Couchiching Ontario Heath Team
COVID-19 Anti-Viral Eligibility- Prescriber/Pharmacist Communication Form

PATIENT INFORMATION:

Last name: First name:

Address:

Phone Number:

DOB: Gender: Health Card with Version Code:

Height (cm):
Weight (kg):
Creatinine:
Date:
eGFR:
Date:

CONSENT:

☐ Informed consent obtained (product monograph will be provided by the pharmacy)

PRESCRIBING PHYSICIAN: Please attach a copy of the patient's current medication list prescription, non-prescription, over the counter and herbal medications with this form completed.

Brief medical history and relevant clinical concerns (where applicable, documentation can be attached)

☐ I confirm this information is provided in attached documents (if not, provided below)

Note: For patients with mild COVID 19 with confirmed COVID 19. These products are available for use under an interim authorization (Interim order) by Health Canada to prevent the progression of mild to moderate COVID 19 in adult patients 18 and up who are at high risk for progression to severe COVID 19, including hospitalization or death.

Criteria for use: All fields must be completed to be eligible for treatment for Paxlovid (nirmatrelvir/ritonavir)

☐ Be symptomatic. Please specify symptoms:

☐ Date of symptom onset: *(treatment must be given within 5 days of symptom onset)*

☐ Date of positive COVID 19 test: Select type: ☐ IDNOW ☐ RAT ☐ PCR

☐ Pregnant: ☐ yes ☐ no

AND

at least one criteria below- (please click on the picture below to bring up tool to circle on form which applies)

OR Prescriber Discretion with informed patient consent: (please add rationale)

AGE (years)	NUMBER OF VACCINE DOSES			RISK FACTORS
	0 doses	1 or 2 doses	3 doses	
<20[1]	**Higher risk** if ≥3 risk factors[1]	Standard risk[1]	Standard risk[1]	• Obesity (BMI ≥30 kg/m²) • Diabetes • Heart disease, hypertension, congestive heart failure • Chronic respiratory disease, including cystic fibrosis • Cerebral palsy • Intellectual disability • Sickle cell disease • Moderate or severe kidney disease (eGFR <60 mL/min) • Moderate or severe liver disease (e.g., Child Pugh Class B)
20 to 39	**Higher risk** if ≥3 risk factors	**Higher risk** if ≥3 risk factors	Standard risk	
40 to 69	**Higher risk** if ≥1 risk factors	**Higher risk** if ≥3 risk factors	Standard risk	
≥70	**Higher risk**	**Higher risk** if ≥1 risk factors	**Higher risk** if ≥3 risk factors	
Immunocompromised[2] individuals of any age	**Higher risk**: Therapeutics should always be recommended for immunocompromised individuals not expected to mount an adequate immune response to COVID-19 vaccination or SARS-CoV-2 infection due to their underlying immune status, regardless of age or vaccine status.[1,2]			
Pregnancy	**Higher risk**[3]	Standard risk	Standard risk	

1. Evidence for the safety and efficacy of sotrovimab and nirmatrelvir/ritonavir (Paxlovid) in children <18 years of age is limited. While early evidence on risk factors for moderate and severe COVID-19 in children is emerging, the ability to reliably predict disease progression in children remains very limited, and the frequency of progression is rare. While not routinely recommended in children <18 years of age, the use of these agents may be considered in exceptional circumstances (e.g., severe immunocompromise and/or multiple risk factors, clinical progression) on a case-by-case basis. Multidisciplinary consultation with Infectious Diseases (or Pediatric Infectious Diseases) and the team primarily responsible for the child's care is recommended to review the individual consideration of these medications.
2. Examples of immunocompromised or immunosuppressed individuals include receipt of treatment for solid tumors and hematologic malignancies (including individuals with lymphoid malignancies who are being monitored without active treatment), receipt of solid-organ transplant and taking immunosuppressive therapy, receipt of chimeric antigen receptor (CAR)-T-cell or hematopoietic stem cell transplant (within 2 years of transplantation or taking immunosuppression therapy), moderate or severe primary immunodeficiency (e.g., DiGeorge syndrome, Wiskott-Aldrich syndrome, common variable immunodeficiency, Good's syndrome, hyper IgE syndrome), advanced or untreated HIV infection, active treatment with high-dose corticosteroids (i.e., ≥20 mg prednisone or equivalent per day when administered for ≥2 weeks), alkylating agents, antimetabolites, transplant-related immunosuppressive drugs, cancer chemotherapeutic agents classified as severely immunosuppressive, tumor-necrosis factor (TNF) blockers, and other biologic agents that are immunosuppressive or immunomodulatory. These individuals should have a reasonable expectation for 1-year survival prior to SARS-CoV-2 infection.
3. Therapeutics should always be recommended for pregnant individuals who have received zero vaccine doses.

**** NOT recommended if eGFR <30ml/min OR with severe hepatic impairment (Child-Pugh Class C)***

eGFR	PAXLOVID Dose
>60mL/min (normal renal function or mild renal impairment)	300mg Nirmatrelvir (two tablets of 150mg each) with 100mg Ritonavir (one tablet of 100mg) taken together twice daily for 5 days
>30 to <60mL/min (moderate renal impairment)	150mg Nirmatrelvir (one tablet of 150mg) with 100mg of Ritonavir (one tablet of 100mg), taken together twice daily for 5 days

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PRESCRIBER ATTESTATION (Must be checked to be eligible for treatment)

☐ **Drug/Drug interactions reviewed** ☐ **Patient is eligible** ☐ **Patient is NOT eligible**

Prescriber name: Direct contact number (not office line):

Signature:

Billing#:

CPSO#:

Date/Time:

☐ **Prescription completed and sent with this tool**

What drug interactions should I consider before prescribing nirmatrelvir/ritonavir?

- **Ritonavir is a potent inhibitor of CYP3A4 isoenzyme and various drug transporters (e.g., P-glycoprotein).**
  - Onset of ritonavir inhibition is rapid and takes a few days to dissipate after completion of therapy.
- **Ritonavir and nirmatrelvir are both CYP3A4 substrates.**
- **Nirmatrelvir/ritonavir is contraindicated in patients taking drugs that are:**
  - Highly metabolized by CYP3A4 where elevated concentrations can be life-threatening.
  - Potent CYP3A4 inducers which may reduce the effectiveness of nirmatrelvir/ritonavir and contribute to the development of drug resistance.

What if my patient is taking therapy for human immunodeficiency virus (HIV)?

Patients taking ritonavir or cobicistat for HIV therapy should continue their complete antiretroviral regimen at usual dosing while taking nirmatrelvir/ritonavir.

Nirmatrelvir/ritonavir has many drug interactions. See page 3 ⟶

What if my patient is taking a drug that interacts with nirmatrelvir/ritonavir?

- ◬ If the patient is taking or has taken a **CYP3A4 enzyme inducer** in the last 14 days (e.g., certain anticonvulsants, antineoplastics, a rifamycin, St. John's wort): Do NOT prescribe nirmatrelvir/ritonavir.
- ▲ If the patient takes an interacting drug with a **long plasma half-life and narrow therapeutic window** (e.g., certain antiarrhythmics, antipsychotics, antineoplastics), the interacting drug will persist in the body after the last dose and may still interact with nirmatrelvir/ritonavir: Do NOT prescribe nirmatrelvir/ritonavir even if the interacting drug can be held.
- ● If the patient takes an interacting drug that can be held, hold the drug starting the first day of nirmatrelvir/ritonavir therapy, and resume 2 days after the last dose of nirmatrelvir/ritonavir treatment.
- ◆ A specialist prescriber or pharmacist may be able to help adjust the dose or dosing interval, replace the drug with an alternative agent, manage side effects, and guide therapeutic drug monitoring.

Nirmatrelvir/Ritonavir (*Paxlovid*) Drug Interactions:

This is not an exhaustive list. Consultation with a pharmacist who can obtain a complete medication, recreational, and natural health product history from the patient is recommended prior to prescribing nirmatrelvir/ritonavir.

Symbol	Severity	Recommendation	Rationale
▲	Contraindicated	Use alternative COVID agent. **Do not use nirmatrelvir/ritonavir.**	Stopping the drug will not mitigate the interaction (e.g., prolonged half-life, narrow therapeutic index, prolonged enzyme-inducing effects which may decrease effectiveness of nirmatrelvir/ritonavir). Do not coadminister due to risk of serious toxicity.
◬	Contraindicated (use within past 14 days)		
●	Do not coadminister	Hold and restart 2 days after completing nirmatrelvir/ritonavir.	Significant ↑ in drug concentrations expected. Do not coadminister due to risk of serious toxicity.
◆	Caution	Therapy modification required (see Appendix).	Significant ↑/↓ in drug concentrations expected, which may lead to serious toxicity or impaired efficacy. Only coadminister if the interacting drug can be safely held or dose-adjusted and closely monitored (see Appendix). Expert consultation may be useful.
✔	Drug interaction not likely to be clinically relevant	Continue with standard dosing.	Although mentioned in the monograph, clinically relevant interaction is not anticipated (e.g., minimal impact on certain metabolic pathways, wide therapeutic index, and short course of nirmatrelvir/ritonavir).

- ◆ Abemaciclib (*Verzenio*)
- ● Alfuzosin (*Xatral*)
- ◆ Alprazolam (*Xanax*)
- ▲ Amiodarone
- ✔ Amitriptyline
- ◆ Amlodipine (*Norvasc*)
- ◬ Apalutamide (*Erleada*)
- ◆ Apixaban (*Eliquis*)
- ◆ Aripiprazole (*Abilify*), oral
- ◆ Atorvastatin (*Lipitor*)
- ✔ Atovaquone
- ▲ Bosentan (*Tracleer*)
- ● Bosutinib (*Bosulif*)
- ◆ Brexpiprazole (*Rexulti*)
- ✔ Budesonide
- ✔ Bupropion
- ◆ Buspirone (*Buspar*)
- ◬ Carbamazepine (*Tegretol*)
- ◆ Ceritinib (*Zykadia*)
- ● Cisapride
- ✔ Citalopram
- ✔ Clarithromycin
- ✔ Clomipramine
- ● Clonazepam
- ◆ Clopidogrel (*Plavix*)
- ● Clorazepate
- ▲ Clozapine (*Clozaril*)
- ● Cobimetinib (*Cotellic*)
- ● Colchicine in renal/hepatic impairment
- ◆ Cyclosporine (*Neoral*)
- ◆ Dabigatran
- ◬ Dabrafenib (*Tafinlar*)
- ◆ Dasatinib (*Sprycel*)
- ◆ Dexamethasone, high dose
- ● Diazepam (*Valium*)
- ◆ Digoxin
- ◆ Diltiazem (*Tiazac, Cardizem*)
- ✔ Divalproex
- ● Dofetilide
- ✔ Dronabinol
- ▲ Dronedarone (*Multaq*)
- ◆ Edoxaban (*Lixiana*)
- ◆ Elagolix (*Orilissa*)
- ◆ Encorafenib (*Braftovi*)
- ◬ Enzalutamide
- ● Ergot alkaloids (e.g., dihydroergotamine, ergonovine)
- ◬ Eslicarbazepine
- ✔ Ethinyl estradiol
- ● Everolimus (*Certican*)
- ◆ Felodipine
- ▲ Fentanyl (*Duragesic*)
- ▲ Flecainide
- ✔ Fluoxetine
- ● Flurazepam
- ✔ Fluvoxamine
- ◆ Fostamatinib (*Tavalisse*)
- ✔ Fusidic acid, topical
- ● Glecaprevir/Pibrentasvir (*Maviret*)
- ◆ Hydrocodone
- ● Ibrutinib (*Imbruvica*)
- ✔ Imipramine
- ✔ Itraconazole
- ✔ Ketoconazole
- ✔ Lamotrigine
- ● Lomitapide (*Juxtapid*)
- ◬ Lorlatinib (*Lorbrena*)
- ● Lovastatin
- ▲ Lurasidone (*Latuda*)
- ✔ Maprotiline
- ✔ Maraviroc
- ● Meperidine (*Demerol*)
- ✔ Methamphetamine
- ✔ Metoprolol
- ● Midazolam, oral
- ◬ Mitotane (*Lysodren*)
- ◆ Modafinil
- ● Neratinib (*Nerlynx*)
- ◆ Nifedipine
- ◆ Nilotinib (*Tasigna*)
- ● Nitrazepam (*Mogadon*)
- ✔ Nortriptyline
- ◬ Oxcarbazepine
- ◆ Oxycodone (*Percocet, OxyNEO*)
- ✔ Paroxetine
- ◬ Phenobarbital
- ◬ Phenytoin (*Dilantin*)
- ▲ Pimozide
- ◬ Primidone
- ▲ Propafenone
- ◆ Quetiapine (*Seroquel*)
- ▲ Quinidine
- ● Quinine
- ✔ Raltegravir
- ▲ Ranolazine (*Corzyna*)
- ◆ Rifabutin
- ◬ Rifampin
- ◬ Rifapentine
- ◆ Risperidone (*Risperdal*), oral
- ▲ Risperidone, long-acting injection (*Risperdal Consta*)
- ● Rivaroxaban (*Xarelto*)
- ◆ Rosuvastatin (*Crestor*)
- ● Salmeterol (*Serevent, Advair*)
- ✔ Sertraline
- ◆ Sildenafil for ED† (*Viagra*)
- ▲ Sildenafil for PAH‡ (*Revatio*)
- ● Silodosin (*Rapaflo*)
- ● Simvastatin
- ● Sirolimus (*Rapamune*)
- ▲ Sonidegib (*Odomzo*)
- ◬ St. John's wort (*Hypericum perforatum*)
- ● Tacrolimus (*Prograf, Advagraf, Envarsus*)
- ◆ Tadalafil for ED† (*Cialis*)
- ▲ Tadalafil for PAH‡ (*Adcirca*)
- ● Tamsulosin (*Flomax*)
- ▲ Tepotinib (*Tepmetko*)
- ✔ Theophylline
- ● Ticagrelor (*Brilinta*)
- ✔ Timolol
- ◆ Tramadol
- ● Triazolam (*Halcion*)
- ✔ Trimipramine
- ● Vardenafil (*Levitra*) for ED†
- ▲ Vardenafil (*Levitra*) for PAH‡
- ▲ Venetoclax (*Venclexta*)
- ✔ Venlafaxine
- ◆ Verapamil
- ◆ Vinblastine
- ◆ Vincristine
- ✔ Voriconazole
- ◆ Warfarin
- ◆ Ziprasidone (*Zeldox*)
- ◆ Zolpidem (*Sublinox, Ambien*)
- ◆ Zopiclone (*Imovane*)

Click here for the Liverpool COVID-19 Interaction Checker

Or visit: https://www.covid19-druginteractions.org/.

†ED = erectile dysfunction ‡PAH = pulmonary arterial hypertension

Updated: February 23, 2022

SCIENCE TABLE
COVID-19 ADVISORY FOR ONTARIO

UNIVERSITY OF WATERLOO | SCHOOL OF PHARMACY

Nirmatrelvir/ Ritonavir (*Paxlovid*)

What Prescribers and Pharmacists Need to Know

Why is nirmatrelvir/ritonavir used to treat COVID-19?

COVID-19 has an initial phase of viral replication and a significant inflammatory response in moderate illness. This inflammation can lead to poor outcomes, including hospitalization, invasive ventilation, and death. However, treatments that target SARS-CoV-2 replication, if administered before the inflammatory phase of COVID-19, can improve outcomes.

Nirmatrelvir works by binding to the SARS-CoV-2 3CL protease, which ultimately causes viral replication to stop. Ritonavir is a potent CYP3A4 inhibitor. It is not active against SARS-CoV-2 but is administered as a "boosting agent" to slow the metabolism of nirmatrelvir, thus increasing concentrations of nirmatrelvir.

Nirmatrelvir/ritonavir is a highly effective outpatient therapy based on available data, but there is uncertainty about effect magnitude in target populations and high certainty for harm with ritonavir **if drug interactions are not mitigated.**

What is the benefit of nirmatrelvir/ritonavir for COVID-19?

The EPIC-HR study[1] has shown a benefit from treatment of adult outpatients with laboratory-proven SARS-CoV-2 infection who were not on supplemental oxygen and were within 5 days of symptom onset. The study suggests that nirmatrelvir/ritonavir may reduce the risk of hospitalization in these patients by 88%.

Research on nirmatrelvir/ritonavir was done in unvaccinated patients and prior to circulation of the Omicron variant. However, a study suggests that nirmatrelvir/ritonavir retains activity against the Omicron variant in vitro.[2] The Ontario Science Advisory Table recommends the use of nirmatrelvir/ritonavir in COVID-19 patients who are not on supplemental oxygen but are at high

How do I dose nirmatrelvir/ritonavir for treatment of COVID-19?

1. Paxlovid consists of 2 drugs packaged together:
   - Nirmatrelvir (pink) 150 mg tablet
   - Ritonavir (white) 100 mg tablet
2. Each carton contains 5 blister cards. One blister card is used each day. The full course of treatment is 5 days.
3. Take 2 pink tablets of nirmatrelvir and 1 white tablet of ritonavir (3 tablets total) together at the same time, once in the morning and once in the evening for 5 days (i.e., 6 tablets per day).
   - Nirmatrelvir/ritonavir may be taken with or without food.

Special Dosing Considerations:

eGFR† 30 to 59 mL/min:
The dose is 1 each of nirmatrelvir 150 mg and ritonavir 100 mg, with both tablets taken together orally BID x 5 days.

eGFR†<30 mL/min:
Nirmatrelvir/ritonavir is not recommended.

Severe hepatic impairment (Child-Pugh Class C):
Nirmatrelvir/ritonavir is not recommended.

What side effects should I be aware of?

Common side effects of nirmatrelvir/ritonavir are generally mild and can include dysgeusia (taste disturbance), diarrhea, hypertension, myalgia, vomiting and headache.

Not many people have taken this drug, and it is still being studied - so it is possible that all the side effects are not yet known, or that rare, but serious side effects may happen.

Click here for the Paxlovid product monograph

Or visit:
https://covid-vaccine.canada.ca/info/pdf/paxlovid-pm-en.pdf