

# Crushing nirmatrelvir and ritonavir tablets

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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 <sup>1,2</sup>.
- 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 <sup>3</sup>. 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 <sup>1,2</sup>.

PK parameter	Nirmatrelvir/ritonavir suspension (250/100 mg, fasted)	Nirmatrelvir/ritonavir tablet (300/100 mg)
C <sub>max</sub> (ng/ml)	2.88	2.21
T <sub>max</sub> (h)	2.75	3.00
AUC <sub>inf</sub> (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 <sup>4</sup>.

### Recommendation

- Nirmatrelvir and ritonavir tablets can be crushed or split and mixed with food or liquid, including dairy-containing products.
- 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 made with crushed nirmatrelvir and ritonavir be consumed immediately.
- This recommendation does 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

- Paxlovid [Summary of Product Characteristics](#), Pfizer Ltd.
- Paxlovid [FDA Emergency Use Authorization](#), Pfizer Inc.
- 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.
- 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](#).