Renal patients are exceptionally vulnerable to COVID-19. The UK Renal Pharmacy Group (UK RPG) have looked at dosing data for Paxlovid (excluding patients taking tacrolimus, ciclosporin or sirolimus) and Remdesivir for adult patients with CKD stage 4 & 5 and conclude that both medications can safely be given to this patient cohort.

RPG members in Wales have been using remdesivir and Paxlovid since Autumn 2022 in these patients as per the table below:

<table>
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<th>Evidence behind recommendations in Wales</th>
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<tr>
<td>Remdesivir</td>
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The antiviral drug remdesivir, whilst recommended for patients undergoing haemodialysis, is not currently licensed for use in patients with an estimated glomerular filtration rate (eGFR) less than 30 mL/min/1.73 m² due to the exclusion of these patients from clinical trials, as they were considered too complicated with further concerns of excipient accumulation, notably the carrier SBECD. Conclusive data on the safety of remdesivir among individuals with eGFR less than 30 ml/min/1.73 m² are lacking. Nevertheless, given the limited duration of treatment (5–10 days) and relatively low concentration of SBECD carrier, this suggests that its benefits may outweigh risk in adult patients with eGFR less than 30 ml/min/ 1.73 m². Much of what is known about the pharmacokinetics and clinical effects of SBECD in kidney failure is gleaned from literature of intravenous voriconazole, which also uses this same carrier. In this setting, short courses are generally well tolerated, without significant adverse events, despite documented accumulation of SBECD above levels in patients with normal kidney function.

In the Canadian Treatments for COVID-19 (CATCO) trial, investigators randomly assigned patients to remdesivir or standard care, regardless of kidney function. Among 1,281 patients (median age 74 years), 34 patients receiving remdesivir and 25 patients receiving standard care had a baseline eGFR less than 30 ml/min/ 1.73 m². Much of what is known about the pharmacokinetics and clinical effects of SBECD in kidney failure is gleaned from literature of intravenous voriconazole, which also uses this same carrier. In this setting, short courses are generally well tolerated, without significant adverse events, despite documented accumulation of SBECD above levels in patients with normal kidney function.

No dose adjustments were made for CKD or dialysis. Clinicians administered intravenous remdesivir at a loading dose of 200 mg on day 1, followed by daily 100mg doses for 9 days or until discharge.

In patients with an eGFR less than 30 mL/min/1.73 m² who received remdesivir, the investigators observed no increased risks for transaminitis or toxic kidney effects at day 5.

Remdesivir Safe Despite Advanced CKD, Study Finds - Renal and Urology News

Remdesivir in Patients with Acute or Chronic Kidney Disease and COVID-19 - PMC (nih.gov)
**Paxlovid**

The antiviral drug Paxlovid is not currently recommended in England for use in patients with an estimated glomerular filtration rate (eGFR) less than 30 mL/min/1.73 m² due to limited evidence; these patients were excluded from clinical trials as considered too complicated.

The prescribing of Paxlovid in Wales was extended in the Autumn 2022 to encompass patients with eGFR less than 30ml/min/1.73 m² including those on haemodialysis or peritoneal dialysis. To date, no safety signals have emerged. 12 outpatients who completed a course of Paxlovid have been followed up by the National Antiviral service in Wales. Reported side effects included nausea, diarrhoea and taste disturbance with all patients completing the prescribed course. Side effects were the same as those reported by patients with eGFR 30-60ml/min/1.73 m² and eGFR 60-90ml/min/1.73 m². Paxlovid has been shown in large clinical studies to be well tolerated with a side effect profile similar to placebo and it is not nephrotoxic.

Prescribing guidance in Wales for COVID-19 therapies includes Paxlovid with a dose regimen:

- eGFR 60 to 90ml/min/1.73 m² Nirmatrelvir 300mg plus Ritonavir 100mg BD for 5 days (normal dose)
- eGFR 30 to 60ml/min/1.73 m² Nirmatrelvir 150mg plus Ritonavir 100mg BD for 5 days (reduced dose)
- eGFR <30ml/min/1.73 m² Nirmatrelvir 150mg plus Ritonavir 100mg BD for 5 days (reduced dose)

Patients taking tacrolimus, ciclosporin or sirolimus should not be given Paxlovid due to interactions.

A pharmacokinetics paper from Germany looked at four patients given this reduced dose and showed no accumulation of nirmatrelvir despite elevated peak plasma concentrations and plasma levels declined rapidly within a few days after end of treatment. Thus supporting that the dose used in Wales is safe.

_A Pharmacokinetics of Nirmatrelvir and Ritonavir in COVID-19 Patients with End-Stage Renal Disease on Intermittent Hemodialysis - PMC (nih.gov)_

There is also evidence from Canada that Paxlovid can be safely given to patients in this cohort. A modified dose of nirmatrelvir/ritonavir (300mg nirmatrelvir + 100mg ritonavir both once daily on day 1, followed by 150mg nirmatrelvir + 100mg ritonavir both once daily for 4 days, given after dialysis for those on haemodialysis) was found to be safe and well tolerated, with no serious adverse events being observed in 134 maintenance haemodialysis patients.

_Early Experience with Modified Dose Nirmatrelvir/Ritonavir i... : Clinical Journal of the American Society of Nephrology (lww.com)_

This modified dose is also recommended by the Liverpool Drug Interactions group.

It is important for patients to be counselled around dosing prior to use and careful vigilance for ongoing inside effects to be reported.

Support for dosing of both medications in CKD patients can be found in the Renal Drug Database.

**The Renal Drug Database**

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