

Antifungal Prophylaxis

Background

Candida is a large group of more than 200 fungal species that colonize the skin, GI tract, and female genitourinary tract. Invasive *Candida* infection (ICI) includes congenital cutaneous candidiasis, bloodstream infections, urinary tract infections, meningitis, peritonitis, and infection of other sterile sites. ICI often presents with non-specific symptoms in preterm infants including lethargy, apnea, cardiorespiratory failure, and leukocytosis or leukopenia. The presence of thrombocytopenia and hyperglycemia have been shown to be associated with a higher likelihood of ICI. ICI is associated with increased mortality and increased risk for neurodevelopmental impairment.

Who is at risk of ICI?

- ELBW (<1,000 g) infants and infants <28 weeks' gestation
- Infants of any gestational age with:
 - Central venous catheters
 - Prolonged periods of NPO (≥ 7 days)
 - Antibiotic treatment for ≥ 7 days
 - Exposure to ≥ 2 days of third- and fourth-generation cephalosporins or carbapenems (i.e. ceftazidime, ceftriaxone, cefepime, meropenem)
 - NEC, bowel perforation, gastroschisis

How to prevent ICI

For high-risk ELBW infants, there is Grade A evidence for antifungal prophylaxis using fluconazole. The American Academy of Pediatrics Red Book (2024) and the Infectious Diseases Society of America recommend that ELBW infants with risk factors that place them at significant risk for ICI or who are in NICUs with significant rates (5-10% or higher) of ICI among ELBW infants receive fluconazole prophylaxis. Fluconazole prophylaxis prevents late-onset but does not prevent early-onset infections.

Targeted Antifungal Prophylaxis

Qualifying Infants	Duration of Prophylaxis
GA $\leq$ 25 6/7 weeks' gestation or BW $<$ 1,000 g	Until 27 6/7 weeks' gestation
GI disease: ▪ Stage 2 or greater NEC ▪ Bowel perforation ▪ Gastroschisis ▪ NPO and/or receiving antibiotics for $\geq$ 7 days	Discontinue when infant is tolerating $\geq$ 40 mL/kg/day of enteral feeds
Receiving 3 rd or 4 th generation cephalosporins or carbapenems for $\geq$ 72 hours AND are preterm or have a central line in place	Discontinue when no longer receiving 3 rd or 4 th generation cephalosporins or carbapenems

Dosing

- 6 mg/kg twice weekly if $<$ 750 g
- 3 mg/kg twice weekly if $\geq$ 750 g

Azole resistance prevention

- Limit length of prophylaxis to high-risk time period defined above
- For antifungal systemic treatment (empiric, suspected, and/or proven) use Amphotericin B or non-azole antifungals
- Use twice weekly dosing of fluconazole prophylaxis

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