Ontario Health
Ontario Renal Network

Nirmatrelvir/Ritonavir (Paxlovid) and Remdesivir Use in Patients on Dialysis with COVID-19: Quick Reference Guide

Paxlovid is currently the most effective therapy for reducing severe outcomes in individuals with mild COVID-19 infection. In cases where Paxlovid is unavailable/contraindicated or would not be well tolerated, Remdesivir may be an option. However, both Paxlovid and Remdesivir lack approved recommendations in their product monographs for use in individuals receiving dialysis treatment, as this patient population was excluded in clinical trials.

The purpose of this document is to summarize the proposed dosing guidance in the use of Paxlovid and Remdesivir in patients receiving dialysis treatment, based on review of recent pharmacological evidence and following consultation with clinical experts.

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PAXLOVID and REMDESIVIR PRESCRIBING GUIDANCE:

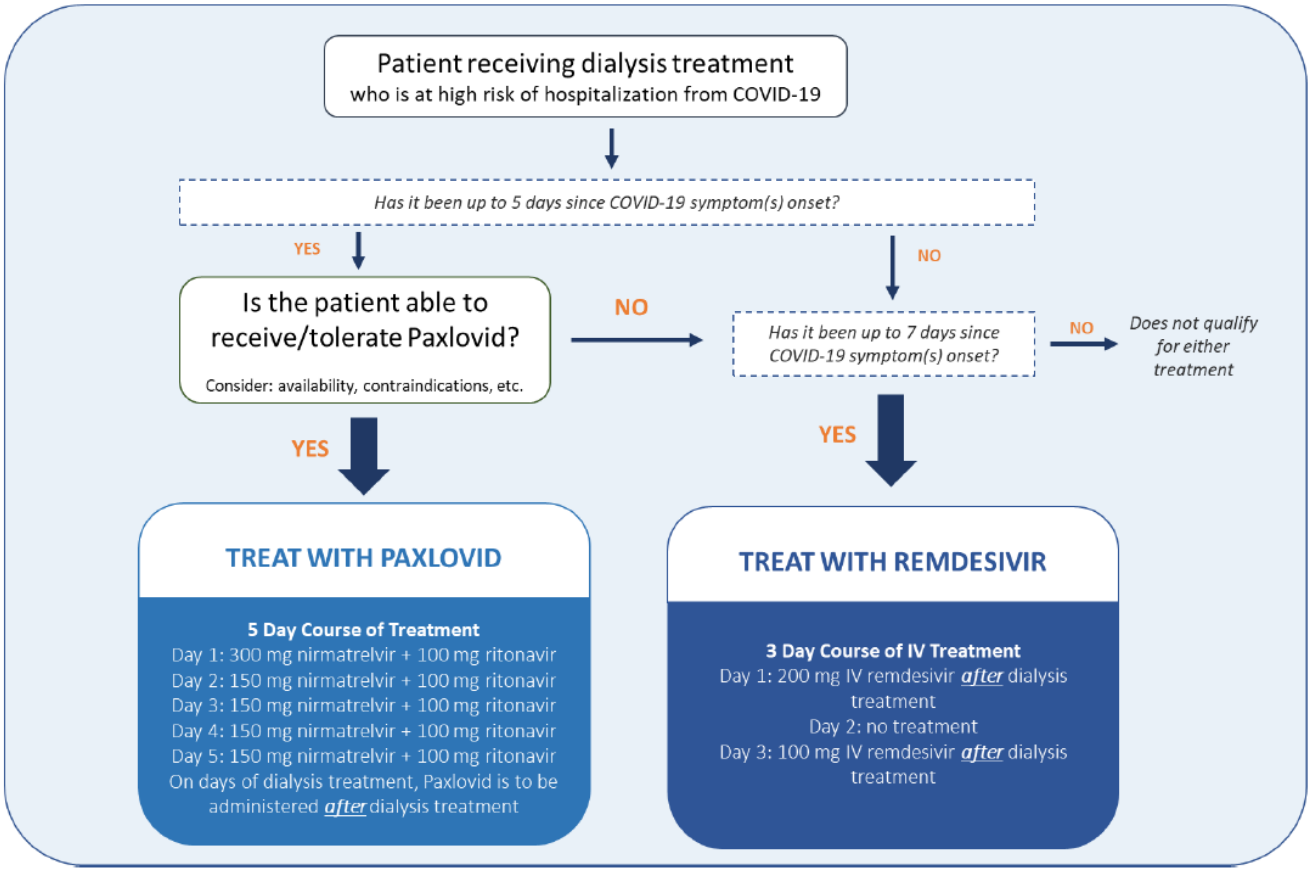

Table 1 Important drug interactions for Paxlovid (nirmatrelvir/ritonavir) and commonly used drugs in kidney patients.

	Drug name/class	Possible action/mitigation
⚠	Calcium channel blockers	Monitor blood pressure (BP); reduce dose or hold if necessary
▲	Statins	Hold statins for duration of nirmatrelvir/ritonavir therapy
⚠	Warfarin	Monitor international normalized ratio (INR) while on therapy
▲	Direct Oral Anticoagulants (DOACs)	Hold or reduce dose of DOACs during active treatment (5 days) based on indication
▲	Clopidogrel	Avoid first 6 weeks – 3 months after stent placement; In these patients, consider use of prasugrel or alternate COVID-19 therapeutics
⚠	Hydromorphone	Warn of reduced analgesic effect, temporarily increase dose as needed
✓	Angiotensin II Receptor Blockers (ARBs)	Drug interaction effect takes several days; no a priori dosage adjustment is recommended.
⚠	Indapamide	Monitor BP; reduce dose or hold if necessary
⚠	Labetolol	Drug interaction effect takes several days; no a priori dosage adjustment is recommended. Monitor BP; reduce dose or hold if necessary
⚠	Mycophenolate mofetil & mycophenolic acid	The effect on MMF/MPA is expected to be minor over 5 days.
▲	Calcineurin Inhibitors (CNIs)	Hold CNIs; monitor levels and restart while monitoring levels after nirmatrelvir/ritonavir course completed[2].
▲	Sirolimus	Hold sirolimus; monitor levels and restart while monitoring levels after nirmatrelvir/ritonavir course completed[2].

▲ Hold drug ⚠ Caution ✓ Drug Interaction not likely relevant

Note: This list of drugs is not exhaustive

APPENDIX:

Drug name/class	Effect of Nirmatrelvir/Ritonavir	Possible action/mitigation
Calcium channel blockers	Metabolized by CYP3A4. Nirmatrelvir/ritonavir is predicted to increase exposure	Monitor blood pressure (BP); reduce dose or hold if necessary
Statins	Some statins (atorvastatin, simvastatin, lovastatin) are metabolized by CYP3A4 and concentrations are expected to increase due to inhibition of CYP3A4 by nirmatrelvir/ritonavir.	Hold statins for duration of nirmatrelvir/ritonavir therapy
Warfarin	Mixed effect; decreased R-warfarin levels may lead to reduced anticoagulation	Monitor international normalized ratio (INR) while on therapy
Direct Oral Anticoagulants (DOACs)	Concentrations of apixaban/rivaroxaban are expected to increase due to CYP3A4 and P-gp inhibition	Hold or reduce dose of DOACs during active treatment (5 days) based on indication
Clopidogrel	Clopidogrel is a prodrug and is converted to its active metabolite mostly via CYP 2C19, and CYPs 3A4, 2B6, and 1A2. May reduce the effect of clopidogrel (minor effect)	Avoid first 6 weeks – 3 months after stent placement; In these patients, consider use of prasugrel or alternate COVID-19 therapeutics
Hydromorphone	Hydromorphone is eliminated via glucuronidation, mainly by UGT2B7. Ritonavir induces glucuronidation and may result in reduced analgesic effect.	Warn of reduced analgesic effect, temporarily increase dose as needed
ARBs	Some ARBs[1] are metabolized by via glucuronidation and oxidation (mainly CYP2C9). Nirmatrelvir/ritonavir could potentially decrease irbesartan exposure.	Drug interaction effect takes several days; no a priori dosage adjustment is recommended.
Indapamide	Indapamide is extensively metabolized by CYP450. Nirmatrelvir/ritonavir could potentially increase indapamide concentrations.	Monitor BP; reduce dose or hold if necessary
Labetolol	Labetalol is mainly glucuronidated by UGTs 1A1 and 2B7. Coadministration could potentially decrease labetalol exposure due to induction of UGT2B7 by ritonavir.	Drug interaction effect takes several days; no a priori dosage adjustment is recommended. Monitor BP; reduce dose or hold if necessary
Mycophenolate mofetil and mycophenolic acid	Mycophenolate mofetil (MMF) is a prodrug of mycophenolic acid (MPA). MPA undergoes glucuronidation; coadministration of inducers or inhibitors of glucuronidation, such as ritonavir, could alter mycophenolate levels.	The effect on MMF/MPA is expected to be minor over 5 days; additionally, these are often held during COVID-19 infection in transplant recipients.

Drug name/class	Effect of Nirmatrelvir/Ritonavir	Possible action/mitigation
Calcineurin Inhibitors (CNIs)	CNIs are metabolized by CYP3A4 and tacrolimus is also a substrate of P-gp. Coadministration with a ritonavir-boosted HIV protease inhibitor has been reported to profoundly increase CNI concentrations which rapidly reach toxic levels.	Hold CNIs; monitor levels and restart while monitoring levels after nirmatrelvir/ritonavir course completed[2].
Sirolimus	Coadministration may increase in sirolimus exposure > 10 fold is predicted in presence of nirmatrelvir/ritonavir.	Hold sirolimus; monitor levels and restart while monitoring levels after nirmatrelvir/ritonavir course completed[2].

Table S2: Important drug interactions for nirmatrelvir/ritonavir and commonly used drugs in kidney patients. This list is not exhaustive. For more consult https://www.covid19-druginteractions.org/checker

[1] Not all ARBs may have this interaction, this has been reported for losartan, candesartan and irbesartan

[2] It is not clear when CNIs could be safely initiated as the enzyme inhibition may persist for a few days; monitor CNI levels closely to decide when these can be re-initiated.

Last Updated: December 1, 2022