

**TITLE: ANTI-INFECTIVE PROPHYLAXIS FOR ADULT
HEMATOLOGY/ONCOLOGY PATIENTS**

GUIDELINES:

These guidelines shall be used by prescribers and pharmacy personnel to address the prevention of infectious complications in patients with cancer.

PURPOSE:

To assist in the optimization of anti-infective prophylaxis in high-risk cancer patients

APPLICABILITY:

NYP/WC and NYP/CU

PROCEDURE:

Please reference Tables I – IV for therapy and Tables V – VII for dosing.

RESPONSIBILITY:

Joint Subcommittee on Anti-Infective Use

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Table I- Anti-Infective Prophylaxis for Hematology/Oncology Patients (Adult)

Infection Risk in Cancer Patients	Disease / Therapy Examples	Anti-Infective
Low	<ul style="list-style-type: none"> Standard chemotherapy regimens for most solid tumors 	<ul style="list-style-type: none"> Bacterial – none Fungal – none Viral – See Table IV PCP - none
Intermediate	<ul style="list-style-type: none"> Autologous HSCT Lymphoma Multiple myeloma CLL Purine analog therapy (ie, fludarabine, clofarabine, nelarabine, 2-CdA) 	<ul style="list-style-type: none"> Bacterial – none Fungal – See Table III Viral – See Table IV PCP – See Table V
High	<ul style="list-style-type: none"> Allogeneic HSCT Acute leukemia Alemtuzumab therapy Severe GVHD requiring treatment 	<ul style="list-style-type: none"> Bacterial – See Table II Fungal – See Table III Viral – See Table IV PCP – See Table V

Key: 2-CdA = cladribine, CLL = chronic lymphocytic leukemia, GVHD = graft versus host disease, HSCT = hematopoietic stem cell transplant, PCP = *Pneumocystis jirovecii* pneumonia

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Table II- Antibacterial Prophylaxis for Hematology/Oncology Patients (Adult)

Disease / Therapy Examples	Antibacterial Prophylaxis	Duration
Autologous HSCT <ul style="list-style-type: none"> • Myeloma patients receiving melphalan Allogeneic HSCT	<ul style="list-style-type: none"> • Levofloxacin (NYP/WC) 	<ul style="list-style-type: none"> • Start at time of stem cell infusion • Until resolution of neutropenia OR initiation antibacterial therapy for febrile neutropenia
Chronic GVHD	<ul style="list-style-type: none"> • Penicillin VK 	<ul style="list-style-type: none"> • Until discontinuation of immunosuppression

Key: HSCT = hematopoietic stem cell transplant, GVHD = graft versus host disease

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Table III- Primary Antifungal Prophylaxis for Hematology/Oncology Patients (Adult)

Disease / Therapy Examples	Primary Antifungal Prophylaxis	Criteria	Duration
ALL CML lymphoid blast crisis	<ul style="list-style-type: none"> Fluconazole 	<ul style="list-style-type: none"> Initial prophylaxis for most patients 	<ul style="list-style-type: none"> During neutropenia with induction and intensification/consolidation chemotherapy cycles
AML MDS CML myeloid blast crisis	<ul style="list-style-type: none"> Fluconazole (NYP/C) Posaconazole (NYP/WC) 	<ul style="list-style-type: none"> Initial prophylaxis for most patients during chemotherapy induction 	<ul style="list-style-type: none"> Start 24 hours after last anthracycline dose or on first day of chemotherapy in patients not receiving anthracycline-based treatment Until resolution of neutropenia AND achievement of complete remission Re-start with each consolidation chemotherapy treatment and continue until resolution of neutropenia
	<ul style="list-style-type: none"> Fluconazole (NYP/WC) 	<ul style="list-style-type: none"> Consolidation chemotherapy 	
	<ul style="list-style-type: none"> Voriconazole (NYP/C) Posaconazole (NYP/WC) 	<ul style="list-style-type: none"> Need for >1 chemotherapy treatment course to achieve complete remission OR Chemotherapy for relapsed or refractory disease 	
	<ul style="list-style-type: none"> Micafungin 	Alternative to voriconazole/posaconazole AND any one of the following: <ul style="list-style-type: none"> Chemotherapy treatment with CYP3A4 substrate Inability to tolerate PO Ongoing diarrhea precluding oral therapy Intolerability to voriconazole/posaconazole 	
Autologous HSCT	<ul style="list-style-type: none"> None Fluconazole 	<ul style="list-style-type: none"> Low probability of developing mucositis High probability of developing mucositis 	<ul style="list-style-type: none"> Until resolution of neutropenia
Allogeneic HSCT	<ul style="list-style-type: none"> Fluconazole Posaconazole Micafungin 	<ul style="list-style-type: none"> Initial prophylaxis for most patients CBT OR T-cell depleted HLA-haploidentical transplant OR Unrelated donor with bone marrow stem cell source Alternative to posaconazole AND any one of the following <ul style="list-style-type: none"> Inability to tolerate PO Intolerability to posaconazole 	<ul style="list-style-type: none"> Start fluconazole with conditioning regimen and continue until Day 75 post-transplant Start posaconazole on day of transplant and continue until discontinuation of immunosuppression
Severe GVHD requiring treatment	<ul style="list-style-type: none"> Posaconazole Micafungin 	<ul style="list-style-type: none"> Initial prophylaxis for most patients Intestinal GVHD OR Diarrhea 	<ul style="list-style-type: none"> Until resolution of severe GVHD AND presumed recovery of immune status

Key: ALL = acute lymphoblastic leukemia, AML = acute myelogenous leukemia, MDS = myelodysplastic syndrome, CML = chronic myelogenous leukemia, HSCT = hematopoietic stem cell transplant, GVHD = graft-versus-host disease, HLA = human leukocyte antigen, CBT = cord blood transplant

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Table IV- Antiviral Prophylaxis for Hematology/Oncology Patients (Adult)

Disease / Therapy Examples	Herpes Viruses	Antiviral Prophylaxis	Duration
Standard chemotherapy regimens for solid tumors	<ul style="list-style-type: none"> • HSV 	<ul style="list-style-type: none"> • None unless prior HSV episode 	<ul style="list-style-type: none"> • During neutropenia
Autologous HSCT	<ul style="list-style-type: none"> • HSV • VZV 	<ul style="list-style-type: none"> • Acyclovir OR • Valacyclovir OR • Famciclovir 	<ul style="list-style-type: none"> • Until day 30 after autologous HSCT • During neutropenia with aggressive lymphoma regimens (e.g., hyperCVAD, CODOX-M/IVAC) • Until 3 months after discontinuation of purine analog therapy
Lymphoma			
Purine analog therapy (ie, fludarabine, clofarabine, nelarabine, cladribine)			
ALL AML MDS CML blast crisis	<ul style="list-style-type: none"> • HSV 	<ul style="list-style-type: none"> • Acyclovir OR • Valacyclovir OR • Famciclovir 	<ul style="list-style-type: none"> • During neutropenia
Bortezomib (multiple myeloma patients only)	<ul style="list-style-type: none"> • VZV 	<ul style="list-style-type: none"> • Acyclovir OR • Valacyclovir OR • Famciclovir 	<ul style="list-style-type: none"> • Until discontinuation of bortezomib
Alemtuzumab Allogeneic HSCT Severe GVHD requiring treatment	<ul style="list-style-type: none"> • HSV • VZV 	<ul style="list-style-type: none"> • Acyclovir OR • Valacyclovir OR • Famciclovir 	<ul style="list-style-type: none"> • Until at least 2 months after discontinuation of alemtuzumab AND CD4 \geq200 cells/mm³ • Start with conditioning regimen for allogeneic HSCT AND continue for 1 year • Until resolution of severe GVHD AND presumed recovery of immune status
	<ul style="list-style-type: none"> • CMV 	<ul style="list-style-type: none"> • No prophylaxis • 	<ul style="list-style-type: none"> • Monitor CMV PCR weekly • Perform surveillance until the respective time points listed above with HSV/VZV

Key: ALL = acute lymphoblastic leukemia, AML = acute myelogenous leukemia, MDS = myelodysplastic syndrome, HSCT = hematopoietic stem cell transplant, GVHD = graft-versus-host disease

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Table V- Anti-PCP Prophylaxis for Hematology/Oncology Patients (Adult)

Disease / Therapy Examples	Anti-PCP Prophylaxis	Criteria	Duration
ALL CML lymphoid blast crisis	<ul style="list-style-type: none"> Trimethoprim-sulfamethoxazole 	<ul style="list-style-type: none"> Initial prophylaxis for most patients 	<ul style="list-style-type: none"> Until completion of anti-leukemic therapy
	<ul style="list-style-type: none"> Dapsone 	<ul style="list-style-type: none"> 1st-line alternative to trimethoprim-sulfamethoxazole 	
	<ul style="list-style-type: none"> Atovaquone 	<ul style="list-style-type: none"> 2nd-line alternative to trimethoprim-sulfamethoxazole 	
Allogeneic HSCT +/- GVHD	<ul style="list-style-type: none"> Trimethoprim-sulfamethoxazole 	<ul style="list-style-type: none"> Initial prophylaxis for most patients 	<ul style="list-style-type: none"> Start with engraftment Until discontinuation of immunosuppression with allogeneic HSCT
	<ul style="list-style-type: none"> Dapsone 	<ul style="list-style-type: none"> 1st-line alternative to trimethoprim-sulfamethoxazole 	
	<ul style="list-style-type: none"> Atovaquone 	<ul style="list-style-type: none"> 2nd-line alternative to trimethoprim-sulfamethoxazole 	
Alemtuzumab Purine analog therapy (i.e., fludarabine, clofarabine, nelarabine, cladribine) Temozolomide + RT	<ul style="list-style-type: none"> Trimethoprim-sulfamethoxazole 	<ul style="list-style-type: none"> Initial prophylaxis for most patients 	<ul style="list-style-type: none"> Until at least 2 months after discontinuation of alemtuzumab AND CD4 ≥ 200 cells/mm³ Until 3-6 months after discontinuation of purine analog therapy Until recovery of lymphocytopenia after temozolomide + RT
	<ul style="list-style-type: none"> Dapsone 	<ul style="list-style-type: none"> 1st-line alternative to trimethoprim-sulfamethoxazole 	
	<ul style="list-style-type: none"> Atovaquone 	<ul style="list-style-type: none"> 2nd-line alternative to trimethoprim-sulfamethoxazole 	

Key: ALL = acute lymphoblastic leukemia, HSCT = hematopoietic stem cell transplant, GVHD = graft versus host disease, RT = radiation therapy

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Table VI- Antibacterial Agents

Drug	Prophylactic Dose	Comments/Cautions
Levofloxacin	500-750 mg PO Q24H	<ul style="list-style-type: none"> • Prophylaxis may increase risk of bacterial resistance and superinfection • Separate administration from antacids, multivitamins, and other products containing aluminum, magnesium, iron, or zinc by 2 hours • Renal adjustment required
Penicillin VK	500 mg PO Q12H	<ul style="list-style-type: none"> • Renal adjustment required

Table VII- Anti-PCP Agents

Drug	Prophylactic Dose	Comments/Cautions
Trimethoprim-sulfamethoxazole	1 DS tablet (160/800 mg) PO Q24H (CrCl >50 mL/min) OR 1 SS tablet (80/400 mg) PO Q24H (CrCl 30-50 mL/min) OR 1 DS tablet (160/800 mg) PO TIW (CrCl <30 mL/min)	<ul style="list-style-type: none"> • Renal adjustment required
Dapsone	100 mg PO Q24H	<ul style="list-style-type: none"> • G6PD required prior to initiating therapy
Atovaquone	1500 mg PO Q24H	<ul style="list-style-type: none"> • Administer with meals to reduce diarrhea and GI adverse effects

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Table VIII- Antiviral Agents

Drug	Prophylactic Dose	Comments/Cautions
Acyclovir	HSV or VZV: 800 mg PO Q12H	<ul style="list-style-type: none">• Renal adjustment required
Valacyclovir	HSV or VZV: 500 mg PO Q12H	<ul style="list-style-type: none">• Renal adjustment required
Famciclovir	HSV or VZV: 250 mg PO Q12H	<ul style="list-style-type: none">• Renal adjustment required

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Table IX- Antifungal Agents

Drug	Prophylactic Dose	Comments/Cautions
Fluconazole	400 mg PO Q24H	<ul style="list-style-type: none"> • Renal adjustment required • Reduce cyclosporine dose by 20-50% when fluconazole initiated and monitor cyclosporine levels • Reduce tacrolimus dose by 40% when fluconazole initiated and monitor tacrolimus levels • Reduce sirolimus dose by 50-70% when fluconazole initiated and monitor sirolimus levels
Posaconazole	200 mg PO Q8H	<ul style="list-style-type: none"> • Potential for hepatotoxicity and nephrotoxicity with cyclophosphamide and neurotoxicity with vinca alkaloids due to CYP 3A4 inhibition – avoid concurrent use • Reduce cyclosporine dose by 50% when posaconazole initiated and monitor cyclosporine levels • Reduce tacrolimus dose by two-thirds when posaconazole initiated and monitor tacrolimus levels • To enhance oral absorption of posaconazole and optimize plasma concentrations: <ul style="list-style-type: none"> ○ Each dose must be administered with full meal (preferably high-fat) or liquid nutritional supplement – consider nutrition consult to improve likelihood of posaconazole absorption ○ Avoid concurrent PPI use ○ Consider monitoring of posaconazole trough concentrations (goal > 0.7 mg/dL) or alternative antifungal prophylaxis if patient is unable to tolerate full meals or nutritional supplements, requires PPI therapy, has ongoing diarrhea, or intestinal GVHD
Voriconazole	200 mg PO Q12H	<ul style="list-style-type: none"> • Potential for hepatotoxicity and nephrotoxicity with cyclophosphamide and neurotoxicity with vinca alkaloids due to CYP 3A4 inhibition – avoid concurrent use • Reduce cyclosporine dose by 50% when voriconazole initiated and monitor cyclosporine levels • Reduce tacrolimus dose by two-thirds when voriconazole initiated and monitor tacrolimus levels • Subsequent to package insert labeling, pharmacokinetic studies^(17-19, 21) have been performed which have identified appropriate pharmacokinetic adjustment of sirolimus when administered concomitantly with voriconazole. Reduce sirolimus dose by 75-90% when voriconazole initiated and monitor sirolimus levels • Consider monitoring of voriconazole trough concentrations (goal >0.5-1 mg/dL) due to high intra- and interpatient variability in drug levels
Micafungin	50 mg IV Q24H	<ul style="list-style-type: none"> • Caution with prolonged use in setting of GVHD or relapsed or refractory hematologic malignancy

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GUIDELINE DATES:

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