

Posaconazole Delayed-Release Tablet Crush Data Summary

Background: Posaconazole is available in intravenous (IV), oral suspension, and oral delayed-release (DR) tablet formulations. In those unable to swallow the DR tablets, there are limited effective enteral options. The posaconazole oral suspension has lower and more erratic bioavailability, and use is associated with difficulty achieving therapeutic drug levels.¹ Long-term IV therapy requires placement of a central venous catheter for administration, which is often impractical and undesirable in this patient population. Due to these limitations, the DR tablet is the preferred formulation, however, is avoided in patients who are unable to tolerate oral (PO) intake due to labelling directions advising against crushing for enteral administration.²

Per the package insert (Noxafil Posaconazole [package insert]. Whitehouse Station, NJ: Merck & Co; 2022.), posaconazole DR tablets are not recommended to be divided, crushed, or chewed, due to theoretical concerns that crushing DR formulations could affect bioavailability. The DR tablet disperses 100 mg of posaconazole in a pH-sensitive solid polymer matrix milled powder which only dissolves at small intestinal pH.² The delayed-release component of the tablets is purely for cosmetic purposes, and crushing these tablets should not significantly alter absorption pharmacokinetics. There have been several retrospective case series published describing outcomes of crushing posaconazole DR tablets for enteral feeding tube administration as detailed below³⁻⁸:

Literature Summary Table

Author/Year	Design	Patients	Results	Other Findings
Mason 2019 ⁴	Retrospective chart review	N = 4	- All patients had detectable serum levels - 2/4 patients had therapeutic levels at first check	
Dieringer 2022 ⁷	Single center retrospective chart review Target trough • Ppx: > 0.7 mg/L • Tx: > 1 mg/L	N = 14 -LTRs (n=8) -Ppx (n=8) -Treatment (n=6)	- 10/14 patients achieved target levels at the time of first assessment (mean 1.61±0.77 mg/L) - The remaining 4/4 patients achieved therapeutic levels on repeat assessment after dose increase (max required 300 mg q12h)	- Cost analysis showed enteral tube administration spared 526 days of IV therapy for posaconazole (37.6 days/patient) equivalent to \$218,063
Manesh 2022 ⁸	Single center prospective	N=19 patients requiring NG administration	- 19/19 patients achieved therapeutic level at 2 weeks (median: 2,639 ng/mL)	

	Target trough: -Tx > 1000 ng/mL	-Uncontrolled DM (n=18) -I&D (n=19) -AmB lead in (n=19)	- All patients had treatment success with no clinical or radiological evidence of disease at 3 and 6 months follow up	
Stevens 2023 ³	Retrospective chart review	N = 10 -Ppx (n=6) -Treatment (n=4)	- 8/10 patients achieved therapeutic levels - 1 who did not was switched to voriconazole, 1 expired due to noninfectious causes prior to repeat levels	- Majority of patients required BID dosing to achieve therapeutic levels
Neuhaus 2023 ⁹	Single center retrospective chart review Target trough ≥ 0.7 mg/L	N=33 -LTRs only	- Thirty of 33 patients achieved therapeutic concentration on 300 mg daily after five days - 82% post-pyloric, 18% gastric routes	- N/A (Abstract only)
Gordon 2025 ⁵	Retrospective chart review Target trough - Ppx: ≥ 0.7 mg/L - Tx: ≥1.2 mg/L	N = 30 LTRs -Ppx (n=28) -Treatment (n=2)	- Median posaconazole level 0.7 mg/L (IQR 0.4-1 mg/L) drawn ~6 days after initiation - 15/30 (50%) achieved goal trough at first level	- Institution protocol was changed from 300 mg crushed daily to 400 mg crushed daily due to internal analysis of low troughs - Those who received a loading dose were more likely to have therapeutic troughs
Kane 2025 ⁶	Single center retrospective chart review Target trough Ppx: > 700 ng/mL	N = 10 patients with available TDM -ICU (n=9) -Ppx (n=4) -Treatment (n=6)	- 2/10 patients achieved indication-specific goals at first level; both were therapeutic prior to initiating crushed posaconazole - 4/4 patients who had a prior posaconazole level experienced a decrease in level when	- With majority of the patients requiring ICU level of care, the reason for subtherapeutic posaconazole levels is likely multifactorial

	Tx: > 1000 ng/mL		transitioning to crushed posaconazole	
Dann 2025 ¹⁰	Single center, cohort control study	N=27 [18 enteral feeding tube (10 received TDM) vs 9 intact oral tabs] -LTRs only (prophylaxis)	<u>First posa trough concentration:</u> 0.41 (crushed) vs 1.44 (PO), p < 0.001 <u>Days to goal trough:</u> 17.8 (crushed) vs 6.7 (PO), p < 0.001	-0 patients in both groups required therapeutic anti-fungals within 3 months -Abstract only

Clinical Application: As described in the above studies, absorption of posaconazole is often erratic and challenging to predict. This aligns with literature evaluating time to therapeutic concentration with administration of posaconazole DR tablet PO. In a retrospective study from the University of Colorado, posaconazole levels were obtained on day 5 of therapy with a target trough of > 0.7 mcg/mL. Of 33 patients receiving the DR tablet, 6 (18%) had subtherapeutic levels. For comparison, 24 of 38 (63.2%) receiving the oral suspension had subtherapeutic levels.¹⁰ Prayag and colleagues further evaluated host factors associated with subtherapeutic posaconazole levels, defined as < 1.25 mg/L, in a retrospective analysis of 164 patients receiving standard dose posaconazole (DR tablet) for therapeutic purposes.¹⁰ The presence of acute myeloid leukemia (AML), bone marrow transplant (BMT), graft versus host disease (GVHD), receipt of chemotherapy, receipt of proton pump inhibitors (PPI), diarrhea, and mucositis were all factors associated with subtherapeutic posaconazole levels in a univariate analysis.¹¹ In a multivariate analysis, factors associated with subtherapeutic posaconazole levels were receipt of PPI (OR 2.45, p 0.028) and diarrhea (OR, p < 0.001).¹¹ Additionally, they conducted a subgroup analysis of patients receiving DR tablet via PEG tube (n=2) and NG tube (n=21), and 14 patients had a therapeutic level with median posaconazole trough of 1.48 for patients receiving via tube administration.¹⁰ The use of enteral tube for administration was not associated with subtherapeutic concentrations, however, there was a small sample size included.¹¹ Higher than normal doses may be required when using crushed posaconazole DR tablets; however, data to support higher initial doses is limited. Prompt TDM should be performed in patients receiving crushed posaconazole DR tablets via tube administration to further guide posaconazole dosing.

References

1. Dodds Ashley ES, Varkey JB, Krishna G, et al. Pharmacokinetics of posaconazole administered orally or by nasogastric tube in healthy volunteers. *Antimicrob Agents Chemother.* 2009;53(7):2960-2964. doi:10.1128/AAC.01178-08

2. Mason MJ, McDanel PM, Musick WL, Kontoyiannis DP. 2019. Serum Levels of Crushed Posaconazole Delayed-Release Tablets. *Antimicrob Agents Chemother* 63:10.1128/aac.02688-18. <https://doi.org/10.1128/aac.02688-18>
3. Stevens RW, O'Connell C, Huang A, Epps KL, Ilges D. Therapeutic drug monitoring following crushed administration of delayed-release posaconazole tablets via enteral feeding tubes. *J Antimicrob Chemother*. 2023;78(2):553-555. doi:10.1093/jac/dkac427
4. Mason MJ, McDanel PM, Musick WL, Kontoyiannis DP. Serum Levels of Crushed Posaconazole Delayed-Release Tablets. *Antimicrob Agents Chemother*. 2019;63(5):e02688-18. Published 2019 Apr 25. doi:10.1128/AAC.02688-18
5. Gordon R, Yen B, Dewey K, et al. Evaluation of Crushed Posaconazole Delayed Release Tablets in Lung Transplant Recipients. *Transpl Infect Dis*. 2025;27(1):e14402. doi:10.1111/tid.14402
6. Kane N, Rikard R, McCrory K, Marx A. Crushed Posaconazole Delayed-Release Tablets Via Enteral Feeding Tubes: A Cautionary Tale. *Ann Pharmacother*. 2025;59(1):92-94. doi:10.1177/10600280241249705
7. Dieringer TD, Schaenman JM, Davis MR. Enteral feeding tube administration with therapeutic drug monitoring of crushed posaconazole tablets and opened isavuconazonium sulfate capsules. *J Antimicrob Chemother*. 2022;77(5):1417-1423. doi:10.1093/jac/dkac035
8. Manesh A, Devasagayam E, Bhanuprasad K, et al. Efficacy of Crushed Delayed-Release Posaconazole Tablets in Rhino-Orbito-Cerebral Mucormycosis. *Antimicrob Agents Chemother*. 2022;66(12):e0108522. doi:10.1128/aac.01085-22
9. Neuhaus K, Xhemali X. Serum Concentrations of Crushed Posaconazole Delayed Release Tablets in Lung Transplant Recipients. *Journal of Heart and Lung Transplantation*. 2023;42(4): S89. doi:10.1016/j.healun.2023.02.215
10. Dann J, Shoemaker C, Anderson R, et al. Early Use of Posaconazole via Enteral Tube Did Not Reduce Time to Goal Trough Concentration Post-Lung Transplant. *AJT*, Volume 25, Issue 8 Supplement 1.
11. Yi, W.M., Schoeppler, K.E., Jaeger, J. et al. Voriconazole and posaconazole therapeutic drug monitoring: a retrospective study. *Ann Clin Microbiol Antimicrob* 16, 60 (2017). <https://doi.org/10.1186/s12941-017-0235-8>
12. Prayag PS, Panchakshari SP, Mahalle NP, et al. Factors associated with subtherapeutic levels of oral posaconazole tablet: a detailed analysis from a tertiary care center in India. *Int J Infect Dis*. 2022;124:76-80. doi:10.1016/j.ijid.2022.09.004
13. Maertens JA, Raad II, Marr KA, et al. Isavuconazole versus voriconazole for primary treatment of invasive mould disease caused by *Aspergillus* and other filamentous fungi (SECURE): a phase 3, randomised-controlled, non-inferiority trial. *Lancet*. 2016;387(10020):760-769. doi:10.1016/S0140-6736(15)01159-9
14. Gómez-López A. Antifungal therapeutic drug monitoring: focus on drugs without a clear recommendation. *Clin Microbiol Infect*. 2020;26(11):1481-1487. doi:10.1016/j.cmi.2020.05.037
15. Isavuconazole. Lexi-Drugs. Lexicomp. Wolters Kluwer Health, Inc. Riverwoods, IL. Available at: <http://online.lexi.com>. Accessed May 7, 2025
16. Posaconazole. Lexi-Drugs. Lexicomp. Wolters Kluwer Health, Inc. Riverwoods, IL. Available at <http://online.lexi.com>. Accessed May 7, 2025