

Ontario Health Recommendation on the Use of Nirmatrelvir/Ritonavir (Paxlovid)

September 2023 – This document was developed in fall 2022 based on best available evidence and expert consensus at the time of publication. This document is currently under review and will be updated in the coming months.

Providers should review Ontario Health's <u>Recommendations</u> on the Outpatient Use of Remdesivir (Veklury) in Adults, published September 2023. These recommendations provide guidance for identifying patients at high risk for severe COVID-19 based on the latest available evidence. These recommendations also provide context on the place in therapy for both nirmatrelvir/ritonavir and remdesivir.

There are limitations to the evidence that is currently available. Prescribers must determine whether adopting suggested information is clinically appropriate for individual patients through a comprehensive risk-benefit assessment.

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Background

During the COVID-19 pandemic in Ontario, the Ontario COVID-19 Science Advisory Table prepared and maintained guidance on the therapeutic management of adult patients with COVID-19. Health care providers have used this guidance, along with criteria from the Ministry of Health, to determine which patients would benefit from receiving nirmatrelvir/ritonavir (Paxlovid) to prevent severe illness due to COVID-19. As of fall 2022, the Ontario COVID-19 Science Advisory Table has been dissolved, and their guidance on the therapeutic management of COVID-19 will no longer be updated.

In fall 2022, Ontario Health established a COVID-19 Therapeutics Interim Working Group (Appendix A) to provide guidance and advice to Ontario Health and the Ministry of Health on priority issues regarding the appropriate use of therapeutics for COVID-19 infection. The first priority issue to be addressed by the Working Group relates to updating the recommendations on which patients would benefit from receiving nirmatrelvir/ritonavir (Paxlovid).

The following consensus-based recommendation was informed by a primary literature review and jurisdictional scan (Appendix B). Prescribers must determine whether adopting suggested information is clinically appropriate for individual patients through a risk-benefit assessment.

Recommendation

Paxlovid should be strongly considered for individuals who have a confirmed COVID-19 diagnosis (based on positive PCR, rapid molecular, or rapid antigen test result), present within 5 days of symptom onset, and meet one or more of the following criteria:

- The individual is 60 years of age or older;
- The individual is 18 years of age or older and is immunocompromised;
- The individual is 18–59 years old and is at higher risk of severe COVID-19. Patients at higher risk of severe COVID-19 include:
 - Those who have one or more <u>comorbidity</u> that puts them at higher risk of severe COVID-19 disease

OR

- Those with inadequate immunity, i.e.:
 - Unvaccinated or incomplete primary series OR
 - Completed primary series AND last COVID-19 vaccine dose was more than 6 months ago AND last SARS-CoV-2 infection was more than 6 months ago

Social determinants of health may confer an increased risk of disease progression. Individuals who are at a higher risk of poor outcomes from COVID-19 infection based on social determinants of health should be considered priority populations for access to Paxlovid. Individuals at higher risk include Indigenous people, Black people, other members of racialized communities, individuals with intellectual, developmental, or cognitive disability, people who use substances regularly (e.g. alcohol), people who live with mental health conditions, and people who are underhoused.

Note: Combinations of risk factors are associated with higher risk of severe COVID-19.



Additional resources

Visit the Ontario Health <u>COVID-19 treatment website</u> for the latest resources on Paxlovid and other COVID-19 therapeutics.





Appendix A: Ontario Health COVID-19 Therapeutics Interim Working Group Members

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	Prevention & Control, Kingston Health Sciences Centre
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Kelly Grindrod	Associate Professor, University of Waterloo School of Pharmacy
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Sarah Salama	Pharmacist, Systemic Treatment, Cancer Programs, Ontario Health

Note: Each member of the Working Group was asked to declare any actual, potential, or perceived conflicts of interest. A summary of disclosures is available here.



Appendix B: References

The following resources informed these recommendations:

- 1. Aggarwal A, Akerman A, Milogiannakis V, et al. SARS-CoV-2 Omicron BA.5: Evolving tropism and evasion of potent humoral responses and resistance to clinical immunotherapeutics relative to viral variants of concern. eBioMedicine. 2022;84:104270. doi:10.1016/j.ebiom.2022.104270
- 2. Ahmed-Belkacem A, Redjoul R, Brillet R, et al. Third early "booster" dose strategy in France of bnt162b2 SARS-CoV-2 vaccine in allogeneic hematopoietic stem cell transplant recipients enhances neutralizing antibody responses. Viruses. 2022;14(9):1928. doi:10.3390/v14091928
- 3. Al Hajji Y, Taylor H, Starkey T, Lee LYW, Tilby M. Antibody response to a third booster dose of SARS-CoV-2 vaccination in adults with haematological and solid cancer: a systematic review. Br J Cancer. 2022;(August):1-10. doi:10.1038/s41416-022-01951-y
- 4. Arbel R, Wolff Sagy Y, Hoshen M, et al. Nirmatrelvir use and severe COVID-19 outcomes during the Omicron surge. N Engl J Med. 2022;387(9):790-798. doi:10.1056/nejmoa2204919
- 5. Becker M, Cossmann A, Lürken K, et al. Longitudinal cellular and humoral immune responses after triple BNT162b2 and fourth full-dose mRNA-1273 vaccination in haemodialysis patients. Front Immunol. 2022;13(October):1-12. doi:10.3389/fimmu.2022.1004045
- 6. Boulware DR, Murray TA, Proper JL, et al. Impact of SARS-CoV-2 vaccination and booster on COVID-19 symptom severity over time in the COVID-OUT trial. Clin Infect Dis. Published online September 17, 2022. doi:10.1093/cid/ciac772
- 7. Britton A, Embi PJ, Levy ME, et al. Effectiveness of COVID-19 mRNA vaccines against COVID-19—associated hospitalizations among immunocompromised adults during SARS-CoV-2 Omicron predominance VISION Network, 10 States, December 2021—August 2022. MMWR Morb Mortal Wkly Rep. 2022;71(42):1335-1342. doi:10.15585/mmwr.mm7142a4
- 8. Brosh-Nissimov T, Hussein K, Wiener-Well Y, et al. Hospitalized patients with severe COVID-19 during the Omicron wave in Israel benefits of a fourth vaccine dose. Clin Infect Dis. Published online June 20, 2022:1-17. doi:10.1093/cid/ciac501
- 9. Busà R, Russelli G, Miele M, et al. Immune response after the fourth dose of SARS-CoV-2 mRNA vaccine compared to natural infection in three doses' vaccinated solid organ transplant recipients. Viruses. 2022;14(10):2299. doi:10.3390/v14102299
- 10. Chalkias S, Harper C, Vrbicky K, et al. A bivalent Omicron-containing booster vaccine against COVID-19. N Engl J Med. 2022;387(14):1279-1291. doi:10.1056/NEJMoa2208343
- 11. Chambers C, Samji H, Cooper CL, et al. COVID-19 vaccine effectiveness among a population-based cohort of people living with HIV. AIDS. 2022; Publish Ah. doi:10.1097/QAD.000000000003405
- 12. Cheung KS, Mok CH, Mao X, et al. COVID-19 vaccine immunogenicity among chronic liver disease patients and liver transplant recipients: A meta-analysis. Clin Mol Hepatol. 2022;28(4):890-911. doi:10.3350/cmh.2022.0087



- 13. Clémenceau B, Le Bourgeois A, Guillaume T, et al. Strong SARS-CoV-2 T-cell responses after one or two COVID-19 vaccine boosters in allogeneic hematopoietic stem cell recipients. Cells. 2022;11(19):3010. doi:10.3390/cells11193010
- 14. Coburn SB, Humes E, Lang R, et al. Analysis of postvaccination breakthrough COVID-19 infections among adults with HIV in the United States. JAMA Netw Open. 2022;5(6):e2215934. doi:10.1001/jamanetworkopen.2022.15934
- 15. Cucchiari D, Egri N, Rodriguez-Espinosa D, et al. Humoral and cellular immune responses after a 3-dose course of mRNA-1273 COVID-19 vaccine in kidney transplant recipients: A prospective cohort study. Transplant Direct. 2022;8(11):e1389. doi:10.1097/TXD.000000000001389
- 16. Dauriat G, Beaumont L, Luong Nguyen LB, et al. Efficacy of 3 COVID-19 vaccine doses in lung transplant recipients: a multicentre cohort study. Eur Respir J. Published online October 20, 2022. doi:10.1183/13993003.00502-2022
- 17. Dryden-Peterson S, Kim A, Kim A, et al. Nirmatrelvir plus ritonavir for early COVID-19 and hospitalization in a large US health system. medRxiv [Preprint]. Published online 2022. doi:10.1101/2022.06.14.22276393
- 18. Fendler A, Shepherd STC, Au L, et al. Functional immune responses against SARS-CoV-2 variants of concern after fourth COVID-19 vaccine dose or infection in patients with blood cancer. Cell Reports Med. 2022;3(10):100781. doi:10.1016/j.xcrm.2022.100781
- 19. Fiorino F, Ciabattini A, Sicuranza A, et al. The third dose of mRNA SARS-CoV-2 vaccines enhances the spike-specific antibody and memory B cell response in myelofibrosis patients. Front Immunol. 2022;13(September):1-11. doi:10.3389/fimmu.2022.1017863
- 20. Frölke SC, Bouwmans P, Messchendorp AL, et al. Predictors of nonseroconversion to SARS-CoV-2 vaccination in kidney transplant recipients. Transplant Direct. 2022;8(11):e1397. doi:10.1097/TXD.000000000001397
- 21. Ganatra S, Dani SS, Ahmad J, et al. Oral nirmatrelvir and ritonavir in non-hospitalized vaccinated patients with COVID-19. Clin Infect Dis. Published online 2022. doi:https://dx.doi.org/10.1093/cid/ciac673
- 22. Greasley SE, Noell S, Plotnikova O, et al. Structural basis for the in vitro efficacy of nirmatrelvir against SARS-CoV-2 variants. J Biol Chem. 2022;298(6):101972. doi:10.1016/j.jbc.2022.101972
- 23. Hammond J, Leister-Tebbe H, Gardner A, et al. Oral nirmatrelvir for high-risk, nonhospitalized adults with COVID-19. N Engl J Med. 2022;386(15):1397-1408. doi:10.1056/nejmoa2118542
- 24. Kane AM, Keenan EM, Lee K, et al. Nirmatrelvir/ritonavir treatment of COVID-19 in a high-risk patient population: a retrospective observational study. JACCP J Am Coll Clin Pharm. Published online November 2, 2022. doi:10.1002/jac5.1729
- 25. Khawaja F, Papanicolaou G, Dadwal S, et al. Frequently asked questions on coronavirus disease 2019 vaccination for hematopoietic cell transplant and chimeric antigen receptor T-cell recipients from the American Society for Transplantation and Cellular Therapy and the American Society of Hematology. Transplant Cell Ther. 2022;(January). doi:10.1016/j.jtct.2022.10.010



- 26. Komorowski AS, Tseng A, Vandersluis S, et al. Evidence-based recommendations on the use of nirmatrelvir/ritonavir (Paxlovid) for adults in Ontario. Ontario COVID-19 Sci Advis Table. 2022;57(3):1-23. https://covid19-sciencetable.ca/sciencebrief/evidence-based-recommendations-on-the-use-of-nirmatrelvir-ritonavir-paxlovid-for-adults-in-ontario
- 27. Lasagna A, Bergami F, Lilleri D, et al. Six-month humoral and cellular immune response to the third dose of BNT162b2 anti-SARS-CoV-2 vaccine in patients with solid tumors: a longitudinal cohort study with a focus on the variants of concern. ESMO Open. 2022;7(5):100574. doi:10.1016/j.esmoop.2022.100574
- 28. Lee JT, Yang Q, Gribenko A, et al. Genetic surveillance of SARS-CoV-2 Mpro reveals high sequence and structural conservation prior to the introduction of protease inhibitor Paxlovid. MBio. 2022;13(4). doi:10.1128/mbio.00869-22
- 29. Lee TC, Pogue JM, McCreary EK, et al. What is the place in therapy for nirmatrelvir/ritonavir? BMJ Evid Based Med. 2022; (November 16). doi: 10.1136/bmjebm-2022-112064
- 30. Lewnard JA, Malden D, Hong V, et al. Effectiveness of nirmatrelvir-ritonavir against hospital admission: a matched cohort study in a large US healthcare system. medRxiv Prepr Serv Heal Sci. 2022;(165):1-13. doi:https://dx.doi.org/10.1101/2022.10.02.22280623
- 31. Lim S, Tignanelli CJ, Hoertel N, Boulware DR, Usher MG. Prevalence of medical contraindications to nirmatrelvir/ritonavir in a cohort of hospitalized and nonhospitalized patients with COVID-19. Open Forum Infect Dis. 2022;9(8):1-4. doi:10.1093/ofid/ofac389
- 32. Lin K, Hsieh M, Chang S, et al. Serological response after COVID-19 mRNA-1273 booster dose in immunocompromised patients, Taiwan, July to August 2021. J Formos Med Assoc. 2022;(January). doi:10.1016/j.jfma.2022.08.017
- 33. Loubet P, Wittkop L, Ninove L, et al. One-month humoral response following two or three doses of mRNA COVID-19 vaccines as primary vaccination in specific populations in France: first results from the ANRS0001S COV-POPART cohort. Clin Microbiol Infect. 2022;(January). doi:10.1016/j.cmi.2022.10.009
- 34. Lu G, Zhang Y, Zhang H, et al. Geriatric risk and protective factors for serious COVID-19 outcomes among older adults in Shanghai Omicron wave. Emerg Microbes Infect. 2022;11(1):2045-2054. doi:10.1080/22221751.2022.2109517
- 35. Ma E, Ai J, Zhang Y, et al. Omicron infections profile and vaccination status among 1881 liver transplant recipients: a multi-centre retrospective cohort. Emerg Microbes Infect. 2022;11(1):2636-2644. doi:10.1080/22221751.2022.2136535
- 36. Macrae K, Martinez-Cajas J, Bessai K, Abdulhamed A, Gong Y. Quantitative analysis of SARS-CoV-2 antibody levels in cancer patients post three doses of immunization and prior to breakthrough COVID-19 infections. Curr Oncol. 2022;29(10):7059-7071. doi:10.3390/curroncol29100554
- 37. Malden DE, Hong V, Lewin BJ, et al. Hospitalization and emergency department encounters for COVID-19 after Paxlovid treatment California, December 2021-May 2022. MMWR Morb Mortal Wkly Rep. 2022;71(25):830-833. doi:https://dx.doi.org/10.15585/mmwr.mm7125e2



- 38. McConeghy KW, White EM, Blackman C, et al. Effectiveness of a second COVID-19 vaccine booster dose against infection, hospitalization, or death among nursing home residents 19 states, March 29-July 25, 2022. MMWR Morb Mortal Wkly Rep. 2022;71(39):1235-1238. doi:10.15585/mmwr.mm7139a2
- 39. Mori Y, Uchida N, Harada T, et al. Predictors of impaired antibody response after SARS-CoV-2 mRNA vaccination in hematopoietic cell transplant recipients: A Japanese multicenter observational study. Am J Hematol. Published online October 31, 2022:0-3. doi:10.1002/ajh.26769
- 40. Najjar-Debbiny R, Gronich N, Weber G, et al. Effectiveness of Paxlovid in reducing severe coronavirus disease 2019 and mortality in high-risk patients. Clin Infect Dis. Published online 2022:1-8. doi:10.1093/cid/ciac443
- 41. Nakagama Y, Chi S, Minami Y, et al. Patients with B-cell malignancies experience reduced antibody responses with class switching defect following BNT162b2 SARS-CoV-2 vaccination. J Infect Chemother. 2022;(July). doi:10.1016/j.jiac.2022.09.018
- 42. Ontario Ministry of Health. Executive Officer Notice: Supplying of publicly funded oral antiviral COVID-19 treatment in Ontario pharmacies (Updated April 25, 2022).; 2022. https://www.ocpinfo.com/wp-content/uploads/2022/04/ministry-of-health-notice-paxlovid.pdf
- 43. Ontario Ministry of Health. Updated: Executive Officer Notice: Administration of Publicly Funded COVID- 19 Vaccines in Ontario Pharmacies Eligibility (Effective November 8th, 2022).; 2022. https://www.health.gov.on.ca/en/pro/programs/drugs/opdp_eo/eo_communiq.aspx#top
- 44. Ontario Ministry of Health; Research, Analysis & Evaluation Branch. Rapid Response Eligibility Criteria for Outpatient COVID-19 Therapeutics; October 13, 2022
- 45. Ontario COVID-19 Drugs and Biologics Clinical Practice Guidelines Working Group. Clinical Practice Guideline Summary: Recommended Drugs and Biologics in Adult Patients with COVID-19. Ontario COVID-19 Science Advisory Table. 2022; Version 11.0. https://doi.org/10.47326/ocsat.cpg.2022.11.0
- 46. Perrier Q, Lupo J, Gerster T, et al. SARS-CoV-2 anti-spike antibodies after a fourth dose of COVID-19 vaccine in adult solid-organ transplant recipients. Vaccine. 2022;40(44):6404-6411. doi:10.1016/j.vaccine.2022.08.065
- 47. Pfizer Canada. Product monograph PAXLOVID. Published online 2022:1-48.
- 48. Pfizer. Pfizer and BioNTech announce updated clinical data for Omicron BA . 4 / BA . 5-adapted bivalent booster demonstrating substantially higher immune response in adults compared to the original COVID-19 vaccine. Published 2022. https://www.pfizer.com/news/press-release/press-release-detail/pfizer-and-biontech-announce-updated-clinical-data-omicron
- 49. Pfizer. Pfizer reports additional data on PAXLOVID[™] supporting upcoming new drug application submission to U.S. FDA. Pfizer press release. Published 2022. https://www.pfizer.com/news/press-release/press-release-detail/pfizer-reports-additional-data-paxlovidtm-supporting
- 50. Public Health Agency of Canada. An Advisory Committee Statement (ACS) National Advisory Committee on Immunization (NACI) Recommendations on the use of bivalent Omicron-containing MRNA COVID-19 vaccines. 2022. https://www.canada.ca/content/dam/phac-



- aspc/documents/services/immunization/national-advisory-committee-on-immunization-naci/recommendations-use-bivalent-Omicron-containing-mrna-covid-19-vaccines.pdf
- 51. Public Health Agency of Canada. Canadian COVID-19 vaccination coverage report. Public Health Agency of Canada. Published 2022. Accessed November 2, 2022. https://health-infobase.canada.ca/covid-19/vaccination-coverage/#a3
- 52. Public Health Agency of Canada. Summary of National Advisory Committee on Immunization (NACI) Statement of October 7, 2022; 2022. https://www.canada.ca/content/dam/phac-aspc/documents/services/immunization/national-advisory-committee-on-immunization-naci/naci-summary-october-7-2022.pdf
- 53. Quiroga B, Soler MJ, Ortiz A, et al. Long-term dynamic humoral response to SARS-CoV-2 mRNA Vaccines in patients on peritoneal dialysis. Vaccines. 2022;10(10):1738. doi:10.3390/vaccines10101738
- 54. Rose DT, Gandhi SM, Bedard RA, et al. Supratherapeutic tacrolimus concentrations with nirmatrelvir/ritonavir in solid organ transplant recipients requiring hospitalization: a case series using rifampin for reversal. Open Forum Infect Dis. 2022;9(7):1-5. doi:10.1093/ofid/ofac238
- 55. Rose E, Magliulo D, Kyttaris VC. Seroconversion among rituximab-treated patients following SARS-CoV-2 vaccine supplemental dose. Clin Immunol. 2022;245:109144. doi:10.1016/j.clim.2022.109144
- 56. Saharia KK, Husson JS, Niederhaus S V, et al. Humoral immunity against SARS-CoV-2 variants including omicron in solid organ transplant recipients after three doses of a COVID-19 mRNA vaccine. Clin Transl Immunol. 2022;11(5). doi:10.1002/cti2.1391
- 57. Salerno DM, Jennings DL, Lange NW, et al. Early clinical experience with nirmatrelvir/ritonavir for the treatment of COVID-19 in solid organ transplant recipients. Am J Transplant. 2022;22(8):2083-2088. doi:10.1111/ajt.17027
- 58. Schwartz KL, Wang J, Tadrous M, et al. Real-world effectiveness of nirmatrelvir/ritonavir use for COVID-19: A population-based cohort study in Ontario, Canada. medRxiv [Preprint]. Published online 2022. https://www.medrxiv.org/content/10.1101/2022.11.03.22281881v1
- 59. Shields AM, Tadros S, Al-Hakim A, et al. Impact of vaccination on hospitalization and mortality from COVID-19 in patients with primary and secondary immunodeficiency: The United Kingdom experience. Front Immunol. 2022;13(September). doi:10.3389/fimmu.2022.984376
- 60. Shrestha LB, Foster C, Rawlinson W, Tedla N, Bull RA. Evolution of the SARS-CoV-2 Omicron variants BA.1 to BA.5: Implications for immune escape and transmission. Rev Med Virol. 2022;32(5). doi:10.1002/rmv.2381
- 61. Syversen SW, Jyssum I, Tveter AT, et al. Immunogenicity and safety of a three-dose SARS-CoV-2 vaccination strategy in patients with immune-mediated inflammatory diseases on immunosuppressive therapy. RMD Open. 2022;8(2):e002417. doi:10.1136/rmdopen-2022-002417
- 62. Takashita E, Yamayoshi S, Simon V, et al. Efficacy of antibodies and antiviral drugs against Omicron BA.2.12.1, BA.4, and BA.5 subvariants. N Engl J Med. 2022;387(5):468-470. doi:10.1056/NEJMc2207519



- 63. Ullrich S, Ekanayake KB, Otting G, Nitsche C. Main protease mutants of SARS-CoV-2 variants remain susceptible to nirmatrelvir. Bioorganic Med Chem Lett. 2022;62(February):128629. doi:10.1016/j.bmcl.2022.128629
- 64. Vangeel L, Chiu W, De Jonghe S, et al. Remdesivir, molnupiravir and nirmatrelvir remain active against SARS-CoV-2 Omicron and other variants of concern. Antiviral Res. 2022;198(January):10-12. doi:10.1016/j.antiviral.2022.105252
- 65. Vitiello A, Ferrara F, Auti AM, Di Domenico M, Boccellino M. Advances in the Omicron variant development. J Intern Med. 2022;292(1):81-90. doi:10.1111/joim.13478
- 66. Wang Q, Bowen A, Valdez R, et al. Antibody responses to Omicron BA.4/BA.5 bivalent mRNA vaccine booster shot. bioRxiv [Preprint]. Published online 2022. doi:https://doi.org/10.1101/2022.10.22.513349
- 67. Wong CKH, Au ICH, Lau KTK, Lau EHY, Cowling BJ, Leung GM. Real-world effectiveness of molnupiravir and nirmatrelvir plus ritonavir against mortality, hospitalisation, and in-hospital outcomes among community-dwelling, ambulatory patients with confirmed SARS-CoV-2 infection during the omicron wave in Hong Kong: a. Lancet. 2022;400(10359):1213-1222. doi:https://dx.doi.org/10.1016/S0140-6736%2822%2901586-0
- 68. Wright BJ, Tideman S, Diaz GA, French T, Parsons GT, Robicsek A. Comparative vaccine effectiveness against severe COVID-19 over time in US hospital administrative data: a case-control study. Lancet Respir Med. 2022;10(6):557-565. doi:10.1016/S2213-2600(22)00042-X
- 69. Yin J, Chen Y, Li Y, Zhang X, Wang C. Seroconversion rate after COVID-19 vaccination in patients with solid cancer: A systematic review and meta-analysis. Hum Vaccin Immunother. 2022. doi:10.1080/21645515.2022.2119763
- 70. Yip TCF, Lui GCY, Lai MSM, et al. Impact of the use of oral antiviral agents on the risk of hospitalization in community COVID-19 patients. Clin Infect Dis. Published online August 29, 2022. doi:https://dx.doi.org/10.1093/cid/ciac687
- 71. Yoo J, Yon DK, Lee SW, Shin J II, Kim BK. Humoral immunogenicity to SARS-CoV-2 vaccination in liver transplant recipients: A systematic review and meta-analysis. Int J Biol Sci. 2022;18(15):5849-5857. doi:10.7150/ijbs.77030
- 72. Zheng Q, Ma P, Wang M, et al. Efficacy and safety of Paxlovid for COVID-19: a meta-analysis. J Infect. 2022;(September 30). doi:10.1016/j.jinf.2022.09.027

