to have received a “Fall Booster”, i.e., between September and December of 2022
- However, such a booster could be delayed for up to 6 months in cases of COVID-19 infection
- Generally, a high-risk patient who has received a booster in the last year is adequately immunized
- Spring boosters are discretionary and not considered herein
- However, such a booster could be delayed for up to 6 months
- Clinical judgement is required when assessing a patient who has received a first or second vaccine dose in the last 3 months or who has had multiple COVID-19 infections; the risk of hospitalization of such patients is likely lower

Examples of vaccine statuses in certain patient groups

Patient type	Vaccine regimen	Vaccine status
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CEV of any age	2-dose primary mRNA series in 2021 without booster	Under-vaccinated
CEV of any age	3-dose primary mRNA series in 2021/22 without booster	Under-vaccinated
CEV of any age	3-dose primary mRNA series and a booster in Dec 2022	Adequately vaccinated
CEV of any age	3-dose primary mRNA series and COVID infection Oct 2022	Under-vaccinated
Healthy 50 y/o	2-dose primary mRNA series in 2021 without booster	Adequately vaccinated
Healthy 50 y/o	1-dose primary series with Janssen vaccine	Under-vaccinated
60 y/o with CHF	2-dose primary series and booster in Sept 2022	Adequately vaccinated
50 y/o with renal disease	2-dose primary mRNA series without booster	Under-vaccinated
40 y/o with MS	2-dose primary mRNA series, COVID infection Sept 2022	Under-vaccinated
30 y/o with diabetes	2-dose primary mRNA series, COVID infection Sept 2022 and Fall booster in April 2023 (delayed due to infection)	Adequately vaccinated
75 y/o	2-dose primary mRNA series without booster	Under-vaccinated
75 y/o	2-dose primary mRNA series and booster in Oct 2022	Adequately vaccinated
80 y/o	2-dose primary mRNA series and COVID infection Apr 2023	Under-vaccinated
85 y/o	2-dose primary mRNA series and COVID infection Sept 2022 and Feb 2023 (delaying booster until 6 mo post-infection)	Adequately vaccinated

6. 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 or have a non-reassuring clinical presentation.**

A non-reassuring clinical presentation is one that poses concern to the health care provider. A CEV-1 patient may only have a low-grade fever; however, this may not be reassuring to their transplant team.

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.*

7. Calculate the Time since Symptom Onset

Symptom windows vary with each therapeutic agent and generally follow study inclusion criteria. **Remdesivir** (and if used in rare cases, sotrovimab) **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.** To facilitate the receipt of oral therapy in the highest risk patients (5% or greater), the nirmatrelvir/ritonavir treatment window can be extended to 7 days if the patient would otherwise be referred for remdesivir based solely remdesivir’s longer treatment window (i.e., the patient exceeds the 5-day window but is within the 7-day window).

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 may 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. Patients who are immunocompromised or very elderly may not have symptoms that are clinically typical and may have protracted courses of illness. Judgement is required in such cases.

Note on Patient Location

This guide refers to patients based on 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.

The recommendations in this Guide apply to all patients irrespective of their physical location.

8. 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) – remdesivir is an option for these patients
- End-stage liver disease (Child-Pugh C or decompensated cirrhosis)
- In patients with hepatitis B and C, or HIV infection regardless of treatment status, *Specialist Consultation (ID, HIV GP or GI) is recommended but treatment should not be delayed or withheld*
- 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. Some can be held depending on the clinical scenario. 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*)

If eGFR or renal function available:	
eGFR ≥50	dabigatran 150 mg BID.
eGFR 30-49	dabigatran 110 mg BID.
eGFR <30	do not use dabigatran.

If eGFR or renal function unknown:	
age < 75	dabigatran 150 mg BID.
age ≥75	dabigatran 110 mg BID.

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.
- **NEW: Apixaban 5mg PO BID:** Recent data support a dose reduction for apixaban 5mg PO BID to 2.5mg PO BID for 7 days (i.e., the duration of the Palxovid treatment and 2 additional days). This option may be used if switching to dabigatran is not feasible.
 - **Antiarrhythmics** like amiodarone and dronedarone: Holding the medication may be considered due to prolonged half-lives and restarted 2 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 2 days after treatment finishes
 - **Some antipsychotics** like clozapine that are hard to adjust, or injectable quetiapine

- **Inhaled salmeterol**; holding salmeterol during a respiratory illness may not be possible but an alternative inhaler (e.g., salbutamol) could be considered
- **Antiepileptics** such as 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 based on the risk of overdose, counselled and monitored

Remdesivir is contraindicated in those with demonstrated hypersensitivity to the product or any of its ingredients. 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. Remdesivir is not officially approved in renal disease or dialysis; however, it has been widely used and deemed safe in this population.

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.

9. Assess/Manage Drug-Drug Interactions (pertains to nirmatrelvir/ritonavir); use Pharmacy Support

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>. 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.

If you need DDI support, community pharmacists who dispense Paxlovid can help. Please contact the community pharmacy that will dispense Paxlovid for the patient for assistance with drug-drug interactions. If drug interactions are found at the time of dispensing, be prepared that the assessing pharmacist will contact you to put a management plan in place.

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 be 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 increased risk

of adverse effects like sedation or dizziness

- Calcium channel blockers like amlodipine, 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

For additional support on how to manage patients on anti-cancer medications or HIV patients, call:

BC Cancer COVID Pharmacist: Regional BC Cancer Centre pharmacists are available to answer questions between the hours of 8am - 4pm Monday through Friday; emails sent on weekends and Statutory Holidays will be responded to by a pharmacist the following working day. Refer to the table below for contacting the correct centre:

Centre	Pharmacist Consult Line
Abbotsford	Email: bcca_acacupharmacists@bccancer.bc.ca Phone: 604-851-4710 EXT. 645242
Kelowna	Email: BCCA_CSIPharmacists@phsa.ca Phone: 250-712-3900 ext 686758
Prince George	Email: cndan@bccancer.bc.ca Phone: 250-645-7317
Surrey	Email: BCCA_FVCCPharmacists@phsa.ca > Phone: 604-930-4002 #2
Vancouver	Email: ACUPharmacist@phsa.ca Phone: 604- 877-6098 ext 672632
Victoria	Email: VICACUPharm@bccancer.bc.ca Phone: 250-519-5500 ext 693795

St. Paul's Hospital Ambulatory Pharmacy (**HIV**): 1-888-511-6222

The RACE line should not be used to obtain peer-peer consultation regarding prescribing practicalities but can be used for clinical consultation services by prescribers in complex patients with COVID-19 who would benefit from Infectious Diseases expertise and input.

11. Pregnancy, Breastfeeding and Pediatrics

Currently available therapies have not been evaluated in pregnancy or breastfeeding. Most BC reproductive experts agree that remdesivir and, in rare occasions, 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 50, 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 (**BCCH Switchboard 604-875-2345**). Sotrovimab is the only approved therapeutic in this age group but due to its reduction in efficacy, remdesivir may be considered based on US labelling.

12. PAXLOVID Prescription

Nirmatrelvir/ritonavir (Paxlovid) is prescribed using a special prescription available [here on the BC Pharmacare webpage](#). E-from prescribing is also available for those registered.

It can be faxed to any pharmacy that stocks nirmatrelvir/ritonavir. For a list of pharmacies that carry Paxlovid kits, [click here](#).

13. Referring for Remdesivir

Patients who are not candidates for nirmatrelvir/ritonavir due to drug-drug interactions or contraindications **and are in the highest risk category (see eligibility above)** need to be referred to the nearest Health Authority remdesivir infusion clinic. If remdesivir administration is not feasible, the clinic COVID doctor may discuss the possibility of sotrovimab with the patient under extenuating circumstances. Numbers are current as of June 10, 2022.

- **Fraser Health Authority:** Directly order infusions. Forms are accessible on the FH Medical Staff website: JPOCSC Clinics & Services Forms -> Medical Day Care -> COVID-19 Therapy Pack. Fax to JPOCSC MDC 604-582-3742. If you need consultation, connect through RACE www.raceapp.ca Infectious Disease - COVID-19 Clinical. Requests will be returned by phone.
- **Vancouver Coastal and Providence Health:** Please make the referrals for remdesivir infusions through the CATe line at 1-888-COVID19
- **Interior Health Authority:** Contact the Interior Health COVID Therapeutics Virtual Clinic at 250-258-7369 or at COVIDTherapeutics@interiorhealth.ca
- **Island Health:** COVID-19 therapeutics clinic: 250-737-2030 (ext 44685) OR RJH ID on call
- **Northern Health:** CATe physician to consult the NH Remdesivir referral document as phone numbers and processes vary by site

14. Provide Patient Information and Counselling

Use patient-specific materials to provide drug information.

Patient information considerations:

- [Patient-facing materials on nirmatrelvir/ritonavir \(Paxlovid\)](#) 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 if drug modifications have been made
- Caution patients of common side effects. For nirmatrelvir/ritonavir these can include:
 - Gastrointestinal upset, nausea, and diarrhea
 - Taste disturbance or altered taste sensation
 - Headache
 - Hypertension
 - 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](#) if you are a pharmacist to ensure all patient information has been provided