Please check [www.covid19-druginteractions.org](http://www.covid19-druginteractions.org) for updates. Please note that if a drug is not listed it cannot automatically be assumed it is safe to coadminister.

No recommendation to use experimental therapy for COVID-19 is made. Data for many agents are limited or absent; therefore, risk-benefit assessment for any individual patient rests with prescribers.

**COVID-19 Antiviral Therapies (Licensed or Under Clinical Investigation)**

Please refer to the additional notes on the following pages for further details and complete dose recommendations.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Renal Impairment eGFR*</th>
<th>Renal Replacement Therapy (RRT)</th>
<th>References</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>≥50 ml/min</td>
<td>30-49 ml/min</td>
<td>10-29 ml/min</td>
</tr>
<tr>
<td>Bamlanivimab/ Etesevimab</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Casirivimab/ Imdevimab</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Favipiravir</td>
<td>100%</td>
<td>No recommendation possible</td>
<td>No recommendation possible</td>
</tr>
<tr>
<td>Molnupiravir</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Niclosamide</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Nirmatrelvir + Ritonavir</td>
<td>100%</td>
<td>Nirmatrelvir: 50% Ritonavir: 100% (i.e. 1 tablet of each)</td>
<td>Not recommended</td>
</tr>
<tr>
<td>Nitazoxanide</td>
<td>100%</td>
<td>100%, with caution</td>
<td>100%, with caution</td>
</tr>
<tr>
<td>Remdesivir</td>
<td>100%</td>
<td>100%</td>
<td>Not recommended in product labels **</td>
</tr>
<tr>
<td>Sotrovimab</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Tixagevimab/ Cilgavimab</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
</tr>
</tbody>
</table>

**Abbreviations**

eGFR Estimated glomerular filtration rate

* Use CKD-EPI formula: the Abbreviated Modification of Diet in Renal Disease (aMDRD) or the Cockcroft-Gault (CG) equation may be used as an alternative; see [www.chip.dk/Tools-Standards/Clinical-risk-scores](http://www.chip.dk/Tools-Standards/Clinical-risk-scores)

** Population pharmacokinetic analysis using data from phase 3 trials conducted in hospitalized COVID-19 patients with impaired renal function indicate that remdesivir can be used in patients with an eGFR of <30 ml/min with no dose adjustment regardless of the need for dialysis (Humeniuk R, et al, CROI 2023, Seattle, abstract 514).
COVID-19 Therapies - Dose Recommendations for Patients with Renal Impairment

Please check www.covid19-druginteractions.org for updates. Please note that if a drug is not listed it cannot automatically be assumed it is safe to coadminister. No recommendation to use experimental therapy for COVID-19 is made. Data for many agents are limited or absent; therefore, risk-benefit assessment for any individual patient rests with prescribers.

Notes - Antiviral Therapies (Licensed or Under Clinical Investigation)

Bamlanivimab/ Etesevimab
Bamlanivimab and etesevimab are not eliminated intact in the urine. Renal impairment is not expected to affect the exposure of bamlanivimab or etesevimab. No dosage adjustment is recommended in patients with renal impairment.

Casirivimab/ Imdevimab
Casirivimab and imdevimab are monoclonal antibodies and are therefore not likely to undergo renal excretion. Renal impairment is not expected to affect the exposure of casirivimab and imdevimab. No dosage adjustment is required in individuals with mild or moderate renal impairment, or in patients with creatinine clearance (CrCl) < 15 mL/min including those on dialysis. Based on population PK analysis, trough concentrations of casirivimab and imdevimab in serum at steady state were comparable between patients with mild or moderate renal impairment, or patients with CrCl <15 ml/min including those on dialysis, and patients with normal renal function. Limited data are available in patients with severe renal impairment (n=3).

Favipiravir
Favipiravir is 90.5% renally excreted, the majority of which (82-92%) as M1 metabolite which is responsible for toxicity. M1 may accumulate in renal impairment with a 2.5-fold increase in moderate impairment based on a single patient studied in global phase 3 with eGFR 30-50 ml/min. Uric acid increases may also be a concern in renal impairment. No data is available to make any statement of safety in patients with renal impairment or dependent on RRT.

Molnupiravir
Molnupiravir is hydrolysed to n-hydroxycytidine (NHC) prior to reaching systemic circulation. Renal clearance is not a meaningful route of elimination for NHC. No dose adjustment in patients with any degree of renal impairment is needed. In a population PK analysis, mild or moderate renal impairment did not have a meaningful impact on the pharmacokinetics of NHC. The pharmacokinetics of molnupiravir and NHC has not been evaluated in patients with eGFR <30 mL/min or on dialysis.

Niclosamide
Niclosamide has poor bioavailability when administered orally and low systemic absorption via the intranasal/inhaled route. Niclosamide may be given safely to patients with kidney diseases.

Nirmatrelvir + ritonavir
The primary route of elimination of nirmatrelvir when administered with ritonavir was renal excretion of intact drug. Approximately 49.6% of the administered dose was recovered in urine. Compared to healthy controls with no renal impairment, nirmatrelvir Cmax and AUC were 30% and 24% higher in patients with mild renal impairment, 38% and 87% higher in patients with moderate renal impairment, and 48% and 204% higher in patients with severe renal impairment. Nirmatrelvir and ritonavir are highly protein bound, therefore, it is unlikely that they will be significantly removed by haemodialysis or peritoneal dialysis.
Notes - Antiviral Therapies (Licensed or Under Clinical Investigation) [continued]

Nitazoxanide

Approximately one third of an oral dose of nitazoxanide is excreted in the urine. Nitazoxanide has not been studied in patients with compromised renal function. No data are available in RRT.

Remdesivir

Remdesivir is not cleared unchanged in urine to any substantial extent, but its main metabolite GS-441524 is renally cleared and the metabolite levels in plasma may theoretically increase in patients with impaired renal function. The excipient betadex sulfobutyl ether sodium is renally cleared and accumulates in patients with decreased renal function.

Product labels for remdesivir advise that all patients should have eGFR determined prior to starting remdesivir and while receiving it as clinically appropriate. Patients with eGFR ≥30 ml/min have received remdesivir for treatment of COVID-19 with no dose adjustment, but remdesivir should not be used in patients with eGFR <30 ml/min as administration of drugs formulated with betadex sulfobutyl ether sodium (such as remdesivir) is not recommended in patients with eGFR <30 ml/min.

Population pharmacokinetic analysis using data from phase 3 trials conducted in hospitalized COVID-19 patients with impaired renal function indicate that remdesivir can be used in patients with an eGFR of <30 ml/min with no dose adjustment regardless of the need for dialysis. At eGFR 10.11 ml/min/1.73m², the mean increase in GS-441524 was 220%, however, this increase was not associated with new safety signals. Analysis of betadex sulfobutyl ether sodium from this study is ongoing but accumulation is not expected based on its observed short plasma elimination half-life (Humeniuk R, et al, CROI 2023, Seattle, abstract 514). This finding is supported by data from a small study in patients with eGFR <30 ml/min (34 on remdesivir vs 25 receiving standard care) showing that there was no increased risk of transaminitis or toxic kidney effects at day 5 (Cheng M et al. JAMA Netw Open, 2022, 5(8):e2229236).

Sotrovimab

Renal impairment is not expected to impact the pharmacokinetics of sotrovimab since mAbs with molecular weight >69 kDa do not undergo renal elimination. No dosage adjustment is recommended in patients with renal impairment. Due to its molecular weight, dialysis is not expected to impact the pharmacokinetics of sotrovimab.

Tixagevimab/Cilgavimab

Tixagevimab and cilgavimab are monoclonal antibodies and are therefore not likely to undergo renal excretion. Renal impairment is not expected to affect the exposure of tixagevimab and cilgavimab.

There is no difference in the clearance of tixagevimab and cilgavimab in individuals with mild or moderate renal impairment compared to individuals with normal renal function. There were insufficient subjects with severe renal impairment to draw conclusions.
# COVID-19 Host-directed Therapies (Licensed or Under Clinical Investigation)

Please refer to the additional notes on the following pages for further details and complete dose recommendations.

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<td></td>
<td>≥50 ml/min</td>
<td>30-49 ml/min</td>
<td>10-29 ml/min</td>
</tr>
<tr>
<td>Anakinra</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Baricitinib</td>
<td>100%</td>
<td>2 mg once daily</td>
<td>Not recommended</td>
</tr>
<tr>
<td>Budesonide (inhaled)</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Canakinumab</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Dexamethasone (low dose)</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Fluvoxamine</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Hydrocortisone</td>
<td>100%</td>
<td>100%, with caution</td>
<td>100%, with caution</td>
</tr>
<tr>
<td>Imatinib</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Infliximab</td>
<td>100%</td>
<td>100%, with caution</td>
<td>100%, with caution</td>
</tr>
<tr>
<td>Methylprednisolone</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Ruxolitinib</td>
<td>100%</td>
<td>100%</td>
<td>5 mg twice daily</td>
</tr>
<tr>
<td>Sarilumab</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Tocilizumab</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
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**Abbreviations**

- eGFR: Estimated glomerular filtration rate
- *: Use CKD-EPI formula: the Abbreviated Modification of Diet in Renal Disease (aMDRD) or the Cockcroft-Gault (CG) equation may be used as an alternative; see [www.chip.dk/Tools-Standards/Clinical-risk-scores](http://www.chip.dk/Tools-Standards/Clinical-risk-scores)

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Notes – Host-directed Therapies (Licensed or Under Clinical Investigation)

Anakinra

Anakinra is eliminated by glomerular filtration and subsequent tubular metabolism. Plasma clearance of anakinra decreases with decreasing renal function. Plasma clearance of anakinra decreased by 70% in severe renal insufficiency and by 75% in end stage renal disease (CrCl <30 ml/min); every other day dosing is recommended. Less than 2.5% of an administered dose was removed by dialysis (HD or CAPD); every other day dosing is recommended.

Baricitinib

Approximately 75% of an administered dose was eliminated in the urine through filtration and active secretion, predominately as unchanged drug (69%). Renal function significantly affects baricitinib exposure. For patients with eGFR 30-60 ml/min, a dose of 2 mg once daily is recommended in the European product label and dose of 1 mg once daily is recommended in the US product label. Given short duration of therapy in COVID-19, 2 mg once daily advised for this indication. Not recommended for use in patients with eGFR <30 ml/min. Baricitinib is likely to be removed during CRRT; dose as in eGFR 30-60 ml/min.

Budesonide (inhaled)

The metabolites of budesonide are excreted as such or in conjugated form mainly via the kidneys. No unchanged budesonide has been detected in the urine. There are no data regarding the specific use of inhaled budesonide in patients with renal impairment. No dose adjustment is required in renal impairment. Budesonide is unlikely to be dialysed.

Canakinumab

Canakinumab is eliminated via intracellular catabolism. Due to its molecular size, little canakinumab is expected to be filtered by the kidney. No formal studies have been conducted to examine the pharmacokinetics of canakinumab administered subcutaneously in patients with renal impairment. Canakinumab is a human IgG immunoglobulin with large molecular size (~150 kDa), and little intact immunoglobulin is expected to be filtered by the kidney. Therefore, impaired renal function or renal replacement therapies are unlikely to affect the pharmacokinetics of canakinumab.

Dexamethasone (low dose)

Dexamethasone is metabolised mainly in the liver, with up to 65% of the dose excreted unchanged in the urine. Particular care is required when considering the use of systemic corticosteroids in patients with renal insufficiency and frequent patient monitoring is necessary.

Fluvoxamine

Fluvoxamine undergoes extensive metabolism in the liver. Fluvoxamine is excreted in the urine predominantly as metabolites, with approximately 2% of the administered dose recovered as unchanged drug. The mean minimum plasma concentrations in renally impaired patients (creatinine clearance 5-45 mL/min) after 4 and 6 weeks of treatment (50 mg twice daily, n=13) were comparable to each other, suggesting no accumulation of fluvoxamine in these patients. Patients with renal insufficiency (<10 ml/min) should start on a low dose and be carefully monitored.

Hydrocortisone

Hydrocortisone is metabolised mainly in the liver and is minimally excreted in the urine. Particular care is required when using systemic hydrocortisone in patients with renal insufficiency (eGFR <50 ml/min); patient monitoring is advised. Hydrocortisone is unlikely to be dialysed.

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Notes – Host-directed Therapies (Licensed or Under Clinical Investigation) [continued]

**Imatinib**

*Imatinib and its metabolites are not excreted via the kidney to a significant extent.*

Patients with mild and moderate impairment of renal function appear to have a higher plasma exposure than patients with normal renal function. The increase is approximately 1.5- to 2-fold, corresponding to a 1.5-fold elevation of plasma AGP, to which imatinib binds strongly. The free drug clearance of imatinib is probably similar between patients with renal impairment and those with normal renal function, since renal excretion represents only a minor elimination pathway for imatinib. The US product label for imatinib recommends a 50% decrease in the recommended starting dose for patients with moderate renal impairment but this is not applicable when imatinib is used at a dose of 400 mg once daily for the treatment of COVID-19.

**Infliximab**

*The elimination pathways for infliximab have not been characterised but it is likely to be eliminated via its target antigen.*

Unchanged infliximab was not detected in urine.

Infliximab has not been studied in patients with renal impairment. No dose recommendations can be made. Infliximab is not dialysed.

**Methylprednisolone**

*Methylprednisolone is metabolized by CYP3A4 to inactive metabolites which are excreted in the urine.*

Particular care is required when considering the use of systemic corticosteroids in patients with renal insufficiency and frequent patient monitoring is necessary. Methylprednisolone is dialysed - dose as in normal renal function.

**Ruxolitinib**

*Approximately 74% of an administered dose was eliminated in the urine, mainly as metabolites (<1% unchanged drug). Clearance of ruxolitinib metabolites decreases with increasing severity of renal impairment. The safety of increased exposure to these metabolites is unknown; close patient monitoring is advised in addition to dose adjustment recommendations.*

The US product label for ruxolitinib recommends to avoid in moderate/severe renal impairment if platelets <100. Avoid if eGFR <15 ml/min.

Use with caution in patients on RRT. Administer post dialysis on dialysis days only. Ruxolitinib metabolites appeared to be dialysable to varying degrees by a 4-hour haemodialysis procedure. No data is available for dosing for patients on PD or CVVH.

**Sarilumab**

*Sarilumab is not metabolised or excreted by the kidneys.*

No effect of renal impairment is expected.

Sarilumab’s large molecular weight prevents clearance via glomerular filtration or RRT.

**Tocilizumab**

*Tocilizumab is not metabolised or excreted by the kidneys.*

No effect of renal impairment is expected.

Tocilizumab’s large molecular weight prevents clearance via glomerular filtration or RRT.
Antiviral Therapies

1. Bamlanivimab and etesevimab FDA Emergency Use Authorization, Lilly USA.
2. Ronapreve (casirivimab/imdevimab) Summary of Product Characteristics, Roche Products Ltd.
3. REGEN-COV (casirivimab/imdevimab) FDA Emergency Use Authorization, Regeneron Pharmaceuticals Inc.
5. Lagevrio (molnupiravir) Summary of Product Characteristics, Merck Sharp and Dohme Ltd.
7. Yomesan (niclosamide) Prescribing Information, Bayer (discontinued).
8. Niclosamide, Jo Drugs Health Inc.
12. Veklury (remdesivir) Summary of Product Characteristics, Gilead Sciences Ltd.

Host-directed Therapies

21. Olumiant (baricitinib) US Prescribing Information, Lilly USA.
24. Ilaris (canakinumab) US Prescribing Information, Novartis Pharmaceuticals.
27. Faverin (fluvoxamine) Summary of Product Characteristics, Mylan.
28. Luvox (fluvoxamine) US Prescribing Information, ANI Pharmaceuticals Inc.
29. Solu-Cortef (hydrocortisone) Summary of Product Characteristics, Pfizer Ltd.
32. Remicade (infliximab) Summary of Product Characteristics, Merck Sharp and Dohme Ltd.
34. Medrone (methylprednisolone) Summary of Product Characteristics, Pfizer Ltd.
35. Medrol (methylprednisolone) US Prescribing Information, Pfizer.
36. Jakavi (ruxolitinib) Summary of Product Characteristics, Novartis Pharmaceuticals Ltd.
40. RoActemra (tocilizumab, for infusion) Summary of Product Characteristics, Roche Products Ltd.
41. Actemra (tocilizumab) US Prescribing Information, Genentech Inc.