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.

Experimental COVID-19 Antiviral Therapies

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

<table>
<thead>
<tr>
<th>Drug</th>
<th>Mild (Childs Pugh A)</th>
<th>Hepatic Impairment Moderate (Childs Pugh B)</th>
<th>Severe (Childs Pugh C)</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atazanavir</td>
<td>400 mg once daily</td>
<td>300 mg once daily</td>
<td>Not recommended</td>
<td>1-4</td>
</tr>
<tr>
<td>Azithromycin</td>
<td>100%</td>
<td>100%</td>
<td>Not recommended</td>
<td>5, 6</td>
</tr>
<tr>
<td>Bamlanivimab/Etesevimab</td>
<td>100%</td>
<td>100% (no data available)</td>
<td>100% (no data available)</td>
<td>7</td>
</tr>
<tr>
<td>Casirivimab/Imdevimab</td>
<td>100%</td>
<td>100% (limited data available)</td>
<td>100% (no data available)</td>
<td>8, 9</td>
</tr>
<tr>
<td>Chloroquine</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
<td></td>
</tr>
<tr>
<td>Favipiravir</td>
<td>Consider dose adjustment. 1200 mg twice daily then 800 mg twice daily to day 5</td>
<td>Consider dose adjustment. 1200 mg twice daily then 800 mg twice daily to day 5</td>
<td>Consider dose adjustment. 800 mg twice daily then 400 mg twice daily to days 2-3</td>
<td>12, 13</td>
</tr>
<tr>
<td>Hydroxychloroquine</td>
<td>100%</td>
<td>100%, with caution and frequent ALT monitoring</td>
<td>Caution. Consider 50% (to a maximum of 400 mg) with frequent ALT monitoring</td>
<td>14, 15</td>
</tr>
<tr>
<td>Interferon beta</td>
<td>100%</td>
<td>Not recommended</td>
<td>Not recommended</td>
<td>16-19</td>
</tr>
<tr>
<td>Ivermectin</td>
<td>100%. Not studied in hepatic disease.</td>
<td>100%. Not studied in hepatic disease.</td>
<td>100%, with caution. Not studied in hepatic disease.</td>
<td>20</td>
</tr>
<tr>
<td>Lopinavir/ritonavir</td>
<td>100%</td>
<td>100%</td>
<td>Contraindicated</td>
<td>21, 22</td>
</tr>
<tr>
<td>Molnupiravir</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
<td>23</td>
</tr>
<tr>
<td>Niclosamide</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
<td>24</td>
</tr>
<tr>
<td>Nitazoxanide</td>
<td>100%, with caution. Not studied in hepatic disease.</td>
<td>100%, with caution. Not studied in hepatic disease.</td>
<td>100%, with caution. Not studied in hepatic disease.</td>
<td>25</td>
</tr>
<tr>
<td>Remdesivir</td>
<td>100% (no data available)</td>
<td>100% (no data available)</td>
<td>100% (no data available)</td>
<td>26, 27</td>
</tr>
<tr>
<td>Ribavirin</td>
<td>100%</td>
<td>100%, with caution and close monitoring of renal function, FBC and LFTs with dose reduction if required.</td>
<td>100%, with caution and close monitoring of renal function, FBC and LFTs with dose reduction if required.</td>
<td>28, 29</td>
</tr>
<tr>
<td>Sotrovimab</td>
<td>100% (no data available)</td>
<td>100% (no data available)</td>
<td>100% (no data available)</td>
<td>30</td>
</tr>
</tbody>
</table>
Liverpool Drug Interactions Group

Charts updated 1 December 2021

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.

Experimental COVID-19 Therapies - Dose recommendations for patients with hepatic impairment

Notes - Antiviral Therapies

Atazanavir
Safety and efficacy in patients with severe hepatic impairment have been suggested in several small studies.

Azithromycin
Hepatic elimination: use with caution in all degrees of hepatic impairment. Discontinue if signs of hepatic dysfunction.

Bamlanivimab/Etesevimab
No dosage adjustment is recommended in patients with mild hepatic impairment. Based on population PK analysis, there is no difference in PK of bamlanivimab or etesevimab in patients with mild hepatic impairment compared to patients with normal hepatic function. Bamlanivimab and etesevimab have not been studied in patients with moderate or severe hepatic impairment.

Casirivimab/Imdevimab
Casirivimab and imdevimab are not expected to undergo significant hepatic elimination. No dosage adjustment is required in patients with mild hepatic impairment. Based on population PK analysis, there is no difference in the exposure of casirivimab and imdevimab in patients with mild hepatic impairment (n=586 for casirivimab; n=599 for imdevimab) (total bilirubin >1.0–1.5 x ULN and any aspartate aminotransferase). No clinically important differences in the exposure of casirivimab and imdevimab were found between patients with mild hepatic impairment and patients with normal hepatic function.

Limited data (n=11) are available in patients with moderate hepatic impairment; no data are available in patients with severe hepatic impairment.

Chloroquine
Use with caution; monitor liver function tests and watch for toxicities.

Favipiravir
Could consider extending treatment duration in COVID as per duration for ongoing trials. Dosing as per study US109.

Hydroxychloroquine
Maximum dosage based on minimal data and risk of hepatotoxicity.

Interferon beta
Caution if ALT >2.5x ULN. Dose reduction advised if ALT >5x ULN. Discontinue if jaundice or clinical symptoms of liver disease.

Ivermectin
Ivermectin has not been studied in patients with hepatic impairment. Patients with abnormal liver tests prior to starting ivermectin should be carefully evaluated.

Lopinavir/ritonavir
Use with caution and monitor for toxicities in patients with mild and moderate hepatic impairment (see product label).

Molnupiravir
No dose adjustment is required for patients with hepatic impairment. The pharmacokinetics of molnupiravir and NHC has not been evaluated in patients with hepatic impairment. Preclinical data indicate that hepatic elimination is not expected to be a major route of NHC elimination therefore hepatic impairment is unlikely to affect NHC exposure.

Niclosamide
Niclosamide may be given safely to patients with liver diseases.

Nitazoxanide
The pharmacokinetics of nitazoxanide in patients with compromised hepatic function have not been studied.

Remdesivir
The pharmacokinetics of remdesivir have not been evaluated in patients with hepatic impairment. The role of the liver in the metabolism of remdesivir is unknown. It is not known if dosage adjustment is appropriate in patients with hepatic impairment. Remdesivir should only be used in patients with hepatic impairment if the potential benefit outweighs the potential risk. Liver function should be determined in all patients prior to starting remdesivir and should be monitored while receiving it as clinically appropriate.

Remdesivir should be discontinued in patients who develop ALT ≥5x ULN (SmPC) or >10x ULN (USPI) during treatment with remdesivir.

Remdesivir should be discontinued in patients who develop ALT elevation accompanied by signs or symptoms of liver inflammation or increasing conjugated bilirubin, alkaline phosphatase, or international normalised ratio (INR).

Ribavirin
Discontinue if progressive and clinically significant ALT rises, despite dose reduction, or accompanied by increased bilirubin.

Sotrovimab
No clinical trials have been conducted to evaluate the effects of hepatic impairment on the pharmacokinetics of sotrovimab. The impact of hepatic impairment on sotrovimab is unknown.
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.

### Experimental COVID-19 Host-directed Therapies

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

<table>
<thead>
<tr>
<th>Drug</th>
<th>Hepatic Impairment</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mild (Childs Pugh A)</td>
<td>Moderate (Childs Pugh B)</td>
</tr>
<tr>
<td>Anakinra</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Baricitinib</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Budesonide (inhaled)</td>
<td>Not studied. Consider 100% with close monitoring.</td>
<td>Not studied. Consider 100% with close monitoring.</td>
</tr>
<tr>
<td>Canakinumab</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Colchicine</td>
<td>100% with close monitoring Contraindicated with P-gp inhibitors or strong CYP3A4 inhibitors.</td>
<td>100% with close monitoring Contraindicated with P-gp inhibitors or strong CYP3A4 inhibitors.</td>
</tr>
<tr>
<td>Dexamethasone (low dose)</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Infliximab</td>
<td>Not studied. No dosing recommendations can be made.</td>
<td>Not studied. No dosing recommendations can be made.</td>
</tr>
<tr>
<td>Methylprednisolone</td>
<td>Not studied. Consider 100%.</td>
<td>Not studied. Consider 100%.</td>
</tr>
<tr>
<td>Ruxolitinib</td>
<td>50% (dosing as per platelet count in product label)</td>
<td>50% (dosing as per platelet count in product label)</td>
</tr>
<tr>
<td>Sarilumab</td>
<td>Not studied. Consider 100% under specialist supervision with frequent ALT monitoring.</td>
<td>Not studied. Consider 100% under specialist supervision with frequent ALT monitoring.</td>
</tr>
<tr>
<td>Tocilizumab</td>
<td>Not studied. Consider 100% under specialist supervision with frequent ALT monitoring.</td>
<td>Not studied. Consider 100% under specialist supervision with frequent ALT monitoring.</td>
</tr>
</tbody>
</table>
Experimental COVID-19 Therapies - Dose recommendations for patients with hepatic 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 - Host-directed Therapies

Anakinra  
The efficacy and safety in patients with AST/ALT ≥1.5x ULN have not been evaluated.

Baricitinib  
There was no clinically relevant effect on the pharmacokinetics of baricitinib in patients with mild or moderate hepatic impairment. The use of baricitinib has not been studied in patients with severe hepatic impairment.

Budesonide (inhaled)  
Formal pharmacokinetic studies with inhaled budesonide have not been conducted in patients with hepatic impairment. However, since budesonide undergoes mainly hepatic metabolism, impairment of liver function may lead to accumulation of budesonide in the plasma. Patients with hepatic disease should be closely monitored.

Canakinumab  
No formal pharmacokinetic studies have been performed in patients with hepatic impairment. Elimination of protein drugs such as canakinumab is thought to occur via proteolytic catabolism in different tissues. Although the liver is known to be a major organ of protein degradation, impaired hepatic function is not expected to be a limiting factor for elimination.

Colchicine  
Use with caution in patients with mild/moderate hepatic impairment. Such patients should be carefully monitored for adverse effects of colchicine. Coadministration is contraindicated in the SmPC for patients with severe hepatic impairment, but the USPI recommends to consider dose reduction. Coadministration is contraindicated in patients with hepatic impairment who are taking a P-gp inhibitor or a strong CYP3A4 inhibitor.

Dexamethasone (low dose)  
Particular care is required when considering the use of systemic corticosteroids in patients with liver failure and frequent patient monitoring is necessary. The elimination half-life is prolonged in severe liver disease.

Hydrocortisone  
There may be an increased effect in patients with liver disease, and monitoring is advised. Reduced dosing may be considered.

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

Methylprednisolone  
Particular care is required when considering the use of systemic corticosteroids in patients with liver failure or cirrhosis and frequent patient monitoring is necessary.

Ruxolitinib  
Recommendations as for polycythaemia vera indication in product labels.

Sarilumab  
Initiating treatment is not recommended in patients with ALT or AST >1.5x ULN.

Tocilizumab  
The European product label does not recommend treatment in patients with baseline ALT or AST >5x ULN. The American product label does not recommend to initiate treatment in patients with elevated transaminases ALT or AST >1.5x ULN.
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.

References

1. Reyataz (atazanavir) Summary of Product Characteristics, Bristol-Myers Squibb Pharmaceuticals Ltd.
2. Reyataz (atazanavir) US Prescribing Information, Bristol-Myers Squibb.
5. Zithromax (azithromycin) Summary of Product Characteristics, Pfizer Ltd.
6. Zithromax (azithromycin) Prescribing Information, Pfizer Inc.
7. Bamlanivimab and etesevimab FDA Emergency Use Authorization, Lilly USA.
8. Ronapreve (casirivimab/imdevimab) Summary of Product Characteristics, Roche Products Ltd.
9. REGEN-COV (casirivimab/imdevimab) FDA Emergency Use Authorization, Regeneron Pharmaceuticals Inc.
10. Avloclor (chloroquine) tablets Summary of Product Characteristics, Alliance Pharmaceuticals.
13. Pharmacokinetics of favipiravir in volunteers with hepatic impairment. ClinicalTrials.gov Identifier: NCT01419457.
15. Plaquenil (hydroxychloroquine) US Prescribing Information, Concordia.
17. Rebif (interferon beta 1a) US Prescribing Information, EMD Serono.
18. Betaferon (interferon beta 1b) Summary of Product Characteristics, Bayer.
20. Soolantra (ivermectin) Summary of Product Characteristics, Galderma (UK) Ltd.
22. Kaletra (lopinavir/ritonavir) US Prescribing Information, Abbvie Inc.
23. Lagevrio (molnupiravir) Summary of Product Characteristics, Merck Sharp and Dohme Ltd.
26. Veklury (remdesivir) Summary of Product Characteristics, Gilead Sciences Ltd.
27. Veklury (remdesivir) US Prescribing Information, Gilead Sciences Inc.
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.

28. Rebetol (ribavirin) Summary of Product Characteristics, Merck Sharpe & Dohme Ltd.
29. Rebetol (ribavirin) US Prescribing Information, Merck & Co Inc.
33. Olumiant (baricitinib) Summary of Product Characteristics, Lilly.
34. Olumiant (baricitinib) US Prescribing Information, Lilly USA.
37. Ilaris (canakinumab) US Prescribing Information, Novartis Pharmaceuticals.
38. Ilaris (canakinumab) CHMP Assessment Report, European Medicines Agency.
40. Colcrys (colchicine) US Prescribing Information, Takeda Pharmaceuticals America Inc.
42. Dexamethasone Summary of Product Characteristics, Consilient Health Ltd.
43. Solu-Cortef (hydrocortisone) Summary of Product Characteristics, Pfizer Ltd.
44. Remicade (infliximab) Summary of Product Characteristics, Merck Sharp and Dohme Ltd.
45. Remicade (infliximab) US Prescribing Information, Janssen Pharmaceuticals.
46. Medrone (methylprednisolone) Summary of Product Characteristics, Pfizer Ltd.
47. Medrol (methylprednisolone) US Prescribing Information, Pfizer.
52. RoActemra (tocilizumab, for infusion) Summary of Product Characteristics, Roche Products Ltd.
53. Actemra (tocilizumab) US Prescribing Information, Genentech Inc.