Antifungal prophylaxis

Immunocompromised patients are at high risk of invasive fungal infections, leading to significant risk of death. Antifungal prophylaxis should be considered when the risk of opportunistic infection is high. As a rule, consider prophylaxis:

- for ***Pneumocystis jiroveci*** pneumonia (PJP) when the risk of infection is **> 3.5-6%**
- for ***invasive candidiasis*** when the risk is **> 10%**
- for ***invasive aspergillosis*** (IA) when the risk is **> 6%.**

The focus of this guideline is on prophylaxis (management of fungal infections is covered elsewhere)

Condition	**Prophylaxis for candida**	**Prophylaxis for mold**	**Prophylaxis for PJP**
Induction chemotherapy for ALL with expected severe neutropenia or GI mucositis	X		
Neutropenia (ANC < 0.5 x 10^9/L) for > 7 days associated with chemotherapy for Acute Myeloid Leukemia (AML) or with myelodysplastic syndrome (MDS)		X	
Autologous HSCT	X		
Allogenic HSCT pre-engraftment (<21 days of neutropenia)	X		
Allogenic HSCT post-engraftment and without severe GVHD			X
Allogenic HSCT with Severe Graft Versus Host Disease (steroid dependent or refractory grade 3 or 4)		X	X
Liver Transplant (OLT) with: - prolonged/repeat operation, - Candida colonization, - high transfusion requirement - choledo-jejunostomy	X		
Liver Transplant (OLT) with - 2nd OLT or more, - Need for CRRT - MELD Score > 30		X	
Liver Transplant (OLT) with: - transplant induction with T-Cell depleting agent (Alemtuzumab or Thymoglobuline) - Receiving treatment for rejection			X
Pancreas transplant with - enteric drainage, - vascular thrombosis or - postperfusion pancreatitis.	X		
Kidney Transplant with - treatment of rejection - Transplant induction with T-cell depleting agent			X
Heart transplant and lung transplant		X	X
Small-bowel recipients with graft rejection/dysfunction, increased immunosuppression, anastomotic disruption, abdominal reoperation or multivisceral transplantation	X		
Corticosteroids > 20 mg/day of prednisone equivalent for 4 weeks			X
HIV with CD4+ < 200 cells/mL or < 20% of total lymphocytes			X
Cancer patient on Alemtuzumab, temolozomide and radiation therapy, fludarabine and T-cell-depleting agents (calcineurin inhibitors, TNF-alpha blockers, lymphocyte-specific monoclonal antibodies, immunosuppressive nucleoside analogues)			X
Rheumatologic diseases, when receiving corticosteroids and other immunosuppressive agents (eg. Wegener's granulomatosis, primary systemic vasculitis, ANCA-associated vasculitis, Rheumatoid arthritis, Connective tissue diseases); Inflammatory bowel disease (if on triple immunomodulators with one of these being either a calcineurin inhibitor or anti-TNF)			X

PHARMACOLOGIC PROPHYLAXIS:

Prophylaxis for	PREFERRED agent for prophylaxis
***Candida spp* infection**	**Fluconazole**[1,2] 400 mg PO q 24h (IV only if cannot tolerate po) Second line **prophylaxis after breakthrough infection:** Micafungin 50 mg IV q24h
Mold infections **(*Aspergillus, Mucormycetes,..*)**	**Posaconazole**[1,2,3] delayed-release tablets 300 mg PO q12h x 2, then 300 mg PO q24h
***Pneumocystis Jiroveci* infection (PJP)**	**Trimethoprim-Sulfamethoxazole**[4] DS 800/160mg PO q M-W-F (or 400/80 mg PO daily) *If hypersensitivity reaction to TMP-SMX or renal failure:* **Atovaquone*** (fatty) 1500 mg PO DIE

[1]Azoles antifungal agents present numerous drug interactions. Refer to Therapeutic drug monitoring (TDM) guideline for azoles and consult pharmacy
[2]Mold prophylaxis is also effective for candida infection prophylaxis, but candida prophylaxis is not effective for mold prophylaxis.
[3]Posaconazole is a "Medicament d'Exception" for RAMQ - outpatient coverage requires completion of RAMQ formulary (available online).

In Pregnancy:

For *Candida* and Mold: the only antifungals with some data in pregnancy are itraconazole and Ampho-B; voriconazole and fluconazole to be avoided - **Consult ID**
For *P.Jiroveci*: add acid folic 5 mg po daily to TMP-SMX or use Atovaquone

DURATION of antifungal prophylaxis:

Hematologic malignancies (neutropenia post-chemo, or recipients of HSCT): continue for the duration of the period of immunocompromise (up to +75d post allo HSCT).

Solid organ transplant recipients on PJP prophylaxis: at least 6-12 months after transplant; at least 6 weeks during and after treatment for acute rejection; Lifelong prophylaxis for *lung transplant.*

HIV on PJP prophylaxis to continue until CD4 > 500 or 3 months while on appropriate antiretroviral therapy, or if CD4+ lymphocytes 100-200 cells/mL **and** undetectable viral load for 3-6 months **while** on appropriate antiretroviral therapy.

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3. Maertens J, et al. ECIL guidelines for preventing Pneumocystis jirovecii pneumonia in patients with haematological malignancies and stem cell transplant recipients. J Antimicrob Chemother. 2016;71(9):2397-404.
5. Martin SI, Fishman JA. Pneumocystis pneumonia in solid organ transplantation. Am J Transplant. 2013;13 Suppl 4:272-9.

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