# nirmatrelvir/ritonavir (Paxlovid)

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The goal of treating mild or moderate COVID-19 is to prevent the illness from progressing to severe disease, which can lead to hospitalization and/or death. A person with mild or moderate COVID-19 can receive treatment at home or in the community without having to receive care in the hospital (Figure 1). Treatment may also quicken recovery and reduce the amount of a time a person is infectious (able to pass SARS-CoV-2, the virus which causes COVID-19, on to others).

This factsheet provides information on a medication called nirmatrelvir/ritonavir, also known by the brand name **Paxlovid**, which is one of the few currently scientifically proven treatment options for mild or moderate COVID-19 among adults, young people, and children 12 years of age and older. We wrote this factsheet to help community-based advocates share accurate information on Paxlovid so that more people with COVID-19 and their caregivers know about the drug, how to take it, and how to access it.

**Figure 1: The spectrum of COVID-19**

| Mild COVID-19 | Moderate COVID-19 | Severe COVID-19 | Critical COVID-19 |
|---|---|---|---|
| Symptoms such as fever, cough, and loss of taste/smell, but no trouble breathing. | Symptoms plus evidence of disease in the lower respiratory tract, but with good oxygen saturation (≥94%). | Poor oxygen saturation (<94%), difficulty breathing (≥30 breaths/minute), signs of pneumonia (lung infiltrates). | Respiratory failure, shock, multiorgan failure. |
| **Can be treated with Paxlovid at home or in the community.** | | Requires hospitalization. Do not start Paxlovid. | Requires hospitalization and critical care. Do not start Paxlovid. |

**PAXLOVID** is the brand name of nirmatrelvir/ritonavir when sold by Pfizer. Generic versions of Paxlovid will be sold under different brand names.

We use the name Paxlovid throughout this factsheet for convenience, but the information here also applies to other versions of nirmatrelvir/ritonavir.

When started within a few days of experiencing COVID-19 symptoms, **Paxlovid can reduce the risk of COVID-19 hospitalization or death by 89%.**

When coupled with rest, supportive care, and monitoring, Paxlovid is one of the best tools people can use at home to prevent mild or moderate COVID-19 from progressing to severe disease. Access to Paxlovid is more important than ever following the surge in COVID-19 cases caused by the Omicron variant. In this stage of the pandemic, Paxlovid should be considered an essential medicine and access to Paxlovid a basic human right.

**What is Paxlovid?** Paxlovid is a medicine used in the treatment of mild or moderate COVID-19 that combines two drugs: **nirmatrelvir** and **ritonavir**. Nirmatrelvir is a new antiviral drug developed by Pfizer. Ritonavir is an older antiviral drug most often used to the enhance the effectiveness of treatments for HIV and hepatitis C.

**Figure 2: Who can take Paxlovid?**

| **Take Paxlovid if you:** | |
|---|---|
| | have mild or moderate COVID-19 |
| ***and*** | a positive SARS-CoV-2 test (either rapid antigen test or PCR) |
| ***and*** | are 12 years of age or older and weigh at least 40 kg (~88 pounds) |
| ***and*** | are at high risk of progression to severe COVID-19 |

**Before starting Paxlovid, give your health care provider a complete list of other medications you take, including herbal and traditional medicines.**

**Who can take Paxlovid?** Paxlovid can be used by adolescents or adults who are 12 years of age and older, weigh at least 40 kg, have received a positive SARS-CoV-2 test result, and are judged at high risk of progression from mild to moderate COVID-19 to severe disease, per an emergency use authorization granted by the U.S. Food and Drug Administration (FDA) and other regulatory authorities (Figure 2). People "at high risk of progression to severe COVID-19" include people with certain comorbidities or other health conditions that are known risk factors for hospitalization or death from COVID-19. This category includes people with diabetes, chronic lung disease, or immunosuppression, as well as elderly individuals regardless of comorbidities. Certain front-line health and essential workers who come into routine contact with large numbers of people who may have undiagnosed, transmissible SARS-CoV-2 should also be prioritized for treatment due to their higher exposure. People who are not yet vaccinated against COVID-19 are at especially high risk of hospitalization and death and should receive Paxlovid.

**How do I take Paxlovid?** One dose of Paxlovid = 300 mg of nirmatrelvir + 100 mg of ritonavir.

As shown in Figure 3, each dose of Paxlovid requires taking three pills: two nirmatrelvir 150 mg tablets (pink) + one ritonavir 100 mg tablet (white). It is important to take both drugs together. Ritonavir helps to boost the amount of nirmatrelvir in the body to the level required for the drug to work against COVID-19. Think of nirmatrelvir as the major character and ritonavir as playing an essential supporting role.

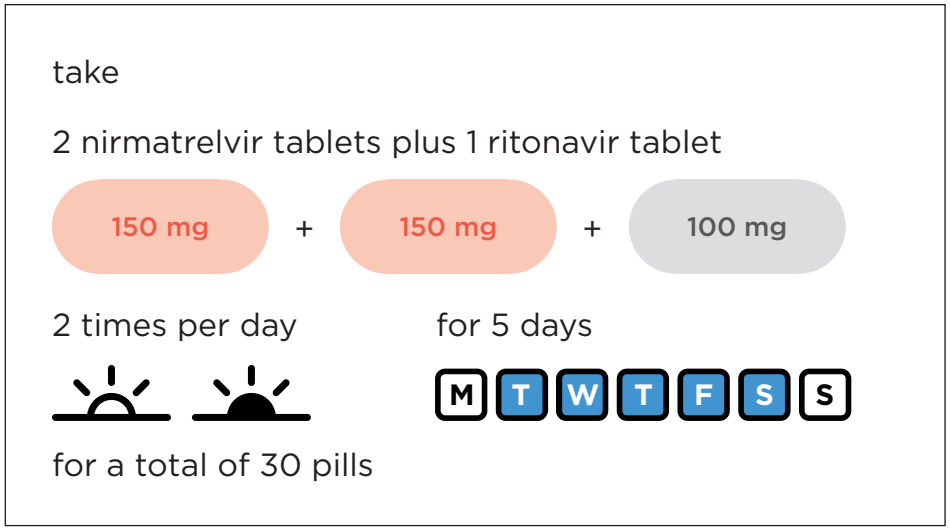
**The positive SARS-CoV-2 test required to receive Paxlovid can be either a rapid antigen test or a PCR test.** Rapid antigen tests have the quickest turn-around and can be taken at home as self-tests.

**People living with HIV, tuberculosis, or hepatitis C virus should be prioritized for access to testing and treatment for mild or moderate COVID-19.** They should also receive early access to COVID-19 vaccines. Read below for more info on using Paxlovid among these groups.

Take Paxlovid twice a day for five days. You should start treatment as soon as possible and within five days of feeling COVID-19 symptoms. You can take Paxlovid with or without food (though taking it with a meal is a good idea since some people have trouble taking ritonavir on an empty stomach). A full five-day treatment course of Paxlovid contains 30 pills.

Paxlovid must be prescribed by a physician, pharmacist, or other qualified health care worker. If you test positive for COVID-19 and believe you may be at high risk of severe disease, contact your primary health care provider immediately to see if you are eligible to take Paxlovid.

**Figure 3: How to take Paxlovid**




**What if I miss a dose?** The most important thing is to take every Paxlovid dose in full, according to a set schedule. This is called adherence and is a way to ensure that enough drug remains in the body to work against COVID-19. For example, each day you can take one dose in the morning (three pills) and the second dose in the evening (three pills) for a total of six pills.

If you forget to take a dose, or only take a partial dose, and less than eight hours have passed, the missed dose or pills should be taken as soon as possible before the next dose. If more than eight hours have passed since the missed dose, you should wait to take the next scheduled dose. In this event, you would take your last dose of Paxlovid on Day 6 after starting treatment.

**How was Paxlovid studied? Is it safe and effective?** The pharmaceutical company Pfizer studied the safety and efficacy of Paxlovid in a clinical trial of over 2,200 people who had just tested positive for COVID-19. Half were randomly assigned to be treated with Paxlovid, and half were randomly assigned to be treated with a placebo, or sugar pill. The study then compared the proportion of each group with COVID-19–related hospitalization or death from any cause and found Paxlovid to be safe and effective: the drug reduced the risk of COVID-19 hospitalization or death by 89% when taken correctly (Table 1). On the basis of these successful results, the FDA granted Paxlovid emergency use authorization in December 2021.

**Taking Paxlovid is not a substitute for getting vaccinated.** Vaccination provides the best protection against severe COVID-19.

**Do not crush, chew, or break tablets.** The tablets in Paxlovid should be swallowed whole.

**Do not make up for a missed dose by taking two doses of Paxlovid at once.**

**More info on Paxlovid clinical trials:**

- The clinical trial that showed the safety and efficacy of Paxlovid was called EPIC-HR (NCT04960202).
- The study of Paxlovid among people at lower risk, including some people who have been vaccinated, is called EPIC-SR (NCT05011513).
- The study of Paxlovid as preventive treatment for people exposed to COVID-19 is called EPIC-PEP (NCT05047601).
- The study of Paxlovid among children is called EPIC-PEDS (NCT05261139).

The clinical trial of Paxlovid did not include people vaccinated for COVID-19. Pfizer is now studying the safety and efficacy of Paxlovid among people who are deemed at lower risk of severe COVID-19, including people who have been vaccinated against COVID-19. Pfizer is conducting a third study to evaluate whether Paxlovid can be taken as preventive treatment by people exposed to COVID-19 by a member of their household. A fourth study of Paxlovid among children aged 6 to 18 years is also underway. These studies will report results in 2022 and, depending on the results, may expand Paxlovid's indicated use to include additional groups of people. In the meantime, people vaccinated against COVID-19 can take Paxlovid if they meet the general eligibility criteria in Figure 2.

**Table 1: Paxlovid safety and efficacy results from the Pfizer EPIC-HR trial**

| | **Paxlovid** (n=697) | **Placebo** (n=682) |
|---|---|---|
| *Efficacy** Number (and proportion) of participants with COVID-19 hospitalization or death through Day 28 | 5 (0.72%) | 44 (6.45%) |
| All-cause mortality (deaths) through Day 28 | 0 | 13 (1.1%) |
| What this means: | Fewer people in the EPIC-HR study who received Paxlovid were hospitalized related to COVID-19 or dead 28 days after entering the study than those who received placebo. There were no deaths in the group receiving Paxlovid compared with 13 deaths in the placebo group. More precisely, Paxlovid reduced the risk of COVID-19 hospitalization or death by 89% compared with placebo. This result was consistent across sub-groups of participants analyzed by age, gender, body mass index, and diabetes status. | |

*This is the primary efficacy analysis of 1,379 participants who started Paxlovid within 3 days of experiencing symptoms. Results were similar in a secondary efficacy analysis among a larger group of participants who began Paxlovid within 5 days of feeling symptoms.

**What are some common side effects of Paxlovid?** In a clinical trial that demonstrated the safety and efficacy of Paxlovid, the drug was well tolerated by most participants who received it. People taking Paxlovid reported fewer serious adverse events than people on placebo. Side effects reported more frequently by people who took Paxlovid instead of placebo included a distorted sense of taste (5.6% for Paxlovid vs. 0.3% for placebo) and diarrhea (3.1% vs. 1.6%). These effects were mild for most people who experienced them.

**Does Paxlovid work against COVID-19 caused by an infection with the Omicron variant?** Yes! Paxlovid is effective against COVID-19 caused by infection with the Omicron variant and previous COVID-19 variants. Early data suggest Paxlovid retains activity against the BA.2 Omicron subvariant.

**Can Paxlovid be taken with medications used to treat other illnesses?** In general, yes. But the specific answer depends on the other medicines you are taking.

You may hear a lot about Paxlovid interacting with other medicines. This is because Paxlovid can affect how quickly the body processes other drugs. At the same time, some other drugs may affect how quickly the body processes Paxlovid. These effects are called drug-drug interactions. Drug-drug interactions can change how well certain medicines work and can sometimes lead to dangerous side effects.

The liver is responsible for processing drugs in the body. There are specific enzymes in the liver that are essential to breaking down drugs. Some medicines can speed up or slow down specific liver enzymes, changing how quickly the body processes medicines and thereby affecting how much drug is in the body. In the case of Paxlovid, the ritonavir in Paxlovid inhibits (slows down) the activity of a liver enzyme called CYP3A that plays an important role in drug metabolism. At the same time that ritonavir inhibits CYP3A, the nirmatrelvir in Paxlovid is itself metabolized by CYP3A. By slowing down CYP3A, the ritonavir ensures that enough nirmatrelvir remains in the body for long enough to have its full effect. But this also means that when Paxlovid is taken with other drugs, things can go in one of two directions:

- Because CYP3A is inhibited (slowed down) by ritonavir, other drugs that are processed by this enzyme will be cleared by the body more slowly. Slower clearance will increase the concentration of these drugs to higher-than-normal levels, potentially leading to more side effects or adverse reactions.
- If Paxlovid is taken together with other drugs that speed up CYP3A, then the body will clear Paxlovid more quickly. This faster clearance could reduce nirmatrelvir drug levels to a point where Paxlovid is less effective against COVID-19.

**Table 2** (on the following page) illustrates drug-drug interactions between Paxlovid and some common medicines that people with HIV, tuberculosis (TB), and hepatitis C virus (HCV) may be taking. For more information on Paxlovid-related drug-drug interactions, you can consult the University of Liverpool COVID-19 drug interaction checker (https://covid19-druginteractions.org/).

**The bottom line: Always tell your health care provider about other medicines you are taking before starting Paxlovid. Depending on the medicine and its interaction with Paxlovid, your health care provider may change the dose of your medicine, switch you to a different medicine, or ask you to stop taking it altogether while on Paxlovid.**

| Table 2: Taking Paxlovid with medicines used to treat TB, HIV, and HCV* | | |
|---|---|---|
| **Condition** | **Medications** | **Effect with Paxlovid** |
| TB | rifampicin | ↓ Paxlovid concentrations |
| | rifapentine | |
| | isoniazid | — no expected interaction |
| | bedaquiline | ↑ bedaquiline concentration |
| | linezolid | — no expected interaction |
| | delamanid | ↑ delamanid concentrations |
| | pretomanid | — no expected interaction |
| | moxifloxacin, levofloxacin | — no expected interaction |
| HIV | dolutegravir | — no expected interaction |
| | bictegravir | — no expected interaction |
| | efavirenz | ↑ efavirenz concentration |
| | emtricitabine/tenofovir alafenamide | — potential weak interaction |
| | cabotegravir/rilpivirine (long acting) | — no expected interaction |
| | ritonavir or cobicistat (including lopinavir/ritonavir, darunavir/ritonavir, darunavir/cobicistat, atazanavir/ritonavir, atazanavir/cobicistat) | monitor for increased side effects |
| HCV | sofosbuvir/velpatasvir/voxilaprevir | ↑sofosbuvir, velpatasvir, voxilaprevir concentrations |
| | glecaprevir/pibrentasvir | ↑ glecaprevir/pibrentasvir concentrations |
| Opioid substitution | methadone | ↓ methadone concentrations |
| | buprenorphine | — potential weak interaction |

* Table lists important or representative medicines for each condition but is not comprehensive. For more information on drug-drug interactions, consult the University of Liverpool COVID-19 drug interactions resource: https://www.covid19-druginteractions.org/checker.

Major interaction expected. Do not use with Paxlovid.

Some interaction expected. Use under supervision and monitor for side effects.

No significant interaction expected. Drugs can be taken together with minimal monitoring.

### Taking Paxlovid if you are receiving treatment for HIV, TB, or HCV

Some evidence suggests that people with HIV, TB, and HCV may be at a higher risk of severe outcomes from COVID-19. (This risk is greatest when people with HIV, TB, or HCV also have additional risk factors for COVID-19 or are unvaccinated.) For this reason, people living with one or more of these three conditions should be prioritized for access to testing and treatment for mild or moderate COVID-19. They should also receive early access to COVID-19 vaccines.

**Can people living with HIV take Paxlovid?** Yes, people living with HIV (PLHIV) can take Paxlovid and Paxlovid may be given antiretroviral therapy (ART) regimens. PLHIV receiving Paxlovid should continue their HIV treatment without interruption. Many PLHIV may already be taking ritonavir as a part of their ART regimen. These people can receive Paxlovid without having to change their ART regimen but should be monitored for increased side effects. ***Treat COVID-19 and continue HIV treatment.***

**Can people with TB take Paxlovid?** The answer depends on the type of TB and the drugs being taken.

- For people with TB infection (sometimes called latent TB infection, or LTBI) who are eligible to take TB preventive treatment, the rifapentine or rifampicin used in common regimens (3HP, 1HP, 3HR, 4R) induces the same CYP3A liver enzyme that the ritonavir in Paxlovid inhibits. This means rifampicin and rifapentine will reduce nirmatrelvir levels, making Paxlovid less effective. People in this category should ***treat and recover from COVID-19 and wait to start TB preventive treatment.*** People who have already started a TB preventive treatment regimen with rifapentine or rifampicin can temporarily pause their regimen while taking Paxlovid and then resume TB preventive treatment several days after taking their last Paxlovid dose.
- For people with drug-sensitive TB, the rifampicin or rifapentine used in first-line TB treatment regimens interacts with the ritonavir in Paxlovid in a way that makes Paxlovid less effective. People in this category should ***continue drug-sensitive TB treatment and seek alternatives to Paxlovid for COVID-19.***
- For people with drug-resistant TB, Paxlovid may increase the concentration of certain drugs such as bedaquiline. People in this category should ***continue drug-resistant TB treatment and consider Paxlovid for COVID-19.*** If Paxlovid is taken, it is important that clinicians and patients work together to monitor for side effects and adjust TB drugs if necessary.

**Can people with HCV take Paxlovid?** Yes, people with HCV can take Paxlovid. Paxlovid is not recommended for use together with an HCV treatment called glecaprevir/pibrentasvir (also known by the brand names Mavyret and Maviret).

**Can pregnant people take Paxlovid?** The short answer is yes. The longer answer is that there are little data on using nirmatrelvir during pregnancy. (Ritonavir is often taken by pregnant people living with HIV and is considered safe for use.) However, while we wait for more data, it is important to allow pregnant people to make an informed choice to take Paxlovid — for at least two reasons. First, people who are pregnant or recently pregnant face a higher risk of severe COVID-19 than non-pregnant people. Second, COVID-19 is associated with poor pregnancy outcomes and poses a risk to the health of the mother and fetus. For these reasons, pregnant people with mild or moderate COVID-19 should have the choice to take Paxlovid after discussing the risks and benefits with their health care provider. The FDA has said that "for a mother and unborn baby, the benefit of taking Paxlovid may be greater than the risk of the treatment." Pregnant people who take Paxlovid should be followed throughout the duration of their pregnancy and after delivery and report pregnancy outcomes to their health care providers.

The option to take Paxlovid is all the more important given that another treatment option for mild and moderate COVID-19, molnupiravir, should *not* be taken by people who are pregnant or breastfeeding. (See Treatment Action Group's *Test and Treat Mild or Moderate COVID-19 Molnupiravir* factsheet for more information.)

**What about people who want to avoid pregnancy?** People taking hormonal birth control (such as Depo Provera) should know that Paxlovid may make their birth control less effective. For this reason, people who remain sexually active while taking Paxlovid should use — or ask their sexual partners to use — a second form of contraception, such as barrier methods like condoms, in addition to their hormonal birth control while taking Paxlovid and for a few days afterward.

**Is Paxlovid available in my country?** Access to Paxlovid will be limited by a critical supply shortage through most of 2022. This is because wealthy countries purchased most of the available supply of Paxlovid through at least the first half of 2022. In November 2021, Pfizer signed an agreement to license Paxlovid to the Medicines Patent Pool (MPP), allowing generic manufacturers anywhere in the world to sell Paxlovid in 95 countries. However, these countries represent just over 50% of the world's population. Additionally, it will take time for generic manufacturers to bring their versions of Paxlovid to the market and produce sufficient quantities to overcome the initial shortage. Generic manufacturers must also assure the quality of their medicines by obtaining approval from the World Health Organization Prequalification Programme or a stringent national regulatory authority. By March 2022, 36 manufacturers in 12 countries had signed up with the MPP to produce nirmatrelvir in combination with ritonavir.

**How much does Paxlovid cost?** In the United States, Pfizer sells Paxlovid for $530 per patient treatment course. For countries outside the MPP license, Pfizer has stated that it will sell Paxlovid under a tiered pricing approach in which high-income countries are charged more than middle-income countries; low-income countries will pay a "not-for-profit" price. This tiered pricing structure is in effect for the 4 million Paxlovid treatment courses Pfizer announced it would make available for procurement in 95 countries via UNICEF. The Global Fund has said that Pfizer plans to make available 10 million Paxlovid treatment courses to low- and middle-income countries in 2022. For countries included under the MPP license, it is not clear at the moment how generic manufacturers will price their versions of nirmatrelvir/ritonavir. The first company to introduce a generic version of Paxlovid, a firm in Bangladesh called Beximco, sells a five-day treatment course for $186. This price should come down substantially with the entry of additional suppliers.

**Where can I get more information?** The information in this factsheet came from the following sources: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