

WHO-PQ RECOMMENDED PATIENT INFORMATION LEAFLET

*This patient information leaflet focuses on uses of the medicine covered by WHO's Prequalification Team - Medicines. The recommendations for use are based on WHO guidelines and on information from stringent regulatory authorities.**

The medicine may be authorised for additional or different uses by national medicines regulatory authorities.

* https://extranet.who.int/prequal/sites/default/files/document_files/75%20SRA%20clarification_Feb2017_newtempl.pdf

Information for the patient

[CV016 trade name][†]
Nirmatrevir + Ritonavir

*The warnings and instructions in this leaflet are intended for the person taking the medicine.
If you are a parent or carer responsible for giving the medicine to someone else such as a child,
you will need to apply the instructions accordingly.*

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have questions about the medicine, ask your health care provider.
- This medicine is for you only. Do not pass it on to others. It may harm them, even if their illness seems to be the same as yours.
- If you are concerned about any side effects, talk to your health care provider. This includes unwanted effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What [CV016 trade name] is and what it is used for
2. What you need to know before you take [CV016 trade name]
3. How to take [CV016 trade name]
4. Possible side effects
5. How to store [CV016 trade name]
6. Contents of the pack and other information

1. What [CV016 trade name] is and what it is used for

The medicine [CV016 trade name] contains two active substances, nirmatrelvir and ritonavir, each in separate tablets. [CV016 trade name] is used for treating adults with COVID-19 who do not need treatment with oxygen. The medicine is used if you are more likely to get seriously ill with COVID-19.

COVID-19 is caused by a virus called SARS-CoV-2, a type of coronavirus. The active substance, nirmatrelvir, stops the virus multiplying in the body and this can help stop you becoming seriously ill and needing hospital treatment. The other active substance in the medicine, ritonavir, reduces the breakdown of nirmatrelvir and so increases its effect against the virus.

2. What you need to know before you take [CV016 trade name]

Do not take [CV016 trade name]

- if you are allergic to nirmatrelvir, ritonavir, or to any of the other ingredients of this medicine (listed in section 6).
- if you are taking any of the following medicines. Taking [CV016 trade name] with these medicines may cause serious or life-threatening side effects or affect how [CV016 trade name] works:
 - Alfuzosin, silodosin (for treating prostate problems)
 - Amiodarone, dronedarone, eplerenone, flecainide, ivabradine, propafenone, quinidine (for treating heart conditions)
 - Apalutamide, neratinib, venetoclax (for treating cancer)

[†] Trade names are not prequalified by WHO. This is the national medicines regulatory agency's responsibility.

- Avanafil, sildenafil, tadalafil, vardenafil (for treating men with erectile disorder; sildenafil and tadalafil are also used for treating high blood pressure in the lungs)
- Carbamazepine, phenobarbital, phenytoin (for treating epilepsy)
- Clorazepate, diazepam, estazolam, flurazepam, triazolam, midazolam (for relieving anxiety and sleeping trouble or for controlling convulsions)
- Clozapine, lurasidone, pimozone, quetiapine (for treating mental conditions such as abnormal thoughts or feelings, schizophrenia, and bipolar disorder)
- Colchicine (for treating gout)
- Dihydroergotamine, eletriptan, ergotamine, (for treating migraine headaches)
- Ergometrine, methylergometrine (for treating excessive bleeding after childbirth)
- Fusidic acid, rifampicin (for treating bacterial infections)
- Lomitapide, lovastatin, simvastatin (used to lower blood cholesterol)
- Ranolazine (for treating angina, a chest pain)
- St John's wort (*Hypericum perforatum*) (a herbal remedy for relieving depression and anxiety)
- Terfenadine (antihistamine for treating allergies such as hayfever)
- Tolvaptan (for treating some kidney disorders and correcting low sodium levels in the blood)
- Voclosporin (for treating conditions caused by overactive immune system)

There may be other medicines that you must not take with [CV016 trade name]. Talk to your health care provider about all the medicines you take before you start taking [CV016 trade name].

Warnings and precautions

Talk to your health care provider about any concerns before you take [CV016 trade name].

Allergic reactions

Allergic reactions, including severe allergic reactions (known as anaphylaxis), can happen in people taking [CV016 trade name], even after only 1 dose. Stop taking [CV016 trade name] and contact your health care provider right away if you get any of the following:

- trouble swallowing or breathing
- swelling of the tongue, mouth, and face
- throat tightness
- hoarseness
- itching
- skin rash

Liver disease

Tell your health care provider if you have ever had liver disease. Liver injury can occur in patients taking the active substance ritonavir.

Kidney disease

Tell your health care provider if you have ever had kidney disease.

High blood pressure

Tell your doctor if you have high blood pressure. Some people taking this medicine may develop increases in their blood pressure, usually temporarily. Your health care provider may want to check your blood pressure during treatment.

Risk of developing HIV-1 resistance

If you have untreated HIV infection, treatment with [CV016 trade name] may reduce how well some HIV medicines work.

Children and adolescents

Do not give [CV016 trade name] to children and adolescents because there is not enough information on its use in children and adolescents aged under 18 years.

Other medicines and [CV016 trade name]

Taking [CV016 trade name] at the same time as many other medicines can have unwanted effects. Tell your health care provider about **all** the medicines you are taking, have recently taken or might take. Your health care provider can tell you if you need to change any of your treatment.

Some medicines that may have unwanted effects with [CV016 trade name] are listed below.

- for cancer—afatinib, abemaciclib, apalutamide, ceritinib, dasatinib, encorafenib, fostamatinib, ibrutinib, nilotinib, vinblastine and vincristine
- for preventing blood clots (anticoagulants)—warfarin, rivaroxaban, dabigatran
- for epilepsy—divalproex (valproic acid and sodium valproate), lamotrigine
- for help to stop smoking—bupropion
- for allergies and hayfever—fexofenadine and loratadine
- for fungal infections—itraconazole and voriconazole
- for Cushing’s syndrome (when the body produces high levels of steroid hormones)—ketoconazole
- for HIV infection—efavirenz, maraviroc, raltegravir and zidovudine
- for various infections—atovaquone, bedaquiline, clarithromycin, delamanid, erythromycin, fusidic acid, rifabutin, sulfamethoxazole/trimethoprim
- for some mental disorders—haloperidol, risperidone, thioridazine
- for reducing high blood pressure in the lungs—bosentan, riociguat
- for high blood pressure and preventing chest pain (angina)—amlodipine, diltiazem, lercanidipine, nifedipine
- for heart conditions—digoxin
- for hepatitis C virus infection—glecaprevir/pibrentasvir
- for lowering blood cholesterol—atorvastatin, fluvastatin, pravastatin, rosuvastatin
- for reducing effects of the immune system—ciclosporin, everolimus, sirolimus, tacrolimus
- for severe pain—buprenorphine, fentanyl, methadone, morphine, other morphine-like medicines, piroxicam
- for mood calming and help with sleeping—alprazolam, buspirone, zolpidem, and midazolam by injection (often used before surgery or some medical procedures)
- corticosteroids (often used to reduce inflammation)—betamethasone, budesonide, ciclesonide, dexamethasone, fluticasone, prednisolone, prednisone, triamcinolone
- for breathing problems such as asthma and chronic obstructive pulmonary disease—salmeterol, theophylline
- for relieving depression—amitriptyline, fluoxetine, imipramine, nortriptyline, paroxetine, sertraline
- for raising thyroid hormone levels—levothyroxine
- for family planning—contraceptive medicine containing ethinylestradiol

Pregnancy and breast-feeding

If you are pregnant, think you may be pregnant or you are planning to have a baby, talk to your health care provider before taking this medicine.

There is not enough information to be sure that [CV016 trade name] is safe to take during pregnancy. If you are pregnant, your health care provider will help you decide if you can take [CV016 trade name].

You should take precautions not to become pregnant during treatment with [CV016 trade name]. Use contraception while taking [CV016 trade name] and for 7 days after completing [CV016 trade name].

[CV016 trade name] may reduce how well some hormone contraceptive medicines work and you and your partner should use another contraceptive method (such as a condom)—your health care provider can give you advice on the right contraception and how long to use it.

There is no information on taking [CV016 trade name] while breast-feeding. As a precaution, do not breast-feed your baby during treatment with [CV016 trade name] and for 7 days after you have finished taking the tablets.

Driving and using machines

[CV016 trade name] is not likely to have an effect on you not likely to have an effect on your ability to drive and to use machines.

Other ingredients of [CV016 trade name]

[CV016 trade name] contains lactose. Lactose is a source of glucose and galactose. The small amount of lactose in each dose is unlikely to cause symptoms of lactose intolerance. If, however, you have one of the rare genetic disorders galactosaemia, glucose-galactose intolerance or congenital lactase deficiency you must talk to your health care provider before taking this medicine.

3. How to take [CV016 trade name]

Always take this medicine exactly as your health care provider has told you. Take it regularly at around the same times each day. Check with your health care provider if you are not sure.

The [CV016 trade name] pack contains two types of tablets: one type contains the active substance nirmatrelvir and the other contains ritonavir. The usual recommended dose is 2 tablets of nirmatrelvir (yellow tablet) together with 1 tablet of ritonavir (white tablet) twice daily, about 12 hours apart (in the morning and in the evening).

A course of treatment lasts 5 days. For each dose, take the nirmatrelvir and ritonavir together at the same time.

If you have kidney disease, talk to your health care provider about the right dose of [CV016 trade name] for you.

You can take [CV016 trade name] either with food or between meals.

Swallow the tablets whole with plenty of water. Do not chew, break, or crush the tablets.

If you take more [CV016 trade name] than you should

If you take more [CV016 trade name] than you should, or if somebody else takes it, contact your health care provider straightaway.

If you forget to take [CV016 trade name]

- You must not miss or skip doses of this medicine.
- If you forget to take a dose and your next regular dose is not due for at least 4 hours, take the dose at once and take the next dose at the usual time.
- If you forget to take a dose and your next regular dose is due in less than 4 hours, do not take the missed dose and instead take the next one at the usual time.
- Do not take a double dose to make up for a missed dose.
- If you are not sure what to do, ask your health care provider.

Do not stop taking [CV016 trade name]

Do not stop taking [CV016 trade name] without first checking with your health care provider. Taking the medicine regularly and finishing the 5-day course gives you the best chance of not falling very ill with COVID-19.

4. Possible side effects

Like all medicines, this medicine can cause side effects but not everybody gets them.

Common side effects that can affect up to 1 in 10 people are:

- diarrhoea
- vomiting
- nausea (feeling sick)
- altered sense of taste
- headache

Uncommon side effects that can affect up to 1 in 100 people are:

- allergic reactions (such as itching and skin rash)
- high blood pressure
- abdominal (belly) pain
- muscle pain

Rare side effects that can affect up to 1 in 1000 people

- severe allergic reactions (anaphylaxis), with swelling of the tongue, mouth and face, trouble swallowing or breathing, throat tightness, hoarseness)
- feeling generally unwell.

Reporting of side effects

If you get a side effect, talk to your health care provider. This includes side effects not listed in this leaflet. You may also be able to report such effects directly to your national reporting system if one is available. By reporting side effects, you can help to improve the available information on this medicine.

5. How to store [CV016 trade name]

Keep this medicine out of the sight and reach of children.

Do not store above 30°C.

Do not use this medicine after the expiry date stated on blister and carton after “EXP”. The expiry date refers to the last day of that month.

Do not use this medicine if you notice description of the visible signs of deterioration that it is different from the description below.

Do not throw away any medicines in wastewater or household waste. Ask your health care provider how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What [CV016 trade name] contains

- The active ingredient of nirmatrelvir tablet is 150 mg nirmatrelvir.
- The active ingredient of ritonavir tablet is 100 mg ritonavir.
- The other ingredients of [CV016 trade name] are:
Nirmatrelvir 150 mg film-coated tablets: microcrystalline cellulose, lactose monohydrate, croscarmellose sodium, colloidal silicon dioxide, sodium stearyl fumarate, hypromellose, titanium dioxide, macrogol/PEG and iron oxide yellow.
Ritonavir 100 mg film-coated tablets: colloidal silicon dioxide, anhydrous dibasic calcium phosphate, copovidone, sorbitan monolaurate, sodium stearyl fumarate, titanium dioxide, hypromellose, macrogol/PEG and polysorbate 80.

There is too little sodium in this medicine to have any effect, even if you are on a low-sodium diet.

What [CV016 trade name] looks like and contents of the pack

Nirmatrelvir 150mg film-coated tablets

Yellow, oval, film-coated tablets. They are biconvex (rounded on top and bottom) with a flat edge. The tablets have ‘150’ debossed (stamped into) one side and are plain on the other side.

Ritonavir 100mg film-coated tablets

White, oval, film-coated tablets. They are biconvex (rounded on top and bottom) with a flat edge. The tablets have “54” debossed (stamped into) on one side and “247” on the other side.

Pack size

Silvery white plastic and aluminium (PA/Alu/PVC) on aluminium foil blister cards, each containing 4 nirmatrelvir 150 mg tablets and 2 ritonavir 100 mg tablets. Available in cartons of 5 × 6 tablets.

Supplier and Manufacturer

Supplier

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For any information about this medicine, contact the supplier.

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Detailed information on this medicine is available on the World Health Organization (WHO) website: <https://extranet.who.int/prequal/medicines/prequalified/finished-pharmaceutical-products>