

1. KEY ACTIVITIES ON DAYS 0-4

TIP: first day of symptoms is arbitrarily labelled day 0

You have up to 5 days to decide about treatment.

Take 24-48 hours, when available, to confirm your patient's eligibility, check the eGFR (if necessary), and confirm the best possible medication history.

The 24-48 hours will also give you a sense of disease trajectory. Many immunocompetent vaccinated patients will get better on their own. In the clinical trial (where **all** patients were UNVACCINATED) 93% did well on placebo....

2. ELIGIBILITY

- Patient has positive PCR or rapid antigen test (RAT), can be self administered RAT
- Patient has symptoms, onset within the last 5 days
- Patient's eGFR is 30 or more
 - **TIP: get the eGFR on day 0-4 if you need it.**
 - **TIP: In the clinical trial eGFR was within last 6 months. But consider the possibility that eGFR may have changed (e.g. reduced oral intake, vomiting, new ACEI Rx)**
- patient does **NOT** have active liver disease (other than nonalcoholic hepatic steatosis), including chronic or active hepatitis B or C infection, primary biliary cirrhosis, Child-Pugh Class B or C, or acute liver failure
- patient does **NOT** have untreated HIV; (viral load **NOT** greater than 400 copies/mL)
- Patient is **NOT** pregnant. Unknown safety in pregnancy.
- patient has updated best possible medication history including herbals, OTCs, and PRNS

3. ASSESS DRUG DRUG INTERACTIONS

a. CYP3A4 inducer within the past 28 days

These drugs will indirectly lead to rapid inactivation of paxlovid, so they are an absolute contraindication. Paxlovid will not be effective. Typical drugs in this category are:

- antiseizure drugs such as phenytoin, carbamazepine, primidone or phenobarbital
- Prostate cancer drugs such as apalutamide or enzalutamide
- Rifampin
- St John's Wort.
 - **TIP Specifically ask about St John's Wort. It's an absolute contraindication**

b. Drugs with Long Half Lives Metabolized by the CYP3A4 Pathway

Coadministration of paxlovid and these drugs can lead to drug toxicity. The long half life means that temporary drug cessation will not ameliorate the risk. These drugs are an absolute contraindication. Typical drugs in this category are:

- Antiarrhythmics such as quinidine, flecainide, dronedarone, propafenone or amiodarone
- Some (not all) antipsychotics such as clozapine, pimozide or lurasidone
- pulmonary arterial hypertension drugs such as bosentan, sildenafil, tadalafil or vardenafil

c. Drugs with Short Half Lives Metabolized by the CYP3A4 Pathway

Coadministration of paxlovid with these drugs can lead to drug toxicity. Temporary cessation, replacing the drug or a dose reduction may be required. Many drugs fit into this category. You will NEVER be able to memorize them.

Some common drugs in this category are: alfuzosin, tamsulosin, colchicine, amlodipine, statins, rivaroxaban, apixaban, clopidogrel, ticagrelor, triazolam, viagra.

Typically patients should NOT take these drugs 12-24 hours before starting paxlovid and for 2-3 days after finishing PAXLVOID. Consult early with your pharmacist.

- **TIP** Get the best possible medication history done over days 0-4 so you are ready to prescribe by day 5
- **TIP:** if you identify potential interactions you can advise patient early
 - Example: stop atorvastatin on day 4, start paxlovid on day 5
- **TIP:** Use drug interaction software OR see a comprehensive list of interactions at <https://covid19-sciencetable.ca/sciencebrief/nirmatrelvir-ritonavir-paxlovid-what-prescribers-and-pharmacists-need-to-know-2-0/>

4. Side effects

- side effects more common than placebo group: metallic taste 5% , diarrhea 3%

5. Safe administration

- - For each dose, patient must take all tablets at the same time
 - Three tablets at a time for most patients; two tablets at a time if eGFR 30-59
 - Patient should finish entire 5 days of treatment
 - Patient should stop or reduce interacting drugs during paxlovid treatment
 - **TIP: Call patient on first day of treatment to reinforce these three points**
 - Patient should know how to resume usual medications after paxlovid treatment
 - **TIP: Call the patient on last day of treatment to make sure they restart usual medications correctly.**