We aim to ensure that information is accurate and consistent with current knowledge and practice. However, the University of Liverpool expressly exclude liability for errors, omissions or inaccuracies to the fullest extent permitted by law.

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.

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.

Analgesics
- Codeine
- Diclofenac
- Fentanyl
- Hydrodine
- Ibuprofen
- Mefenamic acid
- Morphine
- Oxycodone
- Paracetamol
- Tramadol

Antibacterials
- Ampicillin
- Amoxicillin
- Amikacin
- Clindamycin
- Clofazimine
- Clindamycin
- Ciprofloxacin
- Cefalexin
- Ceftriaxone
- Cloxacillin
- Chloramphenicol
- Cefuroxime

Anticoagulants/antiplaetlets
- Apixaban
- Aspirin (antiplatelet)
- Clopidogrel (stented) (c)
- Dalteparin
- Enoxaparin
- Heparin
- Rivaroxaban
- Streptokinase
- Warfarin

Anticonvulsants
- Carbamazepine
- Clonazepam
- Ethosuximide
- Lamotrigin
- Phenytoin
- Valporate

Antidepressants
- Amitriptyline
- Clomipramine
- Fluoxetine
- Lithium
- St John’s Wort

Antidiabetics
- Glibenclamide
- Glitazone
- Insulin
- Metformin

Antifungals
- Amphotericin B
- Fluconazole
- Fluconosine
- Griseofulvin
- Itraconazole (f)
- Ketoconazole (f)
- Nystatin
- Voriconazole

Antimalarials
- Amodiaquine
- Artemether
- Artesunate

Atovaquine
- Lumeferon
- Mefloquine
- Piperaquine
- Primaquine
- Proguanil

Antipsychotics
- Chlorpromazine
- Clozapine
- Fluphenazine
- Haloperidol
- Risperidone

Antioxidics
- Diazepam
- Lorazepam
- Midazolam

Beta blockers
- Atenolol
- Bisoprolol
- Carvedilol
- Metoprolol
- Propranolol
- Timolol

Bronchodilators
- Aminophylline
- Ipratropium bromide
- Salmeterol

Calcium channel blockers
- Nifedipine
- Verapamil

Cancer drugs
- Dasatinib (g)
- Erlotinib (h)
- Imatinib (i)
- Methotrexate
- Vinblastine (i)

Contraceptives
- Ethinylestradiol
- Etonogestrel
- Levonorgestrel

COVID19 therapies
- Budesonide (inhaled)
- Convalescent plasma

Gastrointestinal agents
- Aprepitant
- Domperidone

Herbal supplements
- Folic acid
- Magnesium
- St John’s Wort

HIV antiretrovirals
- Abacavir
- Atazanavir/ritonavir
- Darunavir/ritonavir
- Delavirdine
- Efavirenz
- Emtricitabine
- Lamivudine
- Lopinavir/ritonavir

Hypertension/heart failure
- Amiloride
- Dopamine
- Enalapril

Lipid lowering agents
- Atorvastatin
- Fluvastatin

Lipid lowering agents
- Atorvastatin
- Fluvastatin

Others
- Alopurinol
- Ergotamine
- Levodopa
- Levotheroxine

Steroids
- Beclometasone
- Betamethasone

Steroids
- Beclometasone
- Betamethasone
- Fludrocortisone
- Prednisolone
- Testosterone
- Triamcinolone

HCV antivirals
- Glecaprevir/pibrentasvir
- Ledipasvir/sofosbuvir
- Ombitasvir/paritaprevir/r
- Sofosbuvir/velpatasvir
Interactions with Essential Medicines & Nirmatrelvir/ritonavir (NMV/r)

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

Legend

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

Contraceptive Abbreviations

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

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 an 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.