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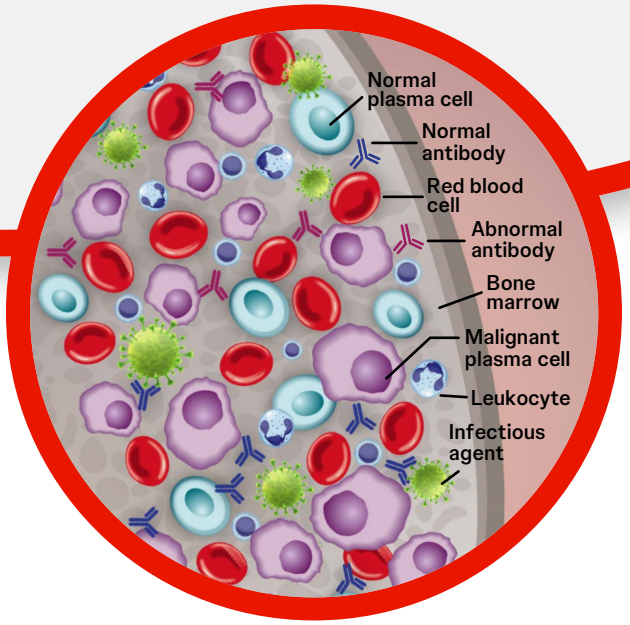
The intent of this handout is to provide background information regarding the risks of infections in multiple myeloma and management recommendations. This handout is not intended to provide treatment guidance for patients.

Infection Risk in Multiple Myeloma



Multiple myeloma is associated with immunosuppression and immune dysregulation that impact the defense against pathogens, increasing the risk of infections.[1] Infections are the leading cause of morbidity and mortality in patients with multiple myeloma.[1,2]

Risk factors[1]

Patient-related

Age ≥65 years | Male sex | Neutropenia
Elevated serum lactic dehydrogenase levels
Pathogen exposure history | High tumor burden | Disease stage
Immune cell dysfunctions (eg, B cells, natural killer cells)
Comorbidities (eg, renal dysfunction)

Treatment-related

Lines of therapy
Therapy type and antigen target
Regimen combinations
Treatment intensity (eg, cycles, dosage)

Treatments that increase risk of infection

Multiple myeloma treatments result in **cumulative immunodeficiencies** that can **increase the risk of infections.**[1,3] Specifically, **multiple myeloma therapies that target the B-cell compartment are associated with a higher incidence of Grade ≥3 infections.**[4,5]

- Stem cell transplant
- Chemotherapy
- Glucocorticoids
- Immunomodulators
- Proteasome inhibitors
- Small-molecule inhibitors (eg, SINEs)
- Antibody-drug conjugates
- mAbs
- T-cell–engaging therapies (bispecific antibodies, CAR-T)

T-cell–engaging therapies are associated with AEs that increase risk of infection[6,7]

Cytopenia, hypogammaglobulinemia, and cytokine release syndrome

Types of infections[1,8]

Gram-positive and Gram-negative bacteria, HBV, HCV, cytomegalovirus, herpes zoster, respiratory viruses, COVID-19, fungal infections, and others

AE, adverse event; CAR-T, chimeric antigen receptor T cell; COVID-19, coronavirus disease 2019; HBV, hepatitis B virus; HCV, hepatitis C virus; HDACi, histone deacetylase inhibitor; mAb, monoclonal antibody; SINE, selective inhibitor of nuclear export.

1. Raje NS, Anaissie E, Kumar SK, et al. *Lancet Haematol.* 2022;9(2):e143-e161. **2.** Augustson BM, Begum G, Dunn JA, et al. *J Clin Oncol.* 2005;23(36):9219-9226. **3.** Badros A, Hyjek E, Ma N, et al. *Blood.* 2017;130(10):1189-1197. **4.** Mikkilineni L, Yates B, Steinberg SM, et al. *Blood Adv.* 2021;5(23):5312-5322. **5.** Watson E, Djebbari F, Rampotas A, Ramasamy K. *Expert Rev Hematol.* 2022;15(6):503-517. **6.** Telli Dizman G, Aguado JM, Fernández-Ruiz M. *Expert Rev Anti Infect Ther.* 2022;20(11):1455-1476. **7.** Longhitano AP, Slavin MA, Harrison SJ, Teh BW. *Blood Rev.* 2021;49:100810. **8.** Hultcrantz M, Richter J, Rosenbaum CA, et al. *Blood Cancer Discov.* 2020;1(3):234-243.

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Infection Risk in Multiple Myeloma

Recommendations for infection prophylaxis and management

Consider National Comprehensive Cancer Network® (NCCN®) and IMWG recommendations for management of infections in patients with cancer.[1-3]

Prophylaxis[1-3]

Consider the following:

- Update patient's immunization status
- Risk-adapted antimicrobials
- Immunoglobulin replacement
- Patient education to avoid pathogen exposure

Immunosuppressed patients may have diminished vaccine responses and increased risk of viral shedding (eg, for COVID-19)[4,5]

Monitoring[1-3]

Consider infection diagnosis testing per the following:

- Fever
- Laboratory and imaging screenings (eg, complete blood panels, blood cultures, CT scans)

Infections may have clinical signs (eg, fever) similar to those of CRS. Appropriate differential diagnosis should be considered when diagnosing and managing infections

Management[1-3]

Consider treatment interruption and administration of the following:

- Antimicrobials
- Supportive care (eg, G-CSF for neutropenia, IVIG for hypogammaglobulinemia)

Consider drug interactions when managing infections in patients undergoing multiple myeloma treatments (eg, CYP450 competitors/inducers)[6]

IMWG recommendations for risk-adapted antimicrobial prophylaxis in patients with multiple myeloma[1]

RISK LEVEL	BACTERIAL	FUNGAL	VIRAL
Low	None	None	None unless prior herpes simplex virus episode, in which case use acyclovir
Intermediate	Consider levofloxacin[a] 500 mg once daily	Consider fluconazole[b] or micafungin in the setting of severe mucositis and prolonged neutropenia (absolute neutrophil count ≤100 cells per µL for ≥7 days)	For patients who are seropositive for herpes simplex virus or herpes zoster virus, provide acyclovir (400 mg or 800 mg orally twice daily for herpes simplex virus and 800 mg orally twice daily for herpes zoster virus) or valacyclovir (500 mg orally twice daily)
High	Consider levofloxacin[a] 500 mg once daily	Consider fluconazole[b] or micafungin in the setting of prolonged neutropenia (absolute neutrophil count ≤100 cells per µL for ≥7 days) and severe mucositis; consider prophylaxis with voriconazole[b] or posaconazole[b] for patients with an absolute neutrophil count ≤100 cells per µL for >7 days; consider prophylaxis against *Pneumocystis jirovecii* pneumonia with trimethoprim–sulfamethoxazole or alternative agents, as clinically indicated[c]	For patients who are seropositive for herpes simplex virus or herpes zoster virus • Provide acyclovir (400 mg or 800 mg orally twice daily for herpes simplex virus and 800 mg orally twice daily for herpes zoster virus) or valacyclovir (500 mg orally twice daily) For patients who are seropositive for HBV, the risk of reactivation depends on HBV serostatus and type and duration of immunosuppressive therapies • For patients at intermediate to high risk of HBV reactivation, consider prophylaxis; for patients at low risk, consider early preemptive treatment.[d] Use tenofovir or entecavir, rather than lamivudine, for treatment and preemptive purposes and select tenofovir in patients with previous exposure to lamivudine; maintain antiviral therapy for several months and monitor HBV viral load. Consider stopping antiviral agents when HBV viral load normalizes and stopping immunosuppressive agents

[a]Levofloxacin is preferred because the trial[7] showing effective infection prevention in this setting used this agent. Additionally, drug-drug interactions exist between ciprofloxacin and pomalidomide, causing a significantly increased drug exposure of pomalidomide and potential toxicity. For patients who are intolerant to levofloxacin and other fluoroquinolones, consider trimethoprim–sulfamethoxazole. [b]Monitor for drug-drug interactions between antifungal triazoles and agents against multiple myeloma: fluconazole, itraconazole, voriconazole, and posaconazole with bortezomib and itraconazole, voriconazole, and posaconazole with panobinostat. The dose of levofloxacin (and other fluoroquinolones), trimethoprim–sulfamethoxazole, acyclovir, and valacyclovir might require a reduction in the presence of renal dysfunction. [c]Trimethoprim–sulfamethoxazole (160 mg or 800 mg twice a day, 2–3 days per week) is the agent of choice for prophylaxis against *P. jirovecii* pneumonia. Alternative agents include aerosolized pentamidine (300 mg once monthly), dapsone (50 mg twice a day), or atovaquone (1500 mg daily). Consider alternative options for patients receiving immunomodulators (eg, thalidomide) because of potentially increased risk of severe skin toxicity with trimethoprim–sulfamethoxazole. [d]Intermediate to high risk of HBV reactivation (>1% risk): HBsAg-positive or -negative but anti–HBc-positive. Low risk of HBV reactivation (<1%): HBsAg-negative and anti–HBc-negative. Patients with evidence of a low circulating viral load of HBV DNA can be given antiviral therapy or closely monitored and treated if there is evidence of increasing viremia, regardless of serum concentrations of alanine aminotransferase.

COVID-19, coronavirus disease 2019; CRS, cytokine release syndrome; CT, computed tomography; G-CSF, granulocyte colony-stimulating factor; HBc, hepatitis B core antibody; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; IMWG, International Myeloma Working Group; IVIG, intravenous immunoglobulin; NCCN, National Comprehensive Cancer Network® (NCCN®).

1. Raje NS, Anaissie E, Kumar SK, et al. *Lancet Haematol*. 2022;9(2):e143-e161. **2.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Prevention and Treatment of Cancer-Related Infections V.1.2026. © National Comprehensive Cancer Network, Inc. 2026. All rights reserved. [Accessed March 12, 2026]. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way. **3.** Rodriguez-Otero P, Usmani S, Cohen AD, et al. *Lancet Oncol*. 2024;25(5):E205-E216. **4.** Meir J, Abid MA, Abid MB. *Transplant Cell Ther*. 2021;27(12):973-987. **5.** Stampfer SD, Goldwater M-S, Jew S, et al. *Leukemia*. 2021;35(12):3534-3541. **6.** Nucci M, Anaissie E. *Clin Infect Dis*. 2009;49(8):1211-1225. **7.** Drayson MT, Bowcock S, Planche T, et al. *Lancet Oncol*. 2019;20(12):1760-1772.

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