

Interactions with Experimental COVID-19 Therapies

Charts updated 16 March 2020

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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. 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

DRV/c	Darunavir/cobicistat	CLQ	Chloroquine
LPV/r	Lopinavir/ritonavir	HCLQ	Hydroxychloroquine
RDV	Remdesivir	NITAZ	Nitazoxanide
FAVI	Favipiravir	RBV	Ribavirin

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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Anaesthetics & Muscle Relaxants

	DRV/c	LPV/r	RDV	FAVI	CLQ	HCLQ	NITAZ	RBV
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.

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

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Analgesics

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

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Notes:

Codeine and Tramadol + DRV/c or LPV/r

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

Diamorphine and Morphine + DRV/c

No effect on systemic exposure but inhibition of P-gp by cobicistat 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 + DRV/c or LPV/r

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

Dihydrocodeine + DRV/c

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

Paracetamol + FAVI

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

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Antiarrhythmics

	DRV/c	LPV/r	RDV	FAVI	CLQ	HCLQ	NITAZ	RBV
Amiodarone	↑♥	↑♥	↔	↔	↑♥	↑♥	↔	↔
Bepiridil	↑♥	↑♥	↔	↔	↑♥	↑♥	↔	↔
Disopyramide	↑♥	↑♥	↔	↔	↔♥	↔♥	↔	↔
Dofetilide	↑♥	↑♥	↔	↔	↔♥	↔♥	↔	↔
Flecainide	↑	↑♥	↔	↔	↑♥	↑♥	↔	↔
Lidocaine (Lignocaine)	↑	↑	↔	↔	↔	↔	↔	↔
Mexiletine	↑	↑	↔	↔	↑♥	↑♥	↔	↔
Propafenone	↑	↑	↔	↔	↔♥	↔♥	↔	↔
Quinidine	↑	↑	↔	↔	↔♥	↔♥	↔	↔

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Notes:

Amiodarone + DRV/c or LPV/r

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

Quinidine + DRV/c

The European product label for DRV/c contraindicates coadministration but the US product label for DRV/c suggests caution and concentration monitoring of quinidine.

Key to abbreviations

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LPV/r	Lopinavir/ritonavir	HCLQ	Hydroxychloroquine
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Antibacterials

	DRV/c	LPV/r	RDV	FAVI	CLQ	HCLQ	NITAZ	RBV
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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♥ One or both drugs may cause QT and/or PR prolongation. ECG monitoring is advised if coadministered.

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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, dapson, doxycycline, ertapenem, ethambutol, ethionamide, gentamicin, imipenem/cilastatin, kanamycin, meropenem, nitrofurantoin, para-aminosalicylic acid, rifaximin, spectinomycin, streptomycin, tetracyclines, trimethoprim/sulfamethoxazole, vancomycin.

Clarithromycin + DRV/c or LPV/r

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

Delamanid + DRV/c 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.

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.

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Anti-coagulant, Anti-platelet and Fibrinolytic

	DRV/c	LPV/r	RDV	FAVI	CLQ	HCLQ	NITAZ	RBV
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 + DRV/c or LPV/r

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

Betrixaban + DRV/c 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 + DRV/c or LPV/r

Decreased conversion to active metabolite leading to non-responsiveness to clopidogrel. Prasugrel should be preferred to clopidogrel with ritonavir- or cobicistat-boosted regimens.

Edoxaban + DRV/c 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 + DRV/c or LPV/r

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

Vitamin K antagonists + DRV/c, LPV/r or NITAZ

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

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Antidepressants

	DRV/c	LPV/r	RDV	FAVI	CLQ	HCLQ	NITAZ	RBV
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	↑	↑	↔	↔	↑	↑	↔	↔

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:

Clomipramine + DRV/c

Coadministration may increase clomipramine concentrations. Use with caution as clomipramine has been shown to prolong the QT interval.

Imipramine + DRV/c

Coadministration may increase imipramine concentrations. Use with caution as imipramine has been shown to prolong the QT interval

Key to abbreviations

DRV/c	Darunavir/cobicistat	CLQ	Chloroquine
LPV/r	Lopinavir/ritonavir	HCLQ	Hydroxychloroquine
RDV	Remdesivir	NITAZ	Nitazoxanide
FAVI	Favipiravir	RBV	Ribavirin

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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Anti-diabetics

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

Text Legend

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

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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/1.73m² 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/1.73m² to <60 mL/min/1.73m² 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 + DRV/c or LPV/r

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

Metformin + DRV/c

Close monitoring is recommended when starting or stopping DRV/c and metformin as a dose adjustment of metformin may be necessary.

Saxagliptin + DRV/c 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 + DRV/c 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

DRV/c	Darunavir/cobicistat	CLQ	Chloroquine
LPV/r	Lopinavir/ritonavir	HCLQ	Hydroxychloroquine
RDV	Remdesivir	NITAZ	Nitazoxanide
FAVI	Favipiravir	RBV	Ribavirin

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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Anti-hypertensives – ACE inhibitors

	DRV/c	LPV/r	RDV	FAVI	CLQ	HCLQ	NITAZ	RBV
Benazepril	↔	↔	↔	↔	↔	↔	↔	↔
Captopril	↔	↔	↔	↔	↔	↔	↔	↔
Cilazapril	↔	↔	↔	↔	↔	↔	↔	↔
Enalapril	↔	↔	↔	↔	↔	↔	↔	↔
Fosinopril	↔	↑	↔	↔	↔	↔	↔	↔
Lisinopril	↔	↔	↔	↔	↔	↔	↔	↔
Perindopril	↔	↔	↔	↔	↔	↔	↔	↔
Quinapril	↔	↔	↔	↔	↔	↔	↔	↔
Ramipril	↔	↔	↔	↔	↔	↔	↔	↔
Trandolapril	↔	↔	↔	↔	↔	↔	↔	↔

Anti-hypertensives – Angiotensin antagonists

	DRV/c	LPV/r	RDV	FAVI	CLQ	HCLQ	NITAZ	RBV
Candesartan	↔	↔	↔	↔	↔	↔	↔	↔
Eprosartan	↔	↔	↔	↔	↔	↔	↔	↔
Irbesartan	↔	↓	↔	↔	↔	↔	↔	↔
Losartan	↔	↓	↔	↔	↔	↔	↔	↔
Olmesartan	↔	↔	↔	↔	↔	↔	↔	↔
Telmisartan	↔	↔	↔	↔	↔	↔	↔	↔
Valsartan	↑	↑	↔	↔	↔	↔	↔	↔

Anti-hypertensives – Diuretics

	DRV/c	LPV/r	RDV	FAVI	CLQ	HCLQ	NITAZ	RBV
Amiloride	↔	↔	↔	↔	↔	↔	↔	↔
Bendroflumethiazide	↔	↔	↔	↔	↔	↔	↔	↔
Chlortalidone	↔	↔	↔	↔	↔	↔	↔	↔
Furosemide	↔	↔	↔	↔	↔	↔	↔	↔
Hydrochlorothiazide	↔	↔	↔	↔	↔	↔	↔	↔
Indapamide	↑	↑	↔	↔	↔	↔	↔	↔
Metolazone	↔	↔	↔	↔	↔	↔	↔	↔
Torasemide	↔	↓	↔	↔	↔	↔	↔	↔
Xipamide	↔	↔	↔	↔	↔	↔	↔	↔

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.

Key to abbreviations

DRV/c	Darunavir/cobicistat	CLQ	Chloroquine
LPV/r	Lopinavir/ritonavir	HCLQ	Hydroxychloroquine
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Anti-hypertensives – Other agents

	DRV/c	LPV/r	RDV	FAVI	CLQ	HCLQ	NITAZ	RBV
Aliskiren	↑	↑	↔	↔	↔	↔	↔	↔
Captopril	↔	↔	↔	↔	↔	↔	↔	↔
Clonidine	↔	↔	↔	↔	↔	↔	↔	↔
Digoxin	↑	↑♥	↔	↔	↑	↑	↔	↔
Dopamine	↔	↔	↔	↔	↔	↔	↔	↔
Doxazosin	↑	↑	↔	↔	↔	↔	↔	↔
Eplerenone	↑	↑	↔	↔	↔	↔	↔	↔
Hydralazine	↔	↔	↔	↔	↔	↔	↔	↔
Isosorbide dinitrate	↑	↑	↔	↔	↔	↔	↔	↔
Ivabradine	↑	↑	↔	↔	↔♥	↔♥	↔	↔
Labetalol	↔	↓	↔	↔	↔	↔	↔	↔
Lacidipine	↑	↑♥	↔	↔	↔	↔	↔	↔
Lercanidipine	↑	↑	↔	↔	↔	↔	↔	↔
Methyldopa	↔	↔	↔	↔	↔	↔	↔	↔
Moxonidine	↔	↔	↔	↑	↔	↔	↔	↔
Prazosin	↑	↑	↔	↔	↔	↔	↔	↔
Ranolazine	↑	↑	↔	↔	↔♥	↔♥	↔	↔
Sacubitril	↑	↑	↔	↔	↔	↔	↔	↔
Sodium nitroprusside	↔	↔	↔	↔	↔	↔	↔	↔
Spironolactone	↔	↔	↔	↔	↔	↔	↔	↔
Terazosin	↑	↑	↔	↔	↔	↔	↔	↔

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:

Doxazosin + DRV/c or LPV/r

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

Isosorbide nitrate + DRV/c or LPV/r

Decreased active metabolite.

Sacubitril + DRV/c or LPV/r

Increased active metabolite

Terazosin + DRV/c or LPV/r

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

Key to abbreviations

DRV/c	Darunavir/cobicistat	CLQ	Chloroquine
LPV/r	Lopinavir/ritonavir	HCLQ	Hydroxychloroquine
RDV	Remdesivir	NITAZ	Nitazoxanide
FAVI	Favipiravir	RBV	Ribavirin

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Anti-hypertensives – Pulmonary hypertension

	DRV/c	LPV/r	RDV	FAVI	CLQ	HCLQ	NITAZ	RBV
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 + DRV/c or LPV/r

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

Bosentan + DRV/c

The European product label for DRV/c does not recommended coadministration as it may lead to decreased cobicistat concentrations and consequently those of darunavir being boosted, leading to loss of therapeutic effect and possible development of resistance. However, the US product label suggests when starting DRV/c in patients stable on bosentan, discontinue bosentan at least 36 h prior to starting cobicistat and resume bosentan at 62.5 mg once daily or every other day based on individual tolerability after at least 10 days following starting darunavir/cobicistat.

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 + DRV/c 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 + DRV/c

The European product label for DRV/c does not recommend coadministration, however, the US product label for DRV/c recommends for patients on tadalafil and starting DRV/c, to avoid the use of tadalafil during the initiation of darunavir/cobicistat and to stop tadalafil at least 24 hours prior to starting DRV/c. After at least one week following the initiation of DRV/c, resume tadalafil at 20 mg once daily. Increase to 40 mg once daily based upon 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

DRV/c	Darunavir/cobicistat	CLQ	Chloroquine
LPV/r	Lopinavir/ritonavir	HCLQ	Hydroxychloroquine
RDV	Remdesivir	NITAZ	Nitazoxanide
FAVI	Favipiravir	RBV	Ribavirin

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

	DRV/c	LPV/r	RDV	FAVI	CLQ	HCLQ	NITAZ	RBV
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

- ↑ 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:

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.

Quetiapine + DRV/c 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

DRV/c	Darunavir/cobicistat	CLQ	Chloroquine
LPV/r	Lopinavir/ritonavir	HCLQ	Hydroxychloroquine
RDV	Remdesivir	NITAZ	Nitazoxanide
FAVI	Favipiravir	RBV	Ribavirin

Colour Legend

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Antivirals

	DRV/c	LPV/r	RDV	FAVI	CLQ	HCLQ	NITAZ	RBV
Darunavir/cobicistat		✗	↔	↔	↑	↑	↔	↔
Lopinavir/ritonavir	✗		↔	↔	↑ ♥	↑ ♥	↔	↔
Remdesivir	↔	↔		↔	↔	↔	↔	↔
Favipiravir	↔	↔	↔		↔	↔	↔	↔
Chloroquine	↑	↑ ♥	↔	↔		✗	↔	↔
Hydroxychloroquine	↑	↑ ♥	↔	↔	✗		↔	↔
Nitazoxanide	↔	↔	↔	↔	↔	↔		↔
Ribavirin	↔	↔	↔	↔	↔	↔	↔	
Oseltamivir	↔	↔	↔	↑ 14%	↔	↔	↔	↔

Text Legend

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

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

Notes:

DRV/c + LPV/r

Darunavir/c and lopinavir/r should not be coadministered due to similar effects of cobicistat and ritonavir on CYP3A4.

CLQ + HCLQ

Chloroquine and hydroxychloroquine should not be coadministered as hydroxychloroquine is a metabolite of chloroquine.

Chloroquine or Hydroxychloroquine + DRV/c

DRV/c may increase concentrations of chloroquine or hydroxychloroquine, but to a moderate extent. DRV/c has not been associated with an increased risk of QT prolongation.

Chloroquine or Hydroxychloroquine + 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.

Key to abbreviations

DRV/c	Darunavir/cobicistat	CLQ	Chloroquine
LPV/r	Lopinavir/ritonavir	HCLQ	Hydroxychloroquine
RDV	Remdesivir	NITAZ	Nitazoxanide
FAVI	Favipiravir	RBV	Ribavirin

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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Anxiolytics/Hypnotics/Sedatives

	DRV/c	LPV/r	RDV	FAVI	CLQ	HCLQ	NITAZ	RBV
Alprazolam	↑	↑	↔	↔	↔	↔	↔	↔
Bromazepam	↑	↑	↔	↔	↔	↔	↔	↔
Bupirone	↑	↑	↔	↔	↔	↔	↔	↔
Chlordiazepoxide	↑	↑	↔	↔	↔	↔	↔	↔
Clobazam	↑	↑	↔	↔	↔	↔	↔	↔
Clorazepate	↑	↑	↔	↔	↔	↔	↔	↔
Diazepam	↑	↑	↔	↔	↔	↔	↔	↔
Estazolam	↑	↑	↔	↔	↔	↔	↔	↔
Flunitrazepam	↑	↑	↔	↔	↔	↔	↔	↔
Flurazepam	↑	↑	↔	↔	↔	↔	↔	↔
Hydroxyzine	↑	↑	↔	↔	↔	↔	↔	↔
Lorazepam	↔	↔	↔	↔	↔	↔	↔	↔
Lormetazepam	↔	↔	↔	↔	↔	↔	↔	↔
Midazolam (oral)	↑	↑	↔	↔	↔	↔	↔	↔
Midazolam (parenteral)	↑	↑	↔	↔	↔	↔	↔	↔
Oxazepam	↔	↔	↔	↔	↔	↔	↔	↔
Temazepam	↔	↔	↔	↔	↔	↔	↔	↔
Triazolam	↑	↑	↔	↔	↔	↔	↔	↔
Zaleplon	↑	↑	↔	↔	↔	↔	↔	↔
Zolpidem	↑	↑	↔	↔	↔	↔	↔	↔
Zopiclone	↑	↑	↔	↔	↔	↔	↔	↔

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.

Key to abbreviations

DRV/c	Darunavir/cobicistat	CLQ	Chloroquine
LPV/r	Lopinavir/ritonavir	HCLQ	Hydroxychloroquine
RDV	Remdesivir	NITAZ	Nitazoxanide
FAVI	Favipiravir	RBV	Ribavirin

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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Beta Blockers

	DRV/c	LPV/r	RDV	FAVI	CLQ	HCLQ	NITAZ	RBV
Atenolol	↑	↔♥	↔	↔	↔	↔	↔	↔
Bisoprolol	↑	↑♥	↔	↔	↔	↔	↔	↔
Carvedilol	↑	↑↓♥	↔	↔	↔	↔	↔	↔
Metoprolol	↑	↑♥	↔	↔	↔♥	↔♥	↔	↔
Nebivolol	↑	↑♥	↔	↔	↔♥	↔♥	↔	↔
Oxprenolol	↔	↓♥	↔	↔	↔	↔	↔	↔
Pindolol	↑	↑♥	↔	↔	↔	↔	↔	↔
Propranolol	↑	↑♥	↔	↔	↔♥	↔♥	↔	↔
Timolol	↑	↑♥	↔	↔	↔♥	↔♥	↔	↔

Text Legend

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Key to abbreviations

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Bronchodilators

	DRV/c	LPV/r	RDV	FAVI	CLQ	HCLQ	NITAZ	RBV
Acclidinium 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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- ↓ Potential decreased exposure of COVID drug
- ↔ No significant effect

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

Notes:

Indacaterol +DRV/c or LPV/r

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

Key to abbreviations

DRV/c	Darunavir/cobicistat	CLQ	Chloroquine
LPV/r	Lopinavir/ritonavir	HCLQ	Hydroxychloroquine
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Calcium Channel Blockers

	DRV/c	LPV/r	RDV	FAVI	CLQ	HCLQ	NITAZ	RBV
Amlodipine	↑	↑♥	↔	↔	↔	↔	↔	↔
Diltiazem	↑	↑♥	↔	↔	↔	↔	↔	↔
Felodipine	↑	↑♥	↔	↔	↔	↔	↔	↔
Nicardipine	↑	↑♥	↔	↔	↔	↔	↔	↔
Nifedipine	↑	↑♥	↔	↔	↔	↔	↔	↔
Nisoldipine	↑	↑♥	↔	↔	↔	↔	↔	↔
Nitrendipine	↑	↑♥	↔	↔	↔	↔	↔	↔
Verapamil	↑	↑♥	↔	↔	↑↑	↑↑	↔	↔

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

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

Notes:

Amlodipine + DRV/c or LPV/r

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

Key to abbreviations

DRV/c	Darunavir/cobicistat	CLQ	Chloroquine
LPV/r	Lopinavir/ritonavir	HCLQ	Hydroxychloroquine
RDV	Remdesivir	NITAZ	Nitazoxanide
FAVI	Favipiravir	RBV	Ribavirin

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Contraceptives

	DRV/c	LPV/r	RDV	FAVI	CLQ	HCLQ	NITAZ	RBV
Desogestrel (COC)	↑	↑	↔	↑	↔	↔	↔	↔
Desogestrel (POP)	↑	↑	↔	↑	↔	↔	↔	↔
Drospirenone (COC)	↑ 58%	↑	↔	↑	↔	↔	↔	↔
Ethinylestradiol	↓ 30%	↓ 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)	↑	↓ 17%	↔	↑ 47%	↔	↔	↔	↔
Norethisterone (IM depot)	↔	↔	↔	↑	↔	↔	↔	↔
Norethisterone(POP)	↑	↑ 50%	↔	↑	↔	↔	↔	↔
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 + DRV/c, 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 + DRV/c or LPV/r

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

Key to abbreviations

DRV/c	Darunavir/cobicistat	CLQ	Chloroquine
LPV/r	Lopinavir/ritonavir	HCLQ	Hydroxychloroquine
RDV	Remdesivir	NITAZ	Nitazoxanide
FAVI	Favipiravir	RBV	Ribavirin

Colour Legend

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Orange	Potential interaction which may require a dose adjustment or close monitoring.
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Gastrointestinal Agents

	DRV/c	LPV/r	RDV	FAVI	CLQ	HCLQ	NITAZ	RBV
Alosetron	↔	↓	↔	↔	↔	↔	↔	↔
Antacids	↔	↔	↔	↔	↓	↓	↔	↔
Bisacodyl	↔	↔	↔	↔	↔	↔	↔	↔
Cimetidine	↔	↔	↔	↔	↔	↔	↔	↔
Cisapride	↑♥	↑♥	↔	↔	↔♥	↔♥	↔	↔
Esomeprazole	↔	↔	↔	↔	↔	↔	↔	↔
Famotidine	↔	↔	↔	↔	↔	↔	↔	↔
Lactulose	↔	↔	↔	↔	↔	↔	↔	↔
Lansoprazole	↔	↔	↔	↔	↔	↔	↔	↔
Loperamide	↑♥	↑♥	↔	↔	↔	↔	↔	↔
Mesalazine	↔	↔	↔	↔	↔	↔	↔	↔
Omeprazole	↔	↔	↔	↔	↔	↔	↔	↔
Pantoprazole	↔	↔	↔	↔	↔	↔	↔	↔
Prucalopride	↔	↔	↔	↔	↔	↔	↔	↔
Rabeprazole	↔	↔	↔	↔	↔	↔	↔	↔
Ranitidine	↔	↔	↔	↔	↔	↔	↔	↔
Senna	↔	↔	↔	↔	↔	↔	↔	↔

Gastrointestinal Agents – Anti-emetics

	DRV/c	LPV/r	RDV	FAVI	CLQ	HCLQ	NITAZ	RBV
Aprepitant	↑	↑	↔	↔	↔	↔	↔	↔
Dolasetron	↔	↔♥	↔	↔	↔♥	↔♥	↔	↔
Domperidone	↑♥	↑♥	↔	↔	↔♥	↔♥	↔	↔
Dronabinol	↑	↑	↔	↔	↔	↔	↔	↔
Granisetron	↑	↑♥	↔	↔	↔♥	↔♥	↔	↔
Metoclopramide	↔	↔	↔	↔	↔	↔	↔	↔
Ondansetron	↑	↑♥	↔	↔	↔♥	↔♥	↔	↔
Prochlorperazine	↑	↑♥	↔	↔	↑♥	↑♥	↔	↔

Text Legend

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

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

Notes:

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.

Loperamide + DRV/c 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.

Key to abbreviations

DRV/c	Darunavir/cobicistat	CLQ	Chloroquine
LPV/r	Lopinavir/ritonavir	HCLQ	Hydroxychloroquine
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Hormone Replacement Therapy

	DRV/c	LPV/r	RDV	FAVI	CLQ	HCLQ	NITAZ	RBV
Drospirenone (HRT)	↑	↑	↔	↔	↔	↔	↔	↔
Dydrogesterone (HRT)	↑	↑	↔	↑	↔	↔	↔	↔
Estradiol	↑	↓	↔	↑	↔	↔	↔	↔
Levonorgestrel (HRT)	↑	↑	↔	↑	↔	↔	↔	↔
Medroxyprogesterone (oral)	↑	↑	↔	↑	↔	↔	↔	↔
Norethisterone (HRT)	↑	↑	↔	↑	↔	↔	↔	↔
Norgestrel (HRT)	↑	↑	↔	↑	↔	↔	↔	↔

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

Notes:

Estradiol and + DRV/c, 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 + DRV/c, 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.

Key to abbreviations

DRV/c	Darunavir/cobicistat	CLQ	Chloroquine
LPV/r	Lopinavir/ritonavir	HCLQ	Hydroxychloroquine
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Immunosuppressants

	DRV/c	LPV/r	RDV	FAVI	CLQ	HCLQ	NITAZ	RBV
Adalimumab	↔	↔	↔	↔	↔	↔	↔	↔
Anti-thymocyte globulin	↔	↔	↔	↔	↔	↔	↔	↔
Azathioprine	↔	↔	↔	↔	↔	↔	↔	↑
Basiliximab	↔	↔	↔	↔	↔	↔	↔	↔
Belatacept	↔	↔	↔	↔	↔	↔	↔	↔
Ciclosporin	↑	↑	↔	↔	↑	↑	↔	↔
Mycophenolate	↔	↑↓	↔	↔	↔	↔	↔	↔
Sirolimus	↑	↑	↔	↔	↑	↑	↔	↔
Tacrolimus	↑	↑	↔	↔	↑	↑	↔	↔

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

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.

Azathioprine + RBV

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

Key to abbreviations

DRV/c	Darunavir/cobicistat	CLQ	Chloroquine
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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.

Inotropes & Vasopressors

	DRV/c	LPV/r	RDV	FAVI	CLQ	HCLQ	NITAZ	RBV
Adrenaline (Epinephrine)	↔	↔	↔	↔	↔	↔	↔	↔
Dobutamine	↔	↔	↔	↔	↔	↔	↔	↔
Noradrenaline	↔	↔	↔	↔	↔	↔	↔	↔
Vasopressin	↔	↔	↔	↔	↔	↔	↔	↔

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:

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.

Key to abbreviations

DRV/c	Darunavir/cobicistat	CLQ	Chloroquine
LPV/r	Lopinavir/ritonavir	HCLQ	Hydroxychloroquine
RDV	Remdesivir	NITAZ	Nitazoxanide
FAVI	Favipiravir	RBV	Ribavirin

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

Interactions with Experimental COVID-19 Therapies

Charts updated 16 March 2020

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Lipid Lowering Agents

	DRV/c	LPV/r	RDV	FAVI	CLQ	HCLQ	NITAZ	RBV
Atorvastatin	↑ 290%	↑ 490%	↔	↔	↔	↔	↔	↔
Bezafibrate	↔	↔	↔	↔	↔	↔	↔	↔
Clofibrate	↔	↔	↔	↔	↔	↔	↔	↔
Evolocumab	↔	↔	↔	↔	↔	↔	↔	↔
Ezetimibe	↑	↔	↔	↔	↔	↔	↔	↔
Fenofibrate	↔	↔	↔	↔	↔	↔	↔	↔
Fish oils	↔	↔	↔	↔	↔	↔	↔	↔
Fluvastatin	↑	↔	↔	↔	↔	↔	↔	↔
Gemfibrozil	↔	↓ 41%	↔	↔	↔	↔	↔	↔
Lovastatin	↑	↑	↔	↔	↔	↔	↔	↔
Pitavastatin	↑	↓ 20%	↔	↔	↔	↔	↔	↔
Pravastatin	↑	↑ 33%	↔	↔	↔	↔	↔	↔
Rosuvastatin	↑ 93%	↑ 108%	↔	↔	↔	↔	↔	↔
Simvastatin	↑	↑	↔	↔	↔	↔	↔	↔

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:

Atorvastatin + DRV/c

A daily dose of 40 mg atorvastatin should not be exceeded with careful safety monitoring. (Note, the US product label for DRV/c states not to exceed atorvastatin 20 mg/day.)

Atorvastatin + LPV/r

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

Rosuvastatin + DRV/c

The US product label for DRV/c states not to exceed rosuvastatin 20 mg/day.

Rosuvastatin + LPV/r

Do not exceed rosuvastatin 10 mg/day.

Key to abbreviations

DRV/c	Darunavir/cobicistat	CLQ	Chloroquine
LPV/r	Lopinavir/ritonavir	HCLQ	Hydroxychloroquine
RDV	Remdesivir	NITAZ	Nitazoxanide
FAVI	Favipiravir	RBV	Ribavirin

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

Interactions with Experimental COVID-19 Therapies

Charts updated 16 March 2020

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Steroids

	DRV/c	LPV/r	RDV	FAVI	CLQ	HCLQ	NITAZ	RBV
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 + DRV/c

DRV/r decreased the AUC of the active metabolite (beclometasone-17-monopropionate) by 11%, but no significant effect on adrenal function was seen. A similar effect may occur with DRV/c.

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 + DRV/c, LPV/r or RDV

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

Ciclesonide + DRV/c or LPV/r

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

Flunisolide + DRV/c or LPV/r

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

Prednisolone or Prednisone + DRV/c or 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

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LPV/r	Lopinavir/ritonavir	HCLQ	Hydroxychloroquine
RDV	Remdesivir	NITAZ	Nitazoxanide
FAVI	Favipiravir	RBV	Ribavirin

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