

Health Advisory

COVID-19 Rebound After Nirmatrelvir/Ritonavir (Paxlovid) Treatment May 25, 2022

SUMMARY POINTS

- There are multiple reports of Nirmatrelvir/Ritonavir related COVID-19 rebound.
- COVID-19 rebound is characterized as the recurrence of COVID-19 symptoms or a new COVID-19 positive test result after having tested negative, usually 2-8 days after the initial recovery.
- There is currently no evidence that additional treatment with Nirmatrelvir/Ritonavir or other anti-SARS-CoV2 therapies is necessary for COVID-19 rebound.
- Healthcare professionals should advise their patients to isolate themselves again for at least 5 days. Individuals can end their re-isolation after 5 full days if fever has resolved for 24 hours (without fever-reducing medicines) and symptoms have improved. Masks must be worn in public for a full 10 days after rebound symptoms start.

Nirmatrelvir/Ritonavir (Paxlovid) is an oral antiviral medication prescribed to people with mild-to-moderate COVID-19 who are at risk of developing severe illness (hospitalization and death). Nirmatrelvir/Ritonavir is currently authorized for people 12 years and older and should be initiated as soon as possible after a diagnosis of COVID-19 or within 5 days of symptom onset.

Case reports have been made about the COVID-19 rebound symptoms. The following are the characteristics of COVID-19 rebound:

- A recurrence of COVID-19 symptoms or a new COVID-19 positive test result after having tested negative.
- Usually occurs between 2 to 8 days after the initial recovery.
- Recurrence of illness and positive test results typically improves or resolves in a median of 3 days without additional anti-COVID-19 treatment.

COVID-19 rebound does not reflect COVID-19 reinfection or development of resistance to Nirmatrelvir/Ritonavir. Degree of transmissibility during COVID-19 rebound remains unknown.

During the Nirmatrelvir/Ritonavir clinical trial (conducted by Pfizer), rebound was identified in both the treatment and placebo groups with no increased occurrence of hospitalization or death. Nirmatrelvir/Ritonavir continues to be the recommended treatment for mild to moderate COVID-19 in those persons at high risk for progression to severe disease.

Please note that a brief return of symptoms may be part of the natural history of COVID-19 infection in some persons, independent of treatment with Nirmatrelvir/Ritonavir and regardless of vaccination status.

There is currently no evidence that additional treatment for COVID-19 is necessary for COVID-19 rebound. Patient monitoring and appropriate management for recurrence of symptoms after completing the treatment course of Nirmatrelvir/Ritonavir continues to be the most appropriate management for patients with recurrence of symptoms after completion of the treatment course of Nirmatrelvir/Ritonavir. Individuals with COVID-19 rebound should restart isolation for at least 5 days. The individual can end their re-isolation after 5 full days if the fever has resolved for 24 hours (without fever-reducing medicines) and symptoms are improving. Individuals with COVID-19 rebound should continue to mask when in public for 10 days after rebound symptoms start.

Healthcare providers are strongly encouraged to report COVID-19 rebound cases to Pfizer via [Pfizer Safety Reporting](#). Healthcare professionals also are recommended to complete and submit [FDA MedWatch](#) or complete FDA form 3500 (healthcare professional) by fax (1-800-FDA-0178). Please call 1-800-FDA-1088 for questions.

Resources:

- [COVID-19 Rebound After Paxlovid Treatment](#)
- [FACT SHEET FOR HEALTHCARE PROVIDERS: EMERGENCY USE AUTHORIZATION FOR PAXLOVID™](#)
- [Pfizer COVID-19 Treatment Adverse Event Reporting](#)
- [MedWatch: The FDA Safety Information and Adverse Event Reporting Program](#)