

## Practice | Five things to know about ...

# Nirmatrelvir-ritonavir for COVID-19

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## 1 Ritonavir-boosted nirmatrelvir (marketed as Paxlovid) is a Health Canada-approved oral antiviral medication with activity against SARS-CoV-2

Treatment is indicated for adult ( $\geq 18$  yr) outpatients with nonhypoxic COVID-19 who are at high risk of severe disease progression (e.g., advanced age, comorbidity, unvaccinated or immunosuppressed).<sup>1,2</sup>

## 2 Studies recruited primarily unvaccinated participants, predated the omicron variant and have not yet undergone peer review

According to available data, patients with 5% risk of hospital admission have an estimated number needed to treat to prevent 1 hospital admission of 24 (95% confidence interval 22–29).<sup>3,4</sup> The most common adverse effects are dysgeusia, diarrhea, vomiting, increased blood pressure and headache.

## 3 The treatment is copackaged as nirmatrelvir (300 mg – two 150 mg tablets) with ritonavir (one 100 mg tablet); the 3 tablets are taken together twice daily for 5 days

Treatment should start as soon as possible after a confirmed diagnosis of COVID-19, ideally within 5 days of symptom onset. Although observational safety data for ritonavir in pregnancy exist, no safety data exist for nirmatrelvir. In moderate renal failure (estimated glomerular filtration rate [eGFR] 30–60 mL/min), the dose is reduced to 1 tablet of nirmatrelvir and 1 tablet of ritonavir twice daily. Nirmatrelvir-ritonavir is contraindicated with eGFR  $< 30$  mL/min.

## 4 The ritonavir component boosts nirmatrelvir levels and is a cytochrome P450 3A4 (CYP3A4) inhibitor when taken short term, leading to important drug–drug interactions<sup>5</sup>

Particular attention should be paid to high-risk medications: antiarrhythmics (amiodarone, digoxin), oral antithrombotics (apixaban, rivaroxaban, ticagrelor), statins (atorvastatin, lovastatin, simvastatin), benzodiazepines (diazepam), opioids (methadone, fentanyl), anti-convulsants, neuropsychiatric drugs and immunosuppressants (Appendix 1, available at [www.cmaj.ca/lookup/doi/10.1503/cmaj.220081/tab-related-content](http://www.cmaj.ca/lookup/doi/10.1503/cmaj.220081/tab-related-content)).

## 5 Mitigation strategies for drug–drug interactions include dose reductions, switching or temporarily holding a drug, and therapeutic drug monitoring

Strategies should be implemented during and 3–5 days after treatment.<sup>5</sup> Some medications (Appendix 1) reduce the efficacy of nirmatrelvir-ritonavir and could lead to treatment failure or virologic resistance,<sup>1</sup> and alternative treatments for COVID-19 should be considered.<sup>4</sup> Pharmacist consultation is recommended in many instances (Appendix 1).

## References

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