

## Information for managing patients with chronic kidney disease

This information is intended to provide specific guidance for using the treatments being tested in RECOVERY in patients with chronic kidney disease (CKD, including those on dialysis or with a kidney transplant). Further information about each treatment is available in its Intervention Sheet which can be downloaded from the study [website](#).

### *Lopinavir-ritonavir*

Lopinavir-ritonavir has negligible renal clearance so no dose modification is required for patients with reduced eGFR or on dialysis.

Lopinavir-ritonavir is highly protein-bound so it not removed by dialysis.

Ritonavir is a potent inhibitor of the cytochrome P<sub>450</sub>3A system so has significant drug-drug interactions, including with calcineurin inhibitors and sirolimus. For patients receiving these drugs (and continuing them despite acute SARS-CoV-2 infection) it would not be appropriate to co-administer lopinavir-ritonavir so it should be marked as “unsuitable” for the participant when completing the randomisation form.

### *Dexamethasone*

Dexamethasone can be used safely in patients with CKD. It may be used in place of prednisolone in transplant immunosuppression (although care must be taken to ensure that it is replaced with another corticosteroid once the 10 day course for RECOVERY is completed).

Dexamethasone may worsen insulin resistance, so care should be taken for patients with poorly-controlled diabetes.

### *Hydroxychloroquine*

Hydroxychloroquine blood concentrations are determined mostly by distribution rather than excretion in the acute phase. The volume of distribution is large (>100 L), hence the large loading doses required to achieve sufficient blood concentration to kill SARS-CoV-2. Hydroxychloroquine has no drug-drug interactions relevant for transplant immunosuppression, although it may increase CNI and sirolimus levels so these should be monitored.

### *Azithromycin*

Azithromycin can be used safely in patients with CKD and on dialysis. Azithromycin may increase ciclosporin concentrations, but can be used safely in people receiving tacrolimus.

## ***Tocilizumab***

Tocilizumab is a humanized monoclonal antibody directed at interleukin-6 receptors which prevents their activation (both membrane-bound and soluble forms). There are no CKD-specific concerns with its use, although it has not been well-studied in people with moderate-severe kidney disease.

Tocilizumab may reduce ciclosporin concentrations so levels should be monitored and doses may need to be adjusted.