

Applicant/PHRC: Hetero Drugs South Africa (Pty) Ltd

Product proprietary name: NIRMACOM

Dosage form and strength: Film-coated tablets (Nirmatrelvir 150 mg and Ritonavir USP 100 mg Co-Pack)

APPROVED PATIENT INFORMATION LEAFLET FOR NIRMACOM

SCHEDULING STATUS

S4

NIRMACOM 150/100 (film-coated tablets)

NIRMACOM is nirmatrelvir tablets co-packaged with ritonavir tablets.

Each film-coated tablet contains nirmatrelvir 150 mg.

Each film-coated tablet contains ritonavir 100 mg.

NIRMACOM contains sugar:

Each nirmatrelvir tablet contains lactose monohydrate 185 mg

Read all of this leaflet carefully before you start taking NIRMACOM

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, pharmacist, nurse or other health care provider.
- NIRMACOM has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

What is in this leaflet

1. What NIRMACOM is and what it is used for
2. What you need to know before you take NIRMACOM
3. How to take NIRMACOM
4. Possible side effects
5. How to store NIRMACOM

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6. Contents of the pack and other information

1. What NIRMACOM is and what it is used for

NIRMACOM contains two medicines packaged together, nirmatrelvir and ritonavir. It belongs to a group of medicines called antivirals. Nirmatrelvir is active against the virus that causes coronavirus disease 2019 (COVID-19). Ritonavir prolongs the therapeutic effect of nirmatrelvir. NIRMACOM is used for treating mild to moderate coronavirus disease 2019 (COVID-19) in adults 18 years of age and older. It is only used in patients who are at high risk for progression to severe COVID-19, including hospitalisation or death. NIRMACOM stops the virus from multiplying in cells and this stops the virus from multiplying in the body. This can help your body to overcome the virus infection and may help you get better faster. You must talk to a health care provider if you do not feel better or if you feel worse while on treatment with NIRMACOM.

2. What you need to know before you take NIRMACOM

Do not take NIRMACOM:

- if you are hypersensitive (allergic) to nirmatrelvir, ritonavir or any of the other ingredients of NIRMACOM (listed in section 6).
- if you have severe liver disease
- if you have severe kidney disease
- If you are taking certain medicines with NIRMACOM because they may lead to serious and /or life-threatening reactions, or may affect how NIRMACOM works. These medicines include, but not limited to:
 - Alfuzosin, used to treat symptoms of enlarged prostate
 - Amiodarone, used to treat heart conditions and correct irregular heartbeats
 - Colchicine, used to treat gout
 - Pimozide, used to treat mood disorders
 - Ergotamine, used to treat migraine

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- Simvastatin, used to control cholesterol
- Sildenafil, used to treat pulmonary arterial hypertension (high blood pressure in the pulmonary artery)
- Pethidine, used for pain
- clonazepam, diazepam, estazolam, flurazepam, triazolam, midazolam taken orally, used to relieve anxiety and/or trouble sleeping
- Cisapride, used to relieve certain stomach problems
- Venetoclax, used to treat cancer
- Phenobarbitone, used to prevent and control seizures
- Fusidic acid, used to treat bacterial infections
- Rifampicin, used to treat tuberculosis
- St. John's Wort (hypericum perforatum), a herbal product used in depression and anxiety.

These are not the only medicines that may cause serious effects if taken with NIRMACOM. NIRMACOM may increase or decrease the levels of other medicines. Therefore, it is very important to tell your doctor or healthcare provider about all the medicines you are taking because changes in the dose of your other medicines may be required while you are taking NIRMACOM.

Warnings and precautions

Take special care with NIRMACOM:

Tell your doctor or health care provider if:

- You have or have had a liver disease. Do not take NIRMACOM if you have a severe liver disease.
- You are taking HIV medicines, as NIRMACOM may result in medicines used in the treatment of HIV to become less effective.

Children and adolescents

NIRMACOM should not be used in children and adolescents under 18 years. NIRMACOM has not been studied

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in children and adolescents.

Other medicines and NIRMACOM

Always tell your health care provider if you are taking any other medicine. (This includes all complementary or traditional medicines.)

Tell your healthcare provider if you are taking combined hormonal contraceptive as NIRMACOM may affect how your birth control pills work.

There are other medicines that should not be taken together with NIRMACOM. Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. Inform your doctor or pharmacist if you are taking any of the following:

- medicines used to treat attention disorders, such as amphetamine derivatives e.g. methylphenidate and dexamfetamine
- medicines used to treat severe pain, such as morphine, fentanyl, methadone, buprenorphine, norbuprenorphine and other morphine-like medicines
- medicines used to treat heart conditions and correct irregular heartbeats, such as digoxin
- medicines used to treat cancer, such as afatinib, abemaciclib, apalutamide, ceritinib, dasatinib, nilotinib, vincristine, vinblastine, encorafenib, fostamatinib, ibrutinib and ivosidenib
- medicines used to thin the blood (anticoagulants), such as warfarin, apixaban, dabigatran, rivaroxaban and vorapaxar
- medicines used to treat seizures, such as lamotrigine and phenytoin
- medicines used to treat depressions, such as amitriptyline, fluoxetine, imipramine, nortriptyline, paroxetine, sertraline and desipramine
- medicines used to treat allergies, such as fexofenadine and loratadine
- medicines used to treat fungal infections (antifungals), such as ketoconazole, itraconazole and voriconazole

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- medicines used to treat bacterial infections (antibiotics and antimycobacterials), such as rifabutin, erythromycin, atovaquone, bedaquiline, delamanid, clarithromycin and sulfamethoxazole/trimethoprim
- medicines used to treat HIV infection, such as amprenavir, atazanavir, darunavir, fosamprenavir, efavirenz, maraviroc, raltegravir and zidovudine
- medicines used to treat mental or mood disorders, such as haloperidol, risperidone and thioridazine
- 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 high blood pressure (hypertension), such as amlodipine, diltiazem and nifedipine
- medicines used to treat high blood pressure in the blood vessels that supply the lungs, such as bosentan and riociguat
- medicines used to treat hepatitis C virus infection, such as glecaprevir/ pibrentasvir
- medicines used to lower blood cholesterol, such as atorvastatin, fluvastatin, pravastatin and rosuvastatin
- medicines used to suppress your immune system, such as cyclosporine, tacrolimus and everolimus
- medicines used to treat erectile dysfunction (also known as impotence), such as sildenafil and tadalafil
- medicines used as sedatives, sleeping medicine, such as alprazolam, buspirone and zolpidem
- steroids including corticosteroids used to treat inflammation, such as budesonide, dexamethasone, fluticasone propionate, prednisolone and triamcinolone
- any of the following other specific medicines:
 - bupropion (used for smoking cessation)
 - oral or patch contraceptive containing ethinylestradiol used to prevent pregnancy
 - 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)
 - levothyroxine (used to treat an underactive thyroid gland [hypothyroidism])

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

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NIRMACOM with food

NIRMACOM can be taken with or without food.

Pregnancy, breastfeeding and fertility

NIRMACOM is not recommended during pregnancy and breastfeeding as there is not enough information to confirm that NIRMACOM is safe during pregnancy and breastfeeding.

If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, please consult your doctor, pharmacist or other health care provider for advice before taking NIRMACOM.

Driving and using machines

Nirmatrelvir with ritonavir have not been specifically tested for possible effects on the ability to drive a car or operate machines.

It is not always possible to predict to what extent NIRMACOM may interfere with the daily activities of a patient. Patients should ensure that they do not engage in the above activities until they are aware of the measure to which NIRMACOM affects them.

NIRMACOM contains lactose monohydrate

If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking NIRMACOM.

NIRMACOM contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially 'sodium-free'.

3. How to take NIRMACOM

Do not share medicines prescribed for you with any other person.

Always take NIRMACOM exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

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NIRMACOM consists of 2 medicines: nirmatrelvir and ritonavir. The recommended dose is two tablets of nirmatrelvir with one tablet of ritonavir by mouth twice daily (in the morning and at night).

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

If you have kidney disease, please talk to your healthcare provider for an appropriate dose of NIRMACOM. If you have moderate kidney disease you will need a lower dose of NIRMACOM. If you have severe kidney disease you must not take NIRMACOM.

Swallow the tablets whole. Do not chew, break or crush the tablets. NIRMACOM can be taken with or without meals.

If you take more NIRMACOM than you should

In the event of overdosage, consult your doctor or pharmacist. If neither is available, contact the nearest hospital or poison centre.

If you forget to take NIRMACOM

If you forget to take a dose of NIRMACOM, take it as soon as you remember. If more than 8 hours have passed since your missed dose, then do not take the missed dose and just carry on as before.

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

If you stop taking NIRMACOM

Even if you feel better, do not stop taking NIRMACOM without talking to your doctor.

4. Possible side effects

NIRMACOM can have side effects.

Not all side effects reported for NIRMACOM are included in this leaflet. Should your general health worsen or if

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you experience any untoward effects while taking NIRMACOM, please consult your health care provider for advice.

Tell your doctor if you notice the following:

Frequent side effects:

- Diarrhoea
- Vomiting
- Altered sense of taste

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

Reporting of side effects

If you get side effects, talk to your doctor, pharmacist or nurse. You can also report side effects to SAHPRA via the "6.04 Adverse Drug Reaction Reporting Form", found online under SAHPRA's publications: <https://www.sahpra.org.za/Publications/Index/8> or to the Holder of certificate of registration through the mail: pvg.cdma@heterogroups.com.

By reporting side effects, you can help provide more information on the safety of NIRMACOM.

5. How to store [PRODUCT NAME]

Store all medicines out of reach of children.

- Store at or below 30 °C
- Do not refrigerate or freeze
- Store in the original package

6. Contents of the pack and other information

What NIRMACOM contains

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NIRMACOM contains nirmatrelvir and ritonavir.

For nirmatrelvir

The active substance is nirmatrelvir 150 mg.

The other ingredients are:

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

Film-coating

Opadry Yellow, Hypromellose, titanium dioxide, macrogol, iron oxide yellow

For ritonavir

The active substance is ritonavir 100 mg.

The other ingredients are:

Copovidone, colloidal silicon dioxide, sorbitan monolaurate, dibasic calcium phosphate, sodium stearyl fumarate

Film coating

Opadry white, Hypromellose, titanium dioxide, macrogol, talc, hydroxypropyl cellulose, polysorbate 80, colloidal anhydrous silica

What NIRMACOM looks like and contents of the pack

Nirmatrelvir film-coated tablet:

Yellow coloured, oval shaped, bevel edged, biconvex film coated tablets debossed with "N 15" on one side and "H" on the other side.

Ritonavir film-coated tablet:

White to off white, capsule shaped, film coated tablets debossed with 'H' on one side and 'R9' on other side.

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10 tablets packed in OPA/PVC aluminium foil blister. And 6 blisters packed in a carton.

Holder of Certificate of Registration

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