JPPT | Commentary

The Pitfalls and Opportunities With Posaconazole DR Oral Suspension

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ABBREVIATIONS DR, delayed release; EMR, electronic medical record; IR, immediate release; ISMP, Institute for Safe Medication Practices; IV, intravenous; NG, nasogastric

KEYWORDS antifungal; drug development; drug supply; inpatient pharmacy; medication administration; medication safety

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Posaconazole is a triazole antifungal that plays an important role in the treatment and prevention of various fungal infections, particularly in immunocompromised patients. It has historically been available as delayed-release (DR) 100-mg tablets, immediate-release (IR) oral suspension 40 mg/mL, and as an intravenous (IV) solution; at the end of 2022, a DR oral suspension for preparation became available on the market in the United States.

Owing to erratic bioavailability of the IR oral suspension, the DR oral suspension has been highly anticipated in the pediatric setting because of the opportunity to provide patient-specific doses in a safe and effective manner.[1,2] The DR oral suspension avoids the crushing of DR tablets (which is not formally approved though studies supporting the practice exist) and associated difficulties in optimizing a dose given tablet sizes; administering the IR suspension multiple times per day (some patients may require dosing 4 times a day to achieve appropriate therapeutic concentrations); and using a less optimal antifungal for the patient.[3–6]

Unfortunately, the currently available product poses several barriers for use in patient care, and particularly in the inpatient setting. This commentary presents identified challenges and solutions with the current formulation of posaconazole DR oral suspension, identified at a large, tertiary pediatric academic medical center.

Product Availability

Posaconazole DR oral suspension is only available for purchase as a drop-ship item; drop-ship medications take more time for order and delivery than other medications. Available in an 8-day supply package, each kit comes with 1 bottle of solution for reconstitution.[1] The medication is supplied in packets with 4 syringes (2 blue [10 mL] syringes and 2 green [3 mL] syringes), 2 mixing cups, a bottle of mixing liquid (contains preservatives), and a bottle adapter.[1]

Challenges.

- Inpatient: The product is available as a medication box/kit and these are essentially patient-specific, complicating medication preparation and dispensing from an inpatient setting. Questions considered by our institution's pharmacy team include:
  - How should packets be prepared when there is 1 primary diluent bottle for each of 8 packets? Would this look different if there were multiple patients needing the medication at once?
  - Where should doses be dispensed from (and are the packets all dispensed at once or individually)?
  - What to do with extra packets?
  - How to allow for appropriate barcode medication administration scanning of the doses?
- Ambulatory: The 8-day supply/counts are challenging for families who are accustomed to receiving medications every 30 days, particularly if an insurance company will not allow a 32-day supply. This requires families to come to the pharmacy more frequently (particularly if receiving other maintenance medications), and both family and pharmacy must identify the need to refill the medication (usually patient-specific ordering by the pharmacy given the cost) in advance. Additionally, this may subject families to a greater number of copayments, adding an additional financial burden.

Solutions.

- Inpatient: The full box is dispensed with the same barcode being used for the multiple packets. An educational handout (see Supplement S1) was created in conjunction with medication safety, pharmacy, and nursing leadership to provide clear instructions on how to prepare individual doses on the floor, and to ensure each dose was appropriately scanned prior to administration. In addition to the educational

handout, administration instructions were added to the medication administration report in the electronic medical record (EMR). The inpatient pharmacist was in close contact with the pharmacy inventory team regarding discharge plans to ensure adequate supply of drug without over-purchasing. Use of the product is strictly limited, and there have not been multiple cases of patients needing treatment simultaneously because of the complexities of the medication and medication safety concerns.[7] If the need were to arise, continuing with an individual supply (1 box per patient) at this time is anticipated.

- Ambulatory: When able and appropriate, change prescription of maintenance medications to a 90-day supply and an 88-day supply for posaconazole DR oral suspension (assuming ongoing clinical need). Have families call for a refill when opening the final box of posaconazole DR suspension (essentially 8 days before the supply is exhausted) to allow adequate time for refill, and as an easy way for families to remember to call.

Preparation and Stability

The product must be prepared by the family/caregiver prior to each dose and expires 1-hour after preparation. Additionally, the preparation is multistep and requires first measuring the correct amount of diluent, then mixing it with the full powder packet, and finally measuring the appropriate patient-specific dose (2 syringes, 1 mixing cup required in addition to the active medication and diluent).[8]

Challenges.

- Inpatient: The short stability of the medication makes it nearly impossible for the medication to be prepared in the inpatient pharmacy, delivered to the floor, and given to the nurse to administer without any delays, which would elapse the beyond-use time.
- Ambulatory: A parent/guardian could not make premeasured doses if the patient were to be cared for by another family member or friend. This means the trained family member would not be able to miss any dosing time for the patient, education would need to extend to multiple family members/friends, or the patient would be at risk of missing a dose.

Solutions.

- Inpatient: Education sheets were created for nursing (Supplement S1), and the inpatient clinical pharmacist checked in daily to ensure there was no confusion or questions about the preparation or administration process (facilitated by nursing in this unique situation only). Comments were also placed in the EMR and dose labels about reviewing these instructions (completed by the verifying inpatient pharmacist).
- Ambulatory: The manufacturer provides a detailed education sheet for families, but it is multiple pages and includes 15 steps, which can be quite overwhelming. A simplified, patient-specific education sheet for families was created and the education process started with the first dose, to ensure families felt confident preparing and administering the correct dose (Supplement S2). Families were observed by nursing and the inpatient pharmacist prior to discharge to "self-lead" the preparation and administration and were asked about the need for additional family member education. How many family members were taught was left up to the family, but all were counseled on the importance of adherence and not missing doses.

The product comes with its own syringes for administration, specified by color; unfortunately, they are not compatible with nasogastric (NG) tubes or ENFit (Multiple manufacturers)) feeding tubes.

Challenges.

- Inpatient: For patients requiring feeding tube administration, the posaconazole DR suspension is not an option at this time because only the manufacturer-provided notched tip syringes should be used when administering the product. Additionally, incompatibility with ENFit syringes/feeding tubes poses a safety risk for route of administration. Color vision–deficient staff need to differentiate syringes by size and cannot rely on the manufacturer's directions, which uses colors specifically.
- Ambulatory: If families are color vision–deficient, manufacturer directions may be confusing, and alternative education would be needed to ensure proper preparation. Patients with NG tubes need alternative formulations.

Solutions. Education sheets (see Supplements S1 and S2) that are not reliant on colors alone, but also clearly relate colors to syringe size, were created for nursing and families. For patients with feeding tubes, the use of crushed posaconazole DR tablets is preferred owing to incompatibility of manufacturer syringes and ENFit system; institutional directions (see Supplement S2) have been created for families and caregivers on how to do this. Therapeutic drug monitoring is used to ensure adequate dosing.

Product Differences

The IV formulation, DR tablets, IR suspension, and DR suspension are not 1:1 dosing conversions. While IR suspension was removed from the market in 2024, orders for the product may still exist in the EMR and cause confusion.

Challenges. When patients are transitioning between products (IV to oral or oral to NG tube), special attention to detail is required. Both suspension

formulations are now hidden in the EMR so that only pharmacists are able to place orders—to prevent confusion for providers during switching. Patient safety events may occur during feeding tube placement and the formulation is switched 1:1 to liquid IR suspension from DR tablets.

Solutions. In conjunction with this, alerts were added to the EMR when ordering posaconazole, and pharmacist education (in the form of a clinical pearl presentation and internal guidance document for further reference) was provided to assist in ordering the right dose/conversion.

Insurance

Challenges. Because the DR suspension is now preferred for pediatric patients, there have been instances where insurance companies specifically prefer the DR suspension product. There have also been instances where insurance-preferred pharmacies are not able to order the product, and on 1 occasion the insurance strictly preferred the DR suspension but would only allow the family to fill the prescription at a pharmacy that was unable to order the product.

Solutions. Early ambulatory prescribing of any posaconazole prescription is recommended (e.g., sending prescriptions as soon as it is known that a patient may require therapy) to allow for prior authorizations and peer to peer, time to order the product, and adequate education for all involved. Historically, most patients requiring any formulation of posaconazole require a minimum of a prior authorization. Several have required significant advocacy in order to receive the medication, with more than a week to receive approval for the medication, and potentially longer to get the product in stock and dispensed. It is an important reminder for all pharmacists, because most (if not all) patients starting to take posaconazole as an inpatient will require continuation in the outpatient setting, and thus early preparation is best.

Discussion

In September 2023, the Institute for Safe Medication Practices (ISMP) issued a safety brief highlighting many of the above concerns.[7] ISMP ultimately recommended carrying only one of the posaconazole suspension formulations to avoid confusion; and emphasized that the inability to use ENFit syringes, as well as the kit design and supply, and the short time frame from preparation to administration all pose significant safety and feasibility issues in the inpatient setting. ISMP highlights the need to develop a plan to operationalize use of the DR suspension (from preparation to administration), prevent the risk of wrong-route drug administration or dosing errors, and provide education to patients/caregivers about home preparation and administration.

In summary, while the posaconazole DR suspension seems like a promising option for pediatric patients, based on trial data, in the real world it falls short. The complexities of preparation, product packaging that is essentially patient-specific (not friendly for multipatient use with no consideration to inpatient administration), incompatibility with feeding tubes, and medication safety concerns, in combination with concern for dosing errors between other formulations, make it essentially unusable in the inpatient setting (which translates to the outpatient setting). Because of these challenges, strong preference has been given to avoid use of the DR suspension in pediatric patients. In situations where DR suspension cannot be avoided, the above solutions provide guidance on safe use and can be adapted to your institution and practice.

Importantly, this should be a call for the manufacturer (and other drug manufacturers) to consider the highlighted issues when developing any medication—these are not challenges unique to the pediatric population, although these challenges disproportionately affect pediatric patients. Continued changes to the formulation, investigation into product compatibility with the ENFit system, and future consideration of pediatric patients during drug development are encouraged.

Article Information

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References

1. McCreary EK, Davis MR, Narayanan N, et al. Utility of triazole antifungal therapeutic drug monitoring: insights from the Society of Infectious Diseases Pharmacists. *Pharmacotherapy.* 2023;43(10):1043–1050.
2. Ashok A, Mangalore RP, Morrissey CO. Azole therapeutic drug monitoring and its use in the management of invasive fungal disease. *Curr Fungal Infect Rep*. 2022;16:55–69.

3. Dieringer TD, Shaenman 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.
4. Neuhas K, Chemali X. Serum concentrations of crushed posaconazole delayed release tablets in lung transplant recipients. *J Heart Lung Transplantation*. 2023;42(4S):S98.
5. Mason MJ, McDaneld PM, Musick WL, Kontoyiannis DP. Serum levels of crushed posaconazole delayed-release tablets. *Antimicrob Agents Chemother*. 2019;63(5):e02688-18.
6. Stevens RW, O'Connell C, Huang A, et al. Therapeutic drug monitoring following crushed administration of delayed-release posaconazole tablets via enteral feeding tubes. *J Antimicrob Chemother*. 2023;78(2):553–555.
7. Safety briefs: limitations of the most recent posaconazole formulation. *Acute Care: ISMP Medication Safety Alert!* 2023;28(18):1–4.
8. Noxafil PowderMix [package insert]. Rahway, NJ: Merck; 2022.