Dosing of Paxlovid in Renal Disease

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Data are limited or absent; therefore, risk-benefit assessment for any individual patient rests with prescribers.

Guidance for the use of nirmatrelvir/ritonavir in patients with advanced chronic kidney disease and patients on dialysis

Background

- Paxlovid (nirmatrelvir/ritonavir) is a very effective therapy in the early management of high-risk patients, such as those with advanced chronic kidney disease or those on dialysis. However it is renally cleared and dose adjustments are required with renal impairment.
- Compared to healthy controls with no renal impairment, following administration of single oral doses of nirmatrelvir (100 mg) and ritonavir (100 mg), Cmax and AUC of nirmatrelvir increased by 30% and 24% in patients with mild renal impairment, by 38% and 87% in patients with moderate renal impairment, and by 48% and 204% in patients with severe renal impairment [1,2].
- Administration of nirmatrelvir/ritonavir 300/100 mg once on Day 1 followed by 150/100 mg once daily on Days 2-5 in subjects with severe renal impairment, either requiring intermittent haemodialysis or not requiring haemodialysis resulted in comparable AUC and Cmax on Day 1 and at steady-state compared to those observed in subjects with normal renal function receiving nirmatrelvir/ritonavir 300 mg/100 mg twice daily for 5 days [2].
- During a 4-hour haemodialysis session, approximately 6.9% of nirmatrelvir dose was cleared through dialysis. Haemodialysis clearance was 1.83 L/h [2].
- Clinical, modelling and patient data [3-5] support an adjusted dosing regimen for use in people with eGFR <30 ml/min and in those on dialysis.

Current Dosing Recommendations

Renal Function	European[1] and American[2] Label Recommendations
eGFR >60 ml/min	*Days 1-5:* 300 mg nirmatrelvir + 100 mg ritonavir, both twice daily
eGFR 30-60 ml/min	*Days 1-5:* 150 mg nirmatrelvir + 100 mg ritonavir, both twice daily
eGFR <30 ml/min	*Day 1:* 300 mg nirmatrelvir + 100 mg ritonavir, both once only *Days 2-5:* 150 mg nirmatrelvir + 100 mg ritonavir, both once daily
Dialysis	*Day 1:* 300 mg nirmatrelvir + 100 mg ritonavir, both once only *Days 2-5:* 150 mg nirmatrelvir + 100 mg ritonavir, both once daily *On haemodialysis days , nirmatrelvir/ritonavir should be administered after haemodialysis.*

Note, in some regions, specific packs are available for patients with moderate or severe renal impairment which contain the correct number of tablets [1,2].

If these packs are not available, patients should be informed that the daily dose pack provided may contain more nirmatrelvir and ritonavir tablets than needed.

References

1. Paxlovid GB Summary of Product Characteristics and European Summary of Product Characteristics, Pfizer Ltd.
2. Paxlovid US Prescribing Information, Pfizer Inc.
3. Early experience with modified dose nirmatrelvir/ritonavir in dialysis patients with coronavirus disease 2019. Hiremath S, Blake PG, Yeung A, et al. Clin J Am Soc Nephrol, 2023, 18(4):485-490.
4. Safety profile and clinical and virological outcomes of nirmatrelvir-ritonavir treatment in patients with advanced chronic kidney disease and coronavirus disease 2019 (COVID-19). Chan GCK, Lui GCY, Wong CNS, et al. Clin Infect Dis. 2023, 77(10):1406-1412.
5. Nirmatrelvir and ritonavir combination in COVID-19 patients with advanced chronic kidney disease. Lafont E, Blez D, Bildan MA, et al. Clin Infect Dis. 2024, 79(3):798-800.

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