CONSENSUS GUIDELINE
Remdesivir and nirmatrelvir plus ritonavir in renal impairment

Background

In Australia, there are currently no approved treatment options for managing COVID-19 patients with severe renal impairment (eGFR < 30 mL/min), including those on dialysis and renal transplant patients. There is limited evidence available to guide COVID-19 treatment in this patient group who are considered to be at high risk for disease progression.[1,2]

This consensus guideline provides guidance for the use of remdesivir (Veklury®) and nirmatrelvir plus ritonavir (Paxlovid®) in renal impairment. It is intended for use in **adult patients when considering the use of nirmatrelvir plus ritonavir, and those aged 12 years and older in relation to remdesivir.** It has been adapted from a similar resource developed by Western Sydney Local Health District Infectious Diseases and Renal Departments (with permission and thanks), and further developed in consultation with the Clinical Excellence Commission (CEC) Antimicrobial Stewardship Expert Advisory Committee. Prior to prescribing, clinicians should conduct a comprehensive risk assessment to consider the risks versus benefits of these treatments for each patient. The use of these treatments in patients with severe renal impairment is considered off-label and requires patient consent, as well as consultation with an Infectious Disease and/or Renal Specialist. Note, the recommendations in this guideline may differ to the CEC developed Drug Guidelines – *Use of remdesivir injection for COVID-19* and *Use of nirmatrelvir and ritonavir tablets for COVID-19*, which include information adapted from the approved Product Information.

Remdesivir and nirmatrelvir plus ritonavir are restricted on the NSW Medicines Formulary (Formulary). Refer to the Formulary online platform for further details.

This guideline requires endorsement by your local Drug and Therapeutics Committee (DTC) prior to implementation. Additional resources to support the safe and appropriate use of remdesivir and nirmatrelvir plus ritonavir are available.

Dosing recommendations based on renal function

Note: Recommendations provided do not override any pre-existing contraindications for the use of remdesivir or nirmatrelvir plus ritonavir. For example, the co-administration of rifampicin with nirmatrelvir plus ritonavir is contraindicated.[1]

Table 1. Dosing recommendations for remdesivir and nirmatrelvir plus ritonavir based on renal function

	Nirmatrelvir/ ritonavir (Paxlovid®)	**Remdesivir (Veklury®)** *For patients (≥ 12 years old) who have pneumonia due to SARS-CoV-2 requiring supplemental oxygen*	**Remdesivir (Veklury®)** *For patients (≥ 12 years old) who do not require supplemental oxygen and who are at high risk of progressing to severe COVID-19*
eGFR ≥ 60 to < 90	300 mg nirmatrelvir plus 100 mg ritonavir taken orally every 12 hours for five days[1]	Day 1: 200 mg IV once Day 2 to 5: 100 mg IV daily[2,4] **Preferred agent in renal impairment**	Day 1: 200 mg IV once Day 2 to 3: 100 mg IV daily[2,4] **Preferred agent in renal impairment**
eGFR ≥ 30 to < 60	**Reduced dose:** 150 mg nirmatrelvir plus 100 mg ritonavir taken orally every 12 hours for five days[1]		
eGFR < 30 and not on dialysis	**Consider only if unable to use remdesivir** Day 1: 300 mg nirmatrelvir plus 100 mg ritonavir taken orally once daily Day 2 to 5: 150 mg nirmatrelvir plus 100 mg ritonavir taken orally once daily[3]		
Dialysis*	**Use with caution**[1]		
Renal transplant	**Use with caution**†		

* Includes peritoneal dialysis and haemodialysis. Remdesivir may be administered without regard to the timing of dialysis.[4]
† Nirmatrelvir plus ritonavir should **not** be used in patients taking tacrolimus. Nirmatrelvir plus ritonavir also has significant interactions with other medicines used in transplant patients including ciclosporin, everolimus and sirolimus. The concurrent use of nirmatrelvir plus ritonavir and these medicines should be with a high level of caution and appropriate monitoring.[1]

References

1. Therapeutic Goods Administration (2022) *Australian Product Information – Paxlovid (nirmatrelvir/ritonavir tablets)*, accessed 18 July 2023.
2. Therapeutic Goods Administration (2022). *Australian Product Information – Veklury (remdesivir) concentrate for injection*, accessed 18 July 2023.
3. University of Liverpool (2023). *Guidance for Paxlovid dosing in patients with renal disease and patients on dialysis*, accessed 19 July 2023.
4. Gilead Sciences (2023). *FDA Approves Veklury (remdesivir) for COVID-19 Treatment in Patients with Severe Renal Impairment, Including Those on Dialysis*, accessed 18 July 2023.
5. The Renal Drug Database (2023). *PAXLOVID (NIRMATRELVIR/RITONAVIR)*, accessed July 19, 2023.
6. The Renal Drug Database (2023). *REMDESIVIR*, accessed 19 July 2023.
7. University of Liverpool (2023). *COVID-19 Therapies – Dose Recommendations for Patients with Renal Impairment* accessed 20 July 2023.