C.S. MOTT CHILDREN'S HOSPITAL
MICHIGAN MEDICINE

INFECTION PROPHYLAXIS IN PEDIATRIC HEMATOLOGY ONCOLOGY GUIDELINE

Patient or disease state specific factors may warrant guideline deviation. Consult primary oncology team (fellow/attending/PharmD) to ensure appropriate prophylaxis is chosen

I. PURPOSE: To describe patients at risk for infections and outline infection prophylaxis since pediatric oncology patients are at risk due to myelosuppression, immunity alteration, disruption of integumentary barrier integrity, changes in colonizing microflora, and undernourishment.

II. SCOPE: This guideline outlines the routine infection prophylaxis for at risk patients based upon primary oncologic diagnosis. The below chart depicts disease specific indications for antimicrobial prophylaxis if not otherwise stated in the patient's current chemotherapy protocol.

Table 1: Antimicrobial Prophylaxis Indicated by Primary Diagnosis/Protocol

Oncologic Diagnosis		Viral[1]	Fungal[2]	Bacterial[3]	PJP[4]	IgG[5]
Leukemia	SR B-cell ALL/Lly				●	●
	HR B-cell ALL/Lly		●		●	●
	T-cell ALL/Lly		●		●	●
	Down Syndrome ALL	●	●	●	●	●
	Infant ALL	●	●	●	●	●
	Relapsed ALL/Lly	●	●	●	●	●
	Refractory ALL/Lly	●	●	●	●	●
	AML/MDS	●	●	●	●	●
	Relapsed/Refractory AML	●	●	●	●	●
Hodgkin Lymphoma	New or Relapsed Hodgkin Lymphoma				●	●
Non-Hodgkin Lymphoma	New or Relapsed Non-Hodgkin Lymphoma	●			●	●
Solid Tumor	Non-CNS Solid Tumors				●	●
	CNS Solid Tumors				●	●
	HEADSTART IV		●	●	●	●

ALL=acute lymphoblastic leukemia; Lly = lymphoblastic lymphoma; AML= acute myelogenous leukemia; MDS= myelodysplastic syndrome; CNS= central nervous system

1. Viral:
    a. Consider Herpes Simplex Virus (HSV) prophylaxis for seropositive patients throughout chemotherapy
    b. **Palivizumab** (Synagis) for Respiratory syncytial virus (RSV) prophylaxis in infants per protocol
2. Fungal:
    a. HR B-cell or T-cell ALL/Lly: Induction: start when ANC <500/µL or on day 10, whichever occurs sooner. Consolidation: initiate when ANC <500/µL.
    b. For all other diagnoses in the table above: prophylaxis is indicated at the start of every chemotherapy cycle expected to cause severe neutropenia (ANC <500/µL) lasting >7 days
    c. Discontinue prophylaxis when ANC >500/µL.
3. Bacterial: Prophylaxis indicated during episodes of severe neutropenia (ANC <500/µL) expected to last >7 days. Discontinue when ANC >500/µL.
4. PJP: Prophylaxis indicated at start of therapy and continued through 3 months off therapy & ALC >1000/µL
5. IgG: supplementation with IVIG indicated when IgG <400 mg/dL. Except in SR B-ALL and T-ALL, routine monthly surveillance recommended in acute leukemia patients and considered in all patients at provider discretion.

III. DOSING GUIDELINES AND PREFERRED AGENTS:

1. **Viral prophylaxis:**

Table 2: Recommended Viral Prophylactic Agents by Pathogen		
Viral pathogen	First Line	Comments
HSV	**Acyclovir** <6 years: 200 mg PO BID ≥6 years: 400 mg PO BID	Intravenous formulation not recommended for routine prophylaxis
RSV	**Palivizumab** (Synagis)	Please refer to institutional Palivizumab (Synagis) prophylaxis guidelines for dosing

2. **Fungal prophylaxis:**

Table 3: Recommended Fungal Prophylactic Agents by Diagnosis/Protocol			
Oncologic Diagnosis	Preferred Agent	Alternative Agent	Agent Rationale
HR B or T-cell ALL/Lly	**Micafungin** IV (inpatient) or **Fluconazole** IV/PO* (outpatient)	none	Yeast; drug PK and interactions
Down Syndrome ALL and Infant ALL	**Micafungin** IV	**Voriconazole** IV/PO or **Posaconazole** IV/PO	Yeast and mold; chemotherapy interactions
Relapsed ALL/Lly	**Voriconazole** IV/PO*	**Posaconazole** IV/PO or **Micafungin** IV	Yeast and mold
Refractory ALL	**Posaconazole** IV/PO	**Isavuconazole** IV/PO > **Micafungin** IV	Yeast, mold (including mucoromycetes)
AML/MDS	**Voriconazole** IV/PO	**Posaconazole** IV/PO or **Micafungin** IV	Yeast and mold
Relapsed/Refractory AML	**Posaconazole** IV/PO	**Isavuconazole** IV/PO > **Micafungin** IV	Yeast, mold (including mucoromycetes)
HEADSTART IV	**Micafungin** IV (inpatient) or **Fluconazole** IV/PO* (outpatient)	none	Yeast; drug PK and interactions
*See below for managing potential DDIs between azoles and vincristine			

- In certain patients in whom neutropenia may last >30 days (relapsed or refractory AML, refractory ALL, etc.), we recommend **posaconazole** or **isavuconazole** for expanded mold coverage for mucoromycetes (e.g., *Mucor* and *Rhizopus* spp.).
- Agents:
  - **Fluconazole** 6 mg/kg PO/IV daily (max: 400 mg/dose)
    - Contraindicated administration <24 hours of vincristine due to increased neurotoxicity. Recommend holding the day prior, the day of, and the day after administration of vincristine.
  - **Micafungin** 3 mg/kg IV daily (max: 100 mg/dose)
  - **Voriconazole**
    - <18 years: 9 mg/kg PO/IV BID (initial maximum dose: 300 mg/dose)
    - ≥18 years: 200 mg PO/IV BID
    - Obtain trough level after 5-7 days
      - Oral formulation preferred
      - Contraindicated administration <24 hours of vincristine due to increased neurotoxicity. Recommend holding the day prior, the day of, and the day after administration of vincristine. For inpatients, consider substituting **micafungin**.
  - **Posaconazole**
    - Delayed-release tablet if ≥40 kg and able to swallow intact tablet: 300 mg PO BID for 2 doses followed by 300 mg PO daily
    - Intravenous: 6 mg/kg IV BID for 2 doses followed by 6 mg/kg IV daily (max: 300 mg/dose)
    - Obtain trough level after 5-7 days
  - **Isavuconazole** if ≥12 years and ≥40 kg: 372 mg PO/IV q8h for 6 doses followed by 372 mg PO/IV daily
    - Obtain trough level after 5-7 days

3. **Bacterial prophylaxis:**
   - Agent:
     - **Levofloxacin**
       - 6 months to <5 years: 10 mg/kg IV/PO BID (max: 375 mg/dose)
       - ≥5 years: 10 mg/kg IV/PO daily (max: 500 mg/dose)
   - Anti-bacterial prophylaxis is not indicated during episodes of febrile neutropenia if not originally on prophylaxis based on Table 1

4. **PJP prophylaxis:**

Table 4: Recommended PJP Prophylactic Agents & Dosing by Age

Age Group	First Line	Second Line	Third Line
<1 month	**Atovaquone** 30 mg/kg PO daily	**Dapsone** 2 mg/kg PO daily (max: 100 mg/dose) or 4 mg/kg PO once weekly (max: 200 mg/dose)	**Pentamidine** 4 mg/kg IV q4 weeks (max: 300 mg/dose)
≥1 - <24 months	**Bactrim** 2.5 mg TMP/kg/dose PO BID 2 days per week (Sat/Sun) (max: 160 mg TMP/dose)	**Atovaquone** PO once daily <3 months: 30 mg/kg ≥3 months-<24 months: 45 mg/kg	**Pentamidine** 4 mg/kg IV q4 weeks (max: 300 mg/dose)
≥24 months – <5 years		**Pentamidine** 4 mg/kg IV q4 weeks (max: 300 mg/dose)	**Atovaquone** 30 mg/kg PO daily (max: 1500 mg/dose)
≥5 years		**Pentamidine** 300 mg inhaled q4 weeks	**Pentamidine** 4 mg/kg IV q4 weeks (max: 300 mg/dose)

   - Agents:
     - **Trimethoprim-sulfamethoxazole (Bactrim)**
       - Contraindicated within 24 hours of High Dose (HD) Methotrexate infusion, allergy to sulfa medications, known G6PD deficiency, or infants <1 month with hyperbilirubinemia
         - Strong recommendation to adjust dosing schedule to avoid administration within 24 hours of HD-methotrexate; should not be restarted until clearance achieved per protocol
       - In the absence of a contraindication, Bactrim is strongly preferred over alternative agents due to increased incidence of breakthrough infections with alternative agents. In patients receiving HD-methotrexate, Bactrim is still preferred if the dosing schedule can be adjusted as described above.
     - **Pentamidine** IV
       - Due to increased breakthrough infections in patients <24 months, use of atovaquone is preferred if unable to take Bactrim
     - **Pentamidine** inhaled (patients ≥5 years old)
       - Must be able to do a PFT test to properly inhale pentamidine
       - Inhaled pentamidine is not recommended in patients that have received lung field radiation or have a history of lung fibrosis, or abnormal PFT
     - **Atovaquone**
       - Recommend prompt transitioning to alternative agent when safe due to poor palatability and expense
     - **Dapsone**
       - Risk of methemoglobinemia 20-30%. Contraindicated in G6PD deficiency (testing recommended).

5. **Immunoglobulin Supplementation:**
   - Agent:
     - IVIG 0.4 g/kg/dose IV

IV. REFERENCES:

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