

Administration of Nirmatrelvir-ritonavir for COVID-19



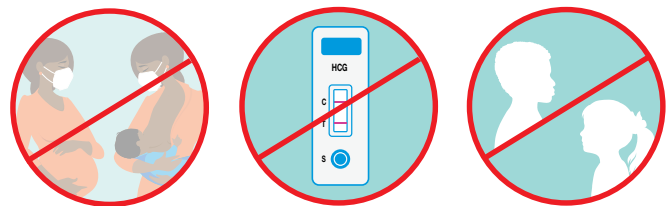
Guidance for
health care workers

CONTRAINDICATIONS

- History of clinically significant hypersensitivity reactions (e.g. toxic epidermal necrolysis [TEN] or Stevens-Johnson Syndrome [SJS]) to its active ingredients (nirmatrelvir or ritonavir) or any of the excipients.
- Patient with history of severe hepatic impairment (Child-Pugh Class C), severe renal impairment (GFR < 30 mL/min) and with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medication, as it contains lactose.
- Certain medicinal products that inhibit or induce CYP3A – please check for drug-drug interactions on the University of Liverpool drug interaction checker (<https://www.covid19-druginteractions.org>).

RECOMMENDATIONS FOR NOT USING NIRMATRELVIR-RITONAVIR

- Women and persons who are pregnant.*
- Women and persons who are breastfeeding.**
- Children < 18 years of age.*



- * Randomized controlled trials (RCTs) enrolled only non-pregnant non-breastfeeding adults. Thus, the applicability of this recommendation to children or women and persons who are pregnant or breastfeeding is currently uncertain. The Guideline Development Group concluded that nirmatrelvir-ritonavir should not be offered to children or women and persons who are pregnant or breastfeeding with non-severe COVID-19 until further clinical data are available.
- ** There are no human data on the use of nirmatrelvir-ritonavir in breastfeeding. It is unknown whether nirmatrelvir is excreted in human or animal milk and the effect it has on the breast-fed newborn or the effects on milk production. Limited published data report that ritonavir is present in human milk but there is no information on its effect on the breast-fed newborn or on milk production.

ADMINISTRATION OF NIRMATRELVIR-RITONAVIR IN CONTEXT OF OTHER COVID-19 THERAPEUTICS

- Several treatment alternatives are available for non-severe COVID-19.
- Nirmatrelvir-ritonavir may represent a superior choice because it may have greater efficacy in preventing hospitalization than alternative COVID-19 medications. There are fewer concerns with respect to harms than with molnupiravir and it is easier to administer than remdesivir and the monoclonal antibodies.
- Ultimate choice of therapeutic will depend on patient characteristics, medication availability, route of administration, duration of treatment and time from onset of symptoms to initiation of treatment.

Remember the
FIVE RIGHTS
of drug administration:



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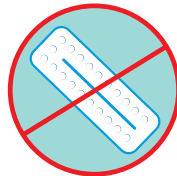
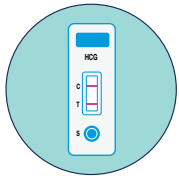
PATIENT POPULATIONS

It is important to carefully evaluate and counsel patients prior to administering nirmatrelvir-ritonavir due to potential adverse effects and drug interactions related to this medicine.

It is also important to clearly describe the treatment course to avoid any medical errors in dosing that may occur as co-administration of pills.

Women and persons who can get pregnant

- If clinically indicated, evaluate patient for pregnancy prior to starting nirmatrelvir-ritonavir for non-severe COVID-19.
- If patient is using hormonal contraception, advise to use an effective alternative method of contraception during treatment and until after **one complete menstrual cycle** after stopping nirmatrelvir-ritonavir. This is due to drug-drug interaction which may reduce the efficacy of hormonal contraception.



Patients receiving concomitant therapy for HIV or HCV with ritonavir or cobicistat-containing regimens

The dose of nirmatrelvir-ritonavir is unchanged.

- Patients should receive **300 mg nirmatrelvir** with **100 mg ritonavir** every 12 hours for a total of 5 days. Dose adjustments may be needed based on renal function.
- Patients taking ritonavir or cobicistat-containing regimens should continue their regimen as indicated. No dose adjustments are necessary.

PREPARATION AND ADMINISTRATION

Nirmatrelvir-ritonavir tablets are administered orally (by mouth).

Instruct patients to take the following measures when taking this medicine at home.

- Wash hands
- Obtain correct dose:
 - **If GFR \geq 60:** 300 mg nirmatrelvir (two 150 mg tablets) with 100 mg ritonavir (one 100 mg tablet).
 - **If GFR 30–60:** 150 mg nirmatrelvir (one 150 mg tablet) with 100 mg ritonavir (one 100 mg tablet).
- Swallow tablets whole with plenty of fluid. The medication can be taken with or without food.
- Advise patients not to stop treatment course early, even if they feel better, as completion of treatment is important to reduce the risk of antiviral resistance, which can lead to reduced efficacy of drug.
- Advise patients that if they do not tolerate this medicine, to immediately discuss with their health care provider before discontinuation of treatment.
- If a patient requires hospitalization due to severe or critical COVID-19 after starting nirmatrelvir-ritonavir, completion of the full 5-day treatment is recommended under direct health care worker supervision.

Missed or forgotten doses

- If a patient forgets to take a dose of nirmatrelvir-ritonavir **within 8 hours** of the time it is usually taken, they should take it as soon as possible and take the next dose at the usual time.
- If a patient forgets to take a dose of nirmatrelvir-ritonavir by **more than 8 hours**, they should **NOT** take the missed dose and take the next one at the usual time.
- Double doses should **NOT** be taken to make up for missed doses.

Overdosage

- In the event of treatment overdose with nirmatrelvir-ritonavir, general supportive measures should be adopted including monitoring of vital signs and observation of the clinical status of the patient.
- There is no specific antidote for overdose with nirmatrelvir-ritonavir.
- Report to national or local pharmacovigilance programmes.

