INVOLVE

A look at the importance of the pharmacists' role in COVID-19 outpatient therapies

Speaker Disclosure

- Faculty: Daniel Thirion
- Relationships with financial sponsors:
  - Grants/Research Support: Pfizer, Sunovion, Département de prévention des infections CUSM, Fonds de la relève UdeM, Ministère de l'éducation, IRSC (fonds de recherche)
  - Speakers Bureau/Honoraria: Vigilance Santé, Sunovion, Sandoz, Pharmaprix, Avir, Verity, Uniprix, APES, McKesson, Merck (speaker); MD Briefcase, CSHP (continuing education author)
  - Consulting Fees: Jamp Pharma, Sunovion, Merck Canada, Pfizer, Gilea (intermittent consultations)

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- Relationships with financial sponsors:
  - Grants/Research Support: CIHR IRSC
  - Speakers Bureau/Honoraria: Emergent, Lilly, Pfizer, AMGEN, Abbvie, Amgen, ENSEMBLE IQ, L'Oreal, BD, Spectrum, Novo Nordsik
  - Advisory Board Participation: JNJ

Disclosure of Financial Support

- This program has received financial support from Pfizer Canada ULC in the form of educational funding.
- Pfizer Canada ULC has developed products that will be discussed in this program.

Mitigating Potential Bias

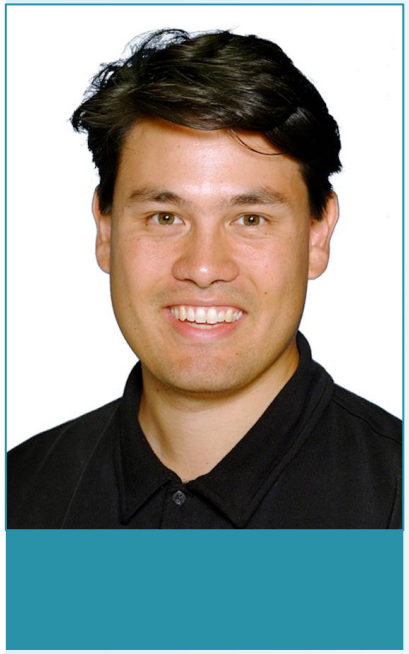
- Bias in this program has been mitigated using independent content validation as follows:
  - All content has been reviewed by an expert steering committee and expert reviewers
  - All data has been sourced from evidence that is clinically accepted
  - All support used in justification of patient care recommendations conform to generally accepted standards, clinical practice guidelines and consensus statements

Disclosure

I had full editorial control over the content of this presentation and wish to advise that it may contain content that is not consistent with the approved Pfizer Canadian Product Monograph.

This presentation includes National Guideline recommendations and other health and/or regulatory body recommendations which may differ from the Pfizer Canadian Product Monograph recommendations.

Scientific Planning Committee



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Aaron Sihota, BSc, BSc Pharm, RPh.

Aaron Sihota is a Primary Care Pharmacist at the UPCC Vancouver and Clinical Instructor at the UBC Faculty of Pharmaceutical Sciences. He is currently leading the development of a national Canadian consensus peer-reviewed publication for COVID-19 testing guidance for pharmacists with a pan-Canadian multidisciplinary Faculty bringing together pharmacists and infectious disease specialists.

Learning Objectives

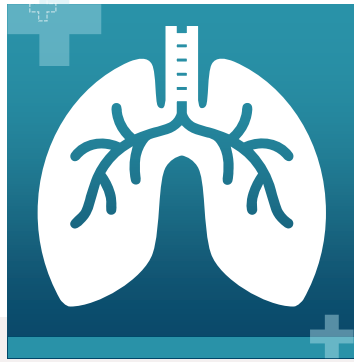
After completing this activity, participants will be able to:

- Describe the role of pharmacists in the outpatient treatment of COVID-19
- Explain the mechanism of action, efficacy and safety of available outpatient therapies for COVID-19
- Apply national and provincial guidelines for the outpatient treatment of COVID-19
- Identify patients eligible for different outpatient therapies based on risk stratification
- Identify and manage drug-drug interactions with common COVID-19 outpatient treatments

Overview of COVID-19

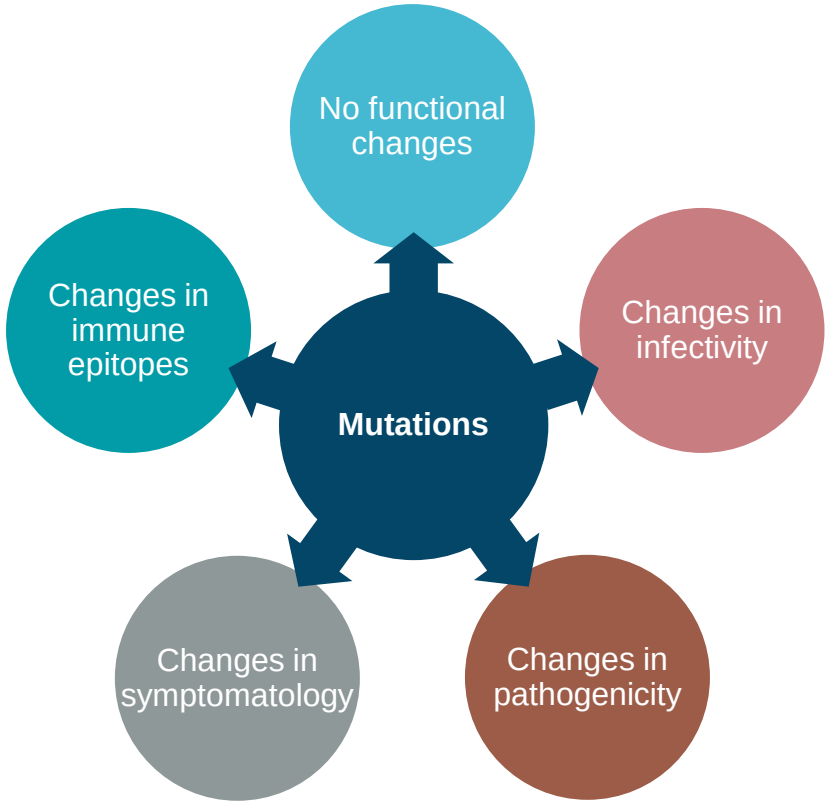
Case 1

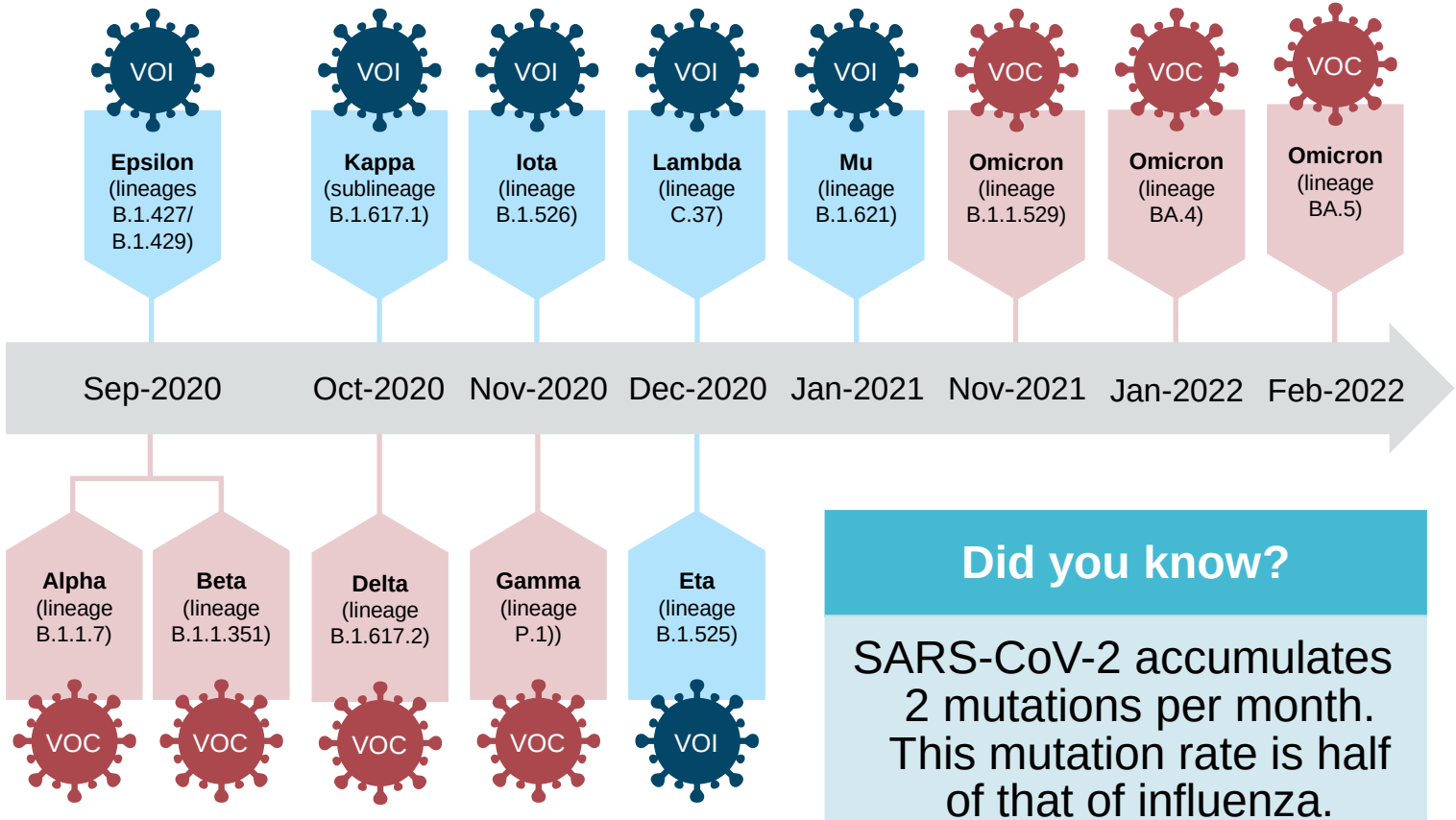
- A patient aged 68 calls to report dry cough, shortness of breath, and fatigue. Symptoms started 1 day ago and are progressively worsening. His wife tested positive for COVID-19 5 days ago.



- **Which signs or symptoms would prompt you to direct the patient for emergency in-person evaluation?**
  a. Confusion
  b. Chest pain
  c. Oxygen saturation (SpO_2) ≤94%
  d. Shortness of breath in daily activities
  e. Dizziness
  f. All of the above

Emergence of New SARS-CoV-2 Strains[1,2,3]





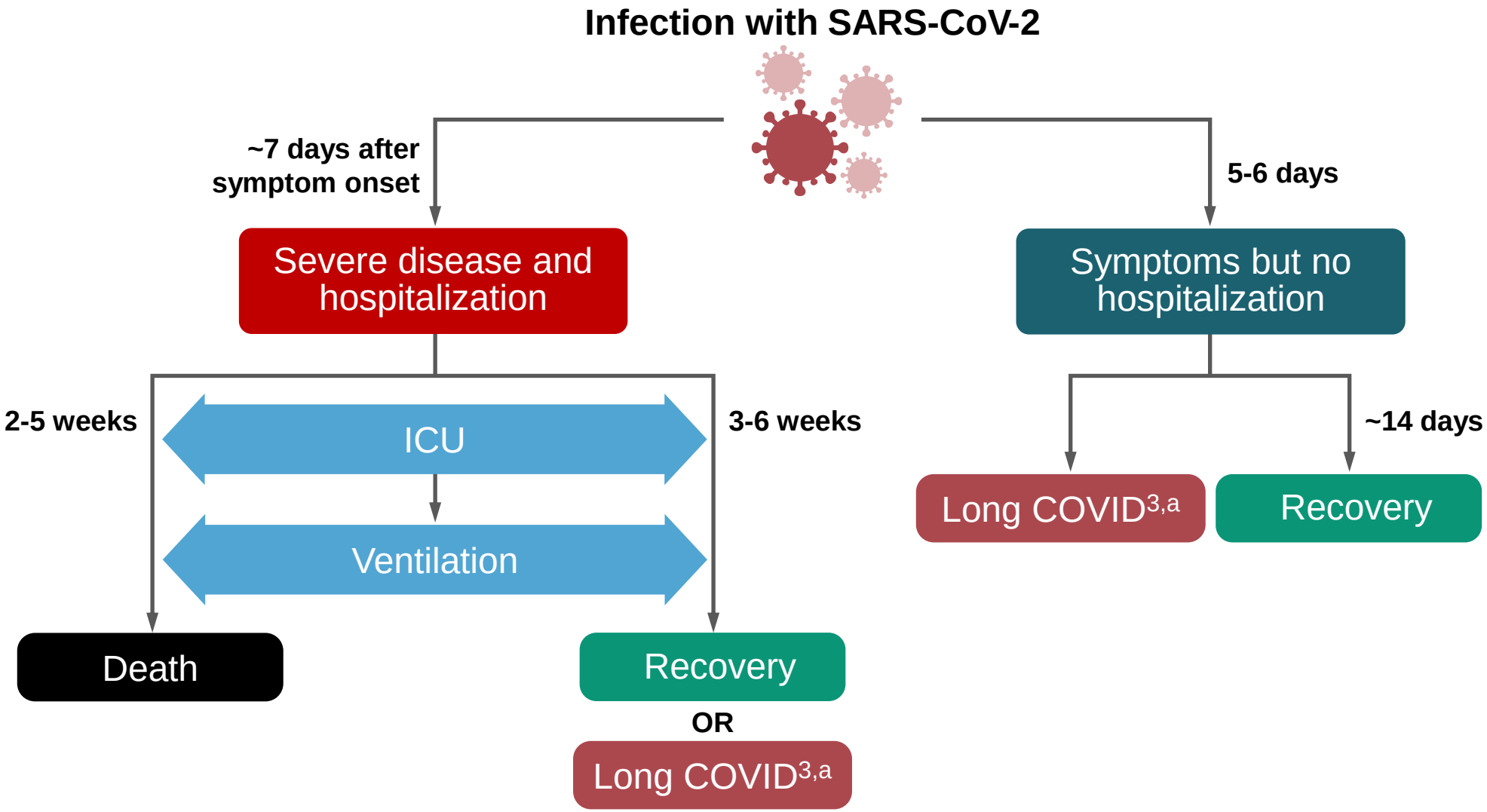
Did you know?

SARS-CoV-2 accumulates 2 mutations per month. This mutation rate is half of that of influenza.

VOC: variants of concern; VOI: variants of interest.

[1]Flores-Vega VR. *Viruses*. 2022; [2]Wang S. *J Med Virol*. 2022. Pango Lineages; [3]Pango Lineages. Tracking the international spread of SARS-CoV-2 lineages. Accessed July 20, 2022. https://cov-lineages.org/lineage_list.html

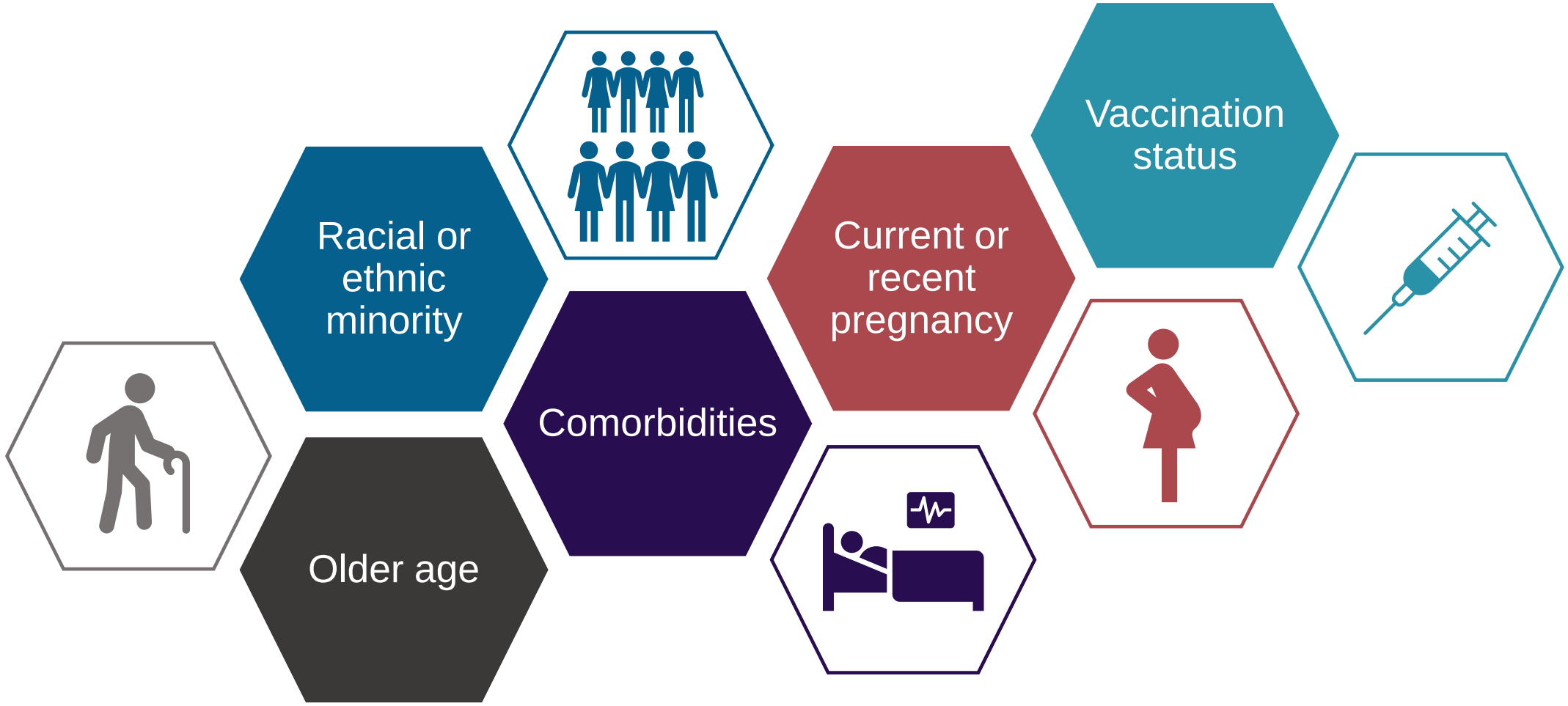
Patient Journey[1,2]



[a] Long COVID (or post COVID-19 condition) is defined as physical or psychological symptoms of COVID-19 lasting more than 12 weeks after SARS-CoV-2 infection.

[1]Estiri H et al. *Sci Rep*. 2021; [2]Report of the WHO-China Joint Mission on Coronavirus Disease 2019 (COVID-19), 16–24 February 2020. [3]Health Canada. Post COVID-19 condition (long COVID). Accessed October 28, 2022. https://www.canada.ca/en/public-health/services/diseases/2019-novel-coronavirus-infection/symptoms/post-covid-19-condition.html

Risk Factors for Severe COVID-19 and Hospitalization[1–4]



[1]CDC. COVID-19 – People with Certain Medical Conditions. Accessed July 20, 2022. www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html; [2]CDC. COVID-19 – Pregnant and Recently Pregnant People. Accessed July 20, 2022. www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/pregnant-people.html; [3]Tenforde MW et al. *JAMA*. 2021. [4]Health Canada. COVID-19 signs, symptoms and severity of disease- A clinician guide. Accessed November 21, 2022. https://www.canada.ca/en/public-health/services/diseases/2019-novel-coronavirus-infection/guidance-documents/

Practice Tip

Advise patients who experience severe dyspnea, shortness of breath in daily activities, confusion, dizziness, and chest pain to seek in-person medical evaluation immediately

Health Canada. COVID-19: Symptoms, treatment, what to do if you feel sick. Accessed November 21, 2022. https://www.canada.ca/en/public-health/services/diseases/2019-novel-coronavirus-infection/symptoms.html

Vaccines Authorized by Health Canada[1,a]

	Type	Indicated age	No. of Primary Vaccination Doses	Indications	Specificity
Comirnaty (BNT162b2)	mRNA	≥ 6 months old	Primary: 2 doses for ages ≥5 years or 3 doses for ages ≥6 months to ≥5 years Booster: 1 dose	Primary vaccination (≥6 months old), booster (≥5 years old)	Original strain
Comirnaty (BNT162b2) Bivalent	mRNA	≥ 12 years old	1 dose	Booster dose	Original strain, Omicron BA.1/BA.4/BA.5
Covifenz	VLP of spike protein	18 to 64	2 (21 days apart)	Primary vaccination	Original strain
JCOVDEN	Viral vector	≥18 years old	Primary: 1 dose Booster: 1 dose (≥2 months after primary)	Primary vaccination, booster (2 months after primary vaccination)	Original strain
Nuvaxovid	Recombinant spike protein	≥18 years old	2 (21 days apart)	Primary vaccination	Original strain
Spikevax	mRNA	≥ 6 months old	Primary: 2 doses (1 month apart) Booster: 1 dose	Primary vaccination (≥6 months old), booster (≥18 years old)	Original strain
Spikevax Bivalent	mRNA	≥ 18 years old	1 dose	Booster dose	Original strain, Omicron BA.1
Vaxzevria	Viral vector	≥18 years old	2 (4 to 12 weeks apart)	Primary vaccination	Original strain

[a] Authorized with terms and conditions; VLP: virus-like particle.

[1]Health Canada. Vaccines for COVID-19. Accessed November 2, 2022. www.canada.ca/en/public-health/services/diseases/coronavirus-disease-covid-19/vaccines.html

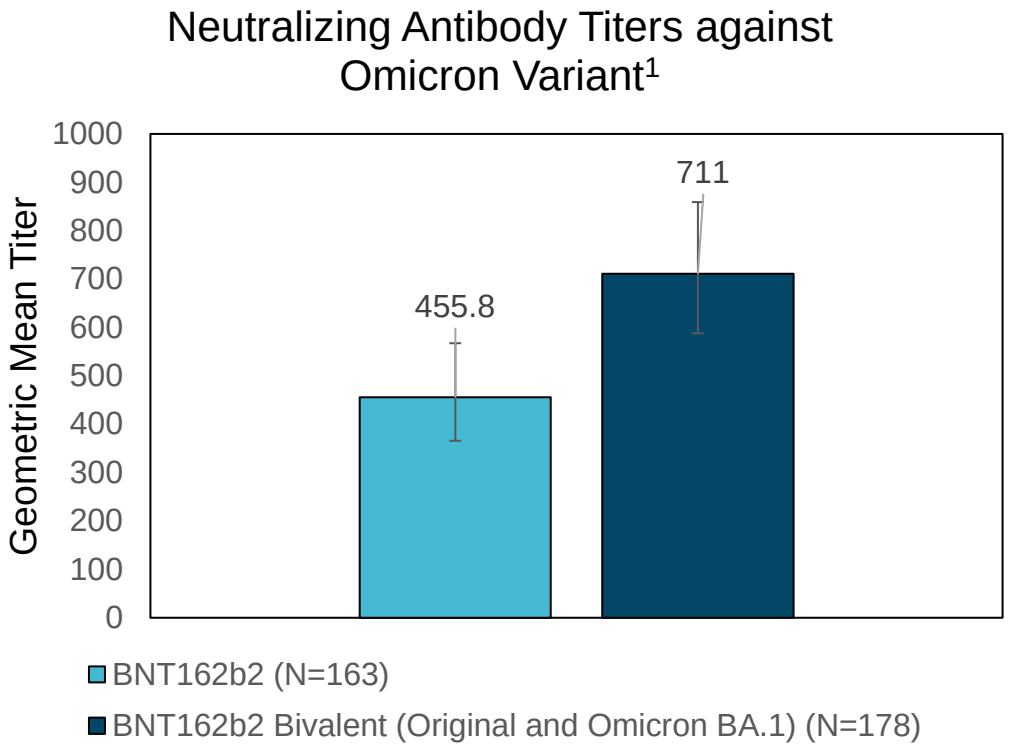
One or Two Booster Doses of BNT162b2 (Comirnaty) Provide Short-term Protection Against Omicron BA.4/BA.5[1,a]

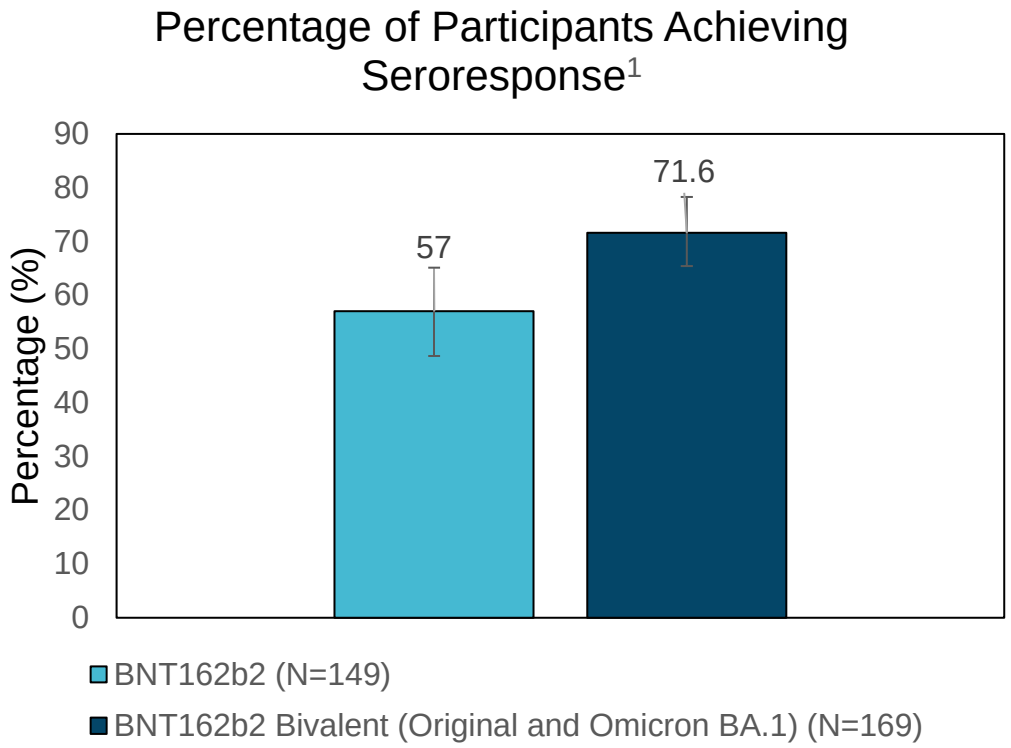
Doses	Hospitalization	Emergency Department	Urgent Care	Outpatient Care
Two doses				
<6 months since second dose	NC	30 (–86 to 74)	50 (10 to 72)	30 (4 to 49)
≥6 months since second dose	–4 (–118 to 50)	44 (20 to 61)	7 (–11 to 22)	19 (9 to 29)
Overall	**–4 (–116 to 50)**	**44 (19 to 61)**	**11 (–7 to 25)**	**21 (11 to 30)**
Three doses				
<6 months since third dose	73 (25 to 91)	43 (10 to 63)	34 (18 to 46)	29 (19 to 37)
≥6 months since third dose	38 (–31 to 71)	37 (8 to 57)	11 (–7 to 26)	6 (–7 to 17)
Overall	**50 (–1 to 76)**	**39 (14 to 57)**	**20 (5 to 33)**	**17 (7 to 26)**
Four doses				
<3 months since fourth dose	66 (20 to 85)	65 (35 to 82)	35 (10 to 54)	28 (10 to 43)
≥3 months since fourth dose	33 (–112 to 79)	78 (50 to 91)	20 (–23 to 48)	11 (–18 to 34)
Overall	**60 (11 to 82)**	**69 (44 to 83)**	**32 (7 to 50)**	**25 (7 to 39)**

[a] Adjusted effectiveness and 95% confidence intervals of BNT162b2 vaccine against Omicron (B.1.1.529) subvariants BA.4 and BA.5; NC: not calculated.

[1]Tartof S et al. *The Lancet Infectious Diseases*. 2022.

Omicron-containing Bivalent Booster (BNT162b2) Induces Antibody Responses Against Omicron BA.1[a]

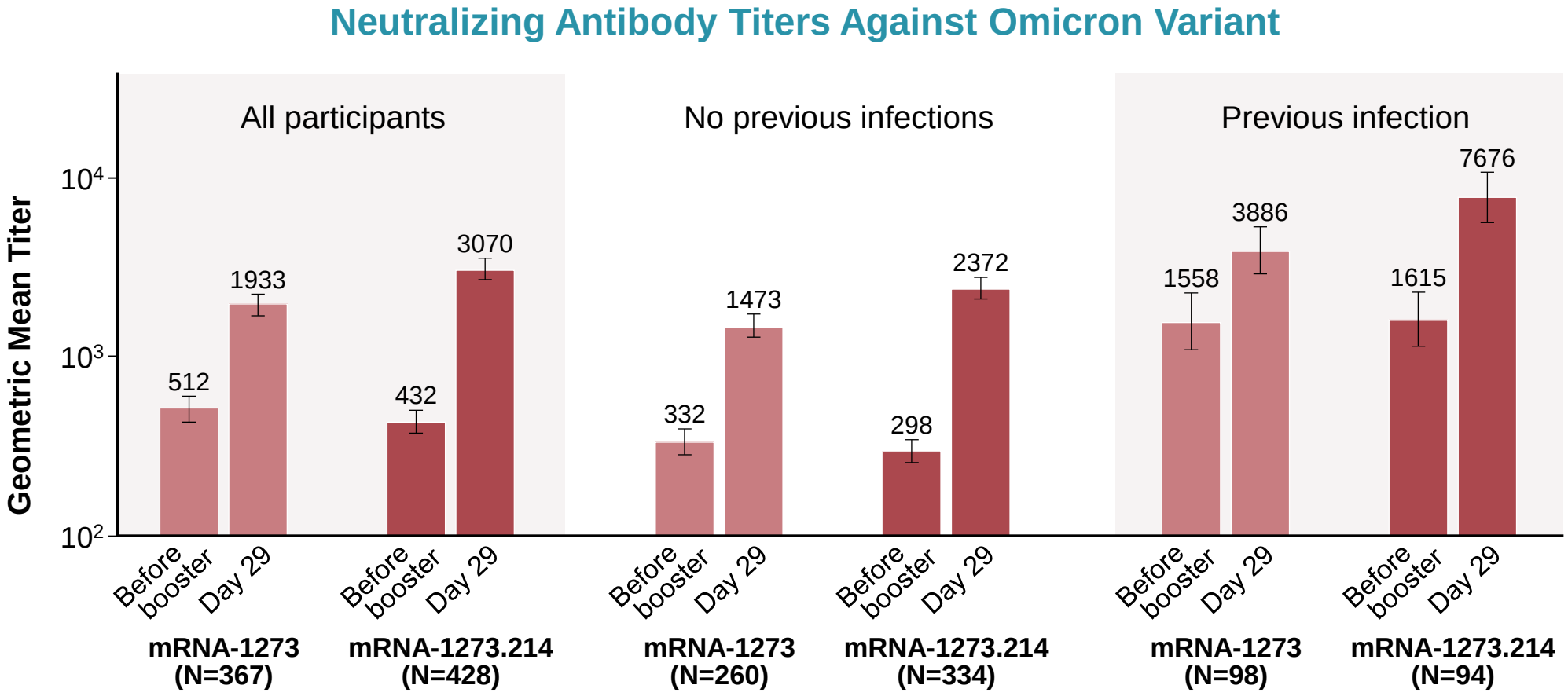




[a] Although the Omicron BA.1 vaccine was not released, its safety and effectiveness as a booster dose was used as reference for the authorization of COMIRNATY Original & Omicron BA.4/BA.5.

[1]COMIRNATY Original & Omicron BA.4/BA.5 Product Monograph. Pfizer Canada ULC. October 7, 2022.

Omicron-containing Bivalent Booster (mRNA-1273.214) Induces Antibody Responses Against Omicron BA.1



[1]Chalkias S et al. *N Engl J Med*. 2022.

Bivalent Boosters (Omicron BA.1 and Original Strain) Induce Antibody Responses Against BA.4/5

Neutralizing Titers Against Omicron BA.4/BA.5 Subvariants after mRNA-1273.214 Administered as Second Booster Doses by Prior SARS-CoV-2 Infection at Pre Booster[1]

	All participants		No prior SARS-CoV-2 infection		Prior SARS-CoV-2 infection	
	mRNA-1273.214 50 µg Booster Dose N=428	mRNA-1273 50 µg Booster Dose N=367	mRNA-1273.214 50 µg Booster Dose N=334	mRNA-1273 50 µg Booster Dose N=260	mRNA-1273.214 50 µg Booster Dose N=94	mRNA-1273 50 µg Booster Dose N=98
Pre-booster, n†	428	367	334	260	94	98
Observed GMT (95% CI)§	172.7 (147.4-202.3)	209.3 (179.5-244.1)	115.6 (98.5-135.6)	139.7 (119.5-163.3)	719.5 (531.6-973.9)	609.1 (448.1-828.1)
Day 29, n†	427	367	333	260	94	98
Observed GMT (95% CI)§	940.6 (826.3-1070.6)	645.4 (570.1-730.6)	727.4 (632.8-836.1)	492.1 (431.1-561.9)	2337.4 (1825.5-2992.9)	1270.8 (987.3-1635.8)
GMFR (95% CI)§	5.4 (5.0-5.9)	3.1 (2.8-3.3)	6.3 (5.7-6.9)	3.5 (3.2-3.9)	3.2 (2.8-3.8)	2.1 (1.8-2.4)
Estimated GMT (95% CI)¶	985.4 (914.8-1061.4)	588.4 (544.1-636.2)	776.4 (719.5-837.9)	458.3 (420.6-499.3)	2246.3 (1975.5-2554.1)	1406.9 (1227.9-1612.0)
GMR (95.0% CI)¶	1.68 (1.52-1.84)		1.69 (1.51-1.90)		1.60 (1.34-1.91)	

CI=confidence interval, GMFR=geometric mean fold rise (post-baseline/baseline titers), GMR=geometric mean ratio (mRNA-1273.214 vs mRNA-1273), GMT=geometric mean titer.

n=Number of participants with non-missing data at baseline and the corresponding post-baseline timepoint. Antibody values assessed by a research-grade pseudovirus neutralizing antibody ID50 assay for omicron (BA.4/BA.5) reported as below the lower limit of detection ([LOD] 10) are replaced by 0.5 x LOD.

† Number of participants with non-missing data at the timepoint (baseline or post-baseline).

§ 95% CI is calculated based on the t-distribution of the log-transformed values or the difference in the log-transformed values for GMT and GMFR, respectively, then back transformed to the original scale for presentation.

¶ The log-transformed antibody levels are analyzed using an analysis of covariance (ANCOVA) model with the treatment variable as fixed effect, adjusting for age group (<65, ≥65 years) and pre-booster antibody titer level (in $\log_{10}$ scale). The treatment variable corresponds to each individual study arm dose. The resulting LS means, difference of LS means, and confidence intervals are back transformed to the original scale for presentation.

[1]Chalkias S et al. *N Engl J Med*. 2022.

NACI: Updated Guidance on COVID-19 Vaccine Booster Doses in Canada

Children 5–11 years old

- Complete series (primary and booster) of the Comirnaty COVID-19 mRNA vaccine (at least 8 weeks between the first and second dose) is recommended for children 5–11 years old who do not have contraindications to the vaccine

Adolescents (12–17 years old)

- Individuals ≥12 years with risk factors for severe COVID-19 should be offered a fall COVID-19 vaccine booster dose regardless of the number of prior booster doses. Comirnaty BA.4/5 bivalent may be offered to adolescents 12–17 years old with moderately to severely immunocompromising conditions and/or biological or social risk factors for severe COVID-19 outcomes

Individuals ≥18 years old

- All individuals 12–64 years old may be offered a fall COVID-19 booster dose regardless of the number of prior booster doses. A bivalent Omicron-containing mRNA COVID-19 vaccine (Spikevax BA.1 bivalent or Comirnaty BA.4/5 bivalent) should be offered as a booster dose to individuals ≥18 years of age

NACI: National Advisory Committee on Immunization.

[1]An Advisory Committee Statement (ACS) National Advisory Committee on Immunization (NACI). Updated guidance on COVID-19 vaccine booster doses in Canada. Accessed October 28, 2022. https://www.canada.ca

Role of Pharmacists in COVID-19 Vaccination[1]

AEs: adverse events.

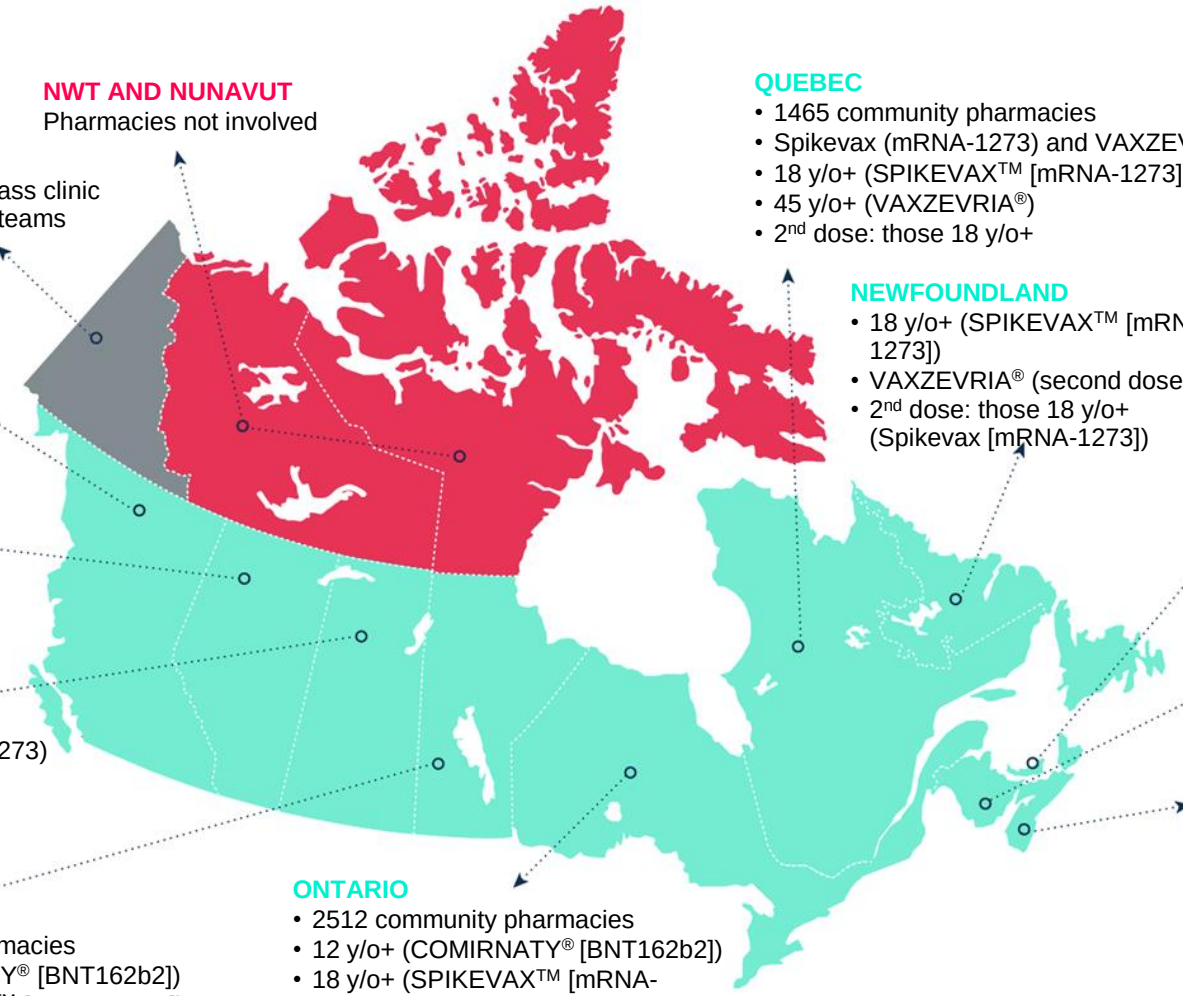
[1]Pharmacies at the ready: Canada's pharmacists and the COVID-19 vaccine. *Can Pharm J (Ott)*. 2021.

Did you know?

In a survey of 1,500 Canadians, 65% of participants indicated they were willing to get vaccinated at a pharmacy, and 43% of participants would prefer it (42% would prefer a physician’s office and 14% a public health clinic)

Canadian Pharmacists Association. Pharmacists and covid-19 vaccinations in Canada. Accessed July 20, 2022. https://www.pharmacists.ca

Pharmacy Involvement in COVID-19 Vaccination



NWT AND NUNAVUT
Pharmacies not involved

YUKON
Yukon pharmacists are part of mass clinic and traveling rural immunization teams

BRITISH COLUMBIA
- 667 community pharmacies
- VAXZEVRIA®
- Second doses only

ALBERTA
- 1300 community pharmacies
- 12 y/o+ (COMIRNATY® [BNT162b2])
- 18 y/o+ (SPIKEVAX™ [mRNA-1273])
- 30 y/o+ (VAXZEVRIA®)
- 2nd dose: those 12 y/o+

SASKATCHEWAN
- 368 community pharmacies
- Comirnaty (BNT162b2) and Spikevax (mRNA-1273)
- 12 y/o+ (COMIRNATY® [BNT162b2]); 18 y/o+ (SPIKEVAX™ [mRNA-1273])
- VAXZEVRIA® (second doses only)
- 2nd dose: those 12 y/o+

MANITOBA
- 315 community pharmacies
- 12 y/o+ (COMIRNATY® [BNT162b2])
- 18 y/o+ (SPIKEVAX™ [mRNA-1273])
- 40 y/o+; 30-39 y/o with certain health conditions (VAXZEVRIA®)
- 2nd dose: those 12 y/o+

ONTARIO
- 2512 community pharmacies
- 12 y/o+ (COMIRNATY® [BNT162b2])
- 18 y/o+ (SPIKEVAX™ [mRNA-1273])
- VAXZEVRIA® (second doses only)
- 2nd dose: those 12 y/o+

QUEBEC
- 1465 community pharmacies
- Spikevax (mRNA-1273) and VAXZEVRIA®
- 18 y/o+ (SPIKEVAX™ [mRNA-1273])
- 45 y/o+ (VAXZEVRIA®)
- 2nd dose: those 18 y/o+

NEWFOUNDLAND
- 18 y/o+ (SPIKEVAX™ [mRNA-1273])
- VAXZEVRIA® (second doses only)
- 2nd dose: those 18 y/o+ (Spikevax [mRNA-1273])

PEI
- 47 community pharmacies
- SPIKEVAX™ (mRNA-1273)
- 18 y/o+
- VAXZEVRIA® paused
- 2nd dose: prebooked during first dose at pharmacy

NEW BRUNSWICK
- 218 community pharmacies
- 12 y/o+ (COMIRNATY® [BNT162b2])
- 18 y/o+ (SPIKEVAX™ [mRNA-1273])
- 55 y/o+ (VAXZEVRIA®)
- 2nd dose: those 12 y/o+

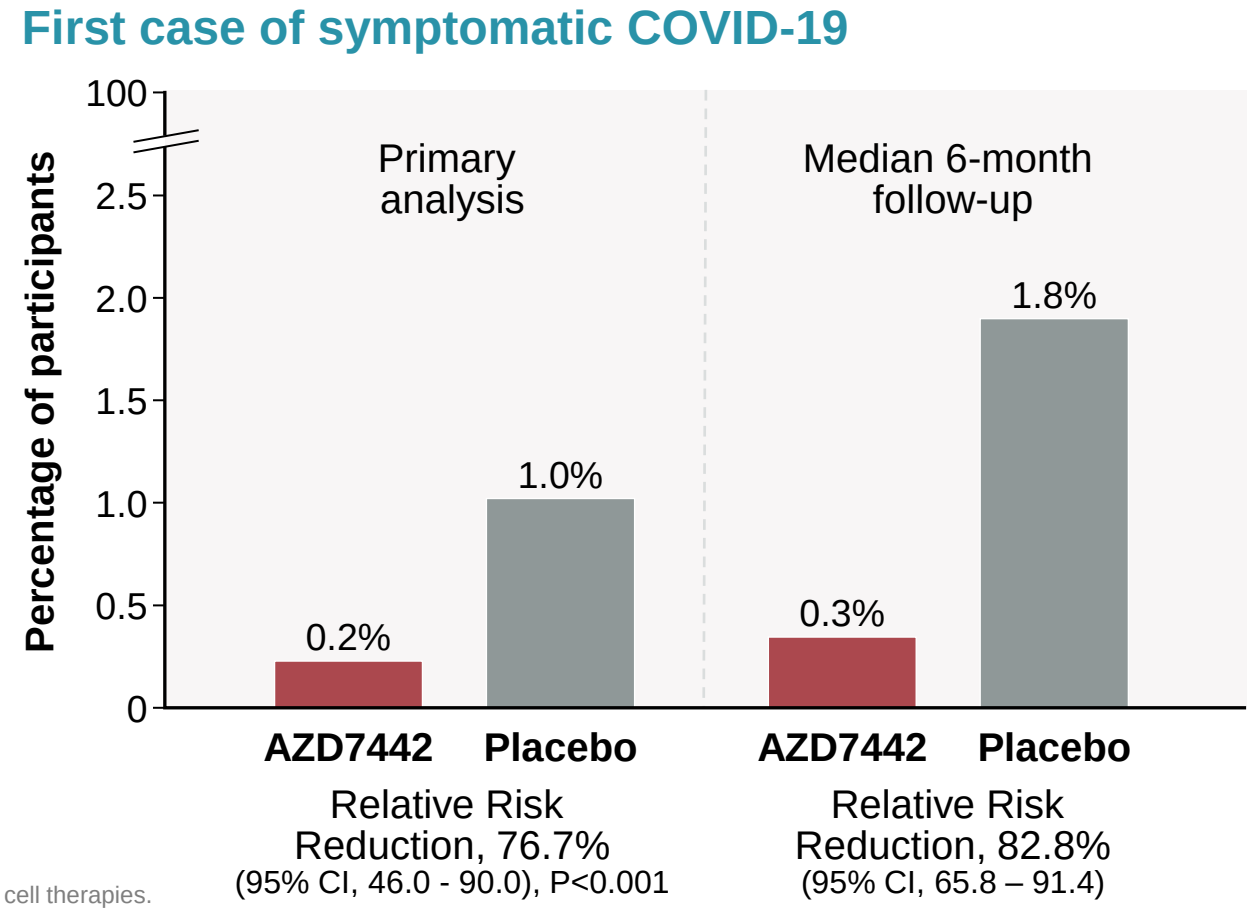
NEW BRUNSWICK
- 295 community pharmacies
- 12 y/o+ (COMIRNATY® [BNT162b2])
- 18 y/o+ (SPIKEVAX™ [mRNA-1273])
- VAXZEVRIA® paused
- 2nd dose: those 12 y/o+; first dose prior to June 15

Canadian Pharmacists Association / Association des pharmaciens du Canada

Canadian Pharmacists Association. Pharmacy Involvement in COVID Vaccination. Accessed October 28, 2022. https://www.pharmacists.ca

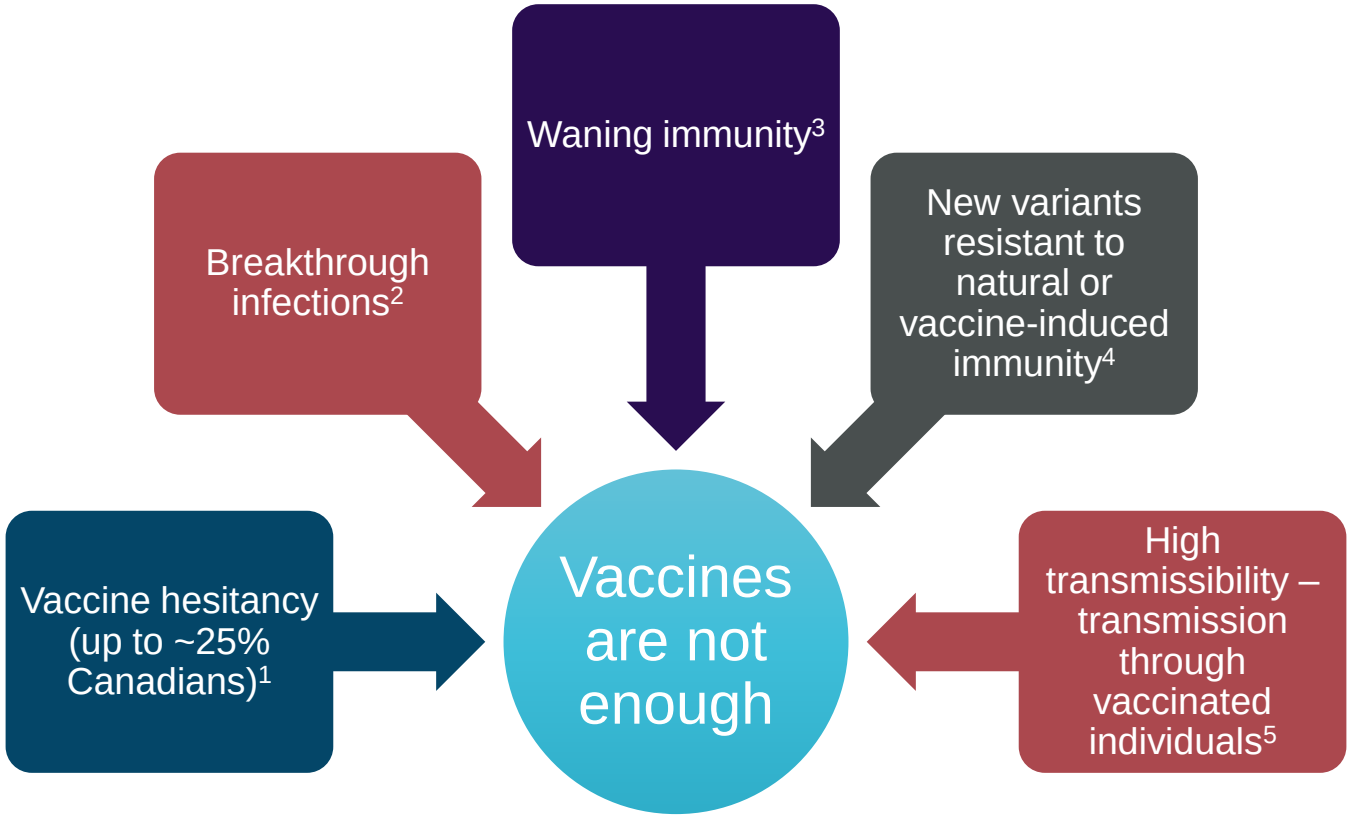
Pre-exposure Prophylaxis Using Tixagevimab plus Cilgavimab Protects Against Symptomatic COVID-19

- **Population:**
  - Increased risk of an inadequate response to vaccine[a]
  - Increased risk of SARS-CoV-2 exposure
- **Treatment:**
  - Single dose (2 consecutive IM injections) of 300 mg AZD7442 (N=3460) **OR**
  - Single dose saline placebo (N=1737)



[a] Solid organ transplant, stem cell transplant, CAR-T cell therapy, blood malignancies, anti-B cell therapies.
AZD7442: tixagevimab + cilgavimab; IM: intramuscular; mAbs: monoclonal antibodies.
[1]Levin MJ et al. *N Engl J Med*. 2022.

Need for Outpatient Treatments to Prevent Hospitalization



In contrast to current management options that are infused or require access to a clinic, outpatient therapies can be taken at home

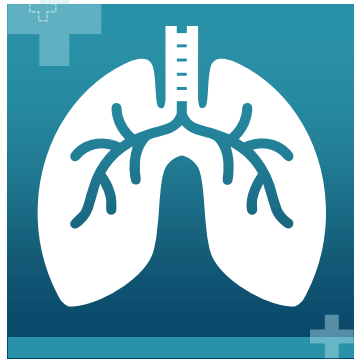
[1]Muhajarine N et al. *PLoS One.* 2021; [2]Gupta RK et al. *Science*. 2021; [3]Naaber P et al. *Lancet Reg Heal - Eur.* 2021; [4]Harvey WT et al. *Nat Rev Microbiol*. 2021; [5]Harris RJ et al. *N Engl J Med*. 2021.

Key Learning Points

- Despite various mitigating factors, the COVID-19 pandemic continues to be a major public health problem and financial burden in Canada
- Older age, comorbidities, vaccination status, and racial or ethnic background are the most important risk factors for severe COVID-19 and hospitalization
- Vaccines remain the first line of defence against COVID-19 – pharmacists play a vital role in vaccination strategies in Canada
- Because of the continuous emergence of new immune-escape SARS-CoV-2 strains, outpatient treatments are needed to prevent hospitalization

Case 2

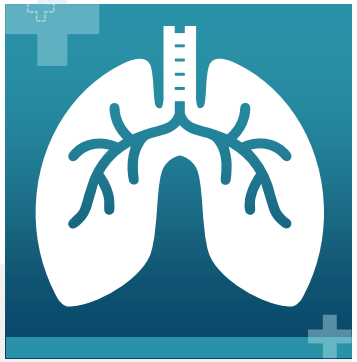
- A patient calls to report experiencing mild COVID-19 symptoms (fever, cough, headache, muscle pain), which started 2 days ago. The patient does not have confusion or alarming signs that would necessitate emergency evaluation.
- You provide the patient with a testing kit and instructions on how to do at-home testing. The test comes back positive.



- To determine eligibility for outpatient treatments, you assess for risk factors for severe illness. **Which of the following factors indicate an increased risk of progression to severe disease?**
  a. Obesity (BMI is 33 kg/m^2)
  b. Diabetes
  c. Age (76 years old)
  d. COPD
  e. Patient on immunosuppressive drug
  f. All of the above

Outpatient Treatment Options

Case 3



- You contact the specialist/prescriber of rivaroxaban to ask for authorization for dose adjustment

- **What would be your next step?**
  a. Increase the dose of rivaroxaban for 7 days and prescribe nirmatrelvir/ritonavir
  b. Not dispense nirmatrelvir/ritonavir and continue rivaroxaban
  c. Add dabigatran to rivaroxaban regimen and additionally prescribe nirmatrelvir/ritonavir
  d. After getting authorization from the prescriber, switch to dabigatran for 10 days (follow-up with the patient via phone every a few days to ensure adherence to therapy) and prescribe nirmatrelvir/ritonavir

Available Therapies in Canada[a]

Agent	Approval Status	Type	Administration Route
Bamlanivimab	✓ Authorized	mAb	IV infusion
Sotrovimab	✓ Authorized	mAb	IV infusion
Casirivimab/imdevimab	✓ Authorized	mAb	IV infusion
Tixagevimab/cilgavimab[b,c]	✓ Authorized	mAb	IM injection
Nirmatrelvir/ritonavir	✓ Authorized	Small molecule inhibitor	Oral
Remdesivir	✓ Authorized	Small molecule inhibitor	IV infusion

[a] With the exception of nirmatrelvir/ritonavir and tixagevimab/cilgavimab, these treatments require access to a hospital; [b] Authorized for pre-exposure prophylaxis and treatment of mild to moderate COVID-19 in select patients; [c] Health Canada has raised a warning alerting healthcare professionals against the use of tixagevimab/cilgavimab because of lack of effectiveness against newer SARS-CoV-2 variants; IM: intramuscular; IV, intravenous; mAb, monoclonal antibody.

[1]www.canada.ca/en/health-canada/services/drugs-health-products/covid19-industry/drugs-vaccines-treatments/treatments.html. Accessed July 21, 2022.

Ideal Patients for Different Outpatient Treatments

Agent	Age	Diagnostic Test	Disease Severity	Primary Risk Factors*	Key Contraindications
Sotrovimab[1]	≥ 12 years old and weighing ≥ 40 kg	Direct SARS-CoV-2 viral testing	Mild to moderate	High risk of COVID-19-related hospitalization and/or death: • ≥ 55 years of age • BMI ≥ 30 kg/m^2 • One or more comorbidities: diabetes, chronic kidney disease, congestive heart failure, chronic obstructive pulmonary disease, moderate to severe asthma	• Hospitalization due to severe COVID-19 respiratory disease • Hypersensitivity to the drug
Tixagevimab/ cilgavimab[2,a]	≥ 12 years old and weighing ≥ 40 kg	Direct SARS-CoV-2 viral testing	Pre-exposure prophylaxis	For patients who have not had a know recent exposure to an individual infected with SARS-CoV-2 and: • Who are immune compromised and unlikely to mount and adequate immune response to COVID-19 vaccination • For whom COVID-19 vaccination is not recommended	• Hospitalization due to severe COVID-19 respiratory disease • Hypersensitivity to the drug
			Mild to moderate COVID-19	High risk of COVID-19-related hospitalization and/or death: • ≥65 years of age, irrespective of comorbidities • <65 years old and presence of one or more comorbidities: obesity, smoking, hypertension, chronic lung disease or moderate to severe asthma, diabetes, cardiovascular disease, immunocompromised state, cancer, chronic kidney or liver disease, sickle cell disease	

*See product monograph for complete list of risk factors.

[a]Health Canada has raised a warning alerting healthcare professionals against the use of tixagevimab/cilgavimab because of lack of effectiveness against newer SARS-CoV-2 variants.

[1]SOTROVIMAB Product Monograph. GlaxoSmithKline Inc. September 14, 2021; [2]EVUSHELD Product Monograph. AstraZeneca Canada Inc. October 18, 2022.

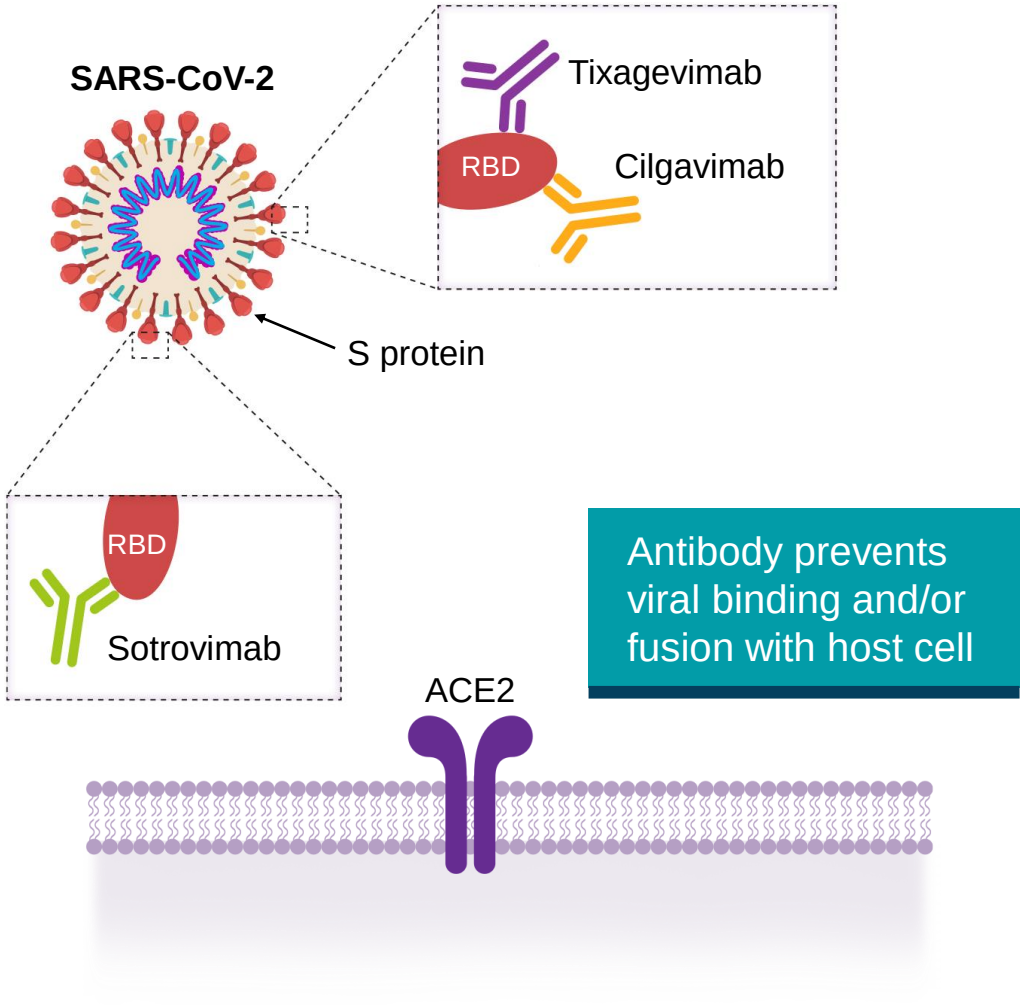
Ideal Patients for Different Outpatient Treatments

Agent	Age	Diagnostic Test	Disease Severity	Primary Risk Factors*	Key Contraindications
Nirmatrelvir/ ritonavir[1]	≥ 18 years old	Direct SARS-CoV-2 viral testing	Mild to moderate	High risk of progression to severe disease, hospitalization or death: • ≥ 60 years of age • BMI ≥ 25 kg/m^2 • One or more comorbidities: diabetes, chronic kidney disease, cardiovascular disease, immunosuppression, chronic lung disease, active cancer, sickle cell disease	• Hospitalization due to severe COVID-19 • Hypersensitivity to the drug • Severe hepatic impairment, severe renal impairment • Concomitant use of drugs that are highly dependent on CYP3A for clearance, and concomitant use of CYP3A inducers • eGFR <30 mL/min
Remdesivir[2]	≥ 12 years old and weighing ≥ 40 kg	Not specified	Patients with pneumonia requiring supplemental oxygen	Not specified	• Hepatic dysfunction, renal dysfunction, previous reactions to the agent

*See product monograph for complete list of risk factors.

[1]PAXLOVID Product Monograph. Pfizer Canada ULC. June 13, 2022; [2]VEKLURY Product Monograph. Gilead Sciences Canada, Inc. April 22, 2022.

MOA of mAbs[1]



Antibody prevents viral binding and/or fusion with host cell

- Specific for S protein
- Neutralize the virus
- Opsonization of virus
- Clearance of infected cells
- Resistance – Efficacy affected by mutations in S protein

mAbs: monoclonal antibodies; MOA: mechanism of action; RBD: receptor binding domain.

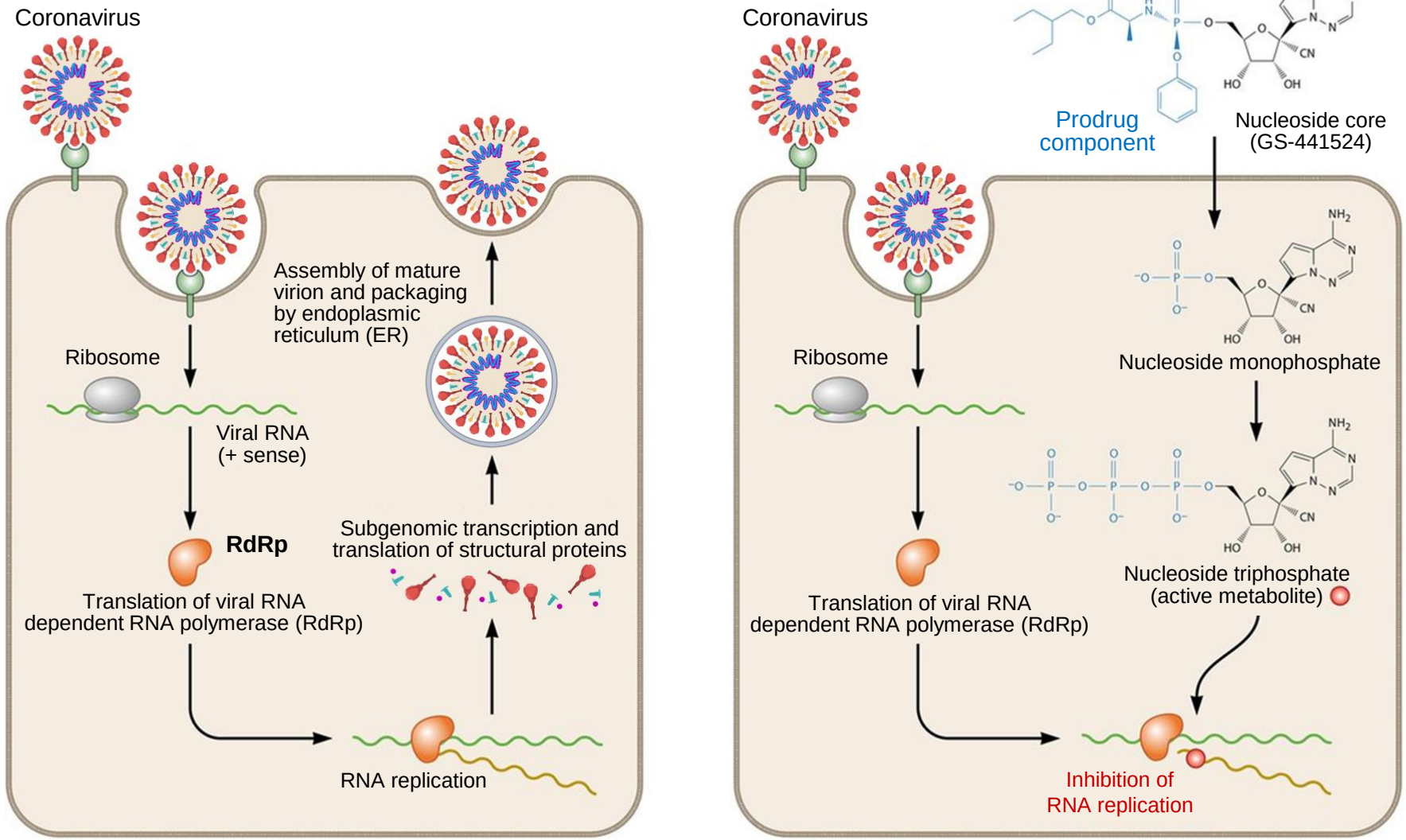
[1]Taylor PC et al. *Nat Rev Immunol*. 2021.

Omicron Subvariants Are Resistance to Existing mAbs[1–5]

Pango lineage	SOT		TIX + CIL	
	In vitro susceptibility[a]	Anticipated clinical activity	In vitro susceptibility[a]	Anticipated clinical activity
B.1.1.529/BA.1.1	No change	Active	Moderate reduction[c]	Active[d]
B.1.1.529/BA.1	No change	Active	Moderate reduction[c]	Active[d]
B.1.1.529/BA.2	Marked reduction	Unlikely to be active	No change	Active
BA.2.12.1	Marked reduction	Unlikely to be active	Marked reduction	Unlikely to be active
BA.4	Marked reduction	Unlikely to be active	Marked reduction	Unlikely to be active
BA.5[e]	Marked reduction	Unlikely to be active	Marked reduction	Unlikely to be active

[a] Based on the fold reduction in susceptibility reported in the FDA EUAs; [b] Marked change for CAS and no change for IMD. The combination of CAS plus IMD appears to retain activity against the variant; [c] Despite the moderately reduced in vitro susceptibility of TIX + CIL, in vitro PK/PD modeling data suggest that the TIX 300 mg + CIL 300 mg dose will retain activity against Omicron; [d] The duration of protection against SARS-CoV-2 infection remains unclear. [e] BA.5 is currently the dominant variant in Canada.
CIL: cilgavimab; EUA: Emergency Use Authorization; PK/PD: pharmacokinetic/pharmacodynamic; SOT: sotrovimab; TIX: tixagevimab.
[1]NIH COVID-19 Guidelines. Anti-SARS-CoV-2 Monoclonal Antibodies. Accessed July 21, 2022. https://files.covid19treatmentguidelines.nih.gov/guidelines/section/section_111.pdf; [2]Cao Y et al. *Nature*. 2022; [3]Yamasoba D et al. *Lancet Infect Dis*. 2022; [4]Wang Q et al. *Nature*. 2022; [5]Takashita E et al. *N Engl J Med*. 2022.

MOA of Remdesivir[1,2]



MOA: mode of action.

[1]Kokic G et al. *Nat Commun.* 2021; [2]Malin JJ et al. *Clin Microbiol Rev*. 2020.

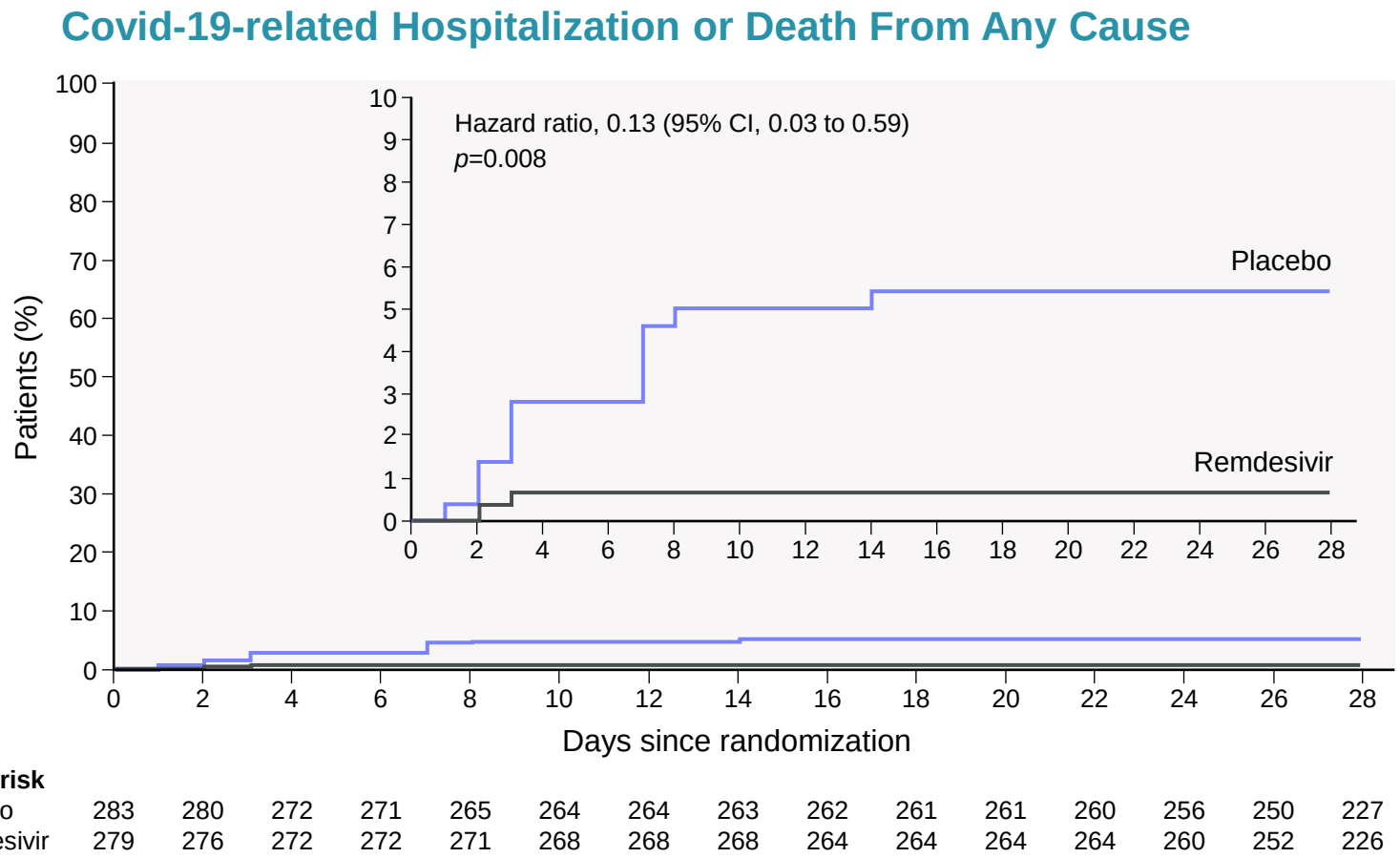
Remdesivir Prevents Progression to Severe COVID-19 in Outpatients[1,a]

3-day course of IV remdesivir or placebo

87% lower risk of hospitalization or death

- 0.7% in remdesivir group vs 5.3% in placebo (*p*=0.008)

No deaths by day 28



[a] The efficacy of remdesivir was assessed when the Delta variant was prevalent; IV: intravenous.

[1]Gottlieb RL et al. *N Engl J Med.* 2022.

Safety of Remdesivir

Event	Remdesivir, n (%)	Placebo n (%)
Any AE	118 (42.3)	131 (46.3)
AE related to trial regimen	34 (12.2)	25 (8.8)
Serious AE	5 (1.8)	19 (6.7)
AE leading to discontinuation of trial regimen	2 (0.7)	5 (1.8)
Death	0	0

AE: adverse event.

[1]Gottlieb RL et al. *N Engl J Med.* 2022.

Nirmatrelvir/ritonavir Is the Only Oral Agent Authorized for Use in Canada

The first oral antiviral therapy approved by Health Canada for use in high-risk adults with mild-to-moderate COVID-19[1]

- Dosage: 300 mg/100 mg BID X 5 days[2]

Provincial healthcare systems have different needs and pressures

- Provinces have established their own guidelines on the use of nirmatrelvir/ritonavir

[1]Press Release: Pfizer Receives Health Canada Authorization for COVID-19 Oral Treatment; [2]PAXLOVID Product Monograph. Pfizer Canada ULC. June 13, 2022.

Practice Tip

Initiate the 5-day treatment course of nirmatrelvir/ritonavir as soon as possible after a diagnosis of COVID-19 has been made, and within 5 days of symptom onset

PAXLOVID Product Monograph. Pfizer Canada ULC. June 13, 2022.

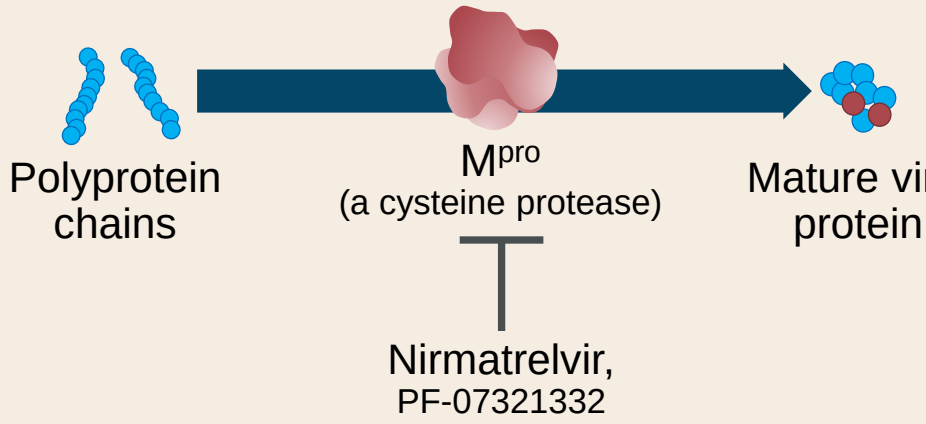
Mechanism of Action of Nirmatrelvir/Ritonavir[1,2]

Did you know?

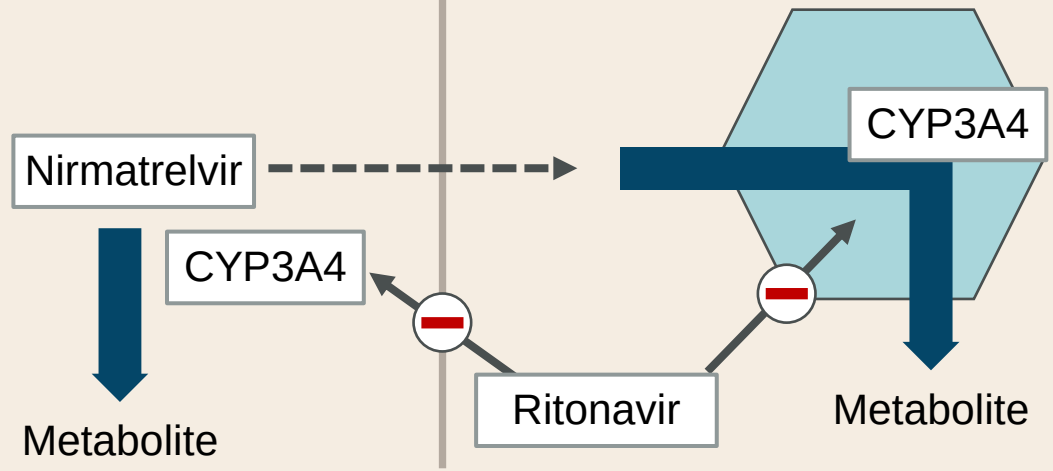
Ritonavir has no antiviral activity against SARS-CoV-2. It is an antiretroviral agent initially developed for HIV and is now used to delay the metabolism of drugs that are CYP3A4 substrates (e.g., nirmatrelvir).

Nirmatrelvir[1–3]

Mechanism: an inhibitor of M^{pro}, a protease critical in viral replication



Ritonavir[1,2]



[1]Owen DR et al. *Science*. 2021; [2]Ahmad B et al. *Int J Mol Sci*. 2021; [3] Hung YP et al. *Antibiotics (Basel)*. 2022.

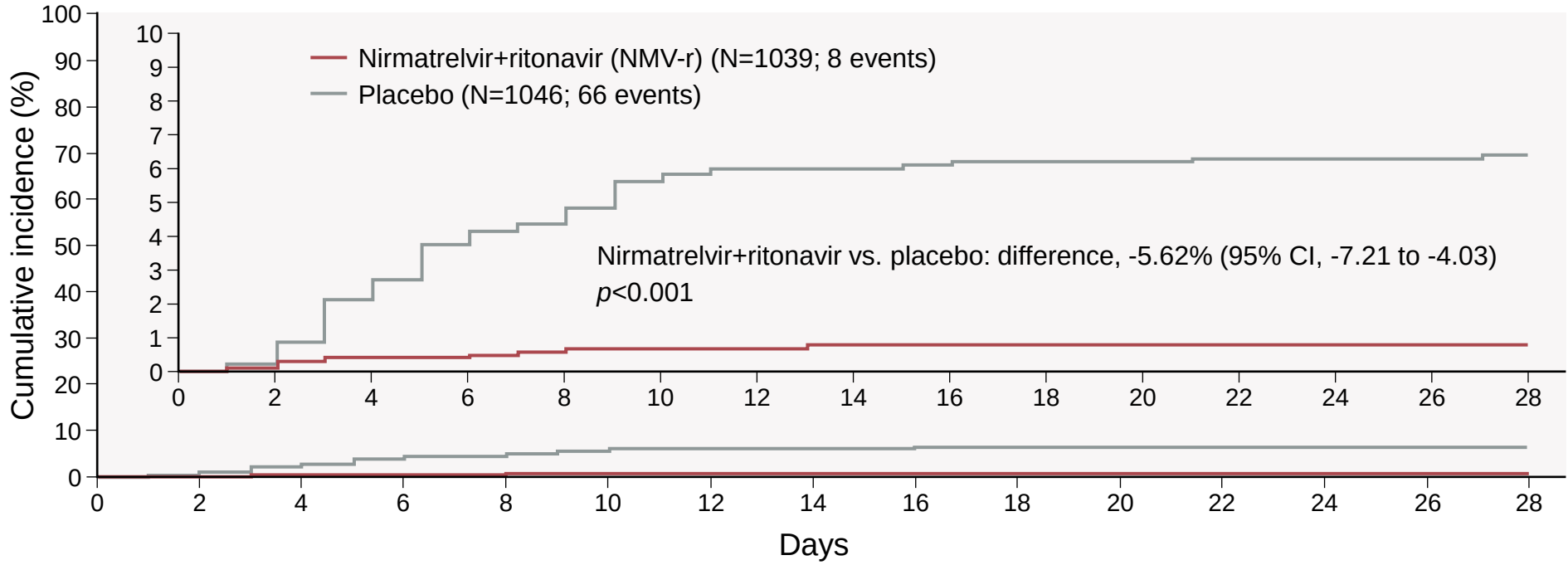
Efficacy of Nirmatrelvir/Ritonavir in High-Risk Patients with COVID-19[1,a]

5-day course of oral nirmatrelvir or placebo

89.1% lower risk of hospitalization or death

- 0.77% in nirmatrelvir group vs 7.01% in placebo (*p*<0.001)

COVID-19-related Hospitalization or Death From Any Cause Through Day 28 Among Patients Treated ≤5 Days After Symptom Onset



No. at risk

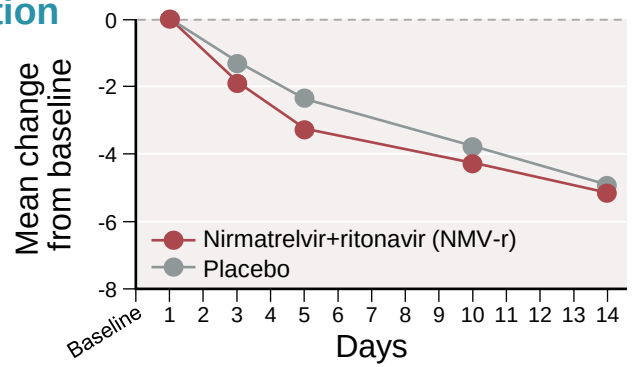
NMV-r	1039	1034	1023	1013	1007	1004	1002	1000	997	995	993	993	993	993	992
Placebo	1046	1042	1015	990	977	963	959	959	955	953	951	948	948	948	945

[a] The efficacy of nirmatrelvir/ritonavir was assessed when the Delta variant was prevalent.

[1]Hammond J et al. *N Engl J Med.* 2022.

Efficacy of Nirmatrelvir/Ritonavir in High-Risk Patients with COVID-19[1,a]

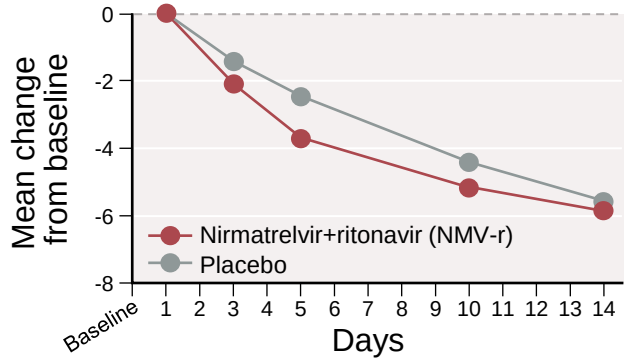
A) Overall Population



No. at risk					
NMV-r	552	529	508	502	507
Placebo	553	525	507	475	500
Mean (±SE) change from baseline vs. placebo		-0.55 ±0.11	-0.08 ±0.10	-0.44 ±0.10	-0.16 ±0.08
P value		<0.001	<0.001	<0.001	<0.045

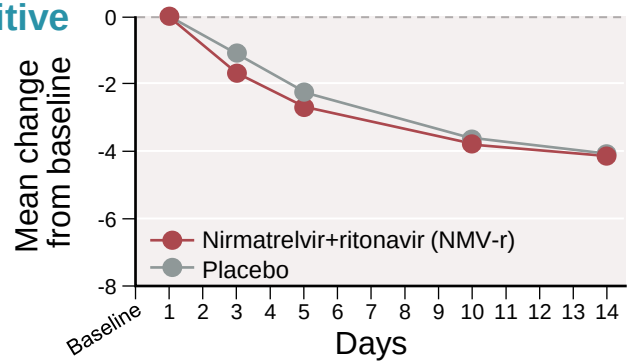
Change from Baseline in Log10-Transformed Viral Load over Time (Modified Intention-to-Treat Population)

B) Seronegative



No. at risk					
NMV-r	318	304	297	296	293
Placebo	312	294	284	267	273
Mean (±SE) change from baseline vs. placebo		-0.56 ±0.14	-1.20 ±0.13	-0.67 ±0.14	-0.21 ±0.12
P value		<0.001	<0.001	<0.001	<0.07

C) Seropositive



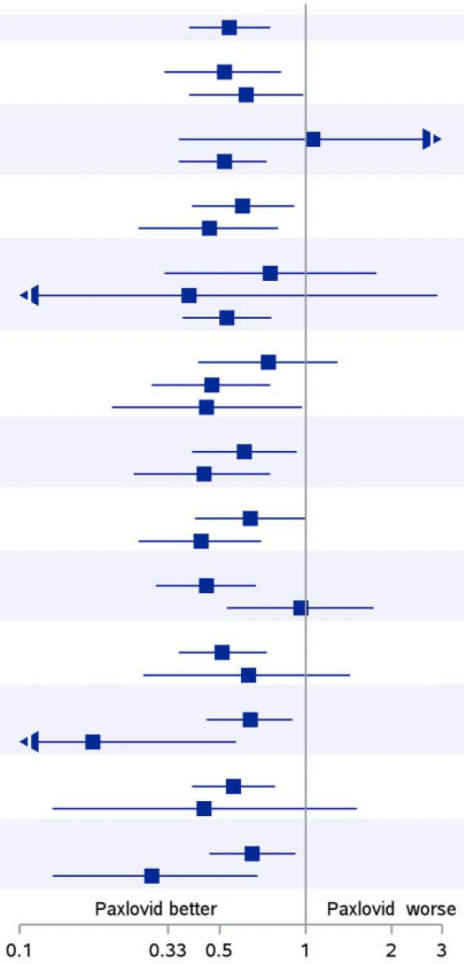
No. at risk					
NMV-r	231	222	208	203	211
Placebo	233	223	215	200	219
Mean (±SE) change from baseline vs. placebo		-0.58 ±0.18	-0.44 ±0.16	-0.11 ±0.12	-0.06 ±0.11
P value		0.001	0.01	0.37	0.60

[a] The efficacy of nirmatrelvir/ritonavir was assessed when the Delta variant was prevalent; [1]Hammond J et al. *N Engl J Med.* 2022.

Nirmatrelvir/Ritonavir Reduces the Risk of Severe COVID-19 or Mortality in High-Risk Patients

Real-World Effectiveness of Nirmatrelvir/Ritonavir in High-Risk Patients[1]

Subgroup	Paxlovid No.	Non-Paxlovid No.	Hazard Ratio (95% CI)	Interaction *P* Value
Overall	4737	175 614	0.54 (.39, .75)	
Adequate COVID-19 vaccination				.129
No	1051	43 818	0.52 (.32, .82)	
Yes	3686	131 796	0.62 (.39, .98)	
Age category				.039
<60 years	973	102 040	1.06 (.36, 3.15)	
≥60 years	3764	73 574	0.52 (.36, .73)	
Sex				.514
Males	1992	71967	0.60 (.40, .91)	
Females	2745	103 647	0.46 (.26, .80)	
Population sector				.708
Arab	300	32 758	0.75 (.32, 1.77)	
Ultra-Orthodox Jewish	202	6835	0.39 (.05, 2.89)	
General Jewish	4234	135 464	0.53 (.37, .76)	
Socioeconomic status				.846
Low	1120	62 618	0.74 (.42, 1.29)	
Middle	2090	74 928	0.47 (.29, .75)	
High	1517	37 022	0.45 (.21, .97)	
Diabetes				.257
No	2911	139 767	0.61 (.40, .93)	
Yes	1826	35 487	0.44 (.25, .75)	
Cardiovascular disease				.028
No	3231	152 121	0.64 (.41, 1.00)	
Yes	1506	23 493	0.43 (.26, .70)	
Chronic lung disease				.114
No	4238	169 385	0.45 (.30, .67)	
Yes	499	6229	0.96 (.53, 1.73)	
Chronic kidney disease				.965
No	4506	170 949	0.51 (.36, .73)	
Yes	231	4665	0.63 (.27, 1.43)	
Neurological disease				.016
No	4410	164 650	0.64 (.45, .90)	
Yes	327	10 964	0.18 (.06, .57)	
Malignancy in the prior year				.387
No	4559	174 090	0.56 (.40, .78)	
Yes	178	1524	0.44 (.13, 1.51)	
Immunosuppression				.042
No	4421	174 400	0.65 (.46, .92)	
Yes	316	1214	0.29 (.13, .68)	



[1]Najjar-Debbiny R et al. *Clinical Infectious Diseases.* 2022.

AEs in EPIC-HR[1]

	Nirmatrelvir/ritonavir N=1109 (%)	Placebo N=1115 (%)
Any AE	251 (22.6)	266 (23.9)
Serious AE	18 (1.6)	74 (6.6)
Maximum grade 3 or 4 AE	45 (4.1)	93 (8.3)
Discontinued drug/placebo because of AE	23 (2.1)	47 (4.2)
Dose reduction or temporary discontinuation owing to AE	4 (0.4)	4 (0.4)

Number of patients with events that emerged during treatment period. Shown are data for all patients who received at least one dose of drug or placebo.

AEs: adverse events.

[1]Hammond J et al. *N Engl J Med.* 2022.

Key Contraindications[1]

Increased substrate drug concentration

CYP3A4 Substrates

Antiarrhythmics
- Amiodarone
- Dronedarone
- Flecainide
- Propafenone
- Quinidine

Antipsychotics
- Lurasidone
- Pimozide

Rivaroxaban (DOAC)

PDE5 inhibitors
- Avanafil
- Sildenafilb
- Vardenafil

CYP3A4 Inducers

Anticonvulsants
- Carbamazepine
- Phenobarbital
- Phenytoin

Anticancer agents
- Apalutamide

Antimycobacterials
- Rifampin

St. John's Wort
(*hypericum perforatum*)

Reduced nirmatrelvir/ritinovir effectiveness

Practice Tip

Do not prescribe nirmatrelvir/ritonavir up to 28 days after administration of a CYP3A4 inducer

DOAC: direct oral anticoagulants.

[1]PAXLOVID Product Monograph. Pfizer Canada ULC. June 13, 2022.

Clinically Significant DDIs[1]

CYP3A4 Substrates

- Increased drug concentration can lead to toxicity
- Stop drug and re-initiate treatment 2 days after completing nirmatrelvir/ritonavir, replace, or adjust dose
- Examples
  - Alpha-blockers
  - Anticoagulants
  - Antipsychotics
  - Calcium channel blockers
  - Corticosteroids
  - Statins
  - Opioids
  - PDE5 inhibitors

CYP3A4 Inhibitors

- CYP3A4 inhibitors that increase nirmatrelvir/ritonavir concentration are tolerated
- Stop, replace, or change the dose of CYP3A4 inhibitors in case of toxicity
- Examples
  - Antifungals (ketoconazole, itraconazole)
  - HCV/HIV protease inhibitors
  - Macrolides (clarithromycin)

[1]PAXLOVID Product Monograph. Pfizer Canada ULC. June 13, 2022.

Key Learning Points

mAbs (bamlanivimab, sotrovimab, casirivimab/imdevimab, tixagevimab/cilgavimaba), oral antivirals (nirmatrelvir/ritonavir), and IV antivirals (remdesivir) are available for the treatment of COVID-19 outpatients in Canada

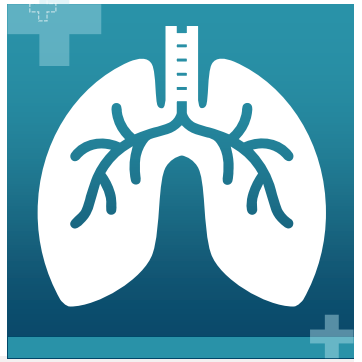
Prevalent Omicron subvariants are resistant to existing mAbs

Oral antivirals remain effective against Omicron subvariants

Role of Pharmacists in the Outpatient Treatment of COVID-19

Case 3

- A patient comes with a positive antigenic test for COVID-19
- Mild symptoms started 3 days ago, and the patient has risk factors for severe disease or hospitalization



- **Given that eligibility for outpatient treatments is time-sensitive and the patient has a positive test, what would your next step be?**
  a. Help patient obtain a prescription based on provincial guidelines (direct to hotline/telehealth or prescribe directly)
  b. Tell your patient to quarantine for 1 day
  c. Send for confirmatory PCR testing
  d. Wait for a couple of days to see if symptoms get worse

Importance of Early Intervention in Patient Outcomes

~13.5% of patients hospitalized with COVID-19 die[1]

Patients hospitalized with COVID-19 are at risk of secondary hospital-acquired bacterial, viral, or fungal infections[2]

Early intervention may reduce mortality in patients with COVID-19[3–5]

[1]Di Fusco M et al. *J Med Econ*. 2021; [2]Smith L et al. *Infect Control Hosp Epidemiol*. 2021; [3]Goyal D et al. *Clin Med*. 2020; [4]Reis G et al. *Lancet Global Health*. 2022; [5]Sun Q et al. *Ann. Intensive Care*. 2020.

Outpatient Treatments Are Underutilized[1,2]

Did you know?

Delays in diagnosis and getting access to therapy are the most important factors contributing to the underutilization of outpatient treatments

Potential factors that can hinder or delay access to outpatient treatments

- Underrecognized early signs and symptoms
- Confusion around patient eligibility
- Getting tested
- Coordinating with the pharmacy, physician, or prescriber

[1]Anderson et al. *J Gen Intern Med*. 2021; [2]Ontario Health. Guidance for primary care providers – Access to outpatient therapies for COVID-19 (sotrovimab and Paxlovid). Accessed July 25, 2022. https://www.ontariohealth.ca/COVID-19/Health-System-Response-Resources#covid19

How to Maximize Use of Outpatient Treatments

Early recognition of symptoms

- Increase awareness of symptoms
- Use of self-assessment tools, online forms/questionnaires, telephone triage/telehealth tools

Testing

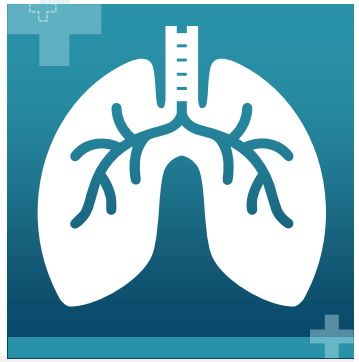
- Early confirmation of diagnosis through rapid and widespread testing and contact-tracing

Easy access to treatment

- Make available through local pharmacies

Case 4

- A patient calls to ask how to access nirmatrelvir/ritonavir
- The patient has mild COVID-19 (diagnosis confirmed through rapid testing) and is at high risk for hospitalization.
  The patient's GP provided a prescription for nirmatrelvir/ritonavir



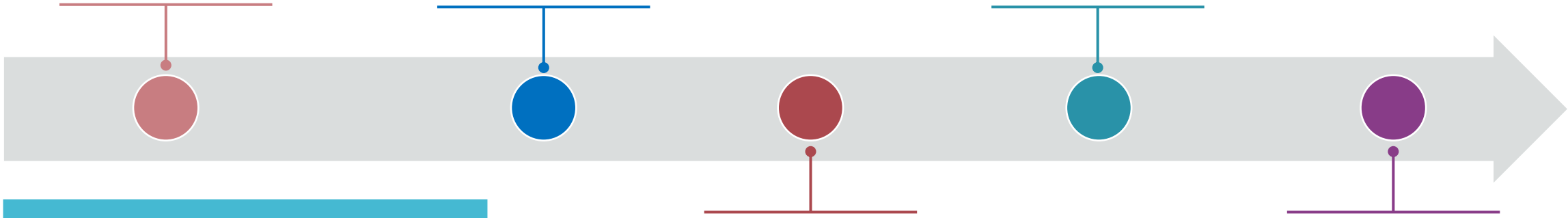
- **What would your next step be?**
  a. Dispense drug because the patient has confirmed diagnosis (mild disease, high risk) and prescription
  b. Ask the patient to get PCR testing because COVID-19 diagnosis was based on rapid testing
  c. Obtain a complete list of the patient's current medications, including over-the-counter agents and herbal supplements, and dispense the drug after having managed any and all significant DDIs that are identified

Pathway for Access to Outpatient Therapies

IDENTIFY individuals at risk before they contract SARS-CoV-2 and inform them about what they should (treatment plan) do if they test positive

PRIORITIZE assessment of patients with COVID-19 symptoms and who are at high risk for severe disease

PRESCRIBE the medication directly to be dispensed at a community pharmacy, or direct the patient to a clinical assessment centre or other local pathway[a]



ASSESS patient to determine if outpatient therapies are appropriate – test patient or direct patient to get tested

FOLLOW UP with the patient – Processes for follow-up within clinical assessment centres and local pathways may vary

Practice Tip

Assess patients with COVID-19 symptoms and who are at high risk for severe disease **within 24h** of the patient seeking support

[a] Who can prescribe varies depending on the province. [1]Ontario Health. Guidance for primary care providers – Access to COVID-19 antiviral treatment (Paxlovid). Accessed July 26, 2022. https://www.ontariohealth.ca/COVID-19/Health-System-Response-Resources#covid19

Prioritizing Access to Outpatient Treatments: Comorbidities

Risk factors:

Immunocompromising conditions[1]	Cell-depleting therapies[a]
	Ongoing treatment with BTKi
	Treatment with CAR-T cells
	Hematopoietic cell transplant recipients[b]
	Active treatment for hematologic malignancies
	Lung transplant recipients
	Severe combined immunodeficiencies
	Untreated HIV and CD4 T cell count <50 cells/mm^3
	Solid organ transplant[a]
Comorbidities[2]	Diabetes
	Heart disease
	Chronic respiratory disease
	Obesity
	Sickle cell disease
	Neurodevelopmental disorders
	Cancer

[a] Within the last year; [b] Hematopoietic cell transplant recipients who have graft versus host disease or take immunosuppressive medications; BTKi: Bruton tyrosine kinase inhibitors.
[1]National Institutes of Health. COVID-19 Treatment Guidelines. Accessed July27, 2022. https://www.covid19treatmentguidelines.nih.gov; [2]CDC COVID-19 People with Certain Medical Conditions. Accessed July27, 2022. www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html

Risk of COVID-19 Hospitalization

Analysis from logistic regression on confirmed cases and hospitalizations from Dec. 14 to Jan. 4, 2022

		Female				Male			
# of at-risk conditions	**Age group**	0 dose	1 dose	2 doses	3 doses	0 dose	1 dose	2 doses	3 doses
0 at-risk conditions	< 20	0,3 %	0,1 %	0,1 %	0,0 %	0,4 %	0,2 %	0,1 %	0,0 %
	20-39	1,5 %	0,5 %	0,4 %	0,2 %	1,8 %	0,7 %	0,4 %	0,2 %
	40-49	1,9 %	0,7 %	0,4 %	0,2 %	2,3 %	0,8 %	0,5 %	0,3 %
	50-59	2,7 %	1,0 %	0,6 %	0,3 %	3,2 %	1,2 %	0,8 %	0,4 %
	60-69	2,9 %	1,1 %	0,7 %	0,3 %	3,6 %	1,3 %	0,8 %	0,4 %
	70-79	5,2 %	1,8 %	1,2 %	0,6 %	6,3 %	2,2 %	1,5 %	0,7 %
	80+	9,5 %	3,3 %	2,2 %	1,1 %	11,8 %	4,0 %	2,7 %	1,3 %
1-2 at-risk conditions	< 20	0,9 %	0,3 %	0,2 %	0,1 %	1,2 %	0,4 %	0,3 %	0,1 %
	20-39	4,5 %	1,7 %	1,1 %	0,5 %	4,7 %	1,8 %	1,1 %	0,6 %
	40-49	5,2 %	1,9 %	1,2 %	0,6 %	5,9 %	2,2 %	1,3 %	0,7 %
	50-59	6,8 %	2,6 %	1,6 %	0,8 %	8,3 %	3,2 %	1,9 %	1,0 %
	60-69	7,5 %	3,0 %	1,8 %	0,9 %	9,5 %	3,6 %	2,2 %	1,1 %
	70-79	13,9 %	5,4 %	3,3 %	1,6 %	17,2 %	6,9 %	4,2 %	2,0 %
	80+	26,2 %	9,7 %	6,2 %	2,9 %	33,9 %	13,1 %	8,1 %	3,9 %
3+ at-risk conditions	< 20	5,5 %	1,8 %	1,3 %	0,5 %	7,3 %	1,8 %	1,4 %	1,4 %
	20-39	23,0 %	10,6 %	5,1 %	2,9 %	25,2 %	11,0 %	6,6 %	3,6 %
	40-49	26,2 %	10,6 %	5,8 %	3,6 %	35,6 %	8,3 %	6,5 %	4,0 %
	50-59	36,0 %	13,2 %	7,7 %	4,3 %	37,0 %	12,3 %	8,9 %	5,1 %
	60-69	33,2 %	14,8 %	7,6 %	3,9 %	40,3 %	16,2 %	9,4 %	5,0 %
	70-79	50,1 %	23,2 %	12,8 %	5,9 %	59,6 %	26,6 %	15,9 %	7,5 %
	80+	71,9 %	31,8 %	20,7 %	9,4 %	83,7 %	43,8 %	26,3 %	12,7 %

Model estimates* of the proportion of cases that would result in hospitalization by demographic group and vaccine status

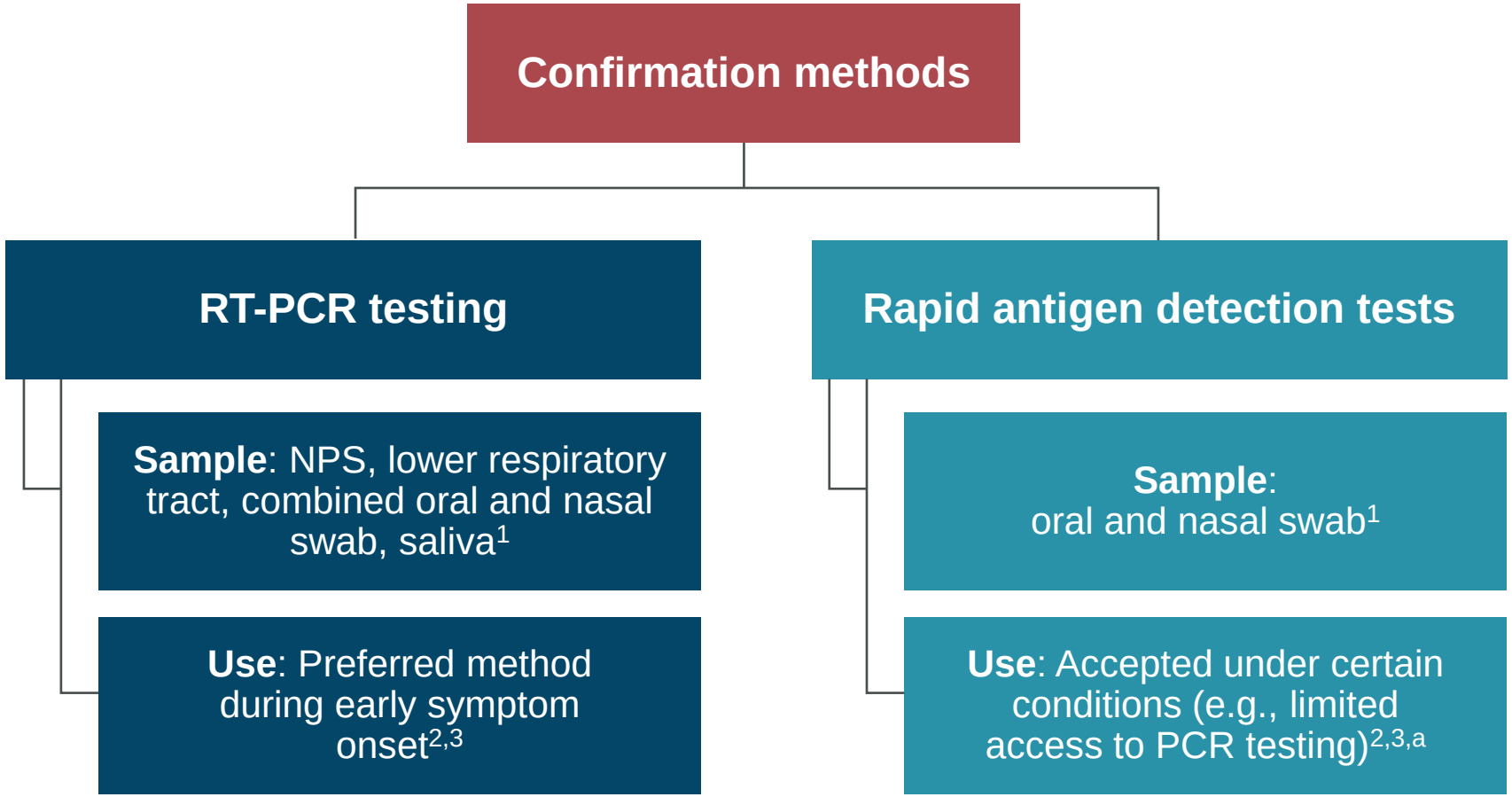
Hospitalization risk for younger people with 2 or more doses approaches zero

Even with 3 doses, substantial risk observed for those over 80+ when multiple risk conditions present

* Point estimates expected to change as more data becomes available. Differences between same-colored cells may not be statistically significant.

BC Centre for Disease Control. COVID-19: Hospitalization Risk. Preliminary Analysis of Cases Dec 14-Jan 6 (Hospitalizations up to Jan 10). Accessed July 27, 2022. https://news.gov.bc.ca/files/1.21.22_COVID_Hospitalizations.pdf

Accepted Confirmation Methods



Practice Tip

Encourage **all** symptomatic patients to get tested regardless of symptom severity

[a] During periods of high community viral prevalence, when the PPV is higher and traditional laboratory test capacity is overwhelmed, this technology can be broadly used. During periods of low prevalence, the use of this technology should be more limited; NPS: nasopharyngeal swab; PPV: positive predictive value; RT-PCR: real-time PCR.

[1]Ontario Health. COVID-19 Provincial Testing Guidance. Accessed July 26, 2022. https://www.health.gov.on.ca/en/pro/programs/publichealth/coronavirus/docs/COVID-19_provincial_testing_guidance.pdf; [2]BC Centre for Disease Control. Assessment Guide for Clinicians. Accessed April 12, 2022. Available at: http://www.bccdc.ca/Health-Professionals-Site/Documents/COVID-treatment/PracticeTool1_AssessmentGuideforClinicians.pdf; [3]Health Canada. Interim guidance on the use of rapid antigen detection tests for the identification of SARS-CoV-2 infection. Accessed July 26. https://www.canada.ca/en/public-health/services/diseases/2019-novel-coronavirus-infection/guidance-documents

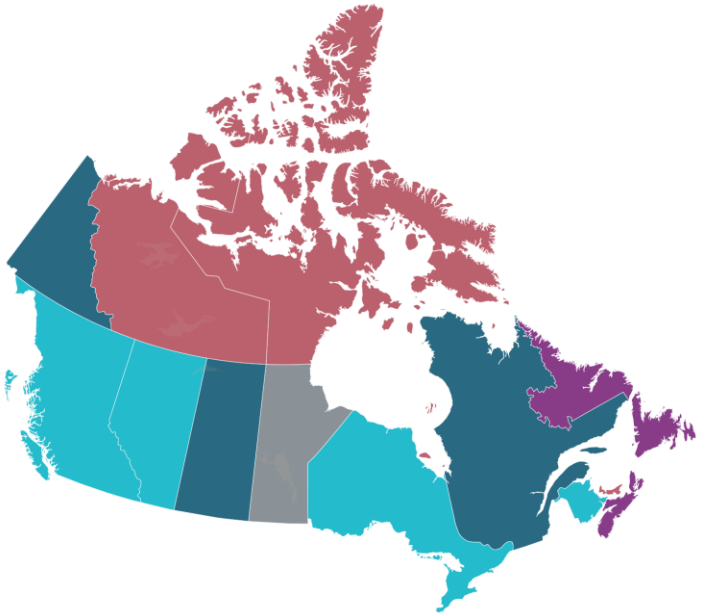
Role of Pharmacists in Rapid POC Testing and Specimen Collection for PCR Testing

NWT and Nunavut
POCT, rapid antigen test, and asymptomatic COVID-19 testing not permitted

Yukon and Quebec
POCT, and rapid antigen tests permitted, with limitations; asymptomatic COVID-19 testing not permitted

British Columbia
POCT, rapid antigen tests, and asymptomatic COVID-19 testing permitted, with some limitations

Alberta
POCT, rapid antigen tests, and asymptomatic COVID-19 testing permitted



Newfoundland
POCT permitted; rapid antigen tests and asymptomatic COVID-19 testing not permitted

PEI
POCT permitted, with limitations; rapid antigen tests and asymptomatic COVID-19 testing not permitted

New Brunswick
POCT and rapid antigen tests permitted; asymptomatic COVID-19 testing permitted, with limitations

Nova Scotia
POCT permitted, with limitations; rapid antigen tests and asymptomatic COVID-19 testing not permitted

Saskatchewan
POCT legislation available, rapid antigen tests permitted, with limitations; COVID-19 testing not permitted

Manitoba
POCT and rapid antigen tests not permitted; asymptomatic COVID-19 testing permitted, with limitations

Ontario
POCT and rapid antigen tests permitted, with limitations; asymptomatic COVID-19 testing permitted

	BC	AB	SK	MB	ON	QC	NB	NS	PEI	NL	YT[1]	NWT	NU
Perform POCT[2]	✓	✓	L[3]	✗	L[4]	L[5]	✓	L[6]	L[7]	✓	L[8]	✗	✗
Perform rapid antigen test[9]	L[10]	✓	L[11]	✗	L[12]	L[13]	✓	✗	✗	✗	L[8]	✗	✗
Specimen collection for asymptomatic COVID-19 test	L[10]	✓[14]	✗	L[15]	✓	✗	L[16]	✗	L[17]	✗	✗	✗	✗

✓ Permitted
L Permitted with certain limitations
✗ Not permitted

POC: point-of-care; [1]Canadian Pharmacists Association. Rapid point-of-care antigen testing and specimen collection for PCR tests by pharmacists. Accessed July 25, 2022. https://www.pharmacists.ca/cpha-ca/assets/File/cpha-on-the-issues/POCT_chart_FINAL_EN.pdf

Who Can Prescribe Outpatient Treatments for COVID-19?

Prescription from a doctor or nurse practitioner[1]

Consult with a health-care provider through telehealth services[1]

Online screening forms (Nova Scotia)[2]

Pharmacy (AB, QC, NL, SK, NB)[3–7]

[1]BC Centre for Disease Control. Assessment Guide for Clinicians. Accessed July 25, 2022. http://www.bccdc.ca; [2]Nova Scotia Health. Report and support online screening form. Accessed July 25, 2022. https://www.nshealth.ca/news/reminder-fill-out-online-screening-tool-ensure-you-are-considered-covid-19-medication; [3]Gouvernement du Québec. Oral COVID-19 treatment. Accessed July 25, 2022. https://www.quebec.ca/en/health/health-issues/a-z/2019-coronavirus/symptoms-transmission-treatment; [4]Government of Newfoundland and Labrador. Nirmatrelvir/Ritonavir (Paxlovid) Guidance for Healthcare Professionals. Accessed July 25, 2022, https://www.gov.nl.ca/covid-19/files/Nirmatrelvir-Ritonavir-Paxlovid-Guidance-for-Health-Care-Professionals-May-2022.pdf; [5]Alberta Health Services. Nirmatrelvir/ritonavir (Paxlovid) Outpatient Treatment. Accessed July 25, 2022; [6]Government of Saskatchewan. COVID-19 Weekly EPI Report. Accessed July 25, 2022. https://www.saskatchewan.ca/government/news-and-media/2022/may/19/covid-19-weekly-epi-report. [7]New Brunswick Health. Assessment and Prescribing for Paxlovid by Pharmacists. Accessed November 21, 2022. https://www2.gnb.ca

Choosing the Right Outpatient Treatment

- **Things to consider[1,2]**
  - Variant
  - mAbs may not be active against circulating variants
  - Local availability
  - Feasibility of prompt access
  - Patient factors (e.g., concomitant treatments/DDIs)
  - Time window from symptom onset
    - **5 days** for nirmatrelvir/ritonavir
    - **7 days** for remdesivir
    - **10 days** for sotrovimab

[1]National Institutes of Health. COVID-19 Treatment Guidelines. Accessed July 27, 2022. https://www.covid19treatmentguidelines.nih.gov; [2]COVID-19 Advisory for Ontario. Evidence-Based Recommendations on the Use of Casirivimab + Imdevimab, and Sotrovimab for Adults in Ontario. Accessed July27, 2022. https://covid19-sciencetable.ca/sciencebrief/evidence-based-recommendations-on-the-use-of-casirivimab-imdevimab-and-sotrovimab-for-adults-in-ontario

Choosing the Right Outpatient Treatment: INESSS Algorithm

- Patients over 18 (If pregnant or adolescent [or >40 kg] → this is a special situation to discuss with a specialist in obstetrics or pediatric infectious diseases)
- Confirmed SARS-CoV-2 test (by PCR or rapid antigen test)
- Mild or moderate symptoms since ≤5 days *for nirmatrelvir/ritonavir or sotrovimab) or ≤7 days (for tixagevimab/cilgavimab or remdesivir)
- Patients non-hospitalized for COVID-19

Patient with high risk of complications?

Severe immunosuppression
(regardless of immunization status or utilization of tixagevimab/cilgavimab as a pre-exposure prophylactic)
OR not adequately vaccinated **AND** Age ≥ 60 years **OR** comorbidities

NO → Treatments is unlikely to reduce the risk of complications. Vaccination with occasional boosters is the be way to protect patients. Consult if unfavorable evolution

If in doubt, for an exceptional case, a discussion with a specialist physician or an experienced colleague could be considered, but the benefits of available treatments are uncertain; the vaccinated population was not included in the studies.

YES

Contraindications to antivirals?

Severe chronic hepatic impairment **OR** Child-Pugh C
OR ALT ≥ 5 ULN (remdesivir)?

YES → Monoclonal antibodies accessible/available?

NO ← Monoclonal antibodies accessible/available?

NO

Drug interactions with ritonavir

Refer to the product monograph and usual pharmacological information sources such as Micromedex, Lexicomp, the HIV/HCV Therapeutic Guide or the Liverpool University COVID-19 drug interactions

YES

NO

Nirmatrelvir/ritonavir | **Tixagevimab/cilgavimab**

Considerations for choosing between the two options:
- Severe immunosuppression
- Use or not of tixagevimab/cilgavimab within the previous 6 months
- Delay since symptom onset
- Availability and accessibility
- Variants, sub-variants, and circulating strains

Consider nirmatrelvir/ritonavir PO x 5 days
Dose adjusted based on renal function

YES → Monoclonal antibodies accessible/available?

NO → May consider remdesivir, 200 mg IV D1 then 100 mg IV D2-3
Vigilance if impaired renal function

YES → **Consider tixagevimab/cilgavimab 600 mg IM x 1 dose OR Sotrovimab 1 g IV x 1 dose**
According to the circulating variants

Variants and subvariants of interest	Neutralizing antibodies to prioritize based on *in vitro* activity
BA.4 and subvariants **except** 4.6 and 4.7	Tixagevimab/ cilgavimab
BA.4.6 and 4.7	Sotrovimab
BA.5 and subvariants **except** 5.9 and BQ.1.1	Tixagevimab/ cilgavimab
BA.5.9 and BQ.1.1	Sotrovimab

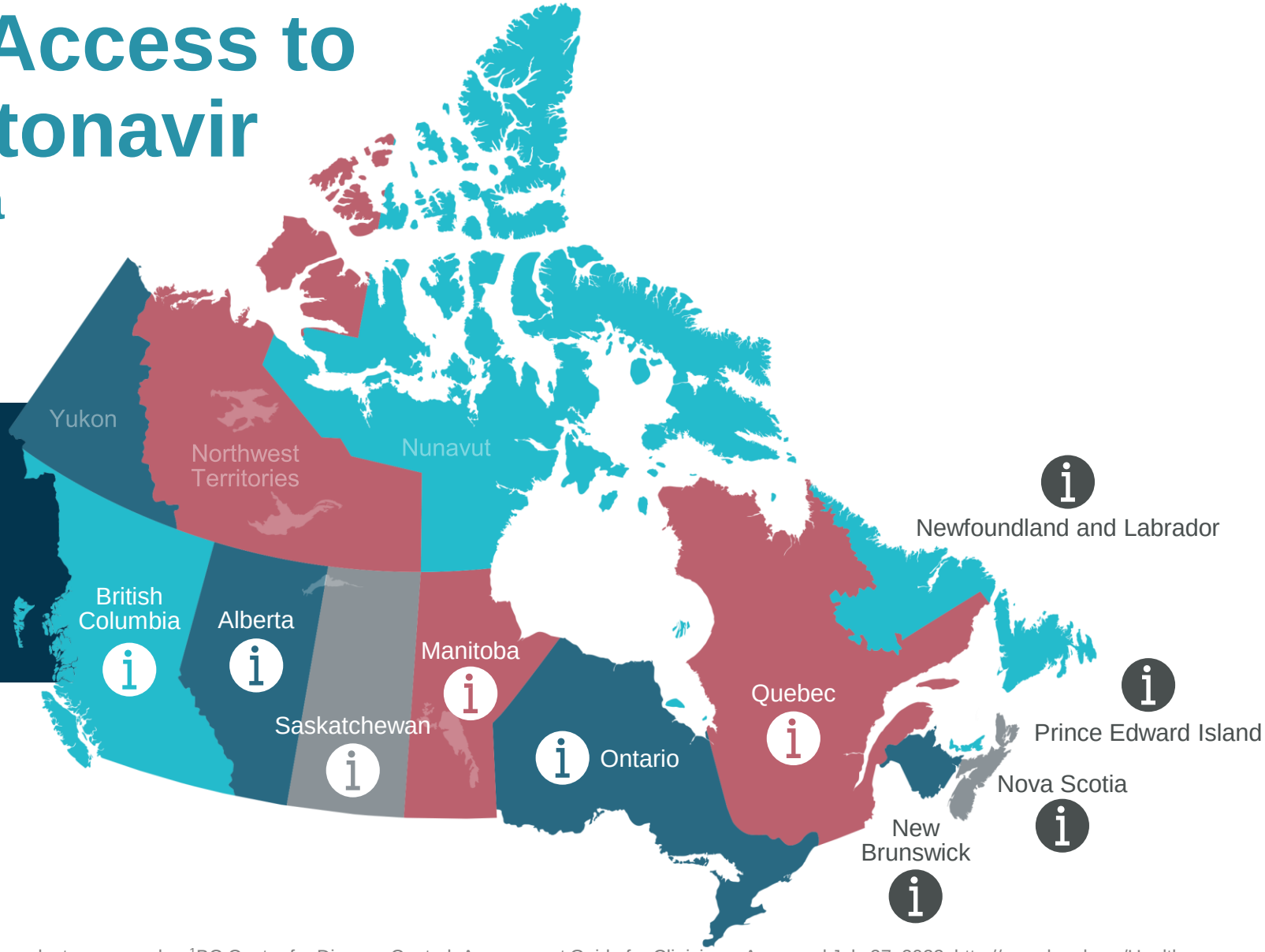
Practice Tip

When prescribing nirmatrelvir/ritonavir, adjust the dose according to renal function

[1]INESSS. Algorithme de traitements contre la covid-19 en ambulatoire pour les personnes à risque élevé de complications. Accessed November 22, 2022. https://www.inesss.qc.ca/fileadmin/doc/INESSS/COVID-19/Algorithme_traitement_COVID_ambulatoire_VF.pdf

Eligibility and Access to Nirmatrelvir/Ritonavir or Remdesivir[a]

Please click on a province's ⓘ icon to read its Eligibility and Access information



[a] Recommendations in the provincial guidelines may differ from the product monographs; [1]BC Centre for Disease Control. Assessment Guide for Clinicians. Accessed July 27, 2022. http://www.bccdc.ca/Health-Professionals-Site/Documents/COVID-treatment/PracticeTool1_AssessmentGuideforClinicians.pdf; [2]Government of Ontario. COVID-19 Treatments. Accessed July 27, 2022. https://covid-19.ontario.ca/covid-19-treatments; [3]Gouvernement du Québec. INESSS. Oral COVID-19 treatment (Paxlovid). Accessed July 27, 2022. https://www.quebec.ca/en/health/health-issues/a-z/2019-coronavirus/symptoms-transmission-treatment/oral-treatment-against-covid-19-paxlovidmc; [4]Alberta Health Services. Outpatient Treatment for COVID-19. Accessed July 27, 2022. https://www.albertahealthservices.ca/topics/Page17753.aspx; [5]Government of Manitoba. Treatment for COVID-19. Accessed July 27, 2022. https://www.gov.mb.ca/covid19/treatment/index.html

Eligibility and Access to Nirmatrelvir/Ritonavir or Remdesivir[a]

BRITISH COLUMBIA[1]

Eligibility:

- Immunocompromised adults
- Unvaccinated adults ≥50 years OR with comorbidities
- ≥50 years with 1-2 vaccine doses and ≥3 comorbidities
- ≥70 years with 1-2 vaccine doses and ≥1 comorbidities
- ≥70 years with ≥3 comorbidities
- Unvaccinated indigenous who are ≥50 with 1-2 vaccine doses, or ≥70 years

Access:

- If tested positive, eligible individuals can access treatment through the local pharmacy after obtaining an electronic prescription

[a] Recommendations in the provincial guidelines may differ from the product monographs; [1]BC Centre for Disease Control. Assessment Guide for Clinicians. Accessed July 27, 2022. http://www.bccdc.ca/Health-Professionals-Site/Documents/COVID-treatment/PracticeTool1_AssessmentGuideforClinicians.pdf; [2]Government of Ontario. COVID-19 Treatments. Accessed July 27, 2022. https://covid-19.ontario.ca/covid-19-treatments; [3]Gouvernement du Québec. INESSS. Oral COVID-19 treatment (Paxlovid). Accessed July 27, 2022. https://www.quebec.ca/en/health/health-issues/a-z/2019-coronavirus/symptoms-transmission-treatment/oral-treatment-against-covid-19-paxlovidmc; [4]Alberta Health Services. Outpatient Treatment for COVID-19. Accessed July 27, 2022. https://www.albertahealthservices.ca/topics/Page17753.aspx; [5]Government of Manitoba. Treatment for COVID-19. Accessed July 27, 2022. https://www.gov.mb.ca/covid19/treatment/index.html

MAP

Eligibility and Access to Nirmatrelvir/Ritonavir or Remdesivir[a]

ALBERTA[4]

Eligibility:

- Immunocompromised individuals who are unvaccinated or vaccinated (any number of doses)
- Living in long-term care or designated supportive living and are unvaccinated or vaccinated (any number of doses)
- Unvaccinated (or one dose) ≥18 years with ≥1 pre-existing health conditions (diabetes (taking medication for treatment), obesity (BMI >30), chronic kidney disease, congestive heart failure, chronic obstructive pulmonary disease, and moderate-to-severe asthma) or pregnancy
- ≥55 years or First Nations, Métis or Inuit and ≥45 years, unvaccinated or one dose
- ≥60 years or First Nations, Métis or Inuit and ≥50 years with ≥1 pre-existing conditions and unvaccinated or 1 or 2 doses
- ≥70 years or First Nations, Métis or Inuit and ≥60 years; with ≥2 pre-existing conditions and unvaccinated or 1, 2 or 3 doses

Access:

- May access treatment at local pharmacies
- **Centralized Call Center:** If patients don't have a family physician, or their physician isn't prescribing nirmatrelvir/ritonavir or remdesivir yet, they may call the dedicated line at 1-844-343-0971 to find out if they qualify to receive treatment

[a] Recommendations in the provincial guidelines may differ from the product monographs; [1]BC Centre for Disease Control. Assessment Guide for Clinicians. Accessed July 27, 2022. http://www.bccdc.ca/Health-Professionals-Site/Documents/COVID-treatment/PracticeTool1_AssessmentGuideforClinicians.pdf; [2]Government of Ontario. COVID-19 Treatments. Accessed July 27, 2022. https://covid-19.ontario.ca/covid-19-treatments; [3]Gouvernement du Québec. INESSS. Oral COVID-19 treatment (Paxlovid). Accessed July 27, 2022. https://www.quebec.ca/en/health/health-issues/a-z/2019-coronavirus/symptoms-transmission-treatment/oral-treatment-against-covid-19-paxlovidmc; [4]Alberta Health Services. Outpatient Treatment for COVID-19. Accessed July 27, 2022. https://www.albertahealthservices.ca/topics/Page17753.aspx; [5]Government of Manitoba. Treatment for COVID-19. Accessed July 27, 2022. https://www.gov.mb.ca/covid19/treatment/index.html

MAP

Eligibility and Access to Nirmatrelvir/Ritonavir or Remdesivir[a]

SASKATCHEWAN[6]

Eligibility:

- ≥18 years
- Positive PCR or rapid test with mild or moderate COVID-19 symptoms and within 5–7 days of symptom onset
- Immunocompromised, regardless of vaccination status
- ≥70 years with designated risk factors, regardless of vaccination status
- Medical condition that puts you at high risk and are not fully vaccinated
- 55–69 years and not fully vaccinated

Access:

- If tested positive, call a participating pharmacist, HealthLine 811 or a nurse practitioner to discuss eligibility

[a] Recommendations in the provincial guidelines may differ from the product monographs; [1]BC Centre for Disease Control. Assessment Guide for Clinicians. Accessed July 27, 2022. http://www.bccdc.ca/Health-Professionals-Site/Documents/COVID-treatment/PracticeTool1_AssessmentGuideforClinicians.pdf; [2]Government of Ontario. COVID-19 Treatments. Accessed July 27, 2022. https://covid-19.ontario.ca/covid-19-treatments; [3]Gouvernement du Québec. INESSS. Oral COVID-19 treatment (Paxlovid). Accessed July 27, 2022. https://www.quebec.ca/en/health/health-issues/a-z/2019-coronavirus/symptoms-transmission-treatment/oral-treatment-against-covid-19-paxlovidmc; [4]Alberta Health Services. Outpatient Treatment for COVID-19. Accessed July 27, 2022. https://www.albertahealthservices.ca/topics/Page17753.aspx; [5]Government of Manitoba. Treatment for COVID-19. Accessed July 27, 2022. https://www.gov.mb.ca/covid19/treatment/index.html

Eligibility and Access to Nirmatrelvir/Ritonavir or Remdesivir[a]

MANITOBA[5]

Eligibility:

- ≥18 years old and immunocompromised, not fully vaccinated, not received a booster dose, not been previously infected with COVID-19, obese, have ≥1 chronic medical conditions, or are pregnant

Access:

- If ≥18 years and meet eligibility criteria, talk with a health care provider or call Health Links - Info Santé (204-788-8200) to access COVID-19 treatment as soon as possible after testing positive

[a] Recommendations in the provincial guidelines may differ from the product monographs; [1]BC Centre for Disease Control. Assessment Guide for Clinicians. Accessed July 27, 2022. http://www.bccdc.ca/Health-Professionals-Site/Documents/COVID-treatment/PracticeTool1_AssessmentGuideforClinicians.pdf; [2]Government of Ontario. COVID-19 Treatments. Accessed July 27, 2022. https://covid-19.ontario.ca/covid-19-treatments; [3]Gouvernement du Québec. INESSS. Oral COVID-19 treatment (Paxlovid). Accessed July 27, 2022. https://www.quebec.ca/en/health/health-issues/a-z/2019-coronavirus/symptoms-transmission-treatment/oral-treatment-against-covid-19-paxlovidmc; [4]Alberta Health Services. Outpatient Treatment for COVID-19. Accessed July 27, 2022. https://www.albertahealthservices.ca/topics/Page17753.aspx; [5]Government of Manitoba. Treatment for COVID-19. Accessed July 27, 2022. https://www.gov.mb.ca/covid19/treatment/index.html

MAP

Eligibility and Access to Nirmatrelvir/Ritonavir or Remdesivir[a]

ONTARIO[2]

Eligibility:

- ≥18 years old and immunocompromised
- ≥70 years old
- ≥60 years old with fewer than 3 vaccine doses
- ≥18 years old with fewer than 3 vaccine doses and at least 1 risk condition

Access:

- Patients with symptoms should seek testing and care immediately by visiting a clinical assessment centre or
- contacting a primary care provider
- List of pharmacy locations that can fill prescriptions: https://covid-19.ontario.ca/covid-19-treatments

[a] Recommendations in the provincial guidelines may differ from the product monographs; [1]BC Centre for Disease Control. Assessment Guide for Clinicians. Accessed July 27, 2022. http://www.bccdc.ca/Health-Professionals-Site/Documents/COVID-treatment/PracticeTool1_AssessmentGuideforClinicians.pdf; [2]Government of Ontario. COVID-19 Treatments. Accessed July 27, 2022. https://covid-19.ontario.ca/covid-19-treatments; [3]Gouvernement du Québec. INESSS. Oral COVID-19 treatment (Paxlovid). Accessed July 27, 2022. https://www.quebec.ca/en/health/health-issues/a-z/2019-coronavirus/symptoms-transmission-treatment/oral-treatment-against-covid-19-paxlovidmc; [4]Alberta Health Services. Outpatient Treatment for COVID-19. Accessed July 27, 2022. https://www.albertahealthservices.ca/topics/Page17753.aspx; [5]Government of Manitoba. Treatment for COVID-19. Accessed July 27, 2022. https://www.gov.mb.ca/covid19/treatment/index.html

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Eligibility and Access to Nirmatrelvir/Ritonavir or Remdesivir[a]

QUEBEC[3]

Eligibility:

- Immunocompromised adults
- ≥60 years old – or ≥ 18 years old, or adolescents ≥ 40 kg or pregnant women, all with comorbidities – not adequately vaccinated (< 2 doses) or not protected against COVID-19
- Exceptionally, adults adequately protected or vaccinated with a very high risk of complications

Access:

- As soon COVID-19 symptoms appear, people must have a screening test to confirm a COVID-19 infection
- If tested positive, they must see a pharmacist, specialized nurse practitioner or physician
- If eligible, they receive treatment free of charge at the pharmacy of their choice

[a] Recommendations in the provincial guidelines may differ from the product monographs; [1]BC Centre for Disease Control. Assessment Guide for Clinicians. Accessed July 27, 2022. http://www.bccdc.ca/Health-Professionals-Site/Documents/COVID-treatment/PracticeTool1_AssessmentGuideforClinicians.pdf; [2]Government of Ontario. COVID-19 Treatments. Accessed July 27, 2022. https://covid-19.ontario.ca/covid-19-treatments; [3]Gouvernement du Québec. INESSS. Oral COVID-19 treatment (Paxlovid). Accessed July 27, 2022. https://www.quebec.ca/en/health/health-issues/a-z/2019-coronavirus/symptoms-transmission-treatment/oral-treatment-against-covid-19-paxlovidmc; [4]Alberta Health Services. Outpatient Treatment for COVID-19. Accessed July 27, 2022. https://www.albertahealthservices.ca/topics/Page17753.aspx; [5]Government of Manitoba. Treatment for COVID-19. Accessed July 27, 2022. https://www.gov.mb.ca/covid19/treatment/index.html

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Eligibility and Access to Nirmatrelvir/Ritonavir or Remdesivir[a]

NEW BRUNSWICK[1]

Eligibility:

- ≥80 years old
- ≥18 years and immunocompromised (active or recent cancer treatment, solid organ transplant, recent stem cell transplant (within 2 years), untreated HIV infection, or immunosuppressive treatment)
- 50-79 years of age and partially or under-vaccinated
- 50-79 years of age and lives in a long-term care (LTC) setting/home care or is from or lives in a First Nations community

Access:

- At symptom onset, people must have a test to confirm infection. If tested positive, eligible individuals can access treatment through the local pharmacy after obtaining a prescription and a signed and completed Eligibility Form

[a] Recommendations in the provincial guidelines may differ from the product monographs; [1]BC Centre for Disease Control. Assessment Guide for Clinicians. Accessed July 27, 2022. http://www.bccdc.ca/Health-Professionals-Site/Documents/COVID-treatment/PracticeTool1_AssessmentGuideforClinicians.pdf; [2]Government of Ontario. COVID-19 Treatments. Accessed July 27, 2022. https://covid-19.ontario.ca/covid-19-treatments; [3]Gouvernement du Québec. INESSS. Oral COVID-19 treatment (Paxlovid). Accessed July 27, 2022. https://www.quebec.ca/en/health/health-issues/a-z/2019-coronavirus/symptoms-transmission-treatment/oral-treatment-against-covid-19-paxlovidmc; [4]Alberta Health Services. Outpatient Treatment for COVID-19. Accessed July 27, 2022. https://www.albertahealthservices.ca/topics/Page17753.aspx; [5]Government of Manitoba. Treatment for COVID-19. Accessed July 27, 2022. https://www.gov.mb.ca/covid19/treatment/index.html

Eligibility and Access to Nirmatrelvir/Ritonavir or Remdesivir[a]

NOVA SCOTIA[3,4]

Eligibility:

- Non-severe COVID-19 with symptom onset within previous 7 days.
- Positive SARS-CoV-2 PCR test (or rapid antigen test while prevalence high)
- Age ≥ 12 years
- Immunocompetent patients who received ≤ 2 doses (primary series) or are < 2 weeks post 1st booster dose
- ≥70 years, vaccinated with 2 dose primary series and >3 months post 1st booster OR < 2 weeks post 2nd booster dose
- Immunocompromised patients who received ≤ 3 dose primary series or are < 2 weeks post 1st booster dose
- Immunocompromised and not expected to mount an adequate immune response to COVID-19 immunization, regardless of vaccine status
- ≥ 1 high risk factor for progression (diabetes, obesity, active cancer, sickle cell disease, chronic lung disease, cardiovascular disease, neurodevelopmental disorder)

Access:

- If tested positive, use the Report and Support Screening Tool or call 1-833-797-7772, and contact your primary care provider (family physician or nurse practitioner) to obtain prescription

[a] Recommendations in the provincial guidelines may differ from the product monographs; [1]BC Centre for Disease Control. Assessment Guide for Clinicians. Accessed July 27, 2022. http://www.bccdc.ca/Health-Professionals-Site/Documents/COVID-treatment/PracticeTool1_AssessmentGuideforClinicians.pdf; [2]Government of Ontario. COVID-19 Treatments. Accessed July 27, 2022. https://covid-19.ontario.ca/covid-19-treatments; [3]Gouvernement du Québec. INESSS. Oral COVID-19 treatment (Paxlovid). Accessed July 27, 2022. https://www.quebec.ca/en/health/health-issues/a-z/2019-coronavirus/symptoms-transmission-treatment/oral-treatment-against-covid-19-paxlovidmc; [4]Alberta Health Services. Outpatient Treatment for COVID-19. Accessed July 27, 2022. https://www.albertahealthservices.ca/topics/Page17753.aspx; [5]Government of Manitoba. Treatment for COVID-19. Accessed July 27, 2022. https://www.gov.mb.ca/covid19/treatment/index.html

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Eligibility and Access to Nirmatrelvir/Ritonavir or Remdesivir[a]

PRINCE EDWARD ISLAND[5]

Eligibility:

- Symptom onset within the last 5 days
- ≥18 years with underlying medical conditions regardless of COVID-19 vaccine status
- ≥ 50 years regardless of vaccine status
- Positive test result by PCR or ID Now/NAAT (e.g. at a testing clinic)

Access:

- If tested positive, contact your family physician/nurse practitioner or call the 811 telehealth service to discuss eligibility

[a] Recommendations in the provincial guidelines may differ from the product monographs; [1]BC Centre for Disease Control. Assessment Guide for Clinicians. Accessed July 27, 2022. http://www.bccdc.ca/Health-Professionals-Site/Documents/COVID-treatment/PracticeTool1_AssessmentGuideforClinicians.pdf; [2]Government of Ontario. COVID-19 Treatments. Accessed July 27, 2022. https://covid-19.ontario.ca/covid-19-treatments; [3]Gouvernement du Québec. INESSS. Oral COVID-19 treatment (Paxlovid). Accessed July 27, 2022. https://www.quebec.ca/en/health/health-issues/a-z/2019-coronavirus/symptoms-transmission-treatment/oral-treatment-against-covid-19-paxlovidmc; [4]Alberta Health Services. Outpatient Treatment for COVID-19. Accessed July 27, 2022. https://www.albertahealthservices.ca/topics/Page17753.aspx; [5]Government of Manitoba. Treatment for COVID-19. Accessed July 27, 2022. https://www.gov.mb.ca/covid19/treatment/index.html

Eligibility and Access to Nirmatrelvir/Ritonavir or Remdesivir[a]

NEWFOUNDLAND AND LABRADOR[2]

Eligibility:

- Immunocompromised (cancer treatment, organ transplantation, immunosuppressive therapy, CAR-T cell treatment, moderate or severe primary immunodeficiency, untreated HIV) regardless of vaccination status
- ≥80 years regardless of vaccination status
- ≥60 years regardless of vaccination status and reside in a rural community, long-term care setting, or Indigenous community

Access:

- If tested positive, contact your primary care provider (family physician or nurse practitioner) to obtain prescription

[a] Recommendations in the provincial guidelines may differ from the product monographs; [1]BC Centre for Disease Control. Assessment Guide for Clinicians. Accessed July 27, 2022. http://www.bccdc.ca/Health-Professionals-Site/Documents/COVID-treatment/PracticeTool1_AssessmentGuideforClinicians.pdf; [2]Government of Ontario. COVID-19 Treatments. Accessed July 27, 2022. https://covid-19.ontario.ca/covid-19-treatments; [3]Gouvernement du Québec. INESSS. Oral COVID-19 treatment (Paxlovid). Accessed July 27, 2022. https://www.quebec.ca/en/health/health-issues/a-z/2019-coronavirus/symptoms-transmission-treatment/oral-treatment-against-covid-19-paxlovidmc; [4]Alberta Health Services. Outpatient Treatment for COVID-19. Accessed July 27, 2022. https://www.albertahealthservices.ca/topics/Page17753.aspx; [5]Government of Manitoba. Treatment for COVID-19. Accessed July 27, 2022. https://www.gov.mb.ca/covid19/treatment/index.html

MAP

Key Learning Points

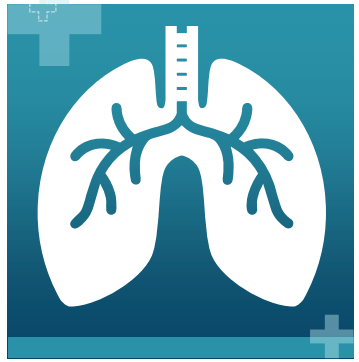
Although early intervention can prevent hospitalization and reduce mortality in patients with COVID-19, outpatient treatments for COVID-19 are underutilized

Early recognition of symptoms, widespread testing, and easy access to treatment can help maximize the use of outpatient treatments

Variant, risk of complications, DDIs, time window from symptom onset, hepatic/renal function, and local drug availability should be considered when choosing the right outpatient treatment for COVID-19

Eligibility criteria for nirmatrelvir/ritonavir and remdesivir is similar across Canada, however, each province establishes their own

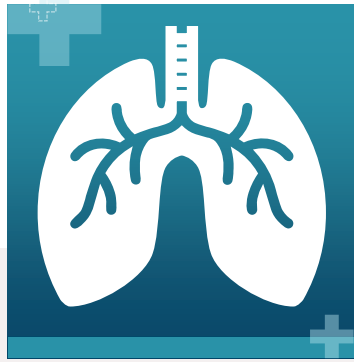
Case 5



- High-risk patient (mild symptoms) tests positive for COVID-19 at your pharmacy in Ontario
- You obtain a list of current medications – current use of rivaroxaban (DOAC) because of nonvalvular atrial fibrillation
- Not eligible for remdesivir – no available clinical times for administering intravenous medications

- **What would be your next step?**
  a. Stop rivaroxaban for 7 days and notify the prescriber in writing and prescribe nirmatrelvir/ritonavir
  b. Not dispense nirmatrelvir/ritonavir and continue rivaroxaban
  c. Add dabigatran to the rivaroxaban regimen without contacting the prescriber and prescribe nirmatrelvir/ritonavir
  d. Contact the specialist/prescriber of rivaroxaban to ask for authorization for dose adjustment

Case 6



- A high-risk patient with COVID-19 is prescribed nirmatrelvir/ritonavir but is also taking oral amlodipine for high blood pressure

- **What is the best way to mitigate potential toxicities from DDIs?**

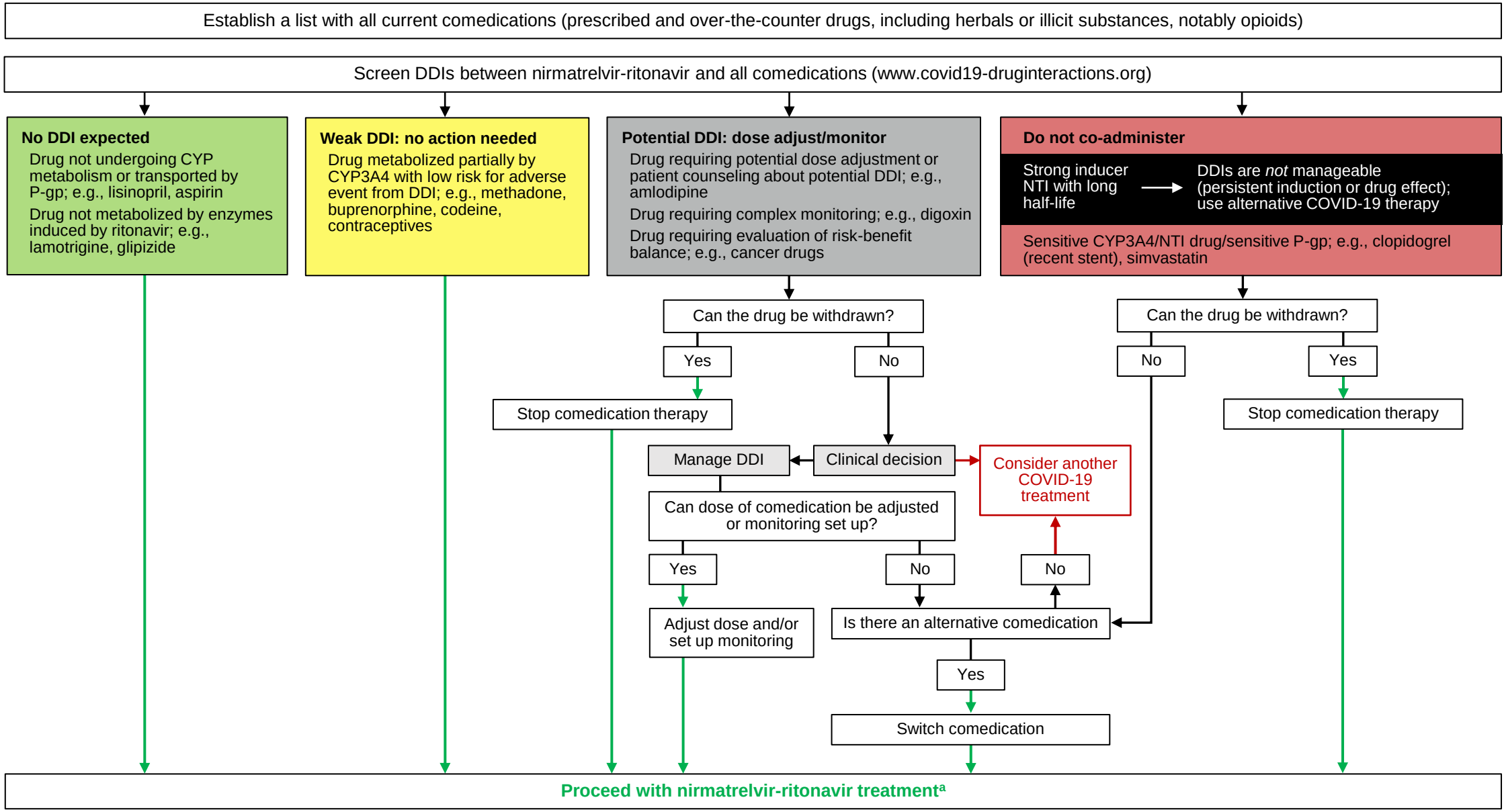
  a. Don’t start nirmatrelvir/ritonavir until the patient completes the amlodipine course

  b. Hold or replace amlodipine if possible and after consulting the prescriber, and start nirmatrelvir/ritonavir. Follow up with the patient to assess adherence

  c. Stop amlodipine without consulting the prescriber and start nirmatrelvir/ritonavir. Re-initiate amlodipine 2 weeks after the patient completes the nirmatrelvir/ritonavir course

  d. Start nirmatrelvir/ritonavir right away without stopping amlodipine—amlodipine does not interact with nirmatrelvir/ritonavir

Management of DDIs[1]



[a] The inhibitory effect of ritonavir takes several days to resolve. Thus, paused comedication therapy should be restarted 3 days after the last dose of nirmatrelvir–ritonavir. The same timeline applies for comedications whose dosage has been adjusted during nirmatrelvir–ritonavir treatment. [1]Marzolini et al. *Ann Intern Med.* 2022.

Discussion Points

How would you mitigate potential toxicities from DDIs in a high-risk patient with COVID-19 who is prescribed nirmatrelvir/ritonavir but is also taking anticoagulants?

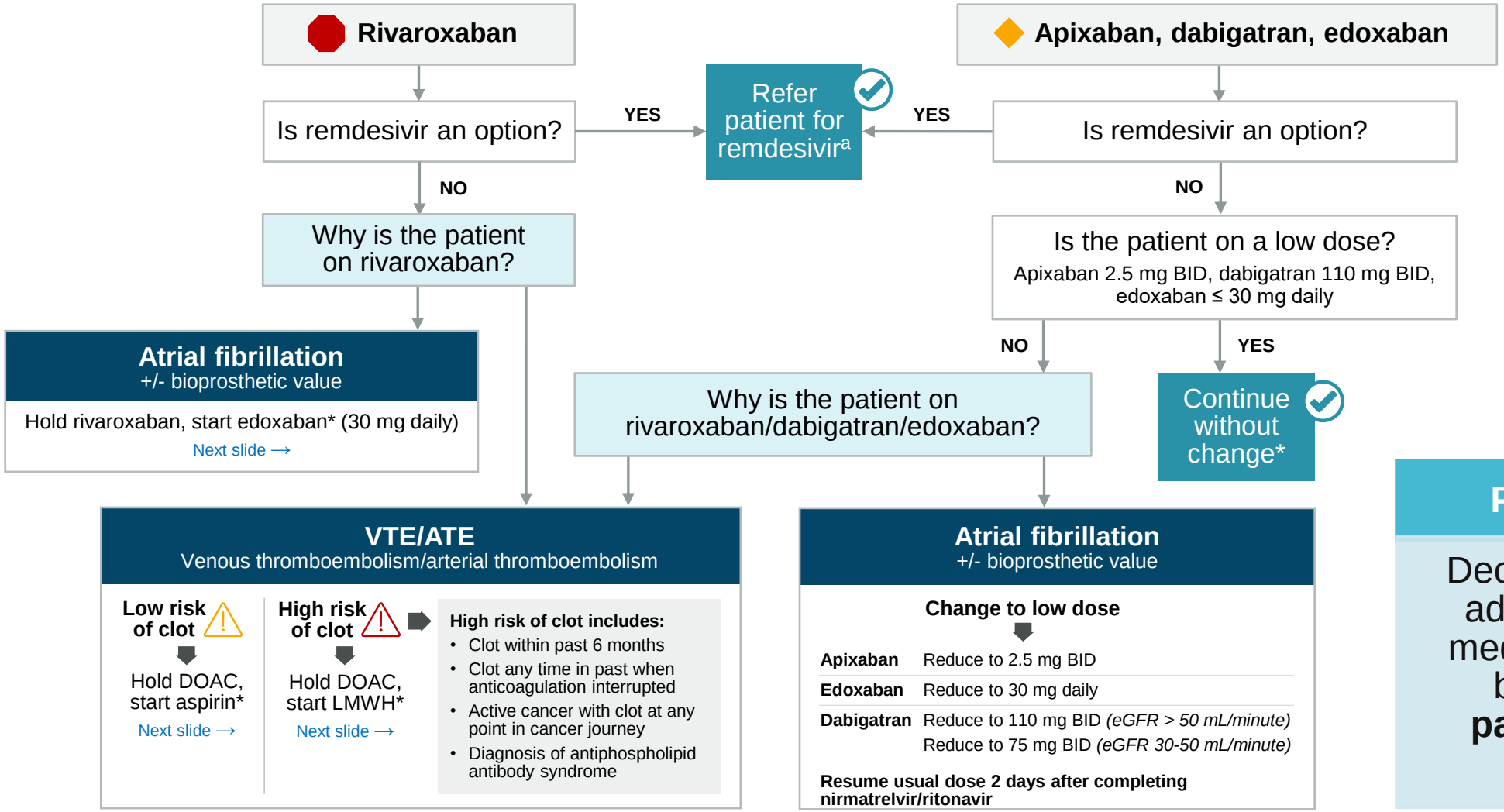
In a patient taking prednisone (rheumatologic disease), would you want to stop prednisone before prescribing nirmatrelvir/ritonavir?

Would you contact the physician/prescriber before stopping or re-initiating a medication?

Practice Tips
Inform the prescriber before adjusting doses of medications
Contact the physician/prescriber and **educate** the patient with clear instructions before stopping and re-initiating a medication. **Follow up** to ensure the patient restarts treatment.

All potential drug-drug interactions should be approached with caution. The drug-drug interaction recommendations on this slide were developed independently of Pfizer Canada ULC and may differ from recommendations in the product monograph of nirmatrelvir/ritonavir and the interacting products. Please consult the relevant product monographs before making any treatment decisions.

Management of DDIs: DOAC[1]



Practice Tip

Decisions to hold, adjust, or change medications should be made on a **patient-specific basis**

[a] Although remdesivir is a good treatment alternative to nirmatrelvir/ritonavir in case of significant drug interactions, timely access to IV treatment is not always feasible, and the use of an IV product may delay COVID-19 management.

BID: twice daily; DOAC: direct oral anticoagulant; LMWH: low-molecular-weight heparin.

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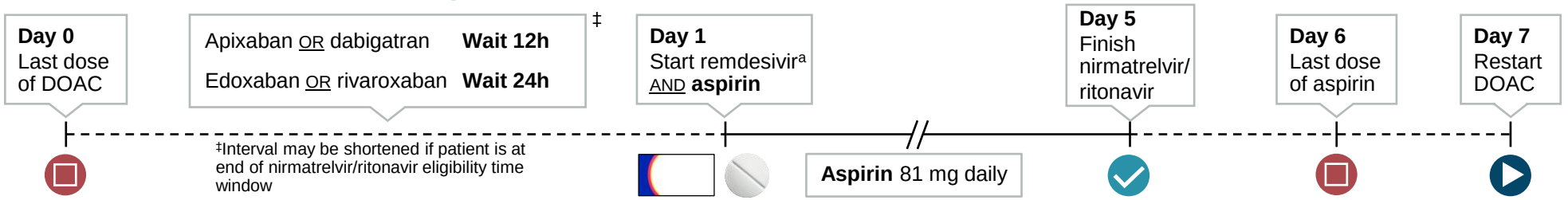
[1]Science Table – COVID-19 Advisory for Ontario. Paxlovid for a Patient on a DOAC. Accessed November 21, 2022. https://covid19-sciencetable.ca/sciencebrief/paxlovid-for-a-patient-on-a-doac-2-0/

Management of DDIs: DOAC[1]

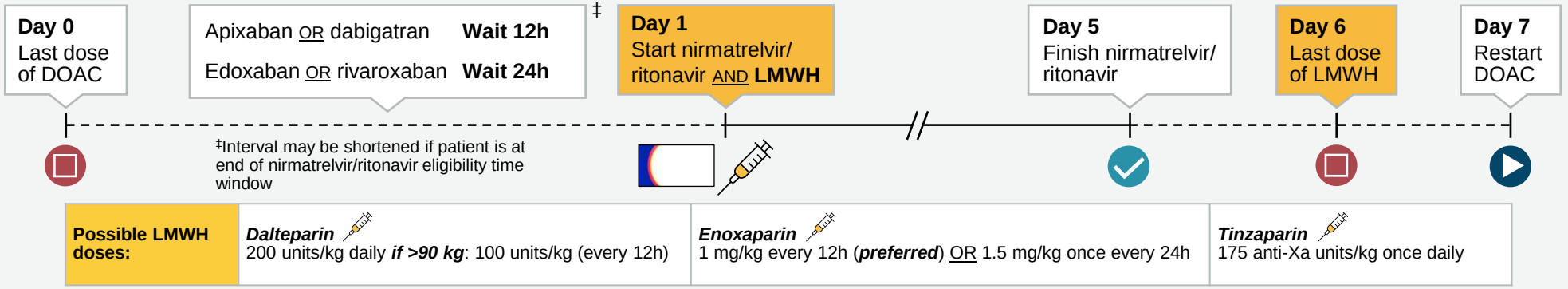
How to hold a DOAC and start aspirin

VTE/ATE: Low risk of clot



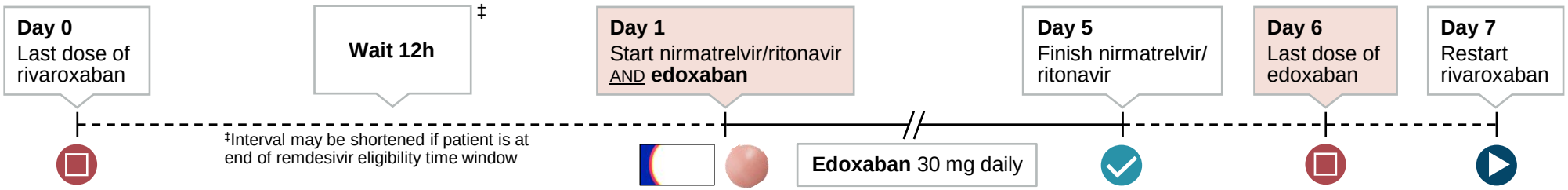
How to hold a DOAC and start LMWH

VTE/ATE: High risk of clot



How to hold rivaroxaban and start edoxaban

Atrial fibrillation



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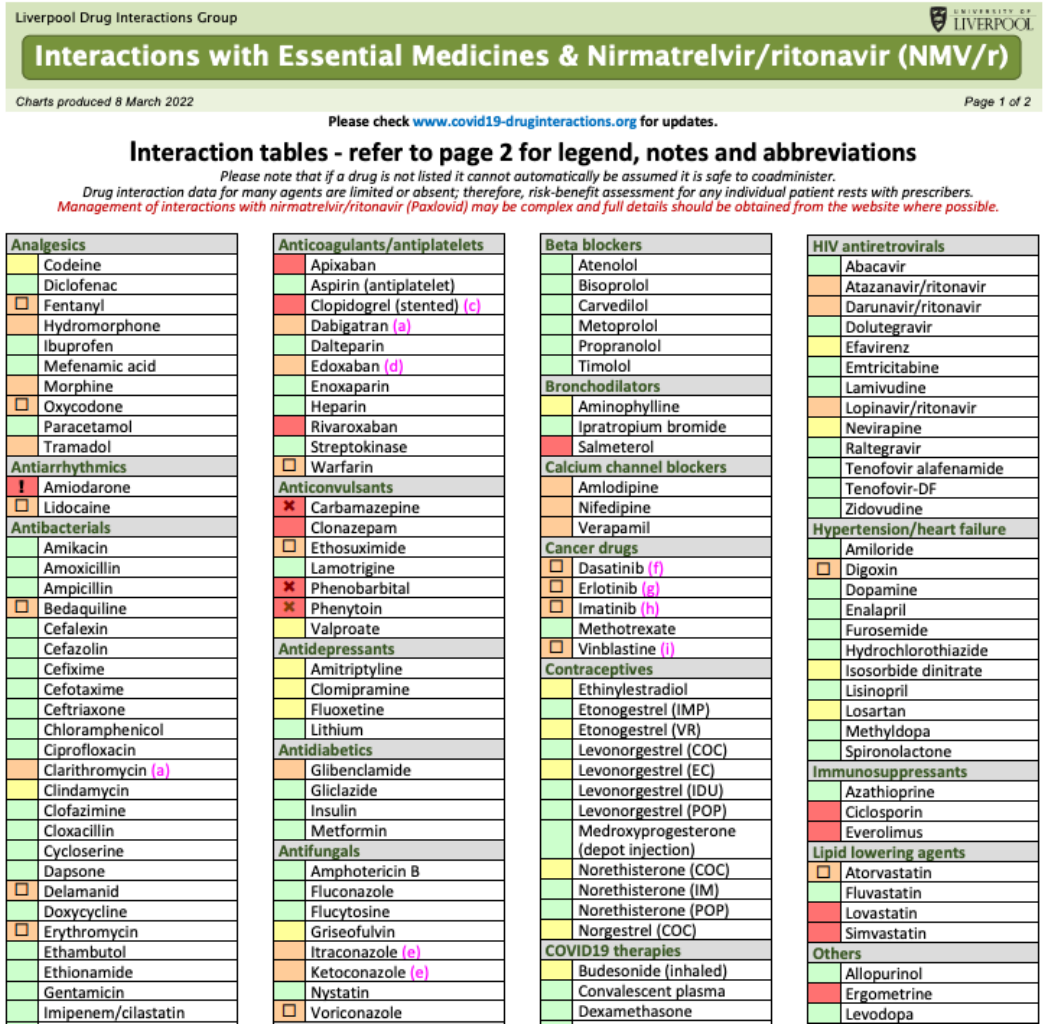
BID: twice daily; DOAC: direct oral anticoagulant; LMWH: low-molecular-weight heparin.

All potential drug-drug interactions should be approached with caution. The drug-drug interaction recommendations on this slide were developed independently of Pfizer Canada ULC and may differ from recommendations in the product monograph of nirmatrelvir/ritonavir and the interacting products. Please consult the relevant product monographs before making any treatment decisions. .

[1]Science Table – COVID-19 Advisory for Ontario. Paxlovid for a Patient on a DOAC. Accessed November 21, 2022. https://covid19-sciencetable.ca/sciencebrief/paxlovid-for-a-patient-on-a-doac-2-0/

DDI Resource: Interactions Chart – Liverpool Drug Interactions Group



Liverpool Drug Interactions Group

UNIVERSITY OF LIVERPOOL

Interactions with Essential Medicines & Nirmatrelvir/ritonavir (NMV/r)

Charts produced 8 March 2022 — *Page 1 of 2*

Please check www.covid19-druginteractions.org for updates.

Interaction tables - refer to page 2 for legend, notes and abbreviations

Please note that if a drug is not listed it cannot automatically be assumed it is safe to coadminister.
Drug interaction data for many agents are limited or absent; therefore, risk-benefit assessment for any individual patient rests with prescribers.
Management of interactions with nirmatrelvir/ritonavir (Paxlovid) may be complex and full details should be obtained from the website where possible.

Analgesics
Codeine
Diclofenac
☐ Fentanyl
Hydromorphone
Ibuprofen
Mefenamic acid
Morphine
☐ Oxycodone
Paracetamol
Tramadol
Antiarrhythmics
! Amiodarone
☐ Lidocaine
Antibacterials
Amikacin
Amoxicillin
Ampicillin
☐ Bedaquiline
Cefalexin
Cefazolin
Cefixime
Cefotaxime
Ceftriaxone
Chloramphenicol
Ciprofloxacin
Clarithromycin (a)
Clindamycin
Clofazimine
Cloxacillin
Cycloserine
Dapsone
☐ Delamanid
Doxycycline
☐ Erythromycin
Ethambutol
Ethionamide
Gentamicin
Imipenem/cilastatin

Anticoagulants/antiplatelets
Apixaban
Aspirin (antiplatelet)
Clopidogrel (stented) (c)
Dabigatran (a)
Dalteparin
Edoxaban (d)
Enoxaparin
Heparin
Rivaroxaban
Streptokinase
☐ Warfarin
Anticonvulsants
✖ Carbamazepine
Clonazepam
☐ Ethosuximide
Lamotrigine
✖ Phenobarbital
✖ Phenytoin
Valproate
Antidepressants
Amitriptyline
Clomipramine
Fluoxetine
Lithium
Antidiabetics
Glibenclamide
Gliclazide
Insulin
Metformin
Antifungals
Amphotericin B
Fluconazole
Flucytosine
Griseofulvin
Itraconazole (e)
Ketoconazole (e)
Nystatin
☐ Voriconazole

Beta blockers
Atenolol
Bisoprolol
Carvedilol
Metoprolol
Propranolol
Timolol
Bronchodilators
Aminophylline
Ipratropium bromide
Salmeterol
Calcium channel blockers
Amlodipine
Nifedipine
Verapamil
Cancer drugs
☐ Dasatinib (f)
☐ Erlotinib (g)
☐ Imatinib (h)
Methotrexate
☐ Vinblastine (i)
Contraceptives
Ethinylestradiol
Etonogestrel (IMP)
Etonogestrel (VR)
Levonorgestrel (COC)
Levonorgestrel (EC)
Levonorgestrel (IDU)
Levonorgestrel (POP)
Medroxyprogesterone (depot injection)
Norethisterone (COC)
Norethisterone (IM)
Norethisterone (POP)
Norgestrel (COC)
COVID19 therapies
Budesonide (inhaled)
Convalescent plasma
Dexamethasone

HIV antiretrovirals
Abacavir
Atazanavir/ritonavir
Darunavir/ritonavir
Dolutegravir
Efavirenz
Emtricitabine
Lamivudine
Lopinavir/ritonavir
Nevirapine
Raltegravir
Tenofovir alafenamide
Tenofovir-DF
Zidovudine
Hypertension/heart failure
Amiloride
☐ Digoxin
Dopamine
Enalapril
Furosemide
Hydrochlorothiazide
Isosorbide dinitrate
Lisinopril
Losartan
Methyldopa
Spironolactone
Immunosuppressants
Azathioprine
Ciclosporin
Everolimus
Lipid lowering agents
☐ Atorvastatin
Fluvastatin
Lovastatin
Simvastatin
Others
Allopurinol
Ergometrine
Levodopa

Legend

Colour/Symbol	Recommendation for NMV/r use
! **Do not co-administer**	**Do not use NMV/r ⇒ alternative COVID-19 therapy** Risk of serious toxicity. Stopping the drug does not mitigate the interaction due to its prolonged half-life.
✖ **Do not co-administer**	**Do not use NMV/r ⇒ alternative COVID-19 therapy** Strong inducer can jeopardize NMV/r efficacy due to persisting induction after stopping the drug.
Do not co-administer	**NMV/r use ONLY possible if drug is paused or replaced by a non-interacting drug** Risk of serious toxicity. Only start NMV/r if the drug can be safely paused or replaced. Drug can be resumed 3 days after completing NMV/r therapy.
☐ **Potential interaction** Dose adjustment and/or close monitoring required.	**Stop or replace drug if possible or consult specialist for dose adjustment/monitoring to allow use with NMV/r** Ideally, only start NMV/r if the drug can be safely paused or replaced. Alternatively, dose adjust/monitor. Refer to www.covid19-druginteractions.org for detailed information.
Potential interaction Manageable by counselling patient	**Proceed with NMV/r** Interaction manageable by counselling the patient about potential interaction and advising to temporarily stop the drug if feeling unwell.
Weak interaction No action needed	**Proceed with NMV/r** Drug metabolized partially by CYP3A4 or with low risk of adverse event from interaction.
No interaction expected	**Proceed with NMV/r**

Link: https://www.covid19-druginteractions.org/home

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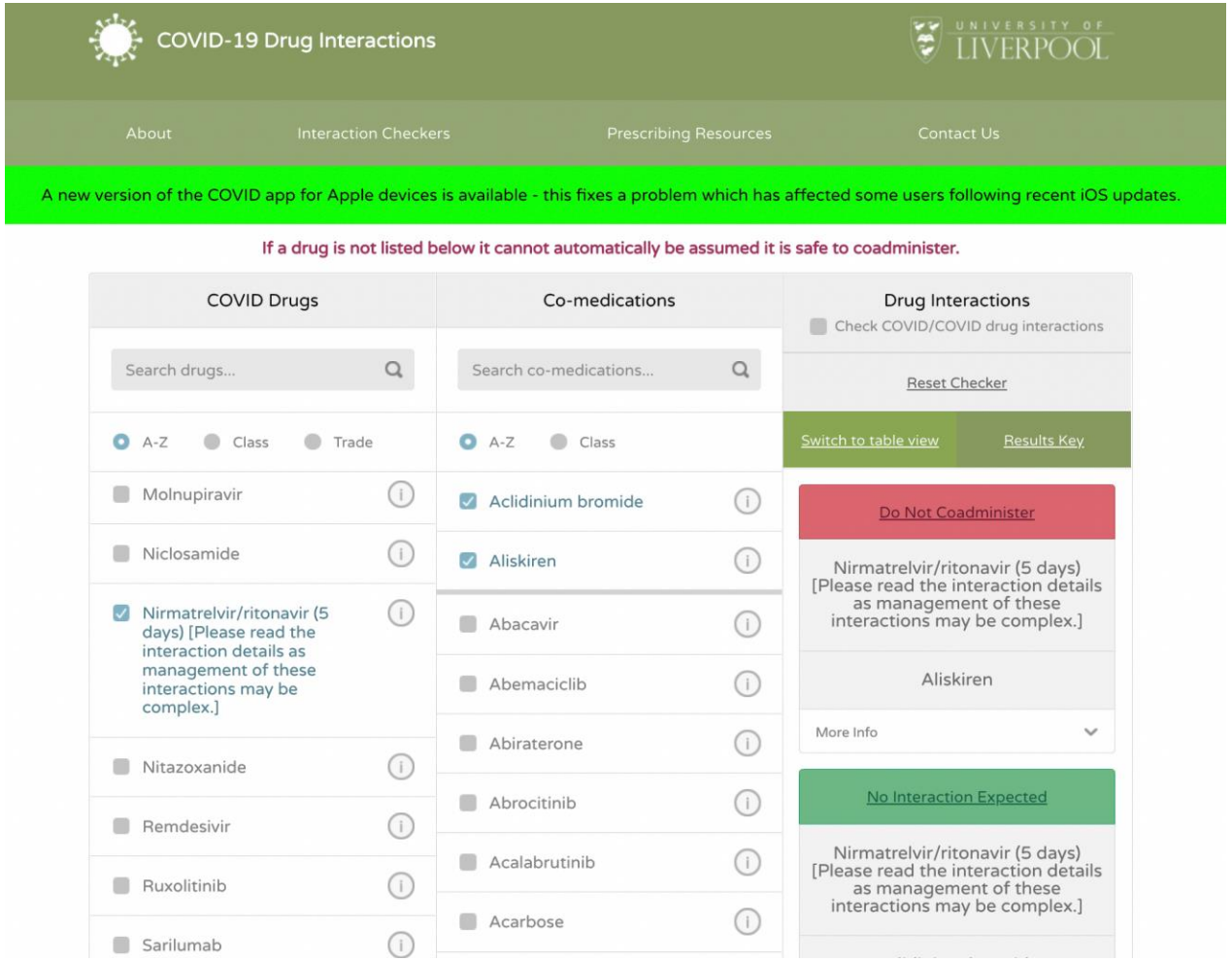
DDI Resource: Interaction Checker



Link: https://www.covid19-druginteractions.org/

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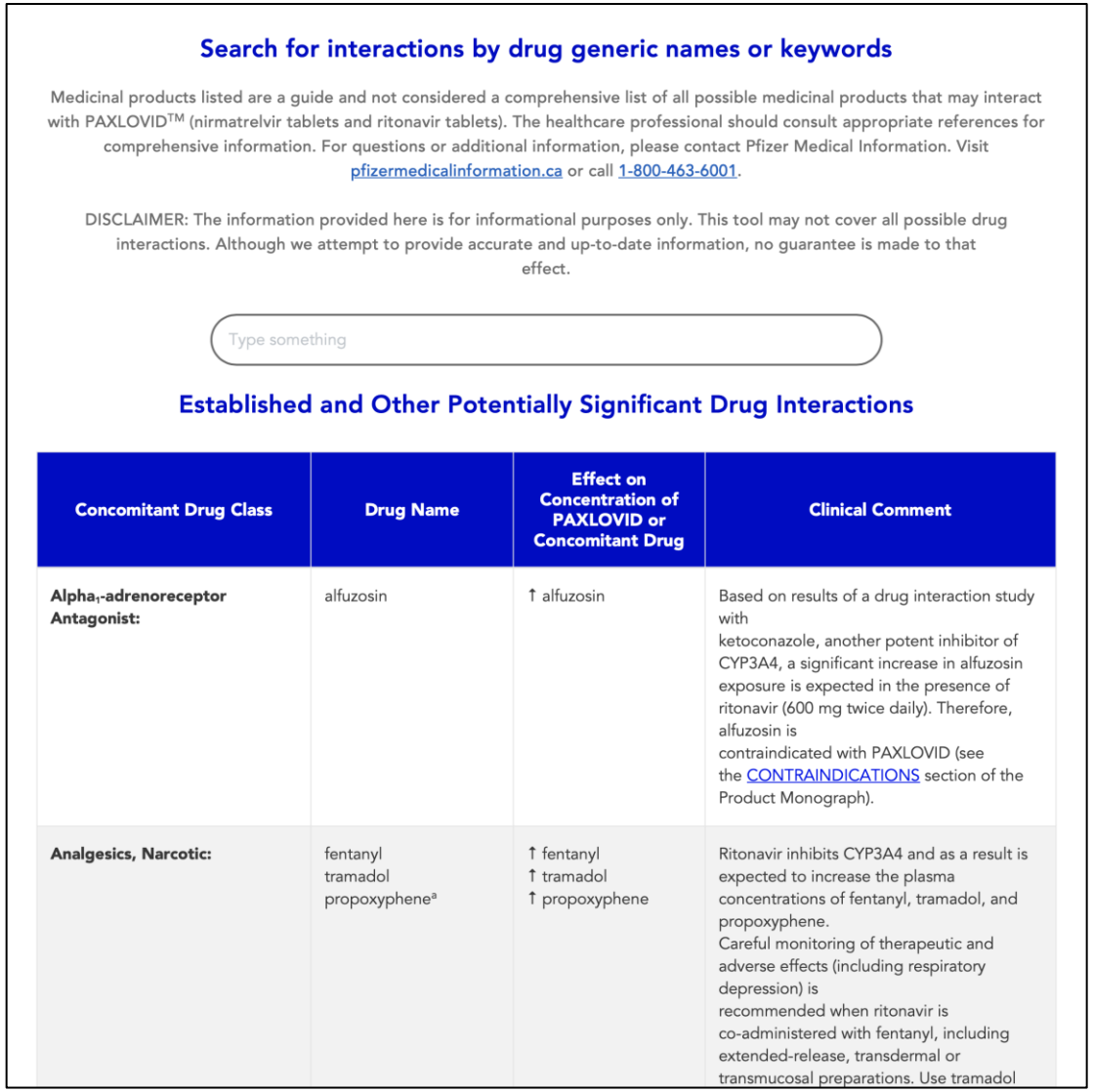
DDI Resource: Drug Interactions Finder



Search for interactions by drug generic names or keywords

Medicinal products listed are a guide and not considered a comprehensive list of all possible medicinal products that may interact with PAXLOVID™ (nirmatrelvir tablets and ritonavir tablets). The healthcare professional should consult appropriate references for comprehensive information. For questions or additional information, please contact Pfizer Medical Information. Visit pfizermedicalinformation.ca or call 1-800-463-6001.

DISCLAIMER: The information provided here is for informational purposes only. This tool may not cover all possible drug interactions. Although we attempt to provide accurate and up-to-date information, no guarantee is made to that effect.

Type something

Established and Other Potentially Significant Drug Interactions

Concomitant Drug Class	Drug Name	Effect on Concentration of PAXLOVID or Concomitant Drug	Clinical Comment
Alpha$_1$-adrenoreceptor Antagonist:	alfuzosin	↑ alfuzosin	Based on results of a drug interaction study with ketoconazole, another potent inhibitor of CYP3A4, a significant increase in alfuzosin exposure is expected in the presence of ritonavir (600 mg twice daily). Therefore, alfuzosin is contraindicated with PAXLOVID (see the CONTRAINDICATIONS section of the Product Monograph).
Analgesics, Narcotic:	fentanyl tramadol propoxyphene[a]	↑ fentanyl ↑ tramadol ↑ propoxyphene	Ritonavir inhibits CYP3A4 and as a result is expected to increase the plasma concentrations of fentanyl, tramadol, and propoxyphene. Careful monitoring of therapeutic and adverse effects (including respiratory depression) is recommended when ritonavir is co-administered with fentanyl, including extended-release, transdermal or transmucosal preparations. Use tramadol

Link: https://www.paxlovid-hcp.ca/en/drug-interaction-finder

Pharmacist Assessment Protocol

Eligibility	Criteria (hyperlinked for information only, pharmacist not required to confirm eligibility)	
Medical History	Allergies, medical conditions, and medications* are updated on patient record	□Yes
	Age < 18 years?	□Yes - STOP □No
	Able to swallow tablets whole?	□Yes □No- STOP
	Is patient pregnant or breastfeeding?	□Yes - STOP □No
	Chronic kidney disease with eGFR < 30 mL/min?	□Yes- STOP □No
	Severe hepatic impairment (Child Pugh C)?	□Yes - STOP □No
Drug Interaction Review	Recommend using University of Liverpool COVID DI Checker (hyperlinked) to screen for drug interactions in addition to pharmacy dispensing software **Select one of the following:** □ No clinically significant interactions with nirmatrelvir/ritonavir (Paxlovid®) and patient's current medications* identified □ Clinically significant interactions with nirmatrelvir/ritonavir (Paxlovid®) and patient's current medications* identified that require monitoring and/or intervention Details: _____ □ Nirmatrelvir/ritonavir (Paxlovid®) CONTRAINDICATED due to interactions with the patient's current medications* Details: _____	
Assessment	**Select one of the following:** □ The patient is eligible for nirmatrelvir and ritonavir (Paxlovid®) Medical history and drug interaction screen do not indicate nirmatrelvir and ritonavir (Paxlovid®) contraindications □ Patient does not qualify for antiviral therapy due to: _____ □ Patient referred to Physician or Nurse Practitioner for assessment due to: _____	

Prescription	Confirm prescription is **one of the following regimens** and **ordered by a designated prescriber** □ eGFR ≥ 60 mL/min: nirmatrelvir 300 mg (2 x 150 mg tablets) and ritonavir 100 mg (1 x 100 mg tablet) po bid x 5 days Dispensed as Paxlovid® x 1 box (5 day treatment course) □ eGFR ≥ 30 to < 60 mL/min: nirmatrelvir 150 mg (1 x 150 mg tablet) and ritonavir 100 mg (1 x 100 mg tablet) po bid x 5 days Dispensed as Paxlovid® x 1 box (5 day treatment course) Dispensing pharmacy to alter packaging to remove 1 nirmatrelvir tablet from each dosing interval in daily blister card
Patient Education/ Follow-up	Patient education sheet reviewed. English (hyperlinked), French (hyperlinked). Self-monitoring for efficacy and toxicity discussed: **Efficacy monitoring** • If COVID-19 signs or symptoms improving, or symptoms are stable, ensure completion of therapy • If COVID-19 signs or symptoms not improving and require support from another healthcare provider for management refer to MD/NP/811 •If COVID-19 progression to severe symptoms such as: difficulty breathing, severe chest pain, loss of consciousness, or feelings of confusion refer to ED or call 911 immediately **Toxicity monitoring** • Side effects including: • Change in sense of taste • Diarrhea • High blood pressure (if patient able to monitor at home) • Muscle aches • Hepatotoxicity: loss of appetite, yellowing of your skin and the whites of eyes (jaundice), dark-colored urine, pale colored stools and itchy skin, stomach area (abdominal) pain □ Faxed notification to primary care provider regarding: _____ Optional: Follow-up date (3 days recommended): _____ (Set reminder in software)

Link: https://pans.ns.ca/sites/default/files/nirmatrelvir_ritonavir_assessment_protocol_0.pdf

Nirmatrelvir/Ritonavir Dose Adjustments for Patients with Renal or Hepatic Impairment[1]

Patients with renal impairment	
Mild (eGFR 60 to <90 mL/min)	No dosage adjustment is needed
Moderate (30 ≤ eGFR < 60 mL/min)	150 mg (1 tablet) nirmatrelvir and 100 mg (1 tablet) ritonavir twice daily for 5 days
Severe (eGFR <30 mL/min)	Not recommended

Patients with hepatic impairment	
Mild (Child-Pugh Class A) or **Moderate** (Child-Pugh Class B)	No dosage adjustment is needed
Severe (Child-Pugh Class C)	Not recommended

Practice Tip

- Pharmacists must have access to a patient's healthcare records within the past 12 months to assess for renal and hepatic function before prescribing nirmatrelvir/ritonavir[2]
- If patients do not have recent kidney function values, complete the patient assessment as fully as possible[3]

[1]PAXLOVID Product Monograph. Pfizer Canada ULC. June 13, 2022; [2]Pfizer Laboratories Inc. Emergency use authorization for Paxlovid. Factsheet for healthcare providers. Accessed October 31, 2022. [3]University of Saskatchewan. College of Pharmacy and Nutrition. Guidelines for Prescribing Paxlovid. Accessed October 31, 2022. https://medsask.usask.ca

Communicating with Patients and Follow-up[a]

Patient preparedness

- Identify high-risk individuals and establish protocols
  - How would they test? (i.e., have rapid tests at home)
  - Medical review
  - Check eligibility for outpatient treatments
  - Develop a treatment plan in case they test positive
  - How could they quickly access treatment for COVID-19 if positive?

Before diagnosis (symptomatic)

- Assess risk, identify patients at high risk, and inform about available treatments
- Monitor (over phone) patients with early symptoms for duration and severity
- Recommend testing for patients with symptoms
- Check eligibility for outpatient treatments

After diagnosis (positive test)

- Prescribe appropriate treatment
- Coordinate with the physician/nurse practitioner

During treatment

- Follow-up (over phone) on day 6–10 after treatment initiation for monitoring and safety[b,c]
- Follow local pathways of adverse reaction reporting if you identify a moderate or severe adverse event
- Monitor treatment adherence
- Ensure adherence to DDI management plan
- Determine if in-person evaluation is needed

[a] Based on faculty experience and opinion; [b] The follow-up guidelines and period may differ between provinces, and local guidelines should be followed. [c] Depending on the province, pharmacists may be able to claim clinical service fee for follow-up and monitoring of patients who receive nirmatrelvir/ritonavir from their pharmacy.

Follow-up Questions

Worsening of COVID-19 symptoms?
AEs? If so, what, duration, and severity? Management?
Treatment completion? If not, how many days were completed? What was the reason for discontinuation (i.e., adverse effects, felt better, etc.)? Did the patient miss any doses?
DDI management plan? What was the follow-up plan suggested by the pharmacist/prescriber? Did the patient have any problems adhering to the management plan?
Remind the patient to follow all public health orders, even if feeling better
Any other relevant follow-up questions per your professional judgement

[1]BC Ministry of Health. Dispensing Paxlovid and Monitoring Adverse Drug Events – A Guide for B.C. Community Pharmacists. Accessed October 29, 2022. https://www2.gov.bc.ca/assets/gov/health/health-drug-coverage/pharmacare/monitoring-paxlovid-ades-guide.pdf

Key Learning Points

Pharmacists play a key role in the identification of potential DDIs and their management

There are multiple tools and algorithms for the management of DDIs in patients receiving outpatient treatment for COVID-19

Test Questions

1. Which patient categories are eligible for outpatient treatments?

a. Patients with mild-to-moderate symptoms and low risk of hospitalization
b. Patients with severe symptoms and low risk of hospitalization
c. Patients with mild-to-moderate symptoms and a high risk of hospitalization
d. Patients with severe symptoms and a high risk of hospitalization
e. Patients on supplemental oxygen

2. Which of the following conditions is a contraindication for nirmatrelvir/ritonavir?

a. Hematological malignancy
b. Treated HIV infection (seronegative status)
c. Renal impairment (eGFR <30 mL/min)
d. Moderate hepatic impairment (Child-Pugh Class B)

3. Which of the following are useful resources when evaluating DDIs in a patient considered for outpatient treatment with nirmatrelvir/ritonavir?

a. Nirmatrelvir/ritonavir product monograph
b. Drug Interactions Finder
c. University of Liverpool COVID-19 DI checker
d. All of the above
e. None of the above

4. Which types of tests are accepted for confirmation of the diagnosis in terms of eligibility for nirmatrelvir/ritonavir?

a. PCR test
b. Rapid antigen test (conducted at the pharmacy)
c. Rapid antigen test (at-home self-test)
d. It varies by province

5. Who can prescribe nirmatrelvir/ritonavir?

a. Doctors, pharmacists, and nurse practitioners in all provinces
b. Doctors in all provinces and nurse practitioners and pharmacists in some provinces
c. Prescription only available through telemedicine
d. Prescription only available through online screening tools

Toolbox – Steps for Facilitating Access to Outpatient Therapies

- **Identify** patients eligible for outpatient therapies
  - Symptom onset and positive test
  - Risk for COVID-19 progression
  - Follow provincial and local eligibility guidelines
- **Determine** the right outpatient treatment
  - Drug interactions and contraindications
  - Follow provincial and local guidelines
- **Manage** directly or direct patient to a clinic or other local pathway
  - Follow provincial and local prescription processes
- **Follow up**
  - Symptoms, treatment adherence, tolerability, adverse events,
  - Follow provincial and local follow-up pathways