

Patient leaflet in accordance with the Pharmacists' Regulations (Preparations) - 1986

This medicine is dispensed with a doctor's prescription only

Paxlovid™

Film-coated tablets

Paxlovid contains 2 types of tablets with the following active substances:

- Each pink film-coated tablet contains: nirmatrelvir 150 mg
- Each white to off-white film-coated tablet contains: ritonavir 100 mg

Inactive ingredients and allergens in the medicine: See section 2 under 'Important information about some of this medicine's ingredients' and section 6 'Further information'.

Read the entire leaflet carefully before using this medicine. This leaflet contains concise information about this medicine. If you have any further questions, consult your doctor or pharmacist.

This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if it seems to you that their medical condition is similar to yours.

1. WHAT IS THIS MEDICINE INTENDED FOR?

Paxlovid is indicated for treatment of confirmed coronavirus disease 2019 (COVID-19) in adults who do not require supplemental oxygen and who are at increased risk of progressing to severe COVID-19 disease.

Therapeutic group: antiviral.

COVID-19 is caused by a virus called a coronavirus. Paxlovid stops the virus multiplying in cells and this stops the virus multiplying in the body. This can help your body to overcome the virus infection, and may prevent the development of severe illness.

2. BEFORE USING THIS MEDICINE

Do not use this medicine if:

- You are sensitive (allergic) to the active ingredients nirmatrelvir, ritonavir or to any of the other ingredients in this medicine (see section 6).
- You are taking any of the following medicines. Taking Paxlovid with these medicines may cause serious or life-threatening side effects or affect how Paxlovid works:
 - Alfuzosin (to treat symptoms of an enlarged prostate)
 - Ranolazine (to treat chronic chest pain [angina])
 - Dronedarone, propafenone, quinidine (to treat heart conditions and correct irregular heartbeats)
 - Rifampicin, rifapentine (to treat bacterial infections)
 - Apalutamide, neratinib, venetoclax (to treat cancer)
 - Carbamazepine, phenobarbital, phenytoin, primidone (to prevent and control seizures)
 - Colchicine (to treat gout)
 - Terfenadine (to treat allergies)
 - Lurasidone (to treat schizophrenia)
 - Pimozide, quetiapine (to treat schizophrenia, bipolar disorder, severe depression and abnormal thoughts or feelings)
 - Silodosin (to treat enlarged prostate gland)
 - Eplerenone and ivabradine (to treat heart and/or blood vessel problems)
 - Dihydroergotamine and ergotamine (to treat migraine headaches)

- Ergonovine and methylergonovine (used to stop excessive bleeding that may occur following childbirth or an abortion)
- Cisapride (to relieve certain stomach problems)
- St. John's wort (*Hypericum perforatum*) (a herbal remedy used for depression and anxiety)
- Voclosporin (to treat immune disorders)
- Lovastatin, simvastatin, lomitapide (to lower blood cholesterol)
- Eletriptan (to treat migraine headaches)
- Lumacaftor/ivacaftor (to treat cystic fibrosis)
- Finerenone (to treat chronic kidney disease associated with Type 2 diabetes)
- Naloxegol (to treat opioid-induced constipation)
- Avanafil, vardenafil (to treat erectile dysfunction [also known as impotence])
- Sildenafil, tadalafil (used to treat erectile dysfunction [also known as impotence] or pulmonary arterial hypertension [high blood pressure in the pulmonary artery])
- Clorazepate, diazepam, estazolam, flurazepam, triazolam, midazolam taken orally (used to relieve anxiety and/or trouble sleeping)
- Tolvaptan used to treat hyponatremia (low sodium levels in the blood)

Special warnings regarding use of the medicine

- **Allergic reactions** - including severe allergic reactions (known as 'anaphylaxis') and serious skin reactions (known as 'toxic epidermal necrolysis' and 'Stevens-Johnson syndrome'), can happen in people taking Paxlovid, even after only 1 dose. Stop taking Paxlovid and call your doctor right away if you get any of the following symptoms of an allergic reaction:
 - trouble swallowing or breathing
 - swelling of the tongue, mouth, and face
 - throat tightness
 - hoarseness
 - itching
 - skin rash
 - red and painful skin
 - blisters and peeling skin
 - blisters or sores in the mouth or lips
- **Risk of HIV-1 resistance development** - If you have untreated and/or uncontrolled HIV infection, Paxlovid may lead to some HIV medicines not working as well in the future.

Before treatment with Paxlovid, tell your doctor if:

- You have or have had **a liver disease**. Liver enzyme abnormalities, hepatitis (inflammation of the liver) and jaundice have occurred in patients receiving ritonavir.
- You have or have had **a kidney disease**.
- You have **high blood pressure**. Your doctor may need to check your blood pressure before taking Paxlovid and while you are taking this medicine. There have been reports of high blood pressure in people taking Paxlovid, particularly in older individuals.

Children and adolescents

Do not give Paxlovid to children and adolescents under 18 years because there is no information regarding the safety and efficacy of its use in children and adolescents.

Drug interactions

If you are taking or have recently taken other medicines, including nonprescription medicines and dietary supplements, tell your doctor or pharmacist.

There are other medicines that may not be taken together with Paxlovid. See section 'Do not use this medicine if'. In addition, tell your doctor if you are taking, have recently taken or might take any other medicines. Particularly tell about:

- medicines used to treat cancer, such as afatinib, abemaciclib, ceritinib, dasatinib, encorafenib, fostamatinib, ibrutinib, ivosidenib, nilotinib, vinblastine and vincristine
- medicines used to thin the blood (anticoagulants), such as warfarin, rivaroxaban, dabigatran and apixaban
- medicines used to treat convulsions, such as divalproex, lamotrigine and clonazepam
- medicines used for smoking cessation, such as bupropion
- medicines used to treat allergies, such as fexofenadine and loratadine
- medicines used to treat fungal infections (antifungals), such as itraconazole and voriconazole
- medicines used to treat Cushing's syndrome - when the body produces an excess of cortisol, such as ketoconazole tablets
- medicines used to treat HIV infection, such as efavirenz, maraviroc, raltegravir, zidovudine and bictegravir/emtricitabine/tenofovir
- medicines used to treat infections (e.g., antibiotics and antimycobacterials), such as atovaquone, clarithromycin, erythromycin, fusidic acid (taken orally or administered by IV route), bedaquiline, rifabutin, delamanid, sulfamethoxazole/trimethoprim
- medicines used to treat schizophrenia and abnormal thoughts or feelings, such as clozapine
- medicines used to treat mental or mood disorders, such as haloperidol, risperidone and thioridazine
- medicines used to treat high blood pressure in the blood vessels that supply the lungs, such as bosentan and riociguat
- medicines used to treat high blood pressure (hypertension), such as amlodipine, diltiazem, felodipine, lercanidipine, nicardipine, nifedipine and verapamil
- medicines used to treat heart and/or blood vessel problems, such as aliskiren, ticagrelor, cilostazol and clopidogrel
- medicines used to treat heart conditions and correct irregular heartbeats, such as digoxin, amiodarone, flecainide and disopyramide
- medicines to treat cystic fibrosis, such as ivacaftor, elexacaftor/tezacaftor/ivacaftor and tezacaftor/ivacaftor
- medicines used to treat diabetes such as saxagliptin
- medicines used to treat hepatitis C virus infection, such as glecaprevir/pibrentasvir and sofosbuvir/velpatasvir/voxilaprevir
- medicines used to lower blood cholesterol, such as atorvastatin, fluvastatin, pravastatin and rosuvastatin
- medicines used to treat migraine headaches, such as rimegepant
- medicines used to treat urinary incontinence, such as darifenacin and solifenacin
- medicines used to treat mental health problems, such as aripiprazole, brexpiprazole and cariprazine
- medicines used to suppress the immune system, such as cyclosporine, everolimus, sirolimus and tacrolimus
- medicines used to treat autoimmune disorders including rheumatoid arthritis, psoriatic arthritis or ulcerative colitis, such as tofacitinib and upadacitinib
- medicines used to treat severe pain, such as morphine, fentanyl, oxycodone, methadone, buprenorphine, other morphine-like medicines, pethidine and piroxicam
- medicines used as sedatives, hypnotics and sleeping agents, such as alprazolam, buspirone and zolpidem
- medicines used to treat attention deficit disorder or a sleep disorder called narcolepsy, such as amphetamines
- steroids including corticosteroids used to treat inflammation, such as budesonide, dexamethasone, fluticasone, prednisolone and triamcinolone
- medicines used to treat asthma and other lung-related problems such as chronic obstructive pulmonary disease [COPD], such as salmeterol and theophylline

- medicines used to treat depression, such as amitriptyline, fluoxetine, imipramine, nortriptyline, paroxetine and sertraline
- medicines used as thyroid replacement therapy, such as levothyroxine
- medicine used to treat enlarged prostate, such as tamsulosin
- any of the following medicines:
 - o oral or patch contraceptive containing ethinyl estradiol used to prevent pregnancy
 - o midazolam administered by injection (used for sedation [an awake but very relaxed state of calm or drowsiness during a medical test or procedure] or anaesthesia)

Many medicines interact with Paxlovid. **Keep a list of your medicines to show your doctor or pharmacist.** Do not start taking a new medicine without telling your doctor. Your doctor can tell you if it is safe to take Paxlovid with other medicines.

Using this medicine and food

Paxlovid can be taken with or without food.

Pregnancy and breastfeeding

If you are pregnant, think you may be pregnant or are planning to have a baby, ask your doctor for advice before taking this medicine. There is not enough information to be sure that Paxlovid is safe for use in pregnancy. If you are pregnant, it is not recommended to use Paxlovid unless your clinical condition requires this treatment.

It is recommended that you refrain from sexual activity or use contraception while taking Paxlovid and for 7 days after completing Paxlovid intake as a precaution. If you are taking hormonal contraceptives, it is recommended to use a condom or other non-hormonal methods of contraception, as Paxlovid may reduce the effectiveness of hormonal contraceptives. Your doctor will advise you on the duration of the required adjustment of your contraceptive measures.

There is no information on the use of Paxlovid during breastfeeding. You should not breastfeed your baby while taking Paxlovid and for 7 days after intake completion as a precaution.

Driving and using machines

Paxlovid is expected to have no influence on the ability to drive and use machines.

Important information about some of this medicine's ingredients

Paxlovid contains lactose - If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicine.

Paxlovid contains sodium - Nirmatrelvir and ritonavir tablets each contain less than 1 mmol (23 mg) sodium per dose, that is to say essentially 'sodium-free'.

3. HOW TO USE THIS MEDICINE?

Always use this medicine according to your doctor's instructions.

Check with the doctor or pharmacist if you are uncertain about the dosage and treatment regimen of the medicine.

The dosage and treatment regimen will be determined by your doctor only.

The standard dosage and treatment regimen are usually:

Paxlovid consists of 2 medicines: nirmatrelvir and ritonavir. The recommended dose is 2 tablets of nirmatrelvir (pink tablets) with 1 tablet of ritonavir (white tablet) by mouth twice daily (in the morning and evening).

Each blister card contains 4 nirmatrelvir tablets (150 mg each) and 2 ritonavir tablets (100 mg each) and indicates which tablets need to be taken in the morning and evening (according to the different background colours).

A course of treatment lasts 5 days. For each dose, take all 3 tablets together at the same time.

If the symptoms worsen or do not improve after 5 days, consult your doctor.

If you have a kidney disease, please talk to your doctor for an appropriate dose of Paxlovid.

Swallow the tablet whole with or without food. Do not chew, break or crush the tablets, since the effect of this administration route has not been examined.

Do not exceed the recommended dose.

Adhere to the treatment as recommended by your doctor.

If you have taken a higher dosage of Paxlovid or if a child has accidentally swallowed some medicine, immediately see a doctor or go to a hospital emergency room and bring the medicine package with you.

If you forget to take Paxlovid

If you miss a dose of Paxlovid within 8 hours of the time it is usually taken, take it as soon as you remember. If you miss a dose by more than 8 hours, skip the missed dose and take the next dose at the regular time. Do not take 2 doses of Paxlovid at the same time.

Do not take a double dose to make up for the forgotten dose.

If you stop taking Paxlovid

Even if you feel better, do not stop taking this medicine without consulting your doctor.

Do not take medicines in the dark! Check the label and dose each time you take medicine. Wear glasses if you need them.

If you have any further questions about using this medicine, consult your doctor or pharmacist.

4. SIDE EFFECTS

As with any medicine, use of Paxlovid may cause side effects in some users. Do not be alarmed by this list of side effects; you may not experience any of them.

Common side effects (occur in up to 1-10 in 100 users):

- Diarrhoea
- Vomiting
- Nausea
- Altered sense of taste (such as metallic, bitter taste)
- Headache

Uncommon side effects (occur in 1-10 in 1,000 users):

- Allergic reaction
- High blood pressure
- Abdominal pain
- Muscle pain
- Skin rash (also reported as part of allergic reaction)

Rare side effects (occur in 1-10 in 10,000 users):

- Severe allergic reaction known as 'anaphylaxis' (such as swelling of the tongue, mouth and face, trouble swallowing or breathing, throat tightness or hoarseness)
- Serious skin reactions known as 'toxic epidermal necrolysis' and 'Stevens-Johnson syndrome' (such as red and painful skin, blisters and peeling skin, blisters or sores in your mouth or lips)
- Malaise
- Itching (also reported as part of allergic reaction)

If you experience any side effect, if any side effect gets worse, or if you experience a side effect not mentioned in this leaflet, consult your doctor.

You can report side effects to the Ministry of Health by following the link 'Reporting Side Effects of Drug Treatment' on the Ministry of Health home page (www.health.gov.il) which links to an online form for reporting side effects or by using the link: <https://sideeffects.health.gov.il> .

5. HOW TO STORE THE MEDICINE?

- Prevent poisoning! This and any other medicine should be kept in a closed place, out of the reach and sight of children and/or infants to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by a doctor.
- Do not use the medicine after the expiry date (exp. date) which is stated on the package. The expiry date refers to the last day of that month.
- No special storage conditions. Storing at room temperature is recommended.

6. FURTHER INFORMATION

In addition to the active ingredients, this medicine also contains:

Nirmatrelvir tablet:

microcrystalline cellulose, lactose monohydrate, croscarmellose sodium, colloidal silicon dioxide, sodium stearyl fumarate

Coating (Opadry Pink):

HPMC 2910/Hypromellose, titanium dioxide, macrogol/PEG, iron oxide red

Ritonavir tablet:

copovidone, calcium hydrogen phosphate, sorbitan laurate, sodium stearyl fumarate, silica, colloidal anhydrous, ethanol (It will not appear in the final product except in trace)

Coating (Opadry White):

HPMC 2910/Hypromellose 6cp (E464), titanium dioxide (E171), macrogol /PEG, MW 400 (E1521), hydroxypropyl cellulose (E463), talc (E553b), macrogol/PEG, MW 3350, MACROGOL 4000 (E1521), silica, colloidal anhydrous (E551), polysorbate 80 (E433)

What the medicine looks like and contents of the pack:

Paxlovid pack contains 30 film-coated tablets divided into 5 blister cards packaged in a carton.

Each blister card contains 4 nirmatrelvir tablets (150 mg each) and 2 ritonavir tablets (100 mg each) and indicates which tablets need to be taken in the morning and evening (according to the different background colours).

Nirmatrelvir 150 mg film-coated tablet: A pink, oval-shaped tablet debossed with 'PFE' on one side and '3CL' on the other side.

Ritonavir 100 mg film-coated tablet: A white to off-white, capsule shaped tablet debossed with 'H' on one side and 'R9' on the other side.

Registration holder and address: Pfizer Pharmaceuticals Israel Ltd., 9 Shenkar St., Herzliya Pituach 46725.

Registration number of the medicine in the Ministry of Health National Drug Registry:
175-58-37720-99

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