# UK Kidney Association (UKKA) position statement on the care of patients with kidney disease and at increased risk from COVID-19

## December 2022

People with kidney disease have been amongst those with the highest risk of mortality and hospitalisation during the COVID-19 pandemic.

Recent observational data show that this risk continues[1]. Whilst the overall absolute risk of dying from COVID-19 has gone down due to the effectiveness of vaccination coupled with naturally acquired immunity and better treatments, the relative risk of death for those with kidney disease, particularly patients with kidney transplants, did not fall in the third wave of the pandemic. These data may be an under-estimate of relative risk as many of the most vulnerable patients continued to shield[2], with impacts on their mental health and that of their family.

The current round of COVID-19 booster vaccines is welcomed, and renal units should continue to strongly encourage patients to receive all COVID-19 vaccines doses offered. Whilst the majority of patients with kidney disease do respond to vaccination against COVID-19[3], a group of at least 13,000 kidney patients are likely to remain unprotected as they have no detectable antibodies against COVID-19 even after four doses of vaccine[4]. The patients most likely to suffer from lower efficacy of vaccination include an estimated 8,000 patients with kidney transplants (from a total of ~40,000 prevalent kidney transplant patients) and up to 5,000 patients who are treated with immunosuppression for immunological diseases that affect the kidneys and other organs. Data suggest that in the Omicron wave (i) people with kidney transplants had around a 3 times higher rate of COVID-19 mortality than over 80-year-olds in the general population and (ii) people with stage 5 CKD had around 8 times higher age-adjusted risk of COVID-19 mortality compared to the general population[5].

## Key recommendations:

1. **<u>UKKA recommends that all kidney patients should continue to be supported to take up all approved COVID vaccine doses</u>** (up to 6 doses in those with a kidney transplant or receiving significant immunosuppression for other kidney disease): All patients with kidney disease in vulnerable groups (transplant recipients, those on significant immunosuppression for autoimmune disease, patients with CKD stage 4 and stage 5 (pre-dialysis) and all those on dialysis) should be strongly encouraged and supported to take up the 2022 Autumn booster dose. Patients should receive education about the potential waning of protection from previous doses of vaccines to allow them to understand the value of continued booster doses. Renal units should be resourced to allow them to continue to support kidney patients to receive vaccination.

2. **<u>UKKA recommends all national guidance on the treatment of COVID-19 should include specific recommendations for patients with kidney disease:</u>** Patients with kidney disease are uniquely vulnerable to COVID-19 due to a combination of increased risk of poor clinical outcomes after infection combined with a limited availability of therapies compatible with renal impairment or immunosuppressive medication.

3. **<u>UKKA recommends urgent clarification and guidance about the use of Remdesivir and modified dose Paxlovid in patients in CKD 4 and 5:</u>** Data is now emerging to suggest that modified dose Paxlovid can be used safely in these patients including in those undergoing dialysis therapy. Current prescribing limitations prevent use of Paxlovid in this group in most areas of the UK, but urgent modification is currently being sought to this to allow use with expert pharmacist guidance. **UKKA currently recommends that Paxlovid should not be used in patients with kidney transplant and other patients receiving immunosuppression with tacrolimus, cyclosporin and sirolimus due to significant drug interactions.**

   **Remdesivir use is also currently restricted in patients with kidney disease. UKKA recommends urgent clarification of a possible role in these patients.**

4. **<u>COVID-19 testing:</u>** UKKA recommends continued use in high-risk settings including for patients who are immunosuppressed.

5. **<u>Antibody testing:</u>** UKKA recommends that the highest risk patients with kidney disease should be offered COVID antibody testing.

6. **<u>Use of antibody therapy in the prevention and treatment of COVID-19:</u>** UKKA recognises the complexity of evolving evidence for the use of Evusheld as prophylaxis for patients who are antibody negative. **UKKA also acknowledges current emerging data about the clinical efficacy of sotrovimab** for patients with kidney disease in the most vulnerable groups particularly in the light of the now dominant BQ.1.1 variant where recent studies suggest clinical efficacy is lost [6.] UKKA acknowledges a need to continually review as further data emerges about circulating variants. Given the importance of providing therapy for this vulnerable group of patients, UKKA continues to request that the further NICE evaluation of Evusheld should be completed and published within the next 6 weeks or that an expert clinical panel be asked to provide a clear recommendation. UKKA also supports the prioritization of trials which evaluate other possible preventative therapeutics (including newer antibody treatment) for kidney patients.

## Background to recommendations

**1. UKKA recommends that all renal patients should continue to be supported to take up all approved COVID vaccine doses.**

New data cited in the recent British Transplantation Society position statement and analysed by linking four national registries including the UK Transplant Registry has shown that vaccination against COVID-19 using vaccines licensed in the UK, is associated with incremental protection in organ transplant patients with those in receipt of four vaccine doses showing a vaccine efficacy of approximately 80% against death and 55% against hospitalisation. Whilst this data is still undergoing peer review, current analysis shows that receipt of 4 vaccine doses is associated with a risk of 1% of dying within 28 days of COVID-19 infection compared to 10% in those who had received no vaccine doses. Although data following doses 5 and 6 is not yet available, it is important to remind patients that laboratory and clinical data show waning of the effect of vaccine doses over time, so up to date vaccination is required to maintain this protection[7].

There is marked variation in uptake of a full course of vaccination, with data from single centres and that linked to UKKR suggesting that people of non-White ethnicity, and/or from socially deprived backgrounds and/or those with severe mental illness being the least likely to have received a full course[8]. Data have also highlighted that where renal units themselves have been able to lead vaccination programmes, increased rates of vaccination have been achieved in comparison to the local population[9,10].

**All renal patients should therefore be encouraged to take up their Autumn booster vaccine dose. Renal services should be resourced to allow them to support patients to be able to access vaccination through close working with vaccination centres, including providing advocacy for patients with kidney disease.**

Education about the importance of vaccination should also allow recommendation of vaccination against influenza given the current increase in prevalence of this infection.

**3. UKKA recommends urgent clarification and guidance about the use of Remdesivir and modified dose Paxlovid in patients in CKD 4 and 5.**

Paxlovid is not a therapeutic option for many kidney patients due to drug interactions with immunosuppressive medication (cyclosporine, tacrolimus and sirolimus) and UKKA continues to recommend that it is not used in combination with these drugs. However, limited safety data is now available for patients with CKD 4 and 5 (those with GFR < 30 ml/min) including those receiving haemodialysis treatment suggesting that it can be used in these patient groups with expert pharmacy guidance. The UKKA is seeking urgent modifications to the regulations concerning prescription of

Paxlovid to allow for use in these groups of patients. Such use will require careful understanding of reduced dosing regimes and clear guidance about other drug interactions requiring modification[11,12,13,14].

Remdesivir is also currently prohibited (by CAS alert and Blueteq) for those with GFR less than 30 ml/min unless on haemodialysis. UKKA feels Remdesivir could be safely and effectively used in kidney patients with no dose modification but remains very concerned about the current national shortage of this drug which may be further disadvantaging patients with kidney disease.

**4. COVID-19 Testing: UKKA recommends continued use in high-risk settings, including for immunocompromised patients who are admitted to hospital for any reason, including as a day case.**

For all patients who are receiving in-centre haemodialysis, we have recently published recommendations that can be accessed here.

**5. Antibody testing: UKKA recommends that the highest risk patients with kidney disease should be offered regular antibody testing.**

This would necessitate testing in approximately 40,000 patients with kidney transplants and an estimated 10,000 patients with autoimmune kidney disease. Patients whose transplants have failed and have returned to dialysis but continue to receive immunosuppressant therapies should also be included in this group. Currently, not all renal units have ready access to antibody testing for their patients.

Around 20% (equating to approximately 8,000 patients) of those with kidney transplants make no antibody response after a four-vaccination course. A further estimated 5,000 patients have recently received B-cell depleting or equivalently immunosuppressant therapies for autoimmune diseases many of whom will also make no antibody response. These patients are at higher risk of hospitalisation and death. Knowledge of antibody status (particularly for those who have made no antibody response) will support these patients in making a risk assessment around social behaviour and management strategies, as it reflects immune status and may encourage those with previous antibody responses to continue booster vaccination rounds.

**6. UKKA acknowledges the complexity of data surrounding the use of antibody therapy for the prevention and treatment of COVID-19 and supports the early inclusion of patients with kidney disease in trials of all new therapeutics for COVID-19 including the trial of new antibody therapies.**

Complex scientific data have been published regarding the efficacy of Evusheld as preventative therapy in COVID-19. However, Evusheld has been used in 32 countries including North America and most European countries with clear efficacy. The Department for Health and Social Care have decided so far

not to proceed with Evusheld prophylaxis for autumn/winter 2022. This is out of alignment with North America and multiple other European countries who have assessed the same evidence. NICE are evaluating Evusheld and a stakeholder consultation on this has been completed. However, NICE are not going to publish this evaluation for some months. We are currently experiencing a further increase in cases this winter and UKKA are therefore requesting that this timescale is significantly accelerated, and the evaluation is completed and published in the next 6 weeks to inform the targeted use of Evusheld for prophylaxis to protect vulnerable patients and the NHS over the winter months. Some patients are currently seeking access to Evusheld through the private sector at considerable cost. As there is uncertainty with regards to efficacy, UKKA would welcome final recommendations from NICE or a panel of clinical experts to clarify this area as soon as possible.

UKKA acknowledges that recent data has raised doubt about the continued efficacy of sotrovimab against the newer BQ.1.1 variant which is thought to be dominant in the UK[6].

However, it also notes that data from early 2022 demonstrated that at that time molnupiravir was not as effective as sotrovimab in many patients with kidney disease, with receipt of sotrovimab being associated with fewer severe outcomes from COVID-19 compared to molnupiravir at 30 and 60 days[15].

Given that many kidney patients will also not be suitable for Paxlovid treatment, this raises concerns about the lack of effective therapeutic options for some kidney patients.

Considering the complexity of using prophylactic antibodies and the uncertainty surrounding the efficacy of Evusheld and sotrovimab, UKKA strongly supports continued inclusion of any candidate antibodies in future clinical trials.

Due to the vulnerability of patients with kidney disease, it remains imperative that access to neutralizing monoclonal antibodies for high-risk kidney patients remains regardless of cost benefit analysis for the more general population.

## Further guidance

**Renal services should work to ensure that all eligible patients are able to access appropriate treatments promptly. Data currently suggest that access is inconsistent.**

Despite patients with moderate to advanced kidney disease (chronic kidney disease stage 3-5) being at increased risk of poor outcomes from COVID-19, UKKA are aware of major differences in care for patients with kidney disease in relation to the COVID-19 pandemic and are recommending a standard of care that some organisations are currently not able to implement. This represents a major inequality in care for people with kidney disease and demands rapid correction. At-risk kidney patients need to be aware of the availability of pre-hospital treatment and how to access it. Ideally, patients should be able to self-refer to CMDUs in all parts of the UK; however, given that they currently cannot, it is vital that

renal units are prepared to facilitate such referrals happening in a timely and effective manner. Such access needs to be supported both pre-hospital and in hospital, given the high relative risk of worse outcomes and the difficulties of using some of the drugs in kidney patients (due to low eGFR and/or drug interactions).

There is also a need for the continued systematic collection of data (e.g., through renal networks) to ensure that early changes in disease burden are identified.

We encourage clinicians to work in their organisations to support implementation for their patients.

UKKA shares recommendations with system leaders (including the Chief Medical Officers) asking for support including to ensure transparency of decision making and equality of access to care. UKKA has received confirmation that our recommendations have been shared with the key advisory committees.

## References


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