

Crushing nirmatrelvir and ritonavir tablets

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Page 1 of 1

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Data are limited or absent; therefore, risk-benefit assessment for any individual patient rests with prescribers.

Administering Paxlovid as Crushed Tablets

Background

- Product labels for nirmatrelvir/ritonavir (Paxlovid®) state that the tablets should be swallowed whole and not chewed, broken or crushed as there is a lack of data to support alternative administration ^{1,2}.
- However, nirmatrelvir and ritonavir tablets are not extended or enteric coated but immediate release film-coated tablets.
- A review of available data suggests that crushing nirmatrelvir and ritonavir tablets does not alter the ritonavir boosting effect and results in comparable nirmatrelvir exposure.

Data supporting crushing nirmatrelvir and ritonavir

- Phase I studies of crushed nirmatrelvir have been carried out where nirmatrelvir was administered as an oral suspension at doses of 50-2500 mg given with or without ritonavir ³. Following administration of a single dose, the nirmatrelvir/ritonavir suspension was shown to have similar pharmacokinetic parameters compared to those reported for the tablet in the product labels ^{1,2}.

PK parameter	Nirmatrelvir/ritonavir suspension (250/100 mg, fasted)	Nirmatrelvir/ritonavir tablet (300/100 mg)
C _{max} (ng/ml)	2.88	2.21
T _{max} (h)	2.75	3.00
AUC _{inf} (µg.h/ml)	28.22	23.01
Half-life (h)	6.9	6.0

- Lopinavir/ritonavir was used in the first COVID-19 wave and plasma concentrations of crushed lopinavir/ritonavir tablets (400/100 mg twice daily) administered through a nasogastric tube were measured in hospitalized COVID-19 patients. When compared to historical data obtained in HIV infected patients, crushing lopinavir/ritonavir tablets did not result in lower lopinavir exposure suggesting that the boosting effect of ritonavir was not impaired ⁴.

Recommendations

- Nirmatrelvir and ritonavir tablets can be crushed or split and mixed with food or liquid, including dairy-containing products.
- Ritonavir powder for oral suspension (if available) could be used instead of crushing the ritonavir tablets.
- Crushed tablets mixed with water can also be considered for administration via feeding tubes (tube should be flushed with water after administration).
- Due to lack of information pertaining to stability, it is recommended that any suspension or preparation made with crushed nirmatrelvir and ritonavir be consumed/administered immediately.
- These recommendations do not replace clinical judgement. An alternative COVID-19 treatment should be considered if crushing or administration of nirmatrelvir and ritonavir solutions are deemed inappropriate.

References

1. Paxlovid [Summary of Product Characteristics](#), Pfizer Ltd.
2. Paxlovid [FDA Emergency Use Authorization](#), Pfizer Inc.
3. Innovative randomized phase I study and dosing regimen selection to accelerate and inform pivotal COVID-19 trial of nirmatrelvir. Singh RSP, et al. *Clin Pharmacol Ther* 2022; 112:101-111.
4. Crushing lopinavir/ritonavir tablets does not result in lower exposure to lopinavir/ritonavir in adult patients with COVID-19. Mohsenian Naghani SM, et al. *Eur J Hosp Pharm* 2021; [ejhpharm-2020-002596](#).