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.

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.

Drug	Hepatic Impairment			References
	Mild (Childs Pugh A)	Moderate (Childs Pugh B)	Severe (Childs Pugh C)	
Bamlanivimab/ Etesevimab	100%	100% (no data available)	100% (no data available)	1
Casirivimab/ Imdevimab	100%	100% (limited data available)	100% (no data available)	2, 3
Favipiravir	Consider dose adjustment. 1200 mg twice daily then 800 mg twice daily to day 5	Consider dose adjustment. 1200 mg twice daily then 800 mg twice daily to day 5	Consider dose adjustment. 800 mg twice daily then 400 mg twice daily to days 2-3	4, 5
Molnupiravir	100%	100%	100%	6, 7
Niclosamide	100%	100%	100%	8
Nirmatrelvir + ritonavir	100%	100%	Contraindicated	9, 10
Nitazoxanide	100%, with caution. Not studied in hepatic disease.	100%, with caution. Not studied in hepatic disease.	100%, with caution. Not studied in hepatic disease.	11
Remdesivir	100%	100%	100%	12, 13
Sotrovimab	100% (no data available)	100% (no data available)	100% (no data available)	14, 15
Tixagevimab/ Cilgavimab	100% (no data available)	100% (no data available)	100% (no data available)	16

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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 individuals with mild hepatic impairment. The effect of hepatic impairment on the exposure of casirivimab and imdevimab was evaluated by population PK analysis 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.
Favipiravir	Could consider extending treatment duration in COVID as per duration for ongoing trials. Dosing as per study US109.
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.
Nirmatrelvir + ritonavir	Nirmatrelvir and ritonavir exposures were similar in subjects with normal hepatic function and those with moderate hepatic impairment. No dosage adjustment is needed for patients with either mild (Child-Pugh Class A) or moderate (Child-Pugh Class B) hepatic impairment. Nirmatrelvir/ritonavir is contraindicated in patients with severe hepatic impairment (Child-Pugh Class C) as it has not been studied and there are no pharmacokinetic or safety data available regarding its use in subjects with severe hepatic impairment.
Nitazoxanide	The pharmacokinetics of nitazoxanide in patients with compromised hepatic function have not been studied.
Remdesivir	Liver function should be determined in all patients prior to starting remdesivir and should be monitored while receiving it as clinically appropriate. The American Prescribing Information states no dosage adjustment of remdesivir is recommended for patients with mild, moderate, or severe hepatic impairment (Child-Pugh Class A, B, or C). Relative to subjects with normal hepatic function, the pharmacokinetics of remdesivir and GS-441524 following a single dose of 100 mg of remdesivir were similar in subjects with moderate hepatic impairment and higher in subjects with severe hepatic impairment. The exposure differences in subjects with severe hepatic impairment are not considered to be clinically significant. The SmPC recommends that remdesivir should only be used in patients with hepatic impairment if the potential benefit outweighs the potential risk and that remdesivir should not be initiated in patients with ALT ≥5x ULN at baseline. 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).
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.
Tixagevimab/ Cilgavimab	No specific studies have been conducted to examine the effects of hepatic impairment on the pharmacokinetics of tixagevimab and cilgavimab. The effect of hepatic impairment on the pharmacokinetics of tixagevimab and cilgavimab is unknown.

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COVID-19 Host-directed Therapies (Licensed or Under Clinical Investigation)

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Drug	Hepatic Impairment			References
	Mild (Childs Pugh A)	Moderate (Childs Pugh B)	Severe (Childs Pugh C)	
Anakinra	100%	100%	100%, with caution	17, 18
Baricitinib	100%	100%	Not recommended	19, 20
Budesonide (inhaled)	Not studied. Consider 100% with close monitoring.	Not studied. Consider 100% with close monitoring.	Not studied. Consider 100% with close monitoring.	21, 22
Canakinumab	100%	100%	100%	23, 24
Dexamethasone (low dose)	100%	100%	100%, with caution	25, 26
Fluvoxamine	100% following slow titration and careful monitoring	100% following slow titration and careful monitoring	100% following slow titration and careful monitoring	27, 28
Hydrocortisone	Not studied. Consider dose reduction.	Not studied. Consider dose reduction.	Not studied. Consider dose reduction.	29
Imatinib	100%	100%	100% (European product label) 75% (American product label)	30, 31
Infliximab	Not studied. No dosing recommendations can be made.	Not studied. No dosing recommendations can be made.	Not studied. No dosing recommendations can be made.	32, 33
Methylprednisolone	Not studied. Consider 100%.	Not studied. Consider 100%.	Not studied. Consider 100%, with caution	34,35
Ruxolitinib	50% (dosing as per platelet count in product label)	50% (dosing as per platelet count in product label)	50% (dosing as per platelet count in product label)	36-38
Sarilumab	Not studied. Consider 100% under specialist supervision with frequent ALT monitoring.	Not studied. Consider 100% under specialist supervision with frequent ALT monitoring.	Not studied. Consider 100% under specialist supervision with frequent ALT monitoring.	39
Tocilizumab	Not studied. Consider 100% under specialist supervision with frequent ALT monitoring.	Not studied. Consider 100% under specialist supervision with frequent ALT monitoring.	Not studied. Consider 100% under specialist supervision with frequent ALT monitoring.	40, 41

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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.
Fluvoxamine	Fluvoxamine undergoes extensive hepatic metabolism. In patients with liver cirrhosis, fluvoxamine AUC increased by ~56% when compared to healthy volunteers.
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.
Imatinib	Imatinib is mainly metabolized in the liver. Mild and moderate hepatic impairment did not influence exposure to imatinib and its major metabolite, CGP74588. In patients with severe hepatic impairment, imatinib Cmax and AUC increased by 63% and 45% and CGP74588 Cmax and AUC increased by 56% and 55%, relative to patients with normal hepatic function.
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.

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Antiviral Therapies

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Host-directed Therapies

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