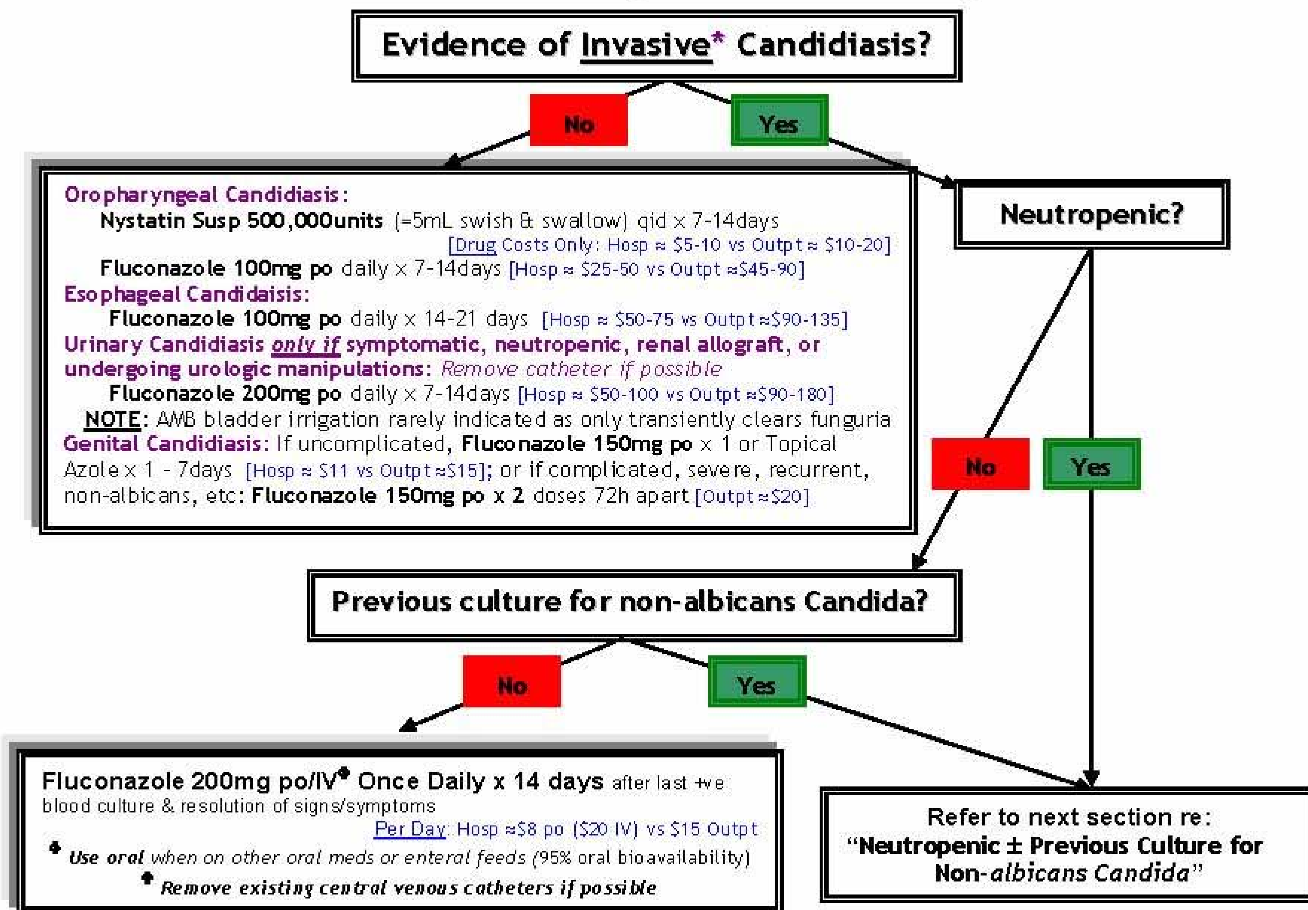
Regina Qu'Appelle HEALTH REGION

Invasive Candidiasis Empiric Treatment Algorithm



* **Invasive Candidiasis** defined as candidemia, *disseminated* candidiasis, deep organ involvement, endocarditis or meningitis

* Risk Factors for Invasive *Candida* Infections *

Iatrogenic ± Nosocomial
- Colonization
- Treatment with broad-spectrum antibiotics
- Central venous catheter
- Parenteral nutrition
- GI or cardiac surgery
- Prolonged hospital stay
- ICU stay
- Burns
- Premature birth

Immunosuppression
- Neutropenia
- Corticosteriod treatment
- *Advanced* HIV disease
- Diabetes mellitus

Fluconazole Drug Interactions of Significance

- **Rifampin**: ↓ fluconazole
- **Fluconazole**: May ↑ amiodarone, benzodiazepines, antidepressants, antidiabetic agents, "statins", phenytoin, calcium channel blockers, propranolol, cyclosporine, tacrolimus, warfarin, ergot derivatives, sildenafil & other substrates of CYP 2C8/9/19 & 3A4

NOTE: Fluconazole strongly inhibits 2C8/9/19; 3A4 moderately; CYP1A2 weakly
** May need to avoid some combinations **

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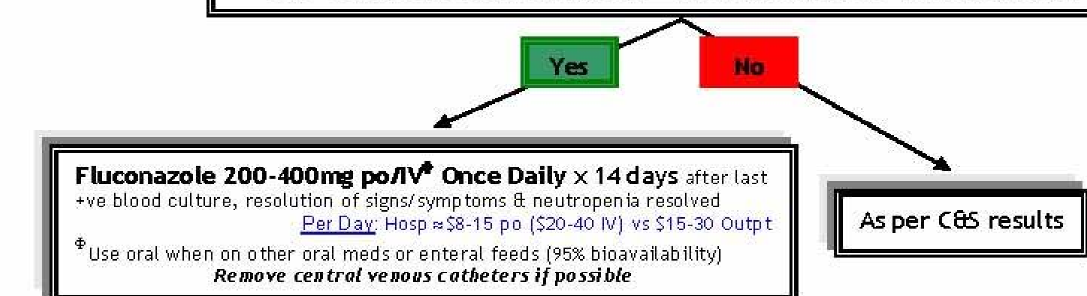
Neutropenic and/or Previous Culture for Non-*albicans Candida*

Scr <150µmol/L: Amphotericin B♣(Fungizone®) ≥ 0.7mg/kg IV ONCE daily (≈$80/day) - *Refer to pre-printed Physician's Orders - PP-218*; *if not neutropenic*: **Consider high dose fluconazole** 800mg po/IV x1, then 400mg IV/po ONCE Daily
♣NOTE: Lipid Amphotericin B more expensive ($700/day) with little/no benefit over caspofungin (or voriconazole)

Scr ≥150µmol/L: Caspofungin 70mg* IV Day 1, then 50mg* IV ONCE Daily ($220/day) Consult ID if oncology patient with Scr <150µmol/L, but receiving active chemotherapy and received fluconazole as prophylaxis (*if hepatic failure, adjust dose)

Alternate, only if above not optimal: Voriconazole* 6mg/kg IV♣ or 400mg po q12h Day 1 (≈$560/$200), then 3mg/kg IV♣ or 200mg po q12h (≈$280 IV vs $100 po/day) ***NOTE: Multiple Drug Interactions listed below!!**
♣Use oral voriconazole for IV-PO step down in fluconazole-resistant isolates in patients on oral meds/enteral feeds, or if Clcr <50mL/min♣



Voriconazole is a *Major Substrate of* **CYP2C8/9/19**; **minor substrate of 3A4**; *Moderate inhibitor* **of 3A4**; **weak inhibitor of CYP2C8/9/19 enzymes**

AVOID: long-acting barbiturates, carbamazepine, efavirenz, ergot alkaloids, pimozide, quinidine, rifampin, rifabutin, ritonavir, sirolimus due to significant ↑↑

Monitor ± ↓ dose of: buspirone, cyclosporine, methadone, methylprednisoline, omeprazole, phenytoin, "statins", sulfonylureas, tacrolimus, warfarin *plus* see previous list of fluconazole DIs
May Need To Avoid Some Combinations

Protease Inhibitors may ↑ **voriconazole**: Monitor for voriconazole toxicity (e.g. visual disturbance, rash, hepatotoxicity)
Carbamazepine, Efavirenz, Nevirapine, Phenytoin, Phenobarb, Rifampin, Ritonavir, Secobarb & other CYP2C8/9/19 *inducers* **may ↓ voriconazole**, sometimes significantly

Candida spp. & % Susceptibility to Fluconazole

RQHR Isolates from Sterile Sites (Apr - Oct '07) *NOTE: *C. kruzei* inherently Resistant to fluconazole

	Candida albicans	*C. glabrata*	*C. parapsilosis*	*C. kruzei* *	*C. tropicalis*	All isolates
Candida Isolates % (n=18)	44 (8)	33 (6)	0.1 (2)	0.06% (1)	0.06% (1)	n=18
Fully Susceptible	88% (7)	67% (4)	100% (2)	-	-	72% (n=13)
Resistant	12 (1)	33 (2)	-	100 (1)	100 (1)	28% (n=5)

References: 1) CID 2004;38(Jan 15):161-89; CID 2006;42(Jan 15):2410-51. **2)** 2007 IDSA presentation by Peter Pappas, primary author of IDSA Guideline update for Treatment of Candidiasis

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