

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

Charts produced 8 March 2022

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

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

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"/>	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 (a)
<input type="checkbox"/>	Dalteparin
<input type="checkbox"/>	Edoxaban (d)
<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
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 (e)
<input type="checkbox"/>	Ketoconazole (e)
<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 (f)
<input type="checkbox"/>	Erlotinib (g)
<input type="checkbox"/>	Imatinib (h)
<input type="checkbox"/>	Methotrexate
<input type="checkbox"/>	Vinblastine (i)
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 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-DP
<input type="checkbox"/>	Zidovudine
Hypertension/heart failure	
<input type="checkbox"/>	Amiloride
<input type="checkbox"/>	Digoxin
<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 type="checkbox"/>	Cyclosporin
<input 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 type="checkbox"/>	Ergometrine
<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 3 days after completing NMV/r therapy.
<input type="checkbox"/> 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

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 The US product label for edoxaban advises no dose adjustment is needed for edoxaban in the presence of a P-gp inhibitor, such as ritonavir.
- e Itraconazole or ketoconazole should not be used at doses >200 mg/day.
- f 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.
- g 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.
- h 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*).
- i 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.

Contraceptive Abbreviations

COC = combined oral contraceptive
 EC = emergency contraception
 IDU = intrauterine device
 IM = intramuscular
 IMP = implant
 POP = progestin only contraceptive pill
 VR = vaginal ring.