

Interactions with Essential Medicines & Nirmatrelvir/ritonavir (NMV/r)

Charts revised 8 June 2022

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Please check www.covid19-druginteractions.org for updates.

Interaction tables - refer to page 2 for legend, abbreviations and notes

Please note that if a drug is not listed it cannot automatically be assumed it is safe to coadminister.

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

Management of interactions with nirmatrelvir/ritonavir (Paxlovid) may be complex and full details should be obtained from the website where possible.

Analgesics	
<input type="checkbox"/> Codeine	
<input type="checkbox"/> Diclofenac	
<input type="checkbox"/> Fentanyl	
<input type="checkbox"/> Hydromorphone	
<input type="checkbox"/> Ibuprofen	
<input type="checkbox"/> Mefenamic acid	
<input type="checkbox"/> Morphine	
<input type="checkbox"/> Oxycodone	
<input type="checkbox"/> Paracetamol	
<input type="checkbox"/> Tramadol	
Antiarrhythmics	
<input checked="" type="checkbox"/> Amiodarone	
<input type="checkbox"/> Digoxin	
<input type="checkbox"/> Lidocaine	
Antibacterials	
<input type="checkbox"/> Amikacin	
<input type="checkbox"/> Amoxicillin	
<input type="checkbox"/> Ampicillin	
<input type="checkbox"/> Bedaquiline	
<input type="checkbox"/> Cefalexin	
<input type="checkbox"/> Cefazolin	
<input type="checkbox"/> Cefixime	
<input type="checkbox"/> Cefotaxime	
<input type="checkbox"/> Ceftriaxone	
<input type="checkbox"/> Chloramphenicol	
<input type="checkbox"/> Ciprofloxacin	
<input type="checkbox"/> Clarithromycin (a)	
<input type="checkbox"/> Clindamycin	
<input type="checkbox"/> Clofazimine	
<input type="checkbox"/> Cloxacillin	
<input type="checkbox"/> Cycloserine	
<input type="checkbox"/> Dapsone	
<input type="checkbox"/> Delamanid	
<input type="checkbox"/> Doxycycline	
<input type="checkbox"/> Erythromycin	
<input type="checkbox"/> Ethambutol	
<input type="checkbox"/> Ethionamide	
<input type="checkbox"/> Gentamicin	
<input type="checkbox"/> Imipenem/cilastatin	
<input type="checkbox"/> Isoniazid	
<input type="checkbox"/> Kanamycin	
<input type="checkbox"/> Levofloxacin	
<input type="checkbox"/> Linezolid	
<input type="checkbox"/> Meropenem	
<input type="checkbox"/> Metronidazole	
<input type="checkbox"/> Moxifloxacin	
<input type="checkbox"/> Nitrofurantoin	
<input type="checkbox"/> Ofloxacin	
<input type="checkbox"/> Para-aminosalicylic acid	
<input type="checkbox"/> Penicillins	
<input type="checkbox"/> Piperacillin	
<input type="checkbox"/> Pyrazinamide	
<input type="checkbox"/> Rifabutin (b)	
<input checked="" type="checkbox"/> Rifampicin	
<input checked="" type="checkbox"/> Rifapentine	
<input type="checkbox"/> Spectinomycin	
<input type="checkbox"/> Streptomycin	
<input type="checkbox"/> Sulfadiazine	
<input type="checkbox"/> Tazobactam	
<input type="checkbox"/> Tetracyclines	
<input type="checkbox"/> Trimethoprim/sulfamethoxazole	
<input type="checkbox"/> Vancomycin	
Anticoagulants/antiplatelets	
<input type="checkbox"/> Apixaban	
<input type="checkbox"/> Aspirin (antiplatelet)	
<input type="checkbox"/> Clopidogrel (stented) (c)	
<input type="checkbox"/> Dabigatran (d)	
<input type="checkbox"/> Dalteparin	
<input type="checkbox"/> Edoxaban (e)	
<input type="checkbox"/> Enoxaparin	
<input type="checkbox"/> Heparin	
<input type="checkbox"/> Rivaroxaban	
<input type="checkbox"/> Streptokinase	
<input type="checkbox"/> Warfarin	
Anticonvulsants	
<input checked="" type="checkbox"/> Carbamazepine	
<input type="checkbox"/> Clonazepam	
<input type="checkbox"/> Ethosuximide	
<input type="checkbox"/> Lamotrigine	
<input checked="" type="checkbox"/> Phenobarbital	
<input checked="" type="checkbox"/> Phenytoin	
<input type="checkbox"/> Valproate	
Antidepressants	
<input type="checkbox"/> Amitriptyline	
<input type="checkbox"/> Clomipramine	
<input type="checkbox"/> Fluoxetine	
<input type="checkbox"/> Lithium	
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Antidiabetics	
<input type="checkbox"/> Glibenclamide	
<input type="checkbox"/> Gliclazide	
<input type="checkbox"/> Insulin	
<input type="checkbox"/> Metformin	
Antifungals	
<input type="checkbox"/> Amphotericin B	
<input type="checkbox"/> Fluconazole	
<input type="checkbox"/> Flucytosine	
<input type="checkbox"/> Griseofulvin	
<input type="checkbox"/> Itraconazole (f)	
<input type="checkbox"/> Ketoconazole (f)	
<input type="checkbox"/> Nystatin	
<input type="checkbox"/> Voriconazole	
Antimalarials	
<input type="checkbox"/> Amodiaquine	
<input type="checkbox"/> Artemether	
<input type="checkbox"/> Artesunate	
<input type="checkbox"/> Atovaquone	
<input type="checkbox"/> Lumefantrine	
<input type="checkbox"/> Mefloquine	
<input type="checkbox"/> Piperaquine	
<input type="checkbox"/> Primaquine	
<input type="checkbox"/> Proguanil	
<input type="checkbox"/> Quinine	
Antipsychotics	
<input type="checkbox"/> Chlorpromazine	
<input type="checkbox"/> Clozapine	
<input type="checkbox"/> Fluphenazine	
<input type="checkbox"/> Haloperidol	
<input type="checkbox"/> Risperidone	
Anxiolytics	
<input type="checkbox"/> Diazepam	
<input type="checkbox"/> Lorazepam	
<input type="checkbox"/> Midazolam	
Beta blockers	
<input type="checkbox"/> Atenolol	
<input type="checkbox"/> Bisoprolol	
<input type="checkbox"/> Carvedilol	
<input type="checkbox"/> Metoprolol	
<input type="checkbox"/> Propranolol	
<input type="checkbox"/> Timolol	
Bronchodilators	
<input type="checkbox"/> Aminophylline	
<input type="checkbox"/> Ipratropium bromide	
<input type="checkbox"/> Salmeterol	
Calcium channel blockers	
<input type="checkbox"/> Amlodipine	
<input type="checkbox"/> Nifedipine	
<input type="checkbox"/> Verapamil	
Cancer drugs	
<input type="checkbox"/> Dasatinib (g)	
<input type="checkbox"/> Erlotinib (h)	
<input type="checkbox"/> Imatinib (i)	
<input type="checkbox"/> Methotrexate	
<input type="checkbox"/> Vinorelbine (j)	
Contraceptives	
<input type="checkbox"/> Ethinylestradiol	
<input type="checkbox"/> Etonogestrel (IMP)	
<input type="checkbox"/> Etonogestrel (VR)	
<input type="checkbox"/> Levonorgestrel (COC)	
<input type="checkbox"/> Levonorgestrel (EC)	
<input type="checkbox"/> Levonorgestrel (IDU)	
<input type="checkbox"/> Levonorgestrel (POP)	
<input type="checkbox"/> Medroxyprogesterone (depot injection)	
<input type="checkbox"/> Norethisterone (COC)	
<input type="checkbox"/> Norethisterone (IM)	
<input type="checkbox"/> Norethisterone (POP)	
<input type="checkbox"/> Norgestrel (COC)	
COVID19 therapies	
<input type="checkbox"/> Budesonide (inhaled)	
<input type="checkbox"/> Convalescent plasma	
<input type="checkbox"/> Dexamethasone	
<input type="checkbox"/> Hydrocortisone	
<input type="checkbox"/> Infliximab	
<input type="checkbox"/> Methylprednisolone	
<input type="checkbox"/> COVID19 vaccines	
Gastrointestinal agents	
<input type="checkbox"/> Aprepitant	
<input type="checkbox"/> Domperidone	
<input type="checkbox"/> Lactulose	
<input type="checkbox"/> Loperamide	
<input type="checkbox"/> Mesalazine	
<input type="checkbox"/> Metoclopramide	
<input type="checkbox"/> Omeprazole	
<input type="checkbox"/> Ondansetron	
<input type="checkbox"/> Ranitidine	
<input type="checkbox"/> Senna	
HCV antivirals	
<input type="checkbox"/> Glecaprevir/pibrentasvir	
<input type="checkbox"/> Ledipasvir/sofosbuvir	
<input type="checkbox"/> Ombitasvir/paritaprevir/r	
<input type="checkbox"/> Sofosbuvir/velpatasvir	
Herbals/supplements	
<input type="checkbox"/> Folic acid	
<input type="checkbox"/> Magnesium	
<input checked="" type="checkbox"/> St John's Wort	
HIV antiretrovirals	
<input type="checkbox"/> Abacavir	
<input type="checkbox"/> Atazanavir/ritonavir	
<input type="checkbox"/> Darunavir/ritonavir	
<input type="checkbox"/> Dolutegravir	
<input type="checkbox"/> Efavirenz	
<input type="checkbox"/> Emtricitabine	
<input type="checkbox"/> Lamivudine	
<input type="checkbox"/> Lopinavir/ritonavir	
<input type="checkbox"/> Nevirapine	
<input type="checkbox"/> Raltegravir	
<input type="checkbox"/> Tenofovir alafenamide	
<input type="checkbox"/> Tenofovir-DF	
<input type="checkbox"/> Zidovudine	
Hypertension/heart failure	
<input type="checkbox"/> Amiloride	
<input type="checkbox"/> Dopamine	
<input type="checkbox"/> Enalapril	
<input type="checkbox"/> Furosemide	
<input type="checkbox"/> Hydrochlorothiazide	
<input type="checkbox"/> Isosorbide dinitrate	
<input type="checkbox"/> Lisinopril	
<input type="checkbox"/> Losartan	
<input type="checkbox"/> Methyldopa	
<input type="checkbox"/> Spironolactone	
Immunosuppressants	
<input type="checkbox"/> Azathioprine	
<input checked="" type="checkbox"/> Ciclosporin (k)	
<input checked="" type="checkbox"/> Everolimus	
Lipid lowering agents	
<input type="checkbox"/> Atorvastatin	
<input type="checkbox"/> Fluvastatin	
<input type="checkbox"/> Lovastatin	
<input type="checkbox"/> Simvastatin	
Others	
<input type="checkbox"/> Allopurinol	
<input checked="" type="checkbox"/> Ergometrine	
<input checked="" type="checkbox"/> Ergotamine	
<input type="checkbox"/> Levodopa	
<input type="checkbox"/> Levothyroxine	
Steroids	
<input type="checkbox"/> Beclomethasone	
<input type="checkbox"/> Betamethasone	
<input type="checkbox"/> Fludrocortisone	
<input type="checkbox"/> Prednisolone	
<input type="checkbox"/> Testosterone	
<input type="checkbox"/> Triamcinolone	

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Legend

Colour/Symbol	Recommendation for NMV/r use
! Do not co-administer	Do not use NMV/r ⇒ alternative COVID-19 therapy Risk of serious toxicity. Stopping the drug does not mitigate the interaction due to its prolonged half-life.
× Do not co-administer	Do not use NMV/r ⇒ alternative COVID-19 therapy Strong inducer can jeopardize NMV/r efficacy due to persisting induction after stopping the drug.
Do not co-administer	NMV/r use ONLY possible if drug is paused or replaced by a non-interacting drug Risk of serious toxicity. Only start NMV/r if the drug can be safely paused or replaced. Drug can be resumed at least 3 days (if possible, up to 5 days for narrow therapeutic index drugs) after completing NMV/r therapy.
□ Potential interaction Dose adjustment and/or close monitoring required.	Stop or replace drug if possible or consult specialist for dose adjustment/monitoring to allow use with NMV/r Ideally, only start NMV/r if the drug can be safely paused or replaced. Alternatively, dose adjust/monitor. Refer to www.covid19-druginteractions.org for detailed information.
Potential interaction Manageable by counselling patient	Proceed with NMV/r Interaction manageable by counselling the patient about potential interaction and advising to temporarily stop the drug if feeling unwell.
Weak interaction No action needed	Proceed with NMV/r Drug metabolized partially by CYP3A4 or with low risk of adverse event from interaction.
No interaction expected	Proceed with NMV/r

Contraceptive Abbreviations

COC = combined oral contraceptive

IDU = intrauterine device

POP = progestin only contraceptive pill

EC = emergency contraception

IM = intramuscular

VR = vaginal ring.

IMP = implant

Notes

- a No dose reduction or monitoring in patients with normal renal function.
- b Rifabutin dosed 150 mg once daily with NMV/r.
- c Ritonavir decreases clopidogrel efficacy therefore NMV/r cannot be prescribed in high risk situation (i.e. initial period (at least 6 weeks) post coronary stenting). NMV/r is allowed if clopidogrel is used outside this period or if clopidogrel is used as alternative to aspirin (intolerant patients).
- d When used for the treatment of atrial fibrillation, reduce dabigatran to 110 mg twice daily in individuals with normal renal function and to 75 mg twice daily in individuals with moderate renal impairment. Consult www.covid19-druginteractions.org for management in other indications.
- e When used for the treatment of atrial fibrillation, reduce edoxaban to 30 mg. Consult www.covid19-druginteractions.org for management in other indications.
- f Itraconazole or ketoconazole should not be used at doses >200 mg/day.
- g The decision to pause or dose adjust dasatinib should be made in conjunction with the patient's oncologist.
Chronic phase chronic myelogenous leukaemia: pause dasatinib and restart 3 days after completing NMV/r. Alternatively, consider reducing dasatinib dose to 20 mg (in patients receiving 100 mg daily) or 40 mg (in patients receiving 140 mg daily) and monitor for toxicity.
Accelerated or blast phase chronic myelogenous leukaemia: do not coadminister, use alternative COVID-19 therapy.
- h The decision to pause or dose adjust erlotinib should be made in conjunction with the patient's oncologist.
If it is decided to pause treatment, restart erlotinib 3 days after completing NMV/r treatment. If pausing erlotinib treatment is not feasible, continue full dose erlotinib with patient self-monitoring for rash and diarrhoea. If these do occur, reduce erlotinib dose in 50 mg decrements or re-assess for a short pause.
- i The decision to pause imatinib should be made in conjunction with the patient's oncologist. If it is decided to hold treatment, restart imatinib 3 days after completing NMV/r treatment. Alternatively, imatinib may be coadministered with monitoring for adverse effects (fluid retention, nausea and neutropenia). NMV/r is expected to have a modest effect on imatinib exposure. Coadministration with ritonavir (600 mg once daily) for 3 days did not significantly alter imatinib exposure (*van Erp NP et al. Clin Cancer Res. 2007;13(24):7394-400*).
- j The decision to pause or dose adjust vinblastine should be made in conjunction with the patient's oncologist. Vinblastine may be paused in the context of acute infection. Restart vinblastine 3 days after completing NMV/r treatment. Alternatively, vinblastine may be coadministered with close monitoring for haematologic toxicity and neurotoxicity. Some providers may wish to empirically reduce vinblastine dose, especially in patients who have previously experienced or are at high risk for toxicity.
- k The management of this interaction is challenging and would require dosage adjustment and therapeutic drug monitoring (TDM) of ciclosporin which may not be possible given the short duration of NMV/r treatment. An alternative COVID treatment should be considered. However, if TDM is available, an empiric dose reduction of ciclosporin has been suggested (reduce total daily dose by 80% and administer once daily) during treatment with NMV/r (days 1-5). Ciclosporin concentrations should be assessed on day 6 or 7 and repeated every 2-4 days.