

molnupiravir (Lagevrio)

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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). Additionally, treatment may quicken recovery and reduce the amount of 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 **molnupiravir**, which is one of the few currently available treatment options for mild or moderate COVID-19 among adults 18 years of age and older. We wrote this factsheet to help community-based advocates share accurate information on molnupiravir so that more people with COVID-19 and their caregivers know about the drug and can make an informed choice about whether to take 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 ($\geq 94\%$).	Poor oxygen saturation ($< 94\%$), difficulty breathing (≥ 30 breaths/minute), signs of pneumonia (lung infiltrates).	Respiratory failure, shock, multiorgan failure.
Can be treated with molnupiravir at home or in the community.		Requires hospitalization. Do not start molnupiravir.	Requires hospitalization and critical care. Do not start molnupiravir.

Molnupiravir is the generic name of this drug. Different manufacturers will sell molnupiravir under different brand names. For example, molnupiravir made by Merck is sold as Lagevrio.

Molnupiravir is not suitable for everyone. It is an option worth considering when more effective oral antivirals against COVID-19, such as nirmatrelvir/ritonavir (Paxlovid), are unavailable.

When coupled with rest, supportive care, and monitoring, molnupiravir is a valuable tool for managing mild or moderate COVID-19 in people at high risk of progressing to severe disease. Molnupiravir is not suitable for everyone. But it is an option worth considering when more effective oral antivirals for treating mild or moderate COVID-19, such as nirmatrelvir/ritonavir (Paxlovid), are unavailable. It may also be a good choice for certain people on medications incompatible with nirmatrelvir/ritonavir. In short, molnupiravir is an important tool for some people, but not all people, with mild or moderate COVID-19.

What is molnupiravir? Molnupiravir is a treatment for mild or moderate COVID-19 developed by Merck and Ridgeback Biotherapeutics. The drug stops SARS-CoV-2, the virus that causes COVID-19, from replicating. It does this by forcing errors (mutations) into the SARS-CoV-2 viral genome (a process called mutagenesis). These forced errors prevent the virus from producing more copies of itself.

Figure 2: Who can take molnupiravir?

Take molnupiravir if you:	
	have mild or moderate COVID-19
and	a positive SARS-CoV-2 test (either rapid antigen test or PCR)
and	are 18 years of age or older
and	are at high risk of progression to severe COVID-19
and	other COVID-19 treatment options such as Paxlovid are either not available or not clinically appropriate
Do not take molnupiravir if you:	
	are younger than 18 years of age
or	are pregnant or planning to become pregnant soon
or	are breastfeeding
or	are able to access an alternative treatment option for mild or moderate COVID-19 such as Paxlovid

Who can take molnupiravir? The U.S. Food and Drug Administration (FDA) granted an emergency use authorization allowing molnupiravir to be used to treat mild or moderate COVID-19 in people who are 18 years of age and older, have received a positive SARS-CoV-2 test result, are judged at high risk of progression to severe COVID-19, and for whom other COVID-19 treatment options are either unavailable or clinically inappropriate (Figure 2). In March 2022, the World Health Organization conditionally recommend molnupiravir in people with non-severe COVID-19 “at highest risk of hospitalization.”

People who cannot access an alternative approved treatment for mild or moderate COVID-19 — such as nirmatrelvir/ritonavir (Paxlovid) — or who cannot take one of these other medicines due to a contraindication may benefit from molnupiravir.

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

The positive SARS-CoV-2 test required to show eligibility to receive molnupiravir can be either a rapid antigen test or a PCR test. Rapid antigen tests have the quickest turnaround and can be taken at home as self-tests.

category includes people with diabetes, high blood pressure, chronic lung disease, or immunosuppression, as well as elderly individuals regardless of comorbidities.

People who are not yet vaccinated against COVID-19 are at especially high risk of hospitalization and death and should be considered for molnupiravir.

How was molnupiravir studied? Is it effective? The pharmaceutical company Merck studied the safety and efficacy of molnupiravir in a clinical trial of over 1,400 people who had just tested positive for COVID-19. Half were randomly assigned to be treated with molnupiravir, 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. The study found molnupiravir to be modestly effective. Molnupiravir reduced the risk of hospitalization and death from COVID-19 by 30%. One person in the group assigned to receive molnupiravir died compared with nine people in the placebo group (Table 1). The proportion of participants reporting adverse events in each group was similar. On the basis of these results, the FDA granted molnupiravir emergency use authorization in December 2021.

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 molnupiravir among these groups.

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

Table 1: Molnupiravir safety and efficacy results from the Merck MOVE-OUT trial

	Molnupiravir (n=709)	Placebo (n=699)
<i>Efficacy*</i> Number (and proportion) of participants with COVID-19 hospitalization or death through Day 29	48 (6.8%)	68 (9.7%)
All-cause mortality (deaths) through Day 29	1 (0.1%)	9 (1.3%)
What this means:	Fewer people in the MOVE-OUT study who received molnupiravir were hospitalized related to COVID-19 or dead 29 days after entering the study than those who received placebo. There was one death in the group receiving molnupiravir compared with nine deaths in the placebo group. More precisely, molnupiravir reduced the risk of COVID-19 hospitalization or death by 30% 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 efficacy analysis that included data from all participants randomized to receive either molnupiravir or placebo. Merck originally reported a higher efficacy of molnupiravir based on an earlier analysis involving a smaller number of participants.		

A second phase III trial of molnupiravir reported results in February 2022. Conducted in India by the generic pharmaceutical company Hetero Labs, this study looked at how well molnupiravir prevented hospitalization through 14 days among over 1,200 adults who had just received a COVID-19 diagnosis and had COVID-19 symptoms for fewer than five days. Participants were assigned to receive either molnupiravir or standard-of-care management. Those who received molnupiravir were less likely to be hospitalized by Day 14. Molnupiravir reduced the risk of

COVID-19 hospitalization by 65% compared to standard of care alone. This is a much greater reduction than observed in the Merck study. The studies had different durations of follow-up (29 days versus 14), and the Hetero trial did not include participants over age 60 years.

Neither of these studies included people vaccinated against COVID-19. People vaccinated for COVID-19 can take molnupiravir if they meet the general eligibility criteria in Figure 2.

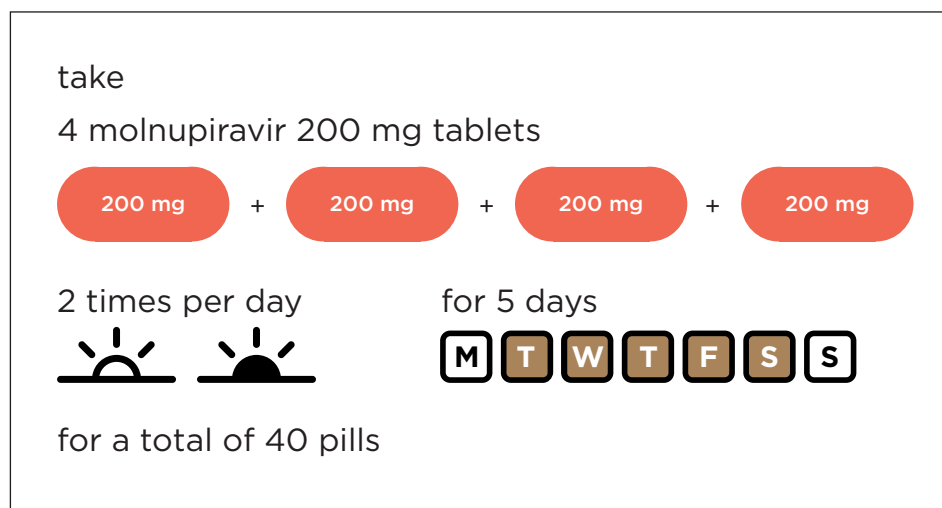
How do I take molnupiravir? One dose of molnupiravir = 800 mg taken as four 200 mg molnupiravir tablets.

As shown in Figure 3, each dose of four pills is taken by mouth every 12 hours (twice a day). A full treatment course of molnupiravir lasts five days. You should start treatment as soon as possible and within 5 days of feeling COVID-19 symptoms. You can take molnupiravir with or without food. Over a full five-day treatment course, you will take 40 molnupiravir tablets.

For molnupiravir to be effective, you should start taking it within five days of experiencing COVID-19 symptoms. It is important to begin the treatment course as soon as possible after feeling symptoms and receiving a positive COVID-19 test.

Molnupiravir 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 molnupiravir.

Figure 3: How to take molnupiravir



What if I miss a dose? The most important thing is to take every molnupiravir 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 (four pills) and the second dose 12 hours later in the evening (four pills) for a total of eight pills.

If you forget to take a dose, or only take a partial dose, and less than 10 hours have passed, the missed dose or pills should be taken as

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

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

soon as possible before the next dose. If more than 10 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 molnupiravir on Day 6 after starting treatment.

Molnupiravir safety

What are some common side effects of molnupiravir? In the Merck clinical trial that demonstrated the safety and efficacy of molnupiravir, the drug was well tolerated by most participants who received it. Side effects reported by more than 1% of people in either the group receiving molnupiravir or those receiving placebo included diarrhea, nausea, and dizziness (though all three were uncommon). Similar side effects were seen in the study by Hetero Labs.

Are there any particular safety concerns? Molnupiravir works against COVID-19 by introducing errors into the SARS-CoV-2 genome. Some people have asked whether molnupiravir can damage the genetic material of human cells in people taking it (an effect called genotoxicity). The FDA has said that “molnupiravir is low risk for genotoxicity.” The FDA’s judgement is based on available evidence, the limited duration of treatment (five days), and on animal studies conducted by Merck in which rodents received molnupiravir at doses much higher than the dose used in people. Reassuringly, these animal studies did not show any genotoxic effects. However, the long-term risks of molnupiravir are unknown at this time. People should know about the potential risk of genotoxicity before taking molnupiravir. These risks are one reason why molnupiravir is not recommended for pregnant people and children (keep reading for more detail).

In order to generate further evidence on the safety of molnupiravir, people taking the drug are advised to report any serious side effects to their health care provider or Merck.

Does molnupiravir work against COVID-19 caused by an infection with the Omicron variant? Yes! Molnupiravir is effective against COVID-19 caused by infection with the Omicron variant (BA.1 and BA.2).

Can molnupiravir prevent infection from SARS-CoV-2? No. Molnupiravir should not be taken either before or after exposure to COVID-19 to prevent infection. At this time, there is no evidence that molnupiravir can prevent infection with SARS-CoV-2.

Who should *not* take molnupiravir? Do not take molnupiravir if you are:

- Younger than 18 years of age.
- Pregnant or breastfeeding.
- Planning to become pregnant soon.

Molnupiravir is not right for children and young people: Molnupiravir has not been studied in people younger than 18 years old. This is because molnupiravir has the potential to disrupt bone growth and cartilage formation. This potential was observed in a preclinical study conducted in rats. For this reason, molnupiravir is currently not recommended for children and adolescents younger than 18 years of age.

Molnupiravir is not right for pregnant people: Molnupiravir should not be taken by people who are pregnant. There are no human data on the safety of molnupiravir taking during pregnancy; information on the risk of the drug in this context comes from animal studies. Preclinical studies in animal models (rats and rabbits) indicate that molnupiravir is teratogenic (able to disrupt fetal development) and may be mutagenic during pregnancy (able to introduce a permanent change to genetic material, i.e., DNA). For these reasons, the FDA and WHO do not recommend molnupiravir for use in pregnancy.

If you are pregnant and take molnupiravir, you should report your exposure to the drug to Merck. The company has established a surveillance program to assess whether exposure to the drug has any effect on pregnancy outcomes. To report molnupiravir exposure during pregnancy, you can

contact Merck — or give permission for your health care provider to get in touch with Merck — at pregnancyreporting.msd.com (or 1-877-888-4231).

Where does this leave people who are pregnant? People who are pregnant should seek other treatment options for mild or moderate COVID-19. One option is nirmatrelvir/ritonavir (Paxlovid). The FDA emergency use authorization for nirmatrelvir/ritonavir clearly states that pregnant people should have the option to take this drug after weighing all of the risks and benefits together with their health care provider. The risks are primarily related to the lack of information on nirmatrelvir given during pregnancy. (Ritonavir is often taken by pregnant people living with HIV and is considered safe for use.) The primary benefit is a lower risk of severe COVID-19 in a high-risk population. Additionally, COVID-19 is associated with adverse pregnancy outcomes and poses a risk to the health of the mother and fetus. For this reason, it is important to have a treatment option for mild or moderate COVID-19 that can be taken during pregnancy; the best option is nirmatrelvir/ritonavir.

The bottom line: people with mild or moderate COVID-19 who are pregnant should have the option to take nirmatrelvir/ritonavir but should avoid taking molnupiravir.

Molnupiravir is not right for people who are breastfeeding: Because molnupiravir might pose a risk to infant development, the FDA recommends that people do not breastfeed while taking molnupiravir. There are no data on molnupiravir in human breastmilk, but a study in rats demonstrated that molnupiravir can pass from mother to nursing pup. Someone who stops breastfeeding in order to take molnupiravir may resume four days after receiving their last dose of the drug. This gives the body enough time to fully process and clear molnupiravir before breastfeeding is resumed.

Is molnupiravir right for people who can become pregnant? What about people whose sexual partners could become pregnant? There are some important things about molnupiravir to consider if you are sexually active and of childbearing potential (can become pregnant) or have a sexual partner of childbearing potential:

- If you are sexually active and have the ability to become pregnant: use a reliable method of birth control while taking molnupiravir and for at least four days afterward. This advice is designed to prevent molnupiravir exposure by mother and fetus during gestation and early pregnancy. The four-day period after completing molnupiravir is like a washout period and ensures your body has fully cleared the drug.
- If your sexual partners are of childbearing potential: use a reliable method of contraception while taking molnupiravir and for at least three months after the last molnupiravir dose. This is important because studies of how molnupiravir may affect sperm have not been completed.

Can molnupiravir be taken with medications used to treat other illnesses? Yes, molnupiravir has very few drug-drug interactions with other medicines. Molnupiravir's compatibility with other medicines is one of its biggest advantages. This is all the more important since nirmatrelvir/ritonavir (Paxlovid), the only other oral antiviral pill for mild or moderate COVID-19, interacts with many other drugs. (For more information on these drug-drug interactions, you can read Treatment Action Group's [nirmatrelvir/ritonavir factsheet](#) or consult the University of Liverpool COVID-19 drug interaction checker: <https://covid19-druginteractions.org/>.)

Can people with HIV, tuberculosis, or hepatitis C take molnupiravir?

Some evidence suggests that people with HIV, tuberculosis (TB), or hepatitis C virus (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.)

- Yes, people living with HIV can take molnupiravir, and molnupiravir may be given with antiretroviral regimens to treat HIV. People taking pre-exposure prophylaxis to prevent HIV may also take molnupiravir.
- Yes, people with TB can take molnupiravir. Molnupiravir is compatible with medicines used for TB preventive treatment in people with TB infection (sometimes called latent TB infection, or LTBI) and with regimens recommended for treating both drug-sensitive and drug-resistant TB. Molnupiravir may be particularly important when managing co-infection with TB and COVID-19 because another COVID-19 oral antiviral drug called nirmatrelvir/ritonavir is not compatible with drug-sensitive TB treatment or TB preventive treatment. (This is due to a drug-drug interaction between nirmatrelvir/ritonavir and TB drugs rifampicin and rifapentine — read TAG’s nirmatrelvir/ritonavir factsheet to learn more.)
- Yes, people with HCV can take molnupiravir. Molnupiravir may be given with oral antivirals used to treat HCV including glecaprevir/pibrentasvir (Mavyret) and ledipasvir/sofosbuvir (Harvoni).

The bottom line: People with HIV, TB, and HCV can take molnupiravir under most circumstances. Whether people with HIV, TB, and HCV *should* take molnupiravir is a decision best made by an individual after talking with their health care provider about the pros and cons of molnupiravir and after assessing the availability of other treatment options, including nirmatrelvir/ritonavir.

Is molnupiravir available in my country? Molnupiravir 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 molnupiravir.

Some countries and regions may experience periods of limited molnupiravir availability through the first half of 2022. Molnupiravir may be easier to access than alternative treatments for mild or moderate COVID-19 such as nirmatrelvir/ritonavir. In October 2021, Merck signed an agreement to license molnupiravir to the Medicines Patent Pool (MPP), allowing generic manufacturers anywhere in the world to sell molnupiravir in 105 countries. These countries represent 100% of the population in regions like South Asia and Sub-Saharan Africa and as little as 5% and 0% of the populations in Europe & Central Asia and North America, respectively. The license excludes large countries such as Brazil, China, Mexico, and the Russian Federation.

By February 2022, 27 generic manufacturers from 11 countries had signed up with the MPP to produce molnupiravir. It will take time for these companies to bring their versions of molnupiravir to the market and obtain the required quality assurance approvals from the World Health Organization or stringent national regulatory authorities. But many of these companies are already close to introducing their versions of the drug, and the initial supply shortage will soon ease. The first generic versions of molnupiravir are already available in India, where Merck signed an earlier licensing agreement with five Indian generic manufacturers.

How much does molnupiravir cost? In the United States, Merck sells molnupiravir for \$712 per patient treatment course. For other countries outside of the MPP license, Merck has stated that it will sell molnupiravir under a tiered pricing approach in which high-income countries are charged more than middle-income countries. For countries included within the MPP license, the price of molnupiravir will be set by generic producers; more information will become available as companies begin to sell their versions of the drug.

One analysis by researchers Melissa Barber and Dzintars Gotham estimates that molnupiravir can be produced for under \$20 per patient course (based on cost of production and including a 10% profit margin and tax on profits). Before entering the licensing agreement with MPP, Merck allowed five Indian pharmaceutical companies to supply the drug to low- and middle-income countries. One of those companies, Dr. Reddy’s, introduced molnupiravir at a price of \$18, in line with the estimate from Barber and Gotham.

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

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