

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

Charts updated 24 September 2020

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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.

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)	
<b>Experimental COVID-19 Antiviral Therapies</b>				
Atazanavir	400 mg once daily	300 mg once daily	Not recommended <sup>a</sup>	1-4
Azithromycin <sup>b</sup>	100%	100%	Not recommended	5, 6
Chloroquine <sup>c</sup>	100%	100%	100%	7, 8
Favipiravir	Consider dose adjustment. 1200 mg twice daily then 800 mg twice daily to day 5 <sup>d</sup>	Consider dose adjustment. 1200 mg twice daily then 800 mg twice daily to day 5 <sup>d</sup>	Consider dose adjustment. 800 mg twice daily then 400 mg twice daily to days 2-3 <sup>d</sup>	9, 10
Hydroxychloroquine <sup>e</sup>	100%	100%, with caution and frequent ALT monitoring	Caution. Consider 50% (to a maximum of 400 mg) with frequent ALT monitoring	11,12
Interferon beta <sup>f</sup>	100%	Not recommended	Not recommended	13-16
Ivermectin <sup>g</sup>	100%. Not studied in hepatic disease.	100%. Not studied in hepatic disease.	100%, with caution. Not studied in hepatic disease.	17
Lopinavir/ritonavir	100% <sup>h</sup>	100% <sup>n</sup>	Contraindicated	18, 19
Nitazoxanide <sup>i</sup>	100%, with caution. Not studied in hepatic disease.	100%, with caution. Not studied in hepatic disease.	100%, with caution. Not studied in hepatic disease.	20
Remdesivir <sup>j</sup>	100% (no data available)	100% (no data available)	100% (no data available)	21, 22
Ribavirin <sup>k</sup>	100%	100%, with caution and close monitoring of renal function, FBC and LFTs with dose reduction if required.	100%, with caution and close monitoring of renal function, FBC and LFTs with dose reduction if required.	23, 24
<b>Experimental COVID-19 Immune Therapies</b>				
Anakinra <sup>l</sup>	100%	100%	100%, with caution	25, 26
Baricitinib <sup>m</sup>	100%	100%	Not recommended	27, 28
Canakinumab <sup>n</sup>	100%	100%	100%	29, 30
Dexamethasone <sup>o</sup>	100%	100%	100%, with caution	31, 32
Hydrocortisone <sup>p</sup>	Not studied. Consider dose reduction.	Not studied. Consider dose reduction.	Not studied. Consider dose reduction.	33
Ruxolitinib <sup>q</sup>	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)	34-36
Sarilumab <sup>r</sup>	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.	37
Tocilizumab <sup>s</sup>	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.	38, 39

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## Notes

### Antiviral Therapies

#### Atazanavir

- a) Safety and efficacy have been suggested in several small studies.

#### Azithromycin

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

#### Chloroquine

- c) Use with caution; monitor liver function tests and watch for toxicities.

#### Favipiravir

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

#### Hydroxychloroquine

- e) Maximum dosage based on minimal data and risk of hepatotoxicity.

#### Interferon beta

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

#### Ivermectin

- g) 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

- h) Use with caution and monitor for toxicities (see product label).

#### Nitazoxanide

- i) The pharmacokinetics of nitazoxanide in patients with compromised hepatic function have not been studied.

#### Remdesivir

- j) ALT 5x ULN exclusion criteria in clinical studies. Discontinuation: ALT >5x ULN or ALT elevation accompanied by signs or symptoms of liver inflammation or increasing conjugated bilirubin, alkaline phosphatase, or INR.

#### Ribavirin

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

### Immune Therapies

#### Anakinra

- l) The efficacy and safety in patients with AST/ALT  $\geq 1.5x$  ULN have not been evaluated.

#### Baricitinib

- m) 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.

#### Canakinumab

- n) 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.

#### Dexamethasone

- o) 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

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

#### Ruxolitinib

- q) Recommendations as for polycythaemia vera indication in product labels.

#### Sarilumab

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

#### Tocilizumab

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

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