

# Interactions with Experimental COVID-19 Therapies

Charts updated 3 April 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. Drug interaction data for many agents are limited or absent; therefore, risk-benefit assessment for any individual patient rests with prescribers.

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### Key to abbreviations

ATV	Atazanavir	CLQ	Chloroquine
LPV/r	Lopinavir/ritonavir	HCLQ	Hydroxychloroquine
RDV	Remdesivir	RBV	Ribavirin
FAVI	Favipiravir	TCZ	Tocilizumab
		IFN-β	Interferon beta

### Colour Legend

<span style="color: red;">■</span>	These drugs should not be coadministered
<span style="color: orange;">■</span>	Potential interaction which may require a dose adjustment or close monitoring.
<span style="color: yellow;">■</span>	Potential interaction likely to be of weak intensity. Additional action/monitoring or dosage adjustment unlikely to be required.
<span style="color: lightgreen;">■</span>	No clinically significant interaction expected

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## Anaesthetics & Muscle Relaxants

	ATV	LPV/r	RDV	FAVI	CLQ	HCLQ	RBV	TCZ	IFN-β
Alcuronium	↔	↔	↔	↑	↔	↔	↔	↔	↔
Bupivacaine	↑	↑	↔	↔	↔	↔	↔	↓	↔
Cisatracurium	↔	↔	↔	↔	↔	↔	↔	↔	↔
Desflurane	↔	↔	↔	↔	↔	↔	↔	↔	↔
Dexmedetomidine	↔	↓	↔	↔	↔	↔	↔	↔	↔
Enflurane	↔	↔	↔	↔	↔	↔	↔	↔	↔
Ephedrine	↔	↔	↔	↔	↔	↔	↔	↔	↔
Etidocaine	↑	↑	↔	↔	↔	↔	↔	↓	↔
Halothane	↔	↔	↔	↔	↔	↔	↔	↔	↔
Isoflurane	↔	↔	↔	↔	↔	↔	↔	↔	↔
Ketamine	↑	↑	↔	↔	↔	↔	↔	↓	↔
Minaxolone	↑	↑	↔	↔	↔	↔	↔	↔	↔
Nitrous oxide	↔	↔	↔	↔	↔	↔	↔	↔	↔
Propofol	↔♥	↓♥	↔	↔	↔♥	↔♥	↔	↔	↔
Rocuronium	↑	↑	↔	↔	↔	↔	↔	↔	↔
Sevoflurane	↔♥	↔♥	↔	↔	↔♥	↔♥	↔	↔	↔
Sufentanil	↑	↑	↔	↔	↔	↔	↔	↓	↔
Suxamethonium (succinylcholine)	↔	↔	↔	↔	↔	↔	↔	↔	↔
Tetracaine	↔	↔	↔	↔	↔	↔	↔	↔	↔
Thiopental	↔	↔	↔	↔	↔	↔	↔	↔	↔
Tizanidine	↔♥	↓♥	↔	↔	↔♥	↔♥	↔	↔	↔
Vecuronium	↔	↔	↔	↔	↔	↔	↔	↔	↔

### Text Legend

- ↑ Potential increased exposure of the comedication
- ↓ Potential decreased exposure of the comedication
- ↑ Potential increased exposure of COVID drug
- ↓ Potential decreased exposure of COVID drug
- ↔ No significant effect

- ♥ One or both drugs may cause QT and/or PR prolongation. ECG monitoring is advised if coadministered.

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## Analgesics

	ATV	LPV/r	RDV	FAVI	CLQ	HCLQ	RBV	TCZ	IFN-β
Alfentanil	↑	↑	↔	↔	↔	↔	↔	↓	↔
Aspirin	↔	↔	↔	↔	↔	↔	↔	↔	↔
Buprenorphine	↑	↑ ~2%	↔	↔	↔	↔	↔	↓	↔
Celecoxib	↔	↔	↔	↔	↔	↔	↔	↔	↔
Codeine	↔	↑	↔	↔	↔	↔	↔	↔	↔
Dextropropoxyphene	↑	↑	↔	↔	↔♥	↔♥	↔	↓	↔
Diamorphine (diacetylmorphine)	↔	↓	↔	↔	↔	↔	↔	↔	↔
Diclofenac	↔	↔	↔	↔	↔	↔	↔	↔	↔
Dihydrocodeine	↑	↑↓	↔	↔	↔	↔	↔	↔	↔
Fentanyl	↑	↑	↔	↔	↔	↔	↔	↓	↔
Hydrocodone	↑↓	↑↓	↔	↔	↑	↑	↔	↔	↔
Hydromorphone	↔	↓	↔	↔	↔	↔	↔	↔	↔
Ibuprofen	↔	↔	↔	↔	↔	↔	↔	↔	↔
Mefenamic acid	↔	↔	↔	↔	↔	↔	↔	↔	↔
Metamizole	↑↓	↑↓	↓	↔	↓	↓	↔	↔	↔
Methadone	↔♥	↓53%♥	↔	↔	↔♥	↔♥	↔	↔	↔
Morphine	↔	↓	↔	↔	↔	↔	↔	↔	↔
Naproxen	↔	↔	↔	↔	↔	↔	↔	↔	↔
Nimesulide	↔	↔	↔	↔	↔	↔	↔	↔	↔
Oxycodone	↑	↑ 160%	↔	↔	↔	↔	↔	↓	↔
Paracetamol (Acetaminophen)	↔	↔	↔	↑14-16%	↔	↔	↔	↔	↔
Pethidine (Meperidine)	↑	↓	↔	↔	↔	↔	↔	↔	↔
Piroxicam	↔	↔	↔	↔	↔	↔	↔	↔	↔
Remifentanil	↔	↔	↔	↔	↔	↔	↔	↔	↔
Tapentadol	↔	↔	↔	↔	↔	↔	↔	↔	↔
Tramadol	↑	↑	↔	↔	↔	↔	↔	↔	↔

## Text Legend

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- ↓↓ Potential decreased exposure of COVID drug
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## Notes:

*Codeine and Tramadol + LPV/r*

Potential decrease of the analgesic effect due to the reduced conversion to the active metabolite.

*Diamorphine and Morphine + ATV*

No effect on systemic exposure but inhibition of P-gp by atazanavir at the blood-brain barrier could potentiate the opiate effect in the CNS.

*Diamorphine and Morphine + LPV/r*

Ritonavir could reduce systemic exposure of diamorphine and morphine due to induction of glucuronidation. Ritonavir also inhibits P-gp at the blood-brain barrier and could potentiate the opiate effect in the CNS.

*Hydrocodone + ATV or LPV/r*

Hydrocodone concentrations are increased, but concentrations of the metabolite hydromorphone (which has also analgesic activity) are reduced.

*Metamizole + CLQ, HCLQ, RBV, TCZ, IFN-β*

Coadministration should be avoided due to the increased risk of haematological toxicity.

*Paracetamol + FAVI*

The daily dose of paracetamol in adults should be no more than 3000 mg/day (rather than 4000 mg/day).

## Key to abbreviations

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## Antiarrhythmics

	ATV	LPV/r	RDV	FAVI	CLQ	HCLQ	RBV	TCZ	IFN-β
Amiodarone	↑♥	↑♥	↔	↔	↑♥	↑♥	↔	↓	↔
Bepidil	↑♥	↑♥	↔	↔	↑♥	↑♥	↔	↔	↔
Disopyramide	↑♥	↑♥	↔	↔	↔♥	↔♥	↔	↔	↔
Dofetilide	↑♥	↑♥	↔	↔	↔♥	↔♥	↔	↔	↔
Flecainide	↑♥	↑♥	↔	↔	↑♥	↑♥	↔	↔	↔
Lidocaine (Lignocaine)	↑	↑	↔	↔	↔	↔	↔	↔	↔
Mexiletine	↔	↑	↔	↔	↑♥	↑♥	↔	↔	↔
Propafenone	↑	↑	↔	↔	↔♥	↔♥	↔	↔	↔
Quinidine	↑	↑	↔	↔	↔♥	↔♥	↔	↓	↔

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## Notes:

### Amiodarone + LPV/r

The European product label for LPV/r contraindicates coadministration but the US product label suggests caution and concentration monitoring of amiodarone.

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## Antibacterials

	ATV	LPV/r	RDV	FAVI	CLQ	HCLQ	RBV	TCZ	IFN-β
Azithromycin	↑ ♥	↔ ♥	↔	↔	↔ ♥	↔ ♥	↔	↔	↔
Bedaquiline	↑ ♥	↑22% ♥	↔	↔	↔ ♥	↔ ♥	↔	↔	↔
Cefalexin	↔	↔	↔	↑	↔	↔	↔	↔	↔
Clarithromycin	↑↑ ♥	↑ ♥	↔	↔	↔ ♥	↔ ♥	↔	↔	↔
Clindamycin	↑	↑	↔	↔	↔	↔	↔	↔	↔
Clofazimine	↔ ♥	↔ ♥	↔	↔	↔ ♥	↔ ♥	↔	↔	↔
Delamanid	↑ ♥	↑ ♥	↔	↔	↔ ♥	↔ ♥	↔	↔	↔
Erythromycin	↑ ♥	↑ ♥	↔	↔	↔ ♥	↔ ♥	↔	↔	↔
Flucloxacillin	↔	↔	↔	↑	↔	↔	↔	↔	↔
Isoniazid	↔	↔	↔	↔	↔	↔	↔	↔	↔
Levofloxacin	↔ ♥	↔ ♥	↔	↔	↔ ♥	↔ ♥	↔	↔	↔
Linezolid	↔	↔	↔	↔	↔	↔	↔	↔	↔
Metronidazole	↔	↔	↔	↔	↔	↔	↔	↔	↔
Moxifloxacin	↑ ♥	↓ ♥	↔	↔	↔ ♥	↔ ♥	↔	↔	↔
Ofloxacin	↔ ♥	↔ ♥	↔	↔	↔ ♥	↔ ♥	↔	↔	↔
Penicillins	↔	↔	↔	↑	↔	↔	↔	↔	↔
Piperacillin	↔	↔	↔	↑	↔	↔	↔	↔	↔
Pyrazinamide	↔	↔	↔	↔	↔	↔	↔	↔	↔
Rifabutin	↑	↑	↓	↔	↓	↓	↔	↔	↔
Rifampicin	↓	↓75%	↓	↔	↓	↓	↔	↔	↔
Rifapentine	↓	↓	↓	↔	↓	↓	↔	↔	↔
Sulfadiazine	↔	↓	↔	↔	↔	↔	↔	↔	↔
Tazobactam	↔	↔	↔	↑	↔	↔	↔	↔	↔
Telithromycin	↑↑ ♥	↑↑ ♥	↔	↔	↔ ♥	↔ ♥	↔	↔	↔
Tinidazole	↑	↑	↔	↔	↔	↔	↔	↔	↔

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### Notes:

No interactions are expected with the COVID-19 therapies listed and the following antibacterials:

*amikacin, amoxicillin, ampicillin, capreomycin, cefazolin, cefixime, cefotaxime, ceftazidime, ceftriaxone, chloramphenicol, ciprofloxacin, clavulanic acid, cloxacillin, cycloserine, dapsone, doxycycline, ertapenem, ethambutol, ethionamide, gentamicin, imipenem/cilastatin, kanamycin, meropenem, nitrofurantoin, para-aminosalicylic acid, rifaximin, spectinomycin, streptomycin, tetracyclines, trimethoprim/sulfamethoxazole, vancomycin.*

#### Clarithromycin + ATV or LPV/r

A dose reduction of clarithromycin may be required for patients with impaired renal function. Refer to product labels for details.

#### Delamanid + ATV or LPV/r

Coadministration is expected to increase concentrations of DM-6705, a delamanid metabolite which is associated with QT prolongation. Frequent ECG monitoring is recommended.

#### Isoniazid + RBV

Use of isoniazid should be carefully monitored with patients with current chronic liver disease. Severe and sometimes fatal hepatitis associated with isoniazid therapy may occur and may develop even after many months of treatment.

#### Linezolid + RBV

Myelosuppression has been reported with both linezolid and ribavirin. Close monitoring of blood counts is recommended.

#### Linezolid + TCZ or IFN-β

Caution is required due to potential additive haematological toxicity.

#### Metronidazole and Tinidazole + LPV/r

No interaction is expected with lopinavir tablets. Coadministration is not recommended with lopinavir oral solution as it contains alcohol.

#### Pyrazinamide + FAVI

No effect on pyrazinamide concentrations but coadministration increased blood uric acid concentrations. Monitor uric acid.

### Key to abbreviations

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## Anti-coagulant, Anti-platelet and Fibrinolytic

	ATV	LPV/r	RDV	FAVI	CLQ	HCLQ	RBV	TCZ	IFN-β
Acenocoumarol	↔	↓	↔	↔	↔	↔	↔	↓	↔
Apixaban	↑	↑	↔	↔	↑	↑	↔	↓	↔
Argatroban	↔	↔	↔	↔	↔	↔	↔	↔	↔
Aspirin (anti-platelet)	↔	↔	↔	↔	↔	↔	↔	↔	↔
Betrixaban	↑♥	↑♥	↔	↔	↑	↑	↔	↔	↔
Clopidogrel	↓	↓	↔	↔	↔	↔	↔	↓	↔
Dabigatran	↑	↔ or ↓	↔	↔	↑	↑	↔	↔	↔
Dalteparin	↔	↔	↔	↔	↔	↔	↔	↔	↔
Dipyridamole	↑	↓	↔	↔	↔	↔	↔	↔	↔
Edoxaban	↑	↑	↔	↔	↑	↑	↔	↔	↔
Eltrombopag	↔	↓ 17%	↔	↔	↔	↔	↔	↔	↔
Enoxaparin	↔	↔	↔	↔	↔	↔	↔	↔	↔
Fondaparinux	↔	↔	↔	↔	↔	↔	↔	↔	↔
Heparin	↔	↔	↔	↔	↔	↔	↔	↔	↔
Phenprocoumon	↑	↑↓	↔	↔	↔	↔	↔	↓	↔
Prasugrel	↔	↔	↔	↔	↔	↔	↔	↓	↔
Rivaroxaban	↑	↑	↔	↔	↑	↑	↔	↓	↔
Streptokinase	↔	↔	↔	↔	↔	↔	↔	↔	↔
Ticagrelor	↑	↑	↔	↔	↔	↔	↔	↓	↔
Warfarin	↑	↓	↔	↔	↔	↔	↓	↓	↔

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### Notes:

#### Apixaban + LPV/r

The US product label for apixaban suggests to use apixaban at a reduced dose (2.5 mg twice daily) if needed.

#### Betrixaban + ATV or LPV/r

The US product label for betrixaban recommends for patients receiving or starting a strong P-gp inhibitor to reduce betrixaban dose and use an initial dose of 80 mg followed by 40 mg once daily.

#### Clopidogrel + ATV or LPV/r

Decreased conversion to active metabolite leading to non-responsiveness to clopidogrel. Prasugrel should be preferred to clopidogrel with ATV or LPV/r.

#### Edoxaban + ATV or LPV/r

The European product label for edoxaban states to consider a dose reduction of edoxaban from 60 mg to 30 mg with strong P-gp inhibitors, however, the US product label recommends no dose modification.

#### Prasugrel + ATV or LPV/r

Concentrations of active metabolite are reduced but without a significant reduction in prasugrel activity.

#### Vitamin K antagonists + ATV or LPV/r

Monitor INR with vitamin K antagonists (e.g., acenocoumarol, phenprocoumon, warfarin).

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## Anticonvulsants

	ATV	LPV/r	RDV	FAVI	CLQ	HCLQ	RBV	TCZ	IFN-β
Carbamazepine	↑↓	↑↓	↓	↔	↓	↓	↔	↓	↔
Clonazepam	↑	↑	↔	↔	↔	↔	↔	↔	↔
Eslicarbazepine	↓♥	↓♥	↓	↔	↓	↓	↔	↔	↔
Ethosuximide	↑	↑	↔	↔	↔	↔	↔	↔	↔
Gabapentin	↔	↔	↔	↔	↔	↔	↔	↔	↔
Lacosamide	↔♥	↔♥	↔	↔	↔	↔	↔	↔	↔
Lamotrigine	↔	↓ 50%	↔	↔	↔	↔	↔	↔	↔
Levetiracetam	↔	↔	↔	↔	↔	↔	↔	↔	↔
Oxcarbazepine	↓	↓	↓	↔	↓	↓	↔	↔	↔
Perampanel	↑	↑	↔	↔	↔	↔	↔	↔	↔
Phenobarbital (Phenobarbitone)	↓	↓	↓	↔	↓	↓	↔	↓	↔
Phenytoin	↓	↓	↓	↔	↓	↓	↔	↓	↔
Pregabalin	↔	↔	↔	↔	↔	↔	↔	↔	↔
Primidone	↓	↓↓	↓	↔	↓	↓	↔	↓	↔
Retigabine	↔	↔	↔	↔	↔	↔	↔	↔	↔
Rufinamide	↓	↓	↓	↔	↓	↓	↔	↔	↔
Sultiame	↑	↑	↔	↔	↔	↔	↔	↔	↔
Tiagabine	↑	↑	↔	↔	↔	↔	↔	↔	↔
Topiramate	↔	↔	↔	↔	↔	↔	↔	↔	↔
Valproate (Divalproex)	↔	↑ 38%	↔	↔	↔	↔	↔	↔	↔
Vigabatrin	↔	↔	↔	↔	↔	↔	↔	↔	↔
Zonisamide	↔	↔	↔	↔	↔	↔	↔	↔	↔

## Text Legend

- ↑ Potential increased exposure of the comedication
- ↓ Potential decreased exposure of the comedication
- ↑ Potential increased exposure of COVID drug
- ↓ Potential decreased exposure of COVID drug
- ↔ No significant effect

- ♥ One or both drugs may cause QT and/or PR prolongation. ECG monitoring is advised if coadministered.

Numbers refer to increase or decrease in AUC as observed in drug-drug interaction studies.

## Notes:

## Valproate + LPV/r

Case report of a 48% decrease in valproate concentration in previously stable patient who developed exacerbated mania on starting lopinavir/ritonavir; dose increase of valproate was required.

## Key to abbreviations

ATV	Atazanavir	CLQ	Chloroquine
LPV/r	Lopinavir/ritonavir	HCLQ	Hydroxychloroquine
RDV	Remdesivir	RBV	Ribavirin
FAVI	Favipiravir	TCZ	Tocilizumab
		IFN-β	Interferon beta

## Colour Legend

	These drugs should not be coadministered
	Potential interaction which may require a dose adjustment or close monitoring.
	Potential interaction likely to be of weak intensity. Additional action/monitoring or dosage adjustment unlikely to be required.
	No clinically significant interaction expected

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## Antidepressants

	ATV	LPV/r	RDV	FAVI	CLQ	HCLQ	RBV	TCZ	IFN-β
Agomelatine	↔	↓	↔	↔	↔	↔	↔	↔	↔
Amitriptyline	↔♥	↑♥	↔	↔	↑♥	↑♥	↔	↔	↔
Bupropion	↔	↓ 57%	↔	↔	↔	↔	↔	↔	↔
Citalopram	↑♥	↑♥	↔	↔	↔♥	↔♥	↔	↔	↔
Clomipramine	↑♥	↑♥	↔	↔	↔♥	↔♥	↔	↔	↔
Desipramine	↔♥	↑ 5%♥	↔	↔	↑♥	↑♥	↔	↔	↔
Doxepin	↔	↑	↔	↔	↔	↔	↔	↔	↔
Duloxetine	↔	↑↓	↔	↔	↑	↑	↔	↔	↔
Escitalopram	↑♥	↑♥	↔	↔	↔♥	↔♥	↔	↔	↔
Fluoxetine	↔	↑	↔	↔	↑	↑	↔	↔	↔
Fluvoxamine	↔	↑	↔	↔	↑	↑	↔	↔	↔
Imipramine	↑♥	↑♥	↔	↔	↔♥	↔♥	↔	↔	↔
Lithium	↔♥	↔♥	↔	↔	↔♥	↔♥	↔	↔	↔
Maprotiline	↔♥	↑♥	↔	↔	↑♥	↑♥	↔	↔	↔
Mianserin	↑	↑	↔	↔	↑	↑	↔	↔	↔
Milnacipran	↔	↔	↔	↔	↔	↔	↔	↔	↔
Mirtazapine	↑	↑	↔	↔	↑	↑	↔	↔	↔
Nefazodone	↑↑	↑	↔	↔	↔	↔	↔	↔	↔
Nortriptyline	↔♥	↑♥	↔	↔	↑♥	↑♥	↔	↔	↔
Paroxetine	↑↓?	↑↓?	↔	↔	↑	↑	↔	↔	↔
Phenelzine	↔	↔	↔	↔	↔	↔	↔	↔	↔
Reboxetine	↑	↑	↔	↔	↔	↔	↔	↔	↔
Sertraline	↑	↓	↔	↔	↔	↔	↔	↔	↔
St John's wort	↓	↓	↓	↔	↓	↓	↔	↔	↔
Tranlycypromine	↑	↑	↔	↔	↔	↔	↔	↔	↔
Trazodone	↑♥	↑♥	↔	↔	↔♥	↔♥	↔	↔	↔
Trimipramine	↔	↑	↔	↔	↑	↑	↔	↔	↔
Venlafaxine	↑	↑	↔	↔	↑	↑	↔	↔	↔
Vortioxetine	↔	↑	↔	↔	↑	↑	↔	↔	↔

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- ↑ Potential increased exposure of the comedication
- ↓ Potential decreased exposure of the comedication
- ↑↑ Potential increased exposure of COVID drug
- ↓↓ Potential decreased exposure of COVID drug
- ↔ No significant effect

♥ One or both drugs may cause QT and/or PR prolongation. ECG monitoring is advised if coadministered.

Numbers refer to increase or decrease in AUC as observed in drug-drug interaction studies.

### Key to abbreviations

ATV	Atazanavir	CLQ	Chloroquine
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### Colour Legend

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	Potential interaction which may require a dose adjustment or close monitoring.
	Potential interaction likely to be of weak intensity. Additional action/monitoring or dosage adjustment unlikely to be required.
	No clinically significant interaction expected



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## Anti-diabetics

	ATV	LPV/r	RDV	FAVI	CLQ	HCLQ	RBV	TCZ	IFN-β
Acarbose	↔	↔	↔	↔	↔	↔	↔	↔	↔
Canagliflozin	↔	↓	↔	↔	↔	↔	↔	↔	↔
Dapagliflozin	↔	↔	↔	↔	↔	↔	↔	↔	↔
Dulaglutide	↓	↔	↔	↔	↔	↔	↔	↔	↔
Empagliflozin	↔	↔	↔	↔	↔	↔	↔	↔	↔
Exanatide	↓	↔	↔	↔	↔	↔	↔	↔	↔
Glibenclamide (Glyburide)	↑	↑	↔	↔	↔	↔	↔	↔	↔
Gliclazide	↔	↓	↔	↔	↔	↔	↔	↔	↔
Glimepiride	↔	↓	↔	↔	↔	↔	↔	↔	↔
Glipizide	↔	↓	↔	↔	↔	↔	↔	↔	↔
Insulin	↔	↔	↔	↔	↔	↔	↔	↔	↔
Linagliptin	↔	↑	↔	↔	↔	↔	↔	↔	↔
Liraglutide	↓	↔	↔	↔	↔	↔	↔	↔	↔
Metformin	↔	↔	↔	↔	↔	↔	↔	↔	↔
Nateglinide	↑	↑↓	↔	↔	↔	↔	↔	↔	↔
Pioglitazone	↑	↑	↔	↑	↔	↔	↔	↔	↔
Repaglinide	↑	↑	↔	↑ 52%	↔	↔	↔	↔	↔
Rosiglitazone	↔	↓	↔	↑	↔	↔	↔	↔	↔
Saxagliptin	↑	↑	↔	↔	↔	↔	↔	↔	↔
Sitagliptin	↑	↑	↔	↔	↔	↔	↔	↔	↔
Tolbutamide	↔	↓	↔	↔	↔	↔	↔	↔	↔
Vildagliptin	↔	↔	↔	↔	↔	↔	↔	↔	↔

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- ↓ Potential decreased exposure of COVID drug
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Numbers refer to increase or decrease in AUC as observed in drug-drug interaction studies.

### Notes:

#### Canagliflozin +LPV/r

If coadministration is deemed necessary, increasing canagliflozin to 300 mg once daily may be considered if patients are currently tolerating canagliflozin 100 mg once daily, have an eGFR ≥60 mL/min/1.73m<sup>2</sup> or CrCl ≥60 mL/min, and require additional glycaemic control. Other glucose-lowering therapies should be considered for patients with an eGFR 45 mL/min/1.73m<sup>2</sup> to <60 mL/min/1.73m<sup>2</sup> or CrCl 45 mL/min to <60 mL/min taking canagliflozin 100 mg who are receiving concurrent therapy with a UGT enzyme inducer and who require additional glycaemic control.

#### Linagliptin + LPV/r

The increase in linagliptin exposure is not considered clinically significant as it is mainly eliminated unchanged and has a large safety window.

#### Saxagliptin + ATV or LPV/r:

The US product label for saxagliptin states the recommended dose of saxagliptin to be 2.5 mg once daily when coadministered with strong CYP3A4/5 inhibitors.

#### Sitagliptin + ATV or LPV/r

The increase in sitagliptin exposure is not considered clinically significant as it is mainly eliminated unchanged and has a large safety window.

### Key to abbreviations

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RDV	Remdesivir	RBV	Ribavirin
FAVI	Favipiravir	TCZ	Tocilizumab
		IFN-β	Interferon beta

### Colour Legend

Red	These drugs should not be coadministered
Orange	Potential interaction which may require a dose adjustment or close monitoring.
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Green	No clinically significant interaction expected

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## Antifungals

	ATV	LPV/r	RDV	FAVI	CLQ	HCLQ	RBV	TCZ	IFN-β
Amphotericin B	↔	↔	↔	↔	↔	↔	↔	↔	↔
Anidulafungin	↔	↔	↔	↔	↔	↔	↔	↔	↔
Caspofungin	↑	↔	↔	↔	↔	↔	↔	↔	↔
Fluconazole	↔	↔	↔	↔	↑	↑	↔	↔	↔
Flucytosine	↔	↔	↔	↔	↔	↔	↔	↔	↔
Griseofulvin	↓	↓	↔	↔	↓	↓	↔	↔	↔
Isavuconazole	↑	↑ 96%	↔	↔	↑	↑	↔	↔	↔
Itraconazole	↑	↑	↔	↔	↑	↑	↔	↔	↔
Ketoconazole	↑	↑	↔	↔	↑	↑	↔	↔	↔
Micafungin	↔	↔	↔	↔	↔	↔	↔	↔	↔
Miconazole	↔	↔	↔	↔	↔	↔	↔	↔	↔
Nystatin	↔	↔	↔	↔	↔	↔	↔	↔	↔
Posaconazole	↑ 270%	↑	↔	↔	↑	↑	↔	↔	↔
Terbinafine	↑	↑	↔	↔	↔	↔	↔	↔	↔
Voriconazole	↓↓	↑↓↑	↔	↔	↑	↑	↔	↔	↔

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- ↑ Potential increased exposure of COVID drug
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- ↔ No significant effect

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Numbers refer to increase or decrease in AUC as observed in drug-drug interaction studies.

### Notes:

#### Griseofulvin + LPV/r

LPV/r oral solution contains alcohol. Consumption of alcohol in association with griseofulvin can result in a 'disulfiram-like' type reaction. No such interaction is expected with LPV/r tablets.

#### Itraconazole or Ketoconazole + ATV or LPV/r

The daily dose of itraconazole or ketoconazole should not exceed 200 mg.

#### Voriconazole + ATV

The effect of atazanavir on voriconazole exposure is dependent on CYP2C19 metaboliser status. In the majority of patients decreases in both voriconazole and atazanavir exposures may be expected, leading to loss of therapeutic effect and possible development of resistance. The European SmPC for atazanavir recommends a patient's CYP2C19 genotype should be performed if feasible. In patients without a functional CYP2C19 allele, increased voriconazole exposures are expected.

#### Voriconazole + LPV/r

Coadministration may result in bidirectional interactions leading to increased concentrations of lopinavir/ritonavir and an increase or decrease in voriconazole. Administration of voriconazole with ritonavir (100 mg twice daily) decreased voriconazole AUC by 39%.

### Key to abbreviations

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## Anti-hypertensives – ACE inhibitors

	ATV	LPV/r	RDV	FAVI	CLQ	HCLQ	RBV	TCZ	IFN-β
Benazepril	↑	↔	↔	↔	↔	↔	↔	↔	↔
Captopril	↔	↔	↔	↔	↔	↔	↔	↔	↔
Cilazapril	↔	↔	↔	↔	↔	↔	↔	↔	↔
Enalapril	↔	↔	↔	↔	↔	↔	↔	↔	↔
Fosinopril	↔	↑	↔	↔	↔	↔	↔	↔	↔
Lisinopril	↔	↔	↔	↔	↔	↔	↔	↔	↔
Perindopril	↔	↔	↔	↔	↔	↔	↔	↔	↔
Quinapril	↔	↔	↔	↔	↔	↔	↔	↔	↔
Ramipril	↔	↔	↔	↔	↔	↔	↔	↔	↔
Trandolapril	↔	↔	↔	↔	↔	↔	↔	↔	↔

## Anti-hypertensives – Angiotensin antagonists

	ATV	LPV/r	RDV	FAVI	CLQ	HCLQ	RBV	TCZ	IFN-β
Candesartan	↔	↔	↔	↔	↔	↔	↔	↔	↔
Eprosartan	↔	↔	↔	↔	↔	↔	↔	↔	↔
Irbesartan	↔	↓	↔	↔	↔	↔	↔	↔	↔
Losartan	↔	↓	↔	↔	↔	↔	↔	↔	↔
Olmесartan	↔	↔	↔	↔	↔	↔	↔	↔	↔
Telmisartan	↔	↔	↔	↔	↔	↔	↔	↔	↔
Valsartan	↑	↑	↔	↔	↔	↔	↔	↔	↔

## Anti-hypertensives – Diuretics

	ATV	LPV/r	RDV	FAVI	CLQ	HCLQ	RBV	TCZ	IFN-β
Amiloride	↔	↔	↔	↔	↔	↔	↔	↔	↔
Bendroflumethiazide	↔	↔	↔	↔	↔	↔	↔	↔	↔
Chlortalidone	↔	↔	↔	↔	↔	↔	↔	↔	↔
Furosemide	↔	↔	↔	↔	↔	↔	↔	↔	↔
Hydrochlorothiazide	↔	↔	↔	↔	↔	↔	↔	↔	↔
Indapamide	↑	↑	↔	↔	↔	↔	↔	↔	↔
Metolazone	↔	↔	↔	↔	↔	↔	↔	↔	↔
Torasemide	↔	↓	↔	↔	↔	↔	↔	↔	↔
Xipamide	↔	↔	↔	↔	↔	↔	↔	↔	↔

## Text Legend

- ↑ Potential increased exposure of the comedication
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- ↑ Potential increased exposure of COVID drug
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## Anti-hypertensives – Other agents

	ATV	LPV/r	RDV	FAVI	CLQ	HCLQ	RBV	TCZ	IFN-β
Aliskiren	↑	↑	↔	↔	↔	↔	↔	↔	↔
Clonidine	↔	↔	↔	↔	↔	↔	↔	↔	↔
Digoxin	↑♥	↑♥	↔	↔	↑	↑	↔	↔	↔
Dopamine	↔	↔	↔	↔	↔	↔	↔	↔	↔
Doxazosin	↑	↑	↔	↔	↔	↔	↔	↔	↔
Eplerenone	↑	↑	↔	↔	↔	↔	↔	↔	↔
Hydralazine	↔	↔	↔	↔	↔	↔	↔	↔	↔
Isosorbide dinitrate	↑	↑	↔	↔	↔	↔	↔	↔	↔
Ivabradine	↑	↑	↔	↔	↔♥	↔♥	↔	↔	↔
Labetalol	↑	↓	↔	↔	↔	↔	↔	↔	↔
Lacidipine	↑♥	↑♥	↔	↔	↔	↔	↔	↔	↔
Lercanidipine	↑	↑	↔	↔	↔	↔	↔	↔	↔
Methyldopa	↔	↔	↔	↔	↔	↔	↔	↔	↔
Moxonidine	↔	↔	↔	↑	↔	↔	↔	↔	↔
Prazosin	↑	↑	↔	↔	↔	↔	↔	↔	↔
Ranolazine	↑	↑	↔	↔	↔♥	↔♥	↔	↔	↔
Sacubitril	↑	↑	↔	↔	↔	↔	↔	↔	↔
Sodium nitroprusside	↔	↔	↔	↔	↔	↔	↔	↔	↔
Spirolactone	↔	↔	↔	↔	↔	↔	↔	↔	↔
Terazosin	↑	↑	↔	↔	↔	↔	↔	↔	↔

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### Notes:

#### Doxazosin + ATV or LPV/r

For patients already taking doxazosin, monitor blood pressure and reduce doxazosin dose as needed if hypotension occurs on starting ATV or LPV/r.

#### Isosorbide nitrate + ATV or LPV/r

Decreased active metabolite.

#### Sacubitril + ATV or LPV/r

Increased active metabolite.

#### Terazosin + ATV or LPV/r

For patients already taking terazosin, monitor blood pressure and reduce terazosin dose as needed if hypotension occurs on starting ATV or LPV/r.

### Key to abbreviations

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## Anti-hypertensives – Pulmonary hypertension

	ATV	LPV/r	RDV	FAVI	CLQ	HCLQ	RBV	TCZ	IFN-β
Ambrisentan	↑	↑	↔	↔	↔	↔	↔	↔	↔
Bosentan	↑↓	↑	↓	↔	↔	↔	↔	↔	↔
Epoprostenol	↔	↔	↔	↔	↔	↔	↔	↔	↔
Iloprost	↔	↔	↔	↔	↔	↔	↔	↔	↔
Macitentan	↑	↑	↔	↔	↔	↔	↔	↔	↔
Riociguat	↑	↑	↔	↔	↔	↔	↔	↔	↔
Selexipag	↔	↔	↔	↔	↔	↔	↔	↔	↔
Sildenafil	↑	↑	↔	↔	↔	↔	↔	↔	↔
Tadalafil	↑	↑	↔	↔	↔	↔	↔	↔	↔
Treprostinil	↔	↔	↔	↑	↔	↔	↔	↔	↔

## Text Legend

- ↑ Potential increased exposure of the comedication
- ↓ Potential decreased exposure of the comedication
- ↑ Potential increased exposure of COVID drug
- ↓ Potential decreased exposure of COVID drug
- ↔ No significant effect

- ♥ One or both drugs may cause QT and/or PR prolongation. ECG monitoring is advised if coadministered.

Numbers refer to increase or decrease in AUC as observed in drug-drug interaction studies.

## Notes:

**Ambrisentan + ATV or LPV/r**

Start ambrisentan at 5 mg and closely monitor the patient for tolerability.

**Bosentan + LPV/r**

When coadministered patients should be closely observed for bosentan toxicity, especially during the first week of co-administration. For patients on bosentan, the US product label for LPV/r suggests to discontinue bosentan at least 36 hours prior to initiation of LPV/r and after at least 10 days of LPV/r, to resume bosentan at 62.5 mg once daily or every other day based upon individual tolerability.

**Riociguat + ATV or LPV/r**

The European product label for riociguat does not recommend its use in presence of strong inhibitors of CYPs, P-gp and BCRP; the US product label recommends to start riociguat at a dose of 0.5 mg three times daily and to monitor for signs and symptoms of hypotension.

**Tadalafil + ATV**

The US product label for ATV suggests for patients receiving atazanavir for at least one week, to start tadalafil at 20 mg once daily and increase to 40 mg once daily based on individual tolerability. For patients on tadalafil, avoid the use of tadalafil when starting atazanavir. Stop tadalafil at least 24 hours before starting atazanavir. At least one week after starting atazanavir, resume tadalafil at 20 mg once daily and increase to 40 mg once daily based on individual tolerability.

**Tadalafil + LPV/r**

The European product label for LPV/r does not recommend tadalafil for the treatment of pulmonary arterial hypertension, but the US product label suggests for patients on tadalafil, to avoid use of tadalafil during the initiation of LPV/r and to stop tadalafil at least 24 hours prior to starting LPV/r. After at least one week following the initiation of LPV/r, resume tadalafil at 20 mg once daily. Increase to 40 mg once daily based upon individual tolerability.

## Key to abbreviations

ATV	Atazanavir	CLQ	Chloroquine
LPV/r	Lopinavir/ritonavir	HCLQ	Hydroxychloroquine
RDV	Remdesivir	RBV	Ribavirin
FAVI	Favipiravir	TCZ	Tocilizumab
		IFN-β	Interferon beta

## Colour Legend

	These drugs should not be coadministered
	Potential interaction which may require a dose adjustment or close monitoring.
	Potential interaction likely to be of weak intensity. Additional action/monitoring or dosage adjustment unlikely to be required.
	No clinically significant interaction expected

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## Antipsychotics/Neuroleptics

	ATV	LPV/r	RDV	FAVI	CLQ	HCLQ	RBV	TCZ	IFN-β
Amisulpride	↔	↔	↔	↔	↔	↔	↔	↔	↔
Aripiprazole	↑	↑	↔	↔	↔	↔	↔	↔	↔
Asenapine	↑	↓	↔	↔	↔	↔	↔	↔	↔
Chlorpromazine	↔♥	↑♥	↔	↔	↑♥	↑♥	↔	↔	↔
Clozapine	↑♥	↑♥	↔	↔	↔♥	↔♥	↔	↔	↔
Fluphenazine	↔♥	↑♥	↔	↔	↑♥	↑♥	↔	↔	↔
Haloperidol	↑♥	↑♥	↔	↔	↔♥	↔♥	↔	↔	↔
Iloperidone	↑♥	↑♥	↔	↔	↔♥	↔♥	↔	↔	↔
Levomepromazine	↔♥	↑♥	↔	↔	↑♥	↑♥	↔	↔	↔
Olanzapine	↔	↓	↔	↔	↔	↔	↔	↔	↔
Paliperidone	↑	↑	↔	↔	↔	↔	↔	↔	↔
Perazine	↑	↑	↔	↔	↔	↔	↔	↔	↔
Periciazine	↑	↑	↔	↔	↔	↔	↔	↔	↔
Perphenazine	↑♥	↑♥	↔	↔	↑♥	↑♥	↔	↔	↔
Pimozide	↑♥	↑♥	↔	↔	↔♥	↔♥	↔	↔	↔
Pipotiazine	↔♥	↑♥	↔	↔	↔♥	↔♥	↔	↔	↔
Quetiapine	↑♥	↑♥	↔	↔	↔♥	↔♥	↔	↔	↔
Risperidone	↑♥	↑♥	↔	↔	↑♥	↑♥	↔	↔	↔
Sulpiride	↔♥	↔♥	↔	↔	↔♥	↔♥	↔	↔	↔
Thioridazine	↑♥	↑♥	↔	↔	↑♥	↑♥	↔	↔	↔
Tiapride	↔♥	↔♥	↔	↔	↔♥	↔♥	↔	↔	↔
Ziprasidone	↑♥	↑♥	↔	↔	↔♥	↔♥	↔	↔	↔
Zotepine	↑♥	↑♥	↔	↔	↔♥	↔♥	↔	↔	↔
Zuclopenthixol	↑♥	↑♥	↔	↔	↑♥	↑♥	↔	↔	↔

## Text Legend

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- ↑ Potential increased exposure of COVID drug
- ↓ Potential decreased exposure of COVID drug
- ↔ No significant effect

- ♥ One or both drugs may cause QT and/or PR prolongation. ECG monitoring is advised if coadministered.

Numbers refer to increase or decrease in AUC as observed in drug-drug interaction studies.

## Notes:

**Clozapine + RBV, CLQ or HCLQ**

The risk of haematological toxicity may be potentially increased as clozapine, ribavirin, chloroquine and hydroxychloroquine can cause myelosuppression. Closely monitor haematological parameters.

**Clozapine + TCZ or IFN-β**

Caution is required due to potential additive haematological toxicity.

**Quetiapine + ATV or LPV/r**

Coadministration contraindicated in the European product label for quetiapine, however, US product label recommends quetiapine should be reduced to one sixth of the original dose if coadministered with a potent CYP3A4 inhibitor.

## Key to abbreviations

ATV	Atazanavir	CLQ	Chloroquine
LPV/r	Lopinavir/ritonavir	HCLQ	Hydroxychloroquine
RDV	Remdesivir	RBV	Ribavirin
FAVI	Favipiravir	TCZ	Tocilizumab
		IFN-β	Interferon beta

## Colour Legend

Red	These drugs should not be coadministered
Orange	Potential interaction which may require a dose adjustment or close monitoring.
Yellow	Potential interaction likely to be of weak intensity. Additional action/monitoring or dosage adjustment unlikely to be required.
Green	No clinically significant interaction expected

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## Antivirals – Covid-19 therapies

	ATV	LPV/r	RDV	FAVI	CLQ	HCLQ	RBV	TCZ	IFN-β
Atazanavir		✗	↔	↔	↑♥	↑♥	↔	↔	↔
Lopinavir/ritonavir	✗		↔	↔	↑♥	↑♥	↔	↔	↔
Remdesivir	↔	↔		↔	↔	↔	↔	↔	↔
Favipiravir	↔	↔	↔		↔	↔	↔	↔	↔
Chloroquine	↑♥	↑♥	↔	↔		✗	↔	↔	↔
Hydroxychloroquine	↑♥	↑♥	↔	↔	✗		↔	↔	↔
Ribavirin	↔	↔	↔	↔	↔	↔		↔	↔
Tocilizumab	↔	↔	↔	↔	↔	↔			↔
Interferon beta-1a	↔	↔	↔	↔	↔	↔	↔	↔	

## Text Legend

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- ↓ Potential decreased exposure of COVID drug
- ↔ No significant effect

- ♥ One or both drugs may cause QT and/or PR prolongation. ECG monitoring is advised if coadministered.

Numbers refer to increase or decrease in AUC as observed in drug-drug interaction studies.

## Notes:

## ATV + LPV/r

These drugs are not intended to be combined for the treatment of COVID-19.

## CLQ + HCLQ

Chloroquine and hydroxychloroquine should not be coadministered.

## CLQ or HCLQ + LPV/r

LPV/r may increase concentrations of chloroquine or hydroxychloroquine, but to a moderate extent. Since LPV/r and chloroquine or hydroxychloroquine can cause QT prolongation, ECG monitoring is recommended when coadministering these agents.

## CLQ or HCLQ + RBV, TCZ or IFN-β

Use with caution due to potential additive toxicity.

## RBV + TCZ

The risk of haematological toxicity may be potentially increased as ribavirin and tocilizumab can cause myelosuppression. Closely monitor haematological parameters.

## TCZ + IFN-β

Use with caution due to increased risk of haematological toxicity.

## Key to abbreviations

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LPV/r	Lopinavir/ritonavir	HCLQ	Hydroxychloroquine
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## Antivirals – HCV DDAs

	ATV	LPV/r	RDV	FAVI	CLQ	HCLQ	RBV	TCZ	IFN-β
Elbasvir/Grazoprevir	↑*	↑*	↔	↔	↔	↔	↔	↔	↔
Glecaprevir/Pibrentasvir	↑*	↑*	↔	↔	↔	↔	↔	↔	↔
Ledipasvir/Sofosbuvir	↔	↔	↔	↔	↔	↔	↔	↔	↔
Ombitasvir/Paritaprevir/r	↑	↑*	↔	↔	↑	↑	↔	↔	↔
Ombitasvir/Paritaprevir/r + Dasabuvir	↑	↑*	↔	↑	↑	↑	↔	↔	↔
Sofosbuvir	↔	↔	↔	↔	↔	↔	↔	↔	↔
Sofosbuvir/Velpatasvir	↔	↔	↔	↑	↔	↔	↔	↔	↔
Sofosbuvir/Velpatasvir/Voxilaprevir	↑*	↑*	↔	↑	↔	↔	↔	↔	↔

### Text Legend

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- ↑ Potential increased exposure of COVID drug
- ↓ Potential decreased exposure of COVID drug
- ↔ No significant effect

- ♥ One or both drugs may cause QT and/or PR prolongation. ECG monitoring is advised if coadministered.

Numbers refer to increase or decrease in AUC as observed in drug-drug interaction studies.

### Notes:

- \* Increased risk of ALT elevations due to an expected or observed significant increase in DAA concentrations.

#### All DAAs + CLQ and HCLQ

The product labels for chloroquine and hydroxychloroquine recommend caution in impaired hepatic function.

#### Ledipasvir/sofosbuvir + LPV/r

Case reports of possible interaction between ledipasvir and LPV with patients having drug-induced liver injury manifesting as significant bilirubin rise within two weeks of starting ledipasvir/sofosbuvir while on LPV-containing HIV regimens.

#### Ombitasvir/Paritaprevir/r + ATV

Paritaprevir AUC increased by 187%. Exposures of paritaprevir greater than this have been evaluated in phase 2 studies and were not expected to have a clinically meaningful impact on safety.

#### Ombitasvir/Paritaprevir/r + Dasabuvir + ATV

Paritaprevir AUC increased by 94%. Exposures of paritaprevir greater than this have been evaluated in phase 2 studies and were not expected to have a clinically meaningful impact on safety. However, the combination carries an increased risk for hyperbilirubinaemia (including ocular icterus), particularly when ribavirin is also prescribed.

#### Ombitasvir/Paritaprevir/r + Dasabuvir + FAVI

Coadministration may increase dasabuvir concentrations. However, due to dasabuvir's large therapeutic index, a clinically relevant effect is not anticipated.

#### Ombitasvir/Paritaprevir/r ± Dasabuvir + CLQ

Inhibition of CYP3A4 by ritonavir may decrease exposure to chloroquine active metabolites, but this may not affect overall activity. No a priori dose alteration for chloroquine is recommended.

#### Ombitasvir/Paritaprevir/r ± Dasabuvir + HCLQ

Inhibition of CYP3A4 by ritonavir may decrease exposure to hydroxychloroquine, although to a moderate extent due to the multiple elimination pathways. No dose alteration is required.

#### Sofosbuvir/Velpatasvir + FAVI

Coadministration may increase velpatasvir concentrations. However, due to velpatasvir's large therapeutic index, a clinically relevant effect is not anticipated.

#### Sofosbuvir/Velpatasvir/Voxilaprevir + FAVI

Coadministration may increase velpatasvir concentrations. However, due to velpatasvir's large therapeutic index, a clinically relevant effect is not anticipated.

### Key to abbreviations

ATV	Atazanavir	CLQ	Chloroquine
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FAVI	Favipiravir	TCZ	Tocilizumab
		IFN-β	Interferon beta

### Colour Legend

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	Potential interaction which may require a dose adjustment or close monitoring.
	Potential interaction likely to be of weak intensity. Additional action/monitoring or dosage adjustment unlikely to be required.
	No clinically significant interaction expected



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## Antivirals – Others

	ATV	LPV/r	RDV	FAVI	CLQ	HCLQ	RBV	TCZ	IFN-β
Oseltamivir	↔	↔	↔	↑ 14%	↔	↔	↔	↔	↔

### Text Legend

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- ↑ Potential increased exposure of COVID drug
- ↓ Potential decreased exposure of COVID drug
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- ♥ One or both drugs may cause QT and/or PR prolongation. ECG monitoring is advised if coadministered.

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### Key to abbreviations

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## Anxiolytics/Hypnotics/Sedatives

	ATV	LPV/r	RDV	FAVI	CLQ	HCLQ	RBV	TCZ	IFN-β
Alprazolam	↑	↑	↔	↔	↔	↔	↔	↔	↔
Bromazepam	↑	↑	↔	↔	↔	↔	↔	↔	↔
Buspirone	↑	↑	↔	↔	↔	↔	↔	↔	↔
Chlordiazepoxide	↑	↑	↔	↔	↔	↔	↔	↔	↔
Clobazam	↑	↑	↔	↔	↔	↔	↔	↔	↔
Clorazepate	↑	↑	↔	↔	↔	↔	↔	↔	↔
Diazepam	↑	↑	↔	↔	↔	↔	↔	↔	↔
Estazolam	↑	↑	↔	↔	↔	↔	↔	↔	↔
Flunitrazepam	↑	↑	↔	↔	↔	↔	↔	↔	↔
Flurazepam	↑	↑	↔	↔	↔	↔	↔	↔	↔
Hydroxyzine	↑♥	↑♥	↔	↔	↔♥	↔♥	↔	↔	↔
Lorazepam	↔	↔	↔	↔	↔	↔	↔	↔	↔
Lormetazepam	↔	↔	↔	↔	↔	↔	↔	↔	↔
Midazolam (oral)	↑	↑	↔	↔	↔	↔	↔	↔	↔
Midazolam (parenteral)	↑	↑	↔	↔	↔	↔	↔	↔	↔
Oxazepam	↔	↔	↔	↔	↔	↔	↔	↔	↔
Temazepam	↔	↔	↔	↔	↔	↔	↔	↔	↔
Triazolam	↑	↑	↔	↔	↔	↔	↔	↔	↔
Zaleplon	↑	↑	↔	↔	↔	↔	↔	↔	↔
Zolpidem	↑	↑	↔	↔	↔	↔	↔	↔	↔
Zopiclone	↑	↑	↔	↔	↔	↔	↔	↔	↔

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## Beta Blockers

	ATV	LPV/r	RDV	FAVI	CLQ	HCLQ	RBV	TCZ	IFN-β
Atenolol	↔♥	↔♥	↔	↔	↔	↔	↔	↔	↔
Bisoprolol	↑♥	↑♥	↔	↔	↔	↔	↔	↔	↔
Carvedilol	↑♥	↑↓♥	↔	↔	↔	↔	↔	↔	↔
Metoprolol	↔♥	↑♥	↔	↔	↔♥	↔♥	↔	↔	↔
Nebivolol	↔♥	↑♥	↔	↔	↔♥	↔♥	↔	↔	↔
Oxprenolol	↑♥	↓♥	↔	↔	↔	↔	↔	↔	↔
Pindolol	↔♥	↑♥	↔	↔	↔	↔	↔	↔	↔
Propranolol	↔♥	↑♥	↔	↔	↔♥	↔♥	↔	↔	↔
Timolol	↔♥	↑♥	↔	↔	↔♥	↔♥	↔	↔	↔

## Text Legend

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## Bronchodilators

	ATV	LPV/r	RDV	FAVI	CLQ	HCLQ	RBV	TCZ	IFN-β
Acidinium bromide	↔	↔	↔	↔	↔	↔	↔	↔	↔
Aminophylline	↔	↓	↔	↔	↔	↔	↔	↓	↑
Formoterol	↔♥	↔♥	↔	↔	↔	↔	↔	↔	↔
Glycopyrronium bromide	↔	↔	↔	↔	↔	↔	↔	↔	↔
Indacaterol	↑	↑	↔	↔	↔	↔	↔	↔	↔
Ipratropium bromide	↔	↔	↔	↔	↔	↔	↔	↔	↔
Montelukast	↑	↑	↔	↑	↔	↔	↔	↔	↔
Olodaterol	↑	↑	↔	↔	↔	↔	↔	↔	↔
Roflumilast	↑	↑	↔	↔	↔	↔	↔	↔	↔
Salbutamol	↔	↔	↔	↔	↔	↔	↔	↔	↔
Salmeterol	↑	↑	↔	↔	↔♥	↔♥	↔	↔	↔
Theophylline	↔	↓	↔	↑17-27%	↔	↔	↔	↓	↑
Tiotropium bromide	↔	↔	↔	↔	↔	↔	↔	↔	↔
Umeclidinium bromide	↑	↑	↔	↔	↑	↑	↔	↔	↔
Vilanterol	↑	↑	↔	↔	↔	↔	↔	↔	↔

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## Notes:

**Aminophylline + TCZ**

Aminophylline is a complex of theophylline and ethylenediamine and is given for its theophylline activity. Co-administration may decrease theophylline concentrations.

**Aminophylline or theophylline + IFN-β**

Co-administration may increase theophylline concentrations but this is unlikely to be clinically significant. (Aminophylline is a complex of theophylline and ethylenediamine and is given for its theophylline activity.)

**Indacaterol + ATV or LPV/r**

Exposure can be increased by up to 2-fold with ritonavir (and may be similar with atazanavir), however, this increase does not raise any concerns based on indacaterol's safety data.

## Key to abbreviations

ATV	Atazanavir	CLQ	Chloroquine
LPV/r	Lopinavir/ritonavir	HCLQ	Hydroxychloroquine
RDV	Remdesivir	RBV	Ribavirin
FAVI	Favipiravir	TCZ	Tocilizumab
		IFN-β	Interferon beta

## Colour Legend

	These drugs should not be coadministered
	Potential interaction which may require a dose adjustment or close monitoring.
	Potential interaction likely to be of weak intensity. Additional action/monitoring or dosage adjustment unlikely to be required.
	No clinically significant interaction expected

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## Calcium Channel Blockers

	ATV	LPV/r	RDV	FAVI	CLQ	HCLQ	RBV	TCZ	IFN-β
Amlodipine	↑♥	↑♥	↔	↔	↔	↔	↔	↔	↔
Diltiazem	↑125%♥	↑♥	↔	↔	↔	↔	↔	↔	↔
Felodipine	↑♥	↑♥	↔	↔	↔	↔	↔	↔	↔
Nicardipine	↑♥	↑♥	↔	↔	↔	↔	↔	↔	↔
Nifedipine	↑♥	↑♥	↔	↔	↔	↔	↔	↔	↔
Nisoldipine	↑♥	↑♥	↔	↔	↔	↔	↔	↔	↔
Nitrendipine	↑♥	↑♥	↔	↔	↔	↔	↔	↔	↔
Verapamil	↑♥	↑♥	↔	↔	↑	↑	↔	↔	↔

## Text Legend

- ↑ Potential increased exposure of the comedication
- ↓ Potential decreased exposure of the comedication
- ↑ Potential increased exposure of COVID drug
- ↓ Potential decreased exposure of COVID drug
- ↔ No significant effect

- ♥ One or both drugs may cause QT and/or PR prolongation. ECG monitoring is advised if coadministered.

Numbers refer to increase or decrease in AUC as observed in drug-drug interaction studies.

## Notes:

*Amlodipine + LPV/r*

If coadministration is indicated, consider a dose reduction for amlodipine of 50%.

*Diltiazem + ATV*

If coadministration is indicated, an initial dose reduction of diltiazem by 50% is recommended, with subsequent titration as needed and ECG monitoring.

## Key to abbreviations

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## Contraceptives

	ATV	LPV/r	RDV	FAVI	CLQ	HCLQ	RBV	TCZ	IFN-β
Desogestrel (COC)	↑	↑	↔	↑	↔	↔	↔	↔	↔
Desogestrel (POP)	↑	↑	↔	↑	↔	↔	↔	↔	↔
Drospirenone (COC)	↑	↑	↔	↑	↔	↔	↔	↔	↔
Ethinylestradiol	↑ 48%	↓ 42%	↔	↑ 43%	↔	↔	↔	↔	↔
Etonogestrel (implant)	↑	↑ 52%	↔	↑	↔	↔	↔	↔	↔
Etonogestrel (vaginal ring)	↑	↑	↔	↑	↔	↔	↔	↔	↔
Gestodene (COC)	↑	↑	↔	↑	↔	↔	↔	↔	↔
Levonorgestrel (COC)	↑	↑	↔	↑	↔	↔	↔	↔	↔
Levonorgestrel (emergency con.)	↑	↑	↔	↑	↔	↔	↔	↔	↔
Levonorgestrel (implant)	↑	↑	↔	↑	↔	↔	↔	↔	↔
Levonorgestrel (IUD)	↔	↔	↔	↔	↔	↔	↔	↔	↔
Levonorgestrel (POP)	↑	↑	↔	↑	↔	↔	↔	↔	↔
Medroxyprogesterone (depot inj)	↔	↑ 70%	↔	↔	↔	↔	↔	↔	↔
Norelgestromin (patch)	↑	↑ 83%	↔	↑	↔	↔	↔	↔	↔
Norethisterone (COC)	↑ 110%	↓ 17%	↔	↑ 47%	↔	↔	↔	↔	↔
Norethisterone (IM depot)	↔	↔	↔	↑	↔	↔	↔	↔	↔
Norethisterone(POP)	↑	↑	↔	↑	↔	↔	↔	↔	↔
Norgestimate (COC)	↑	↑	↔	↑	↔	↔	↔	↔	↔
Norgestrel (COC)	↑	↑	↔	↑	↔	↔	↔	↔	↔
Ulipristal	↑	↑	↔	↑	↔	↔	↔	↔	↔

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Numbers refer to increase or decrease in AUC as observed in drug-drug interaction studies.

### Notes:

COC – Combined oral contraceptive; POP – Progestogen only pill; IUD – Intra-uterine device

#### Contraceptives + RBV

Extreme care must be taken to avoid pregnancy in female patients and in female partners of male patients taking ribavirin. The European product labels for ribavirin state that effective contraception must be used during ribavirin treatment and for 4 months after treatment has been concluded in female patients and for 7 months in female partners of male patients. The US product labels for ribavirin state that effective contraception must be used during ribavirin treatment and for 6 months after treatment has been concluded in female patients and female partners of male patients.

#### Ethinylestradiol and/or progestins + ATV, LPV/r, FAVI

Concentrations of ethinylestradiol and progestins may be affected but no action is needed due to the short treatment duration of the COVID-19 therapy.

#### Levonorgestrel (emergency contraception) and Ulipristal + ATV or LPV/r

Any increase in exposure of levonorgestrel or ulipristal is unlikely to be clinically significant when used as a single dose.

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## Interactions with Experimental COVID-19 Therapies

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## Gastrointestinal Agents

	ATV	LPV/r	RDV	FAVI	CLQ	HCLQ	RBV	TCZ	IFN-β
Alosetron	↔	↓	↔	↔	↔	↔	↔	↔	↔
Antacids	↓	↔	↔	↔	↓	↓	↔	↔	↔
Bisacodyl	↔	↔	↔	↔	↔	↔	↔	↔	↔
Cimetidine	↓	↔	↔	↔	↔	↔	↔	↔	↔
Cisapride	↑♥	↑♥	↔	↔	↔♥	↔♥	↔	↔	↔
Esomeprazole	↓	↔	↔	↔	↔	↔	↔	↔	↔
Famotidine	↓ 41%	↔	↔	↔	↔	↔	↔	↔	↔
Lactulose	↔	↔	↔	↔	↔	↔	↔	↔	↔
Lansoprazole	↓	↔	↔	↔	↔	↔	↔	↔	↔
Loperamide	↑♥	↑♥	↔	↔	↔	↔	↔	↔	↔
Mesalazine	↔	↔	↔	↔	↔	↔	↔	↔	↔
Omeprazole	↓	↔	↔	↔	↔	↔	↔	↔	↔
Pantoprazole	↓	↔	↔	↔	↔	↔	↔	↔	↔
Prucalopride	↔	↔	↔	↔	↔	↔	↔	↔	↔
Rabeprazole	↓	↔	↔	↔	↔	↔	↔	↔	↔
Ranitidine	↓	↔	↔	↔	↔	↔	↔	↔	↔
Senna	↔	↔	↔	↔	↔	↔	↔	↔	↔

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Numbers refer to increase or decrease in AUC as observed in drug-drug interaction studies.

## Notes:

**Antacids + ATV**

Antacids can reduce absorption of atazanavir. Atazanavir should be taken at least 2 h before or 1 h after antacids.

**Antacids + CLQ**

Antacids can reduce absorption of chloroquine. Antacids should be taken at least 2 h before or 2 h after chloroquine.

**Antacids +HCLQ**

Antacids can reduce absorption of hydroxychloroquine. Antacids should be taken at least 4 h before or 4 h after hydroxychloroquine.

**Cimetidine, famotidine, ranitidine + ATV**

Unboosted atazanavir is not recommended with H2RAs as they can reduce absorption of atazanavir. If coadministration is necessary, atazanavir 400 mg once daily with food should be administered at least 2 hours before and at least 10 hours after a dose of the H2RA.

**Esomeprazole, lansoprazole, omeprazole, pantoprazole, rabeprazole + ATV**

When possible, discontinue proton pump inhibitor treatment for the duration of atazanavir treatment.

**Loperamide + ATV or LPV/r**

Caution is advised with high doses of loperamide used for reducing stoma output, particularly as patients may be at increased risk of cardiac events due to electrolytes disturbances.

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## Gastrointestinal Agents – Anti-emetics

	ATV	LPV/r	RDV	FAVI	CLQ	HCLQ	RBV	TCZ	IFN-β
Aprepitant	↑	↑	↔	↔	↔	↔	↔	↔	↔
Dolasetron	↑♥	↔♥	↔	↔	↔♥	↔♥	↔	↔	↔
Domperidone	↑♥	↑♥	↔	↔	↔♥	↔♥	↔	↔	↔
Dronabinol	↑	↑	↔	↔	↔	↔	↔	↔	↔
Granisetron	↑♥	↑♥	↔	↔	↔♥	↔♥	↔	↔	↔
Metoclopramide	↔	↔	↔	↔	↔	↔	↔	↔	↔
Ondansetron	↑♥	↑♥	↔	↔	↔♥	↔♥	↔	↔	↔
Prochlorperazine	↔♥	↑♥	↔	↔	↑♥	↑♥	↔	↔	↔

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## Hormone Replacement Therapy

	ATV	LPV/r	RDV	FAVI	CLQ	HCLQ	RBV	TCZ	IFN-β
Drospirenone (HRT)	↑	↑	↔	↔	↔	↔	↔	↔	↔
Dydrogesterone (HRT)	↑	↑	↔	↑	↔	↔	↔	↔	↔
Estradiol	↑	↓	↔	↑	↔	↔	↔	↔	↔
Levonorgestrel (HRT)	↑	↑	↔	↑	↔	↔	↔	↔	↔
Medroxyprogesterone (oral)	↑	↑	↔	↑	↔	↔	↔	↔	↔
Norethisterone (HRT)	↑	↑	↔	↑	↔	↔	↔	↔	↔
Norgestrel (HRT)	↑	↑	↔	↑	↔	↔	↔	↔	↔

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## Notes:

*Estradiol and + ATV, LPV/r or FAVI*

Concentrations of estradiol may alter but no action is needed due to the short treatment duration of the COVID-19 therapy.

*Progestins + ATV, LPV/r or FAVI*

Concentrations of progestins may increase but no action is needed due to the short treatment duration of the COVID-19 therapy.

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## Immunosuppressants

	ATV	LPV/r	RDV	FAVI	CLQ	HCLQ	RBV	TCZ	IFN-β
Adalimumab	↔	↔	↔	↔	↔	↔	↔	↔	↔
Anti-thymocyte globulin	↔	↔	↔	↔	↔	↔	↔	↔	↔
Azathioprine	↔	↔	↔	↔	↔	↔	↑	↔	↔
Basiliximab	↔	↔	↔	↔	↔	↔	↔	↔	↔
Belatacept	↔	↔	↔	↔	↔	↔	↔	↔	↔
Ciclosporin	↑	↑	↔	↔	↑	↑	↔	↓	↔
Mycophenolate	↔	↕	↔	↔	↔	↔	↔	↔	↔
Pirfenidone	↔	↓	↔	↔	↔	↔	↔	↔	↑
Sirolimus	↑	↑	↔	↔	↑	↑	↔	↓	↔
Tacrolimus	↑	↑	↔	↔	↑	↑	↔	↓	↔

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### Notes:

#### Adalimumab and azathioprine + CLQ or HCLQ

The risk of haematological toxicity may be potentially increased as adalimumab, azathioprine, chloroquine and hydroxychloroquine can cause myelosuppression. Closely monitor haematological parameters.

#### Adalimumab + RBV

The risk of haematological toxicity may be potentially increased as adalimumab and ribavirin can cause myelosuppression. Closely monitor haematological parameters.

#### Adalimumab and basiliximab + TCZ

Avoid coadministration due to the enhanced immunosuppressive effect.

#### Adalimumab + IFN-β

Caution is required due to potential additive haematological toxicity.

#### Azathioprine + RBV

Ribavirin may interfere with azathioprine metabolism possibly leading to an accumulation of 6-methylthioinosine monophosphate, which has been associated with myelotoxicity.

#### Azathioprine + TCZ or IFN-β

Caution is required due to potential additive haematological toxicity.

#### Pirfenidone + IFN-β

Any increase in pirfenidone is unlikely to be clinically relevant, except in the presence of hepatic impairment as moderate hepatic impairment also increases pirfenidone exposure (by 60%). No a priori dosage adjustment is recommended in patients with hepatic impairment but monitor for increased toxicity.

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## Inotropes & Vasopressors

	ATV	LPV/r	RDV	FAVI	CLQ	HCLQ	RBV	TCZ	IFN-β
Adrenaline (Epinephrine)	↔	↔	↔	↔	↔	↔	↔	↔	↔
Dobutamine	↔	↔	↔	↔	↔	↔	↔	↔	↔
Noradrenaline	↔	↔	↔	↔	↔	↔	↔	↔	↔
Vasopressin	↔	↔	↔	↔	↔	↔	↔	↔	↔

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### Notes:

#### Remdesivir

Pressor requirement to maintain blood pressure is a key exclusion criteria to eligibility for remdesivir use.

See <https://rdvcu.gilead.com/> for further details.

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## Lipid Lowering Agents

	ATV	LPV/r	RDV	FAVI	CLQ	HCLQ	RBV	TCZ	IFN-β
Atorvastatin	↑	↑ 490%	↔	↔	↔	↔	↔	↔	↔
Bezafibrate	↔	↔	↔	↔	↔	↔	↔	↔	↔
Clofibrate	↔	↔	↔	↔	↔	↔	↔	↔	↔
Evolocumab	↔	↔	↔	↔	↔	↔	↔	↔	↔
Ezetimibe	↑	↔	↔	↔	↔	↔	↔	↔	↔
Fenofibrate	↔	↔	↔	↔	↔	↔	↔	↔	↔
Fish oils	↔	↔	↔	↔	↔	↔	↔	↔	↔
Fluvastatin	↑	↔	↔	↔	↔	↔	↔	↔	↔
Gemfibrozil	↔	↓ 41%	↔	↔	↔	↔	↔	↔	↔
Lovastatin	↑	↑	↔	↔	↔	↔	↔	↔	↔
Pitavastatin	↑ 31%	↓ 20%	↔	↔	↔	↔	↔	↔	↔
Pravastatin	↑	↑ 33%	↔	↔	↔	↔	↔	↔	↔
Rosuvastatin	↑	↑ 108%	↔	↔	↔	↔	↔	↔	↔
Simvastatin	↑	↑	↔	↔	↔	↔	↔	↔	↔

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### Notes:

#### Atorvastatin + ATV

Coadministration is not recommended. If the use of atorvastatin is considered necessary, use the lowest possible dose of atorvastatin with careful safety monitoring. The daily atorvastatin dose should not exceed 10 mg.

#### Atorvastatin + LPV/r

Do not exceed a daily dose of 20 mg with careful safety monitoring.

#### Evolocumab + TCZ

Avoid coadministration due to the enhanced immunosuppressive effect.

#### Rosuvastatin + ATV or LPV/r

Do not exceed rosuvastatin 10 mg/day.

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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. Drug interaction data for many agents are limited or absent; therefore, risk-benefit assessment for any individual patient rests with prescribers.

## Steroids

	ATV	LPV/r	RDV	FAVI	CLQ	HCLQ	RBV	TCZ	IFN-β
Beclometasone	↔	↑	↔	↔	↔	↔	↔	↔	↔
Betamethasone	↑* ↓	↑* ↓	↓	↔	↔	↔	↔	↔	↔
Budesonide	↑*	↑*	↔	↔	↔	↔	↔	↔	↔
Ciclesonide	↑	↑	↔	↔	↔	↔	↔	↔	↔
Clobetasol	↑*	↑*	↔	↔	↔	↔	↔	↔	↔
Dexamethasone	↑* ↓	↑* ↓	↓	↔	↔	↔	↔	↔	↔
Fludrocortisone	↑*	↑*	↔	↔	↔	↔	↔	↔	↔
Flunisolide	↑	↑	↔	↔	↔	↔	↔	↔	↔
Fluocinolone	↑*	↑*	↔	↔	↔	↔	↔	↔	↔
Fluticasone	↑*	↑*	↔	↔	↔	↔	↔	↔	↔
Hydrocortisone (oral)	↑*	↑*	↔	↔	↔	↔	↔	↔	↔
Hydrocortisone (topical)	↔	↔	↔	↔	↔	↔	↔	↔	↔
Megestrol acetate	↔	↔	↔	↔	↔	↔	↔	↔	↔
Methylprednisolone	↑*	↑*	↔	↔	↔	↔	↔	↔	↔
Mometasone	↑*	↑*	↔	↔	↔	↔	↔	↔	↔
Nandrolone	↔	↔	↔	↔	↔	↔	↔	↔	↔
Oxandrolone	↔	↔	↔	↔	↔	↔	↔	↔	↔
Prednisolone	↑*	↑*	↔	↔	↔	↔	↔	↔	↔
Prednisone	↑*	↑*	↔	↔	↔	↔	↔	↔	↔
Stanazolol	↑	↑	↔	↔	↔	↔	↔	↔	↔
Testosterone	↑	↑	↔	↔	↔	↔	↔	↔	↔
Triamcinolone	↑*	↑*	↔	↔	↔	↔	↔	↔	↔

## Text Legend

- ↑ Potential increased exposure of the comedication
- ↓ Potential decreased exposure of the comedication
- ↑↑ Potential increased exposure of COVID drug
- ↓↓ Potential decreased exposure of COVID drug
- ↔ No significant effect

- ♥ One or both drugs may cause QT and/or PR prolongation. ECG monitoring is advised if coadministered.

Numbers refer to increase or decrease in AUC as observed in drug-drug interaction studies.

## Notes:

- \* Risk of elevated corticosteroid levels, Cushing's syndrome and adrenal suppression. This risk is present for oral and injected administration, and also for topical, inhaled or eye drops corticosteroids

### Beclometasone + LPV/r

Ritonavir (100 mg twice daily) increased the AUC of the active metabolite by 108% but no significant effect on adrenal function was seen. Caution is still warranted, use the lowest possible corticosteroid dose and monitor for corticosteroid side effects.

### Betamethasone or Dexamethasone + ATV, LPV/r or RDV

Betamethasone and dexamethasone are moderate inducers of CYP3A4 and could decrease exposure and efficacy of ATV, LPV/r or RDV particularly when administered orally or intravenously at high doses or for a long duration.

### Ciclesonide + ATV or LPV/r

No dose adjustment required but monitor closely, especially for Cushing's syndrome, when using a high dose or prolonged administration.

### Flunisolide + ATV or LPV/r

Use the lowest possible flunisolide dose with monitoring for corticosteroid side effects.

### Prednisolone or Prednisone + LPV/r

Based on DDI study with LPV/r, exposure of prednisolone (obtained also after conversion from prednisone) is increased modestly (+30%). A 30% dose reduction of the corticosteroid might be considered during concomitant treatment.

## Key to abbreviations

ATV	Atazanavir	CLQ	Chloroquine
LPV/r	Lopinavir/ritonavir	HCLQ	Hydroxychloroquine
RDV	Remdesivir	RBV	Ribavirin
FAVI	Favipiravir	TCZ	Tocilizumab
		IFN-β	Interferon beta

## Colour Legend

	These drugs should not be coadministered
	Potential interaction which may require a dose adjustment or close monitoring.
	Potential interaction likely to be of weak intensity. Additional action/monitoring or dosage adjustment unlikely to be required.
	No clinically significant interaction expected