

Drug interactions when using Paxlovid for >5 days

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

Data are limited or absent; therefore, risk-benefit assessment for any individual patient rests with prescribers.

Differences in the drug interaction potential of Paxlovid when used for 5 days or for an extended duration

Background

- An extended treatment duration of Paxlovid (nirmatrelvir/ritonavir) may be used in a clinical trial setting or in patients with persistent SARS-CoV-2 viral shedding and relapsing COVID-19 pneumonia (for example, in immunocompromised patients)
- When Paxlovid is used for 10 days or more, its interaction profile differs from that of a 5 day treatment duration.

Key differences

- **Induction of CYPs (CYP1A, CYP2B6, CYP2C9, CYP2C19) and UGTs** by ritonavir may result in clinically significant interactions as induction takes several days to reach maximal effect.
- **Pausing of medications** may not be possible or may be challenging when Paxlovid is used for an extended duration.
- **Dosing of immunosuppressants** needs to be adjusted using therapeutic drug monitoring.
- The **risk of corticosteroids adverse effects** increases when Paxlovid is given for an extended duration. Prescribers should be aware of and to look out for signs of systemic corticosteroid side effects.

Examples of comedications with potentially clinically relevant interactions

- The list below gives examples of drugs which may have a potentially significant interaction due to enzyme induction by ritonavir when Paxlovid is given for an extended duration.

Artesunate (UGT)	Lamotrigine (UGT1A4)
Asenapine (UGT1A1/CYP1A2)	Letermovir (UGT1A1)
Acenocoumarol (CYP2C9/1A2/2C19)	Levothyroxine (UGT)
Agomelatine (CYP1A2)	Minoxidil (UGT)
Aminophylline (CYP1A2)	Moxifloxacin (UGT1A1)
Artemether (UGT)	Mycophenolate (UGT)
Atovaquone (UGT)	Olanzapine (CYP1A2)
Binimetinib (UGT1A1)	Oxprenolol (UGT)
Bupropion (CYP2B6)	Rasagiline (CYP1A2)
Abrocitinib (CYP2C19/2C9)	Ropinirole (CYP1A2)
Canagliflozin (UGT1A9/2B4)	Pirfenidone (CYP1A2)
Cyclophosphamide (CYP2B6>2C9, 3A4)	Pizotifen (UGT2B10)
Dabigatran (P-gp)	Prazosin (CYP/UGT)
Dacarbazine (CYP1A2)	Proguanil (CYP2C19>3A4)
Dexmedetomidine (UGT)	Sertraline (CYP2B6>2C9/2C19)
Dipyridamole (UGT1A)	Siponimod (CYP2C9>3A4)
Dronabinol (CYP2C9>3A4)	Sodium valproate (UGT/CYP2C9)
Eltrombopag (UGT1A1/CYP1A2)	Phenprocoumon (CYP2C9/3A4)
Epirubicin (UGT2B7)	Theophylline (CYP1A2)
Febuxostat (CYP1A2/UGT)	Ticlopidine (CYP2B6/2C19/1A2 + other CYPs)
Frovatriptan (CYP1A2)	Tolbutamide (CYP2C9/2C8/2C19)
Gliclazide (CYP2C19)	Triamterene (CYP1A2)
Glimepiride (CYP2C9)	Valproate semisodium (UGT/CYP2C9/2C19)
Glipizide (CYP2C9)	Valproic acid (UGT/CYP2C9/2C19)
Hydromorphone (UGT2B7)	Warfarin (CYP1A2/CYP2C9/3A4)
Isavuconazole (CYP3A4/UGT)	