



# Fungal Infections – Primary Prophylaxis

Recommendations from the society for diagnosis and therapy of haematological and oncological diseases

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# Fungal Infections - Primary Prophylaxis

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- [Guideline creation rules](#)
- [Conflict of interests](#)

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on behalf of the AGIHO Infectious Diseases Working Party of the DGHO

## 1 Definition and Basic Information

The rising incidence of invasive fungal infections compromises therapeutic outcomes in hematologic cancer patients and in transplant recipients. This guideline is based on a systematic literature search for clinical trials on antifungal prophylaxis [1]. Data were extracted by two of the authors. A review committee with experts for hematology and infectious diseases discussed and interpreted the data in a consensus process. A total of 86 studies were identified including 16,922 patients. Only few trials yielded significant differences in efficacy. Fluconazole 400 mg/day improved the incidence rates of invasive fungal infections and attributable mortality in allogeneic stem cell recipients with severe graft versus host disease, in patients with acute myeloid leukemia or myelodysplastic syndrome. Posaconazole 600 mg/day reduced the incidence of invasive fungal infections and the attributable mortality of patients with graft versus host disease after allogeneic stem cell transplantation and in patients with acute myeloid leukemia or with myelodysplastic syndrome. In the latter group, posaconazole prophylaxis led to a significant decrease in overall mortality. Aerosolized liposomal amphotericin B reduced the incidence of invasive pulmonary aspergillosis.

Categories are based on the evaluation of study results and the recommendations developed by the Infectious Diseases Society of America, ISDA, see [Table 1](#).

**Table 1: Categories of Evidence**

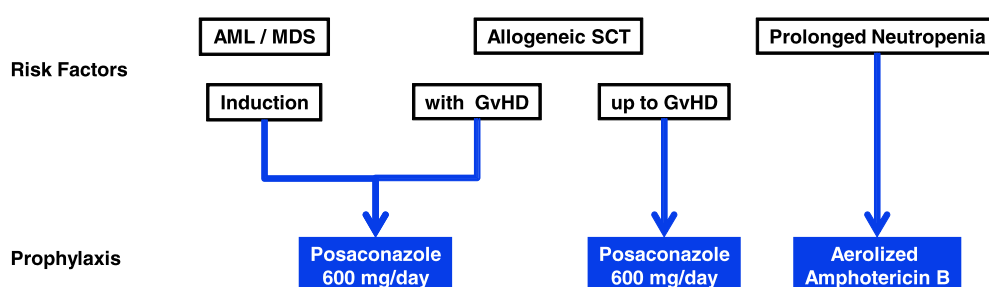
Category, grade Strength of Recommendation	Definition
A	Good evidence to support a recommendation for use
B	Moderate evidence to support a recommendation for use
C	Poor evidence to support a recommendation for use
D	Moderate evidence to support a recommendation against use
E	Good evidence to support a recommendation against use
Quality of Evidence	Definition
I	Evidence from $\geq 1$ properly randomized, controlled trial
II	Evidence from $\geq 1$ well-designed clinical trial, without randomization; from cohort or case-controlled analytic studies (preferable from $>1$ centre); from multiple time series; or from dramatic results of uncontrolled experiments
III	Evidence from opinions of respected authorities, based on clinical experience, descriptive studies, or reports from expert committees

## 2 Primary Prophylaxis

Posaconazole 600 mg/day is recommended in patients with acute myeloid leukemia (AML) / myelodysplastic syndrome (MDS) or undergoing allogeneic stem cell recipients for the prevention of invasive fungal infections and reduction of mortality [A-I] [2, 3]. Fluconazole 400 mg/day is recommended in allogeneic stem cell recipients until development of graft versus host disease [A-I] [4, 5]. Aerolized liposomal amphotericin B is recommended during prolonged neutropenia [B-II] [6].

The algorithm for primary prophylaxis is depicted of fungal infections is depicted in [Figure 1](#).

**Figure 1: Algorithm for Primary Prophylaxis of Fungal Infections**



## 3 References

1. Oliver A, Cornely A, Angelika Böhme, Dieter Buchheidt, Hermann Einsele, Werner J. Heinz, Meinolf Karthaus, Stefan W. Krause, William Krüger, Georg Maschmeyer, Olaf Penack, Jörg Ritter, Markus Ruhnke, Michael Sandherr, Michal Sieniawski, Jörg-Janne Vehreschild, Hans-Heinrich Wolf, and Andrew J. Ullmann: Primary prophylaxis of invasive fungal infections in patients with hematologic malignancies. Recommendations of the Infectious Diseases Working Party of the German Society for Haematology and Oncology. *Haematologica*. 2009, 94:113–122. DOI: [10.3324/haematol.11665](https://doi.org/10.3324/haematol.11665)
2. Goodman JL, Winston DJ, Greenfield RA, Chandrasekar PH, Fox B, Kaizer H, et al. A controlled trial of fluconazole to prevent fungal infections in patients undergoing bone marrow transplantation. *N Engl J Med* 1992;326:845-51. PMID: [1542320](https://pubmed.ncbi.nlm.nih.gov/1542320/)
3. Slavin MA, Osborne B, Adams R, Levenstein MJ, Schoch HG, Feldman AR, et al. Efficacy and safety of fluconazole prophylaxis for fungal infections after marrow transplantation--a prospective, randomized, double-blind study. *J Infect Dis* 1995;171:1545-52. PMID: [7769290](https://pubmed.ncbi.nlm.nih.gov/7769290/)
4. Cornely OA, Maertens J, Winston DJ, Perfect J, Ullmann AJ, Walsh TJ, et al. Posaconazole vs. fluconazole or itraconazole prophylaxis in patients with neutropenia. *N Engl J Med* 2007;356:348-359. [http://content.nejm.org/cgi/content/abstract/356/4/348?ijkey=f0258d123c5ce59d3c5d8839d2407c1416824d6f&keytype2=tf\\_ipsecsha](http://content.nejm.org/cgi/content/abstract/356/4/348?ijkey=f0258d123c5ce59d3c5d8839d2407c1416824d6f&keytype2=tf_ipsecsha)
5. Ullmann AJ, Lipton JH, Vesole DH, Chandrasekar P, Langston A, Tarantolo SR, et al. Posaconazole or fluconazole for prophylaxis in severe graft-versus-host disease. *N Engl J Med* 2007;356:335-347 <http://content.nejm.org/cgi/content/full/356/4/335?ijkey=f9ed79644e3af0e3b49a4567c6bf6ac946cb28c9>
6. Rijnders BJ, Cornelissen JJ, Slobbe L, Becker MJ, Doorduijn JK, Hop WC, et al. Aerosolized liposomal amphotericin B for the prevention of invasive pulmonary aspergillosis during prolonged neutropenia: a randomized, placebo-controlled trial. *Clin Infect Dis* 2008;46:1401-8. DOI: [10.1086/586739](https://doi.org/10.1086/586739)

## 4 Drugs and Dose

Table 2: Antifungal Prophylaxis

Substance	Dose	Application
Amphotericin, liposomal	12,5 mg twice weekly	Inhalation
Fluconazole	1 x 400 mg daily	PO
Posaconazole	3 x 200 mg daily	PO

## 10 Links

<https://www.agiho.de/ueber-die-agiho>

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