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# Antiviral Treatment for COVID-19 in Adults With Renal Impairment

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Reference List

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**About CADTH:** CADTH is an independent, not-for-profit organization responsible for providing Canada's health care decision-makers with objective evidence to help make informed decisions about the optimal use of drugs, medical devices, diagnostics, and procedures in our health care system.

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Questions or requests for information about this report can be directed to **requests@cadth.ca**

## Key Messages

- We did not find any studies about the clinical effectiveness of nirmatrelvir and ritonavir for COVID-19 in adults with renal impairment.
- We found 1 systematic review and 7 non-randomized studies about the clinical effectiveness of remdesivir for COVID-19 in adults with renal impairment.
- We did not find any evidence-based guidelines for the use of nirmatrelvir and ritonavir for COVID-19 in adults with renal impairment.
- We found 1 evidence-based guideline for the use of remdesivir for COVID-19 in adults with renal impairment.

## Research Questions

1. What is the clinical effectiveness of nirmatrelvir and ritonavir for COVID-19 in adults with renal impairment?
2. What is the clinical effectiveness of remdesivir for COVID-19 in adults with renal impairment?
3. What are the evidence-based guidelines for the use of nirmatrelvir and ritonavir for COVID-19 in adults with renal impairment?
4. What are the evidence-based guidelines for the use of remdesivir for COVID-19 in adults with renal impairment?

## Methods

### Literature Search Methods

A limited literature search was conducted by an information specialist on key resources including MEDLINE, Embase, the Cochrane Database of Systematic Reviews, the International HTA Database, the websites of Canadian and major international health technology agencies, as well as a focused internet search. The search strategy comprised both controlled vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords. The main search concepts were COVID-19 and renal impairment and remdesivir or nirmatrelvir and ritonavir (Paxlovid). A CADTH-developed search filter was applied to limit retrieval to guidelines for a secondary search of concepts COVID-19 and remdesivir or nirmatrelvir and ritonavir (Paxlovid). Conference abstracts were omitted from the Embase search. The search was completed on November 16, 2022, and limited to English-language documents published since January 1, 2020. Internet links were provided, where available.

### Selection Criteria

One reviewer screened literature search results (titles and abstracts) and selected publications according to the inclusion criteria presented in Table 1. Full texts of study publications were not reviewed. Open access full-text versions of evidence-based guidelines were reviewed when available.

## Table 1: Selection Criteria

| Criteria | Description |
|---|---|
| **Population** | Adults with renal impairment and symptomatic COVID-19 |
| **Intervention** | Q1 and Q3: Nirmatrelvir and ritonavir<br>Q2 and Q4: Remdesivir |
| **Comparator** | Q1 and Q2: Any comparator (e.g., standard care, placebo, no treatment); no comparator<br>Q3 and Q4: Not applicable |
| **Outcomes** | Q1 and Q2: Clinical benefits (e.g., mortality, hospitalization, severity of clinical symptoms, viral load, time to clinical improvement) and harms (e.g., adverse events, intolerability)<br>Q3: Recommendations regarding the use of nirmatrelvir and ritonavir for COVID-19<br>Q4: Recommendations regarding the use of remdesivir for COVID-19 |
| **Study designs** | Health technology assessments, systematic reviews, randomized controlled trials, non-randomized studies, evidence-based guidelines |

# Results

One systematic review[1] and 7 non-randomized studies[2-8] were identified regarding the clinical effectiveness of remdesivir for COVID-19 in adults with renal impairment. One evidence-based guideline[9] was identified regarding the use of remdesivir for COVID-19 in adults with renal impairment. No relevant health technology assessments or randomized controlled trials were identified.

Additional references of potential interest that did not meet the inclusion criteria are provided in Appendix 1.

# References

## Health Technology Assessments

No literature identified.

## Systematic Reviews

1. Davoudi-Monfared E, Ahmadi A, Karimpour-Razkenari E, Shahrami B, Najmeddin F, Mojtahedzadeh M. Remdesivir administration in COVID-19 patients with renal impairment: a systematic review. *Am J Ther*. 2022;29(5):e520-e533. PubMed

## Randomized Controlled Trials

No literature identified.

## Non-Randomized Studies

2. Seethapathy R, Zhao S, Long JD, Strohbehn IA, Sise ME. A propensity score-matched observational study of remdesivir in patients with COVID-19 and severe kidney disease. *Kidney360*. 2022;3(2):269-278. PubMed
3. Selvaraj V, Lal A, Finn A, et al. Efficacy of remdesivir for hospitalized COVID-19 patients with end stage renal disease. *World J Crit Care Med*. 2022;11(1):48-57. PubMed
4. Shah MK, Parikh M, Prajapati D, et al. Safety and tolerability of remdesivir in patients with end-stage renal disease on maintenance hemodialysis. *Indian J Crit Care Med*. 2022;26(5):619-625. PubMed
5. Stancampiano F, Jhawar N, Alsafi W, et al. Use of remdesivir for COVID-19 pneumonia in patients with advanced kidney disease: a retrospective multicenter study. *Clin Infect Pract*. 2022;16:100207. PubMed
6. Wang S, Huynh C, Islam S, Malone B, Masani N, Joseph D. Assessment of safety of remdesivir in Covid - 19 patients with estimated glomerular filtration rate (eGFR) < 30 ml/min per 1.73 m2. *J Intensive Care Med*. 2022;37(6):764-768. PubMed
7. Zaki KE, Huang CW, Zhou H, et al. Comparison of safety and outcomes related to remdesivir treatment among dialysis patients hospitalized with COVID-19. *Clin Kidney J.* 2022;15(11):2056-2062. PubMed
8. Ackley TW, McManus D, Topal JE, Cicali B, Shah S. A valid warning or clinical lore: an evaluation of safety outcomes of remdesivir in patients with impaired renal function from a multicenter matched cohort. *Antimicrob Agents Chemother*. 2021; 65(2):20. PubMed

## Guidelines and Recommendations

9. National Institutes of Health. Remdesivir. 2022 Aug 8; https://www.covid19treatmentguidelines.nih.gov/therapies/antiviral-therapy/remdesivir/. Accessed 2022 Nov 22.
   See Recommendations, page 175; Considerations in Patients With Renal Insufficiency, page 176.

# Appendix 1: References of Potential Interest

## Non-Randomized Studies

### *Population Age Not Specified*

Al Bishawi A, Abdel Hadi H, Elmekaty E, et al. Remdesivir for COVID-19 pneumonia in patients with severe chronic kidney disease: a case series and review of the literature. *Clin Case Rep*. 2022;10(2):e05467. PubMed

Butt B, Hussain T, Jarrar M, et al. Efficacy and safety of remdesivir in COVID-19 positive dialysis patients. *Antibiotics (Basel)*. 2022;11(2):25. PubMed

Aiswarya D, Arumugam V, Dineshkumar T, et al. Use of remdesivir in patients with COVID-19 on hemodialysis: a study of safety and tolerance. *Kidney Int Rep*. 2021;6(3):586-593. PubMed

### *Preprints*

Brown PA, McGuinty M, Argyropoulos C, et al. Early experience with modified dose nirmatrelvir/ritonavir in dialysis patients with coronavirus disease-2019 **[non peer-reviewed preprint]**. *medRxiv*. 2022: doi: https://doi.org/10.1101/2022.05.18.22275234. https://www.medrxiv.org/content/10.1101/2022.05.18.22275234v1 Accessed Nov 22.

Selvaraj V, Baig M, Dapaah-Afriyie K, Finn A, Jindal A, Bayliss G. Outcomes of COVID-19 among patients with end stage renal disease on remdesivir. **[non peer-reviewed preprint]**. medRxiv; 2021: doi:10.1101/2021.02.10.21251527. https://www.medrxiv.org/content/10.1101/2021.02.10.21251527v1. Accessed 2022 Nov 22.

### *Alternative Population — Kidney Transplant Patients*

Cacho J, Burgos E, Molina M, et al. Remdesivir in kidney transplant patients with SARS-CoV-2 pneumonia. *Nefrologia (Engl Ed)*. 2022;42(3):311-317. PubMed

Gouthami B, Naik ND, Bennikal M, et al. COVID-19 in kidney transplant recipients; an Indian experience. *J Nephropathol*. 2022;11(2):e17232. https://nephropathol.com/Article/jnp-17232 . Accessed 2022 Nov 22.

Latief M, Abbas F, Iqbal M, Hassan Z, Naresh Goud L, Shafi O. Remdesivir in renal transplant patients with coronavirus disease 2019: an observational study. *Ind J Transplant*. 2022;16(2):216-219.

Buxeda A, Arias-Cabrales C, Perez-Saez MJ, et al. Use and safety of remdesivir in kidney transplant recipients with COVID-19. *Kidney Int Rep*. 2021;6(9):2305-2315. PubMed

Meshram HS, Kute VB, Patel H, et al. Feasibility and safety of remdesivir in SARS-CoV2 infected renal transplant recipients: a retrospective cohort from a developing nation. *Transpl Infect Dis*. 2021;23(4):e13629. PubMed

Tatapudi RR, Kopparti VR, Poosapati A, Metta S, Gongada AR, Vedulla B. SARS-CoV-2 infection in kidney transplant recipients: a single-centre study of 20 cases from India. *Int J Nephrol*. 2021;2021:2243095. PubMed

### *Case Series*

Ito J, Kimura M, Toya T, et al. Remdesivir administration for Japanese COVID-19 patients undergoing maintenance hemodialysis: a retrospective observation with six case reports. *Ren Replace Ther*. 2022;8(1):14. PubMed

### *Alternative Comparator — People Without Renal Impairment*

Sunny S, Samaroo-Campbell J, Abdallah M, Luka A, Quale J. Is remdesivir safe in patients with renal impairment? Experience at a large tertiary urban medical center. *Infection*. 2022;26:26. PubMed

Pettit NN, Pisano J, Nguyen CT, et al. Remdesivir use in the setting of severe renal impairment: a theoretical concern or real risk? *Clin Infect Dis*. 2021;73(11):e3990-e3995. PubMed

### *Mixed Population — Patients With and Without Baseline Renal Impairment*

Shakir A, Bhasin N, Swami R, et al. Renal and hepatic outcomes after remdesivir therapy in Coronavirus disease-2019-positive patients with renal dysfunction at baseline or after starting therapy. *Saudi J Kidney Dis Transpl*. 2021;32(4):1034-1042. PubMed

## Guidelines and Recommendations

### *Unclear Methodology*

BC COVID Therapeutics Committee. Clinical practice guide for the use of therapeutics in mild-moderate COVID-19. Vancouver (BC): BC Centre for Disease Control; 2022 Oct 12: http://www.bccdc.ca/Health-Professionals-Site/Documents/COVID-treatment/ClinicalPracticeGuide_Therapeutics_MildModerateCOVID.pdf. Accessed 2022 Nov 22.
See Contraindications, Nirmatrelvir/ritonavir, Remsdesivir, page 11 and Dosing, Remdesivir, page 14.

Hamilton Family Medicine. Antiviral / Paxlovid access [clinical care pathway]. 2022; https://hfam.ca/clinical-pathways-and-evidence/covid/hamilton-monoclonal-antibody-pilot/. Accessed 2022 Nov 22.
See Writing a Prescription for Paxlovid.

Komorowski AS, Tseng A, Vandersluis S, et al. Evidence-based recommendations on the use of nirmatrelvir/ritonavir (Paxlovid) for adults in Ontario. *Science Briefs of the Ontario COVID-19 Science Advisory Table*. 2022;3(57). https://covid19-sciencetable.ca/wp-content/uploads/2022/02/Evidence-Based-Recommendations-on-the-Use

-of-Nirmatrelvir-Ritonavir-Paxlovid-for-Adults-in-Ontario_published_20220223.pdf. Accessed 2022 Nov 22.
See Patients with Renal Impairment, page 18.

Ontario Health; Ontario Renal Network. COVID-19 supplemental clinical guidance #4: nirmatrelvir/ritonavir (Paxlovid) use in patients with advanced chronic kidney disease and patients on dialysis with COVID19. Toronto (ON): Ontario Health; 2022 Apr 13: https://www.ontariohealth.ca/sites/ontariohealth/files/2022-04/PaxlovidClinicalGuide.pdf. Accessed 2022 Nov 22.
See Table 2: Proposed dosing guidance for Nirmatrelvir/Ritonavir in Chronic Kidney Disease, page 10.

Marra F, Smolders EJ, El-Sherif O, et al. Recommendations for dosing of repurposed COVID-19 medications in patients with renal and hepatic impairment. *Drugs R D.* 2021;21(1):9-27. PubMed
See section 3.4.1, page 13.

## Review Articles

Wilt TJ, Kaka AS, MacDonald R, et al. COVID-19: remdesivir for hospitalized adults: a living rapid review. Washington (DC): Evidence Synthesis Program, Health Services Research and Development Service, Office of Research and Development, Department of Veteran Affairs: 2022 Feb; https://www.hsrd.research.va.gov/publications/esp/covid-19-remdesivir.pdf. Accessed 2022 Nov 22.
See page 38; ongoing studies or studies completed after our search date.

Kusztal M, Myslak M. Therapeutic dilemmas in dialysis patients hospitalized for COVID-19: balancing between nihilism, off-label treatment and side effects. *Clin Kidney J.* 2021;14(4):1039-1041. PubMed

Roberto P, Francesco L, Emanuela C, Giorgia G, Pasquale N, Sara D. Current treatment of COVID-19 in renal patients: hope or hype? *Intern Emerg Med*. 2020;15(8):1389-1398. PubMed

## Additional References

### *Research Letters*

Cuadrado-Payan E, Rodriguez-Espinosa D, Broseta JJ, Guillen-Olmos E, Maduell F. Safety profile and clinical results of remdesivir in hemodialysis patients infected with SARS-CoV-2. A single-center Spanish cohort study. *J Nephrol*. 2022;1-2. PubMed

Lim JH, Park SD, Jeon Y, et al. Clinical effectiveness and safety of remdesivir in hemodialysis patients with COVID-19. *Kidney Int Rep*. 2022;7(11):2522-2525. PubMed

Estiverne C, Strohbehn IA, Mithani Z, et al. Remdesivir in patients with estimated GFR <30 ml/min per 1.73 m2 or on renal replacement therapy. *Kidney Int Rep*. 2021;6(3):835-838. PubMed

Thakare S, Gandhi C, Modi T, et al. Safety of remdesivir in patients with acute kidney injury or CKD. *Kidney Int Rep*. 2021;6(1):206-210. PubMed

### *Letter to the Editor*

Haddad I, Agarwal P, Hassanein M. Remdesivir use in COVID-19 patients with end-stage kidney disease on intermittent hemodialysis: an absolute contraindication? *Therap Apher Dial*. 2022;26(4):850-851. PubMed

### *Case Report*

Patel RH, Pella PM, Haider N, Blanco R. Case report: severe SARS-CoV-2 infection treated with remdesivir in a patient with ESRD. *Infect Disord Drug Targets*. 2022;22(3):e011221198456. PubMed

### *Case Report — Kidney Transplant Patients*

Fahim P, Nicolaysen A, Yabu JM, Zuckerman JE. Osmotic tubulopathy and acute thrombotic microangiopathy in a kidney transplant recipient with a breakthrough SARS-CoV-2 infection. *Kidney Med*. 2022;4(7):100492. PubMed