Evidence Brief for Primary Care: Ontario Health Recommendation on the Use of Paxlovid (Nirmatrelvir/Ritonavir)

Centre for Effective Practice | Ontario College of Family Physicians — Leaders for a healthy Ontario

✓ **Growing evidence base supports use of Paxlovid.** 18 studies published since the HR-EPIC trial in April 2022 support its effectiveness in reducing hospitalization and death from COVID-19 across varied patient groups.[1,2,3,5,6]

✓ **Paxlovid should be offered regardless of vaccination status.** Current evidence suggests that effectiveness and benefit of Paxlovid may not be affected by vaccination status.[1]

✓ **Boosters reduce but do not remove risk of poor outcomes.** While Omicron is predominant, individuals vulnerable to poor outcomes from infection should be considered higher risk even when up to date with booster doses.

Recent emerging evidence

A December 2022 systematic review and meta-analysis, pooling data from patients of varied age, vaccination and risk status and including ON data, showed a significant difference between the Paxlovid and non-Paxlovid groups in both mortality rate (OR = 0.25, 95% CI: 0.14 to 0.45) and hospitalization or death rate (OR = 0.17, 95% CI: 0.06 to 0.46).[3]

OH recommendations are based on evidence current to November 2022. References for additional evidence on pg 2.

PAXLOVID BENEFIT

Benefit is likely to:

- **Be seen in older patients**
- **Be seen in patients with comorbidities**
- **Increase with the number of coincident factors**
- **Be greater in those unvaccinated or inadequately vaccinated**
- **Be seen in groups vulnerable to poor COVID-19 outcomes:** Black people and other members of racialized communities disproportionately affected by covid-19; Individuals with developmental or cognitive disability; People who use substances regularly, who live with mental health conditions, or who are underhoused.

	Group	Outcome	NNT (number needed to treat)
EPIC-HR	Patients < 5 days from symptom onset[2]	Hospitalization or death	NNT = ~19
		Hospitalization	NNT = 19
		Death	NNT = 87
ON Data	Age >= 70[4]	Hospitalization or death	NNT = 45
	Age < 70[4]		NNT = 181
	Comorbidities 3+[4]	Hospitalization or death	NNT = 97
	Comorbidities < 3[4]		NNT = 42
	OST** High risk[4]	Hospitalization or death	NNT = 37

<u>Groups at high risk for disease progression *and* vulnerable to poor outcomes:</u>

- Indigenous people
- Intellectual disability of any severity

****Ontario Science Table (OST) High risk factors for disease progression:**
BMI ≥ 30, diabetes; heart disease, hypertension, congestive heart failure; chronic respiratory disease, cystic fibrosis, cerebral palsy, sickle cell disease, kidney disease (eGFR <60mL/min), moderate or severe liver disease

PAXLOVID RISK

No new evidence on the safety profile of Paxlovid in a real-world setting has been identified.[1]

Risk is likely to stem from:[1]

- Renal impairment
- Potential drug interactions with medications that are highly dependent on liver enzyme CYP3A4-mediated metabolism
- Clinical impact of interrupting or replacing another medication to mitigate drug interactions.

For details on how to manage these risks, see:
Nirmatrelvir/Ritonavir: What Prescribers and Pharmacists Need to Know[7]
(Dec 12 2022)

	Group	Outcome	NNT/NNH (number needed to harm)
EPIC-HR	Unvaccinated COVID-19 pts with 1+ Risk Factors treated with Paxlovid[2]	Adverse Events (AE): Any, related to treatment	NNH = 26
ON Data	Pts with no Drug-Drug Interactions (DDI)[4]	Hospitalization or death	NNT = 34
	Pts with DDI Level 1*[4]	Hospitalization or death	*NA*
	Pts with DDI Level 2**[4]	Hospitalization or death	NNT = 54

DDIs were not evaluated for patients <70 years of age. Defined as severity level 1 or level 2 co-medications with an ODB claim/overlap in days supplied and dispense date of Paxlovid, where:

- *Level 1: Co-medications contraindicated with Paxlovid
- **Level 2: Co-medications with clinically significant DDIs requiring a mitigation strategy while on Paxlovid according to Ontario Science Table guidelines.

1. Ontario Health Recommendation on the Use of Nirmatrelvir/Ritonavir (Paxlovid) – Executive Summary. 9 November 2022.
2. 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.
3. Amani et al. Efficacy and safety of nirmatrelvir/ritonavir (Paxlovid) for COVID-19 : a rapid review and meta-analysis. JMV 28 Dec 2022.
4. 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]*. Oct 2022.
5. CDC. MMWR: Paxlovid Associated with Decreased Hospitalization Rate Among Adults with COVID-19. 2 December 2, 2022
6. Yang et al. Early administration of Paxlovid reduces the viral elimination time in patients infected with SARS-CoV-2 Omicron variants. JMV 29 Dec 2022
7 Nirmatrelvir/Ritonavir: What Prescribers and Pharmacists Need to Know. University of Toronto/University of Waterloo, 12 Dec 2022