CHILDREN'S ONCOLOGY GROUP

The world's childhood cancer experts

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Primary Antifungal Prophylaxis for Pediatric Patients with Cancer or Hematopoietic Stem Cell Transplant Recipients

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The "Guideline for Primary Antifungal Prophylaxis for Pediatric Patients with Cancer or Hematopoietic Stem Cell Transplant Recipients" was endorsed by the COG Supportive Care Guideline Committee in October 2015. The entire document is available at: http://www.c17.ca/index.php?cID=86
A summary was published (Science M, Robinson P, MacDonald T, Rassekh SR, Dupuis LL, Sung L. Guideline for primary antifungal prophylaxis for pediatric patients with cancer or hematopoietic stem cell transplant recipients. Pediatr Blood Cancer 2014; 61:393-400) and is available at: http://onlinelibrary.wiley.com/doi/10.1002/pbc.24847/epdf

The purpose of this guideline is to provide healthcare professionals with evidence-based recommendations on the use of primary antifungal prophylaxis in children with cancer or undergoing hematopoietic stem cell transplant.

The recommendations of the endorsed guideline are presented below.

I. Summary of Recommendations for Primary Antifungal Prophylaxis for Pediatric Patients with Cancer or Hematopoietic Stem Cell Transplant Recipients

RECOMMENDATIONS	Strength of Recommendation and Quality of Evidence
ALLOGENEIC HSCT	
• For children 1 month to <19 years of age undergoing allogeneic HSCT, administer fluconazole 6–12 mg/kg/day (maximum 400 mg/day) intravenous (IV) or oral (PO) from the start of conditioning until engraftment	Strong recommendation, High quality evidence
• For the above children where fluconazole is contraindicated, administer an echinocandin as an alternative to fluconazole	Strong recommendation, Moderate quality evidence
ALLOGENEIC HSCT WITH ACUTE GRADE II–IV GVHD OR CHRONIC EXTENSIVE GVHD	
• For children 13 years of age or older undergoing allogeneic HSCT with acute Grade II–IV or chronic extensive GVHD, prophylaxis with posaconazole 200 mg PO TID from GVHD diagnosis until resolution of acute Grade II–IV GVHD or chronic extensive GVHD is suggested	Weak recommendation Moderate quality evidence
• For the above children where posaconazole is contraindicated, fluconazole 6–12 mg/kg/day (maximum 400 mg/day) IV/PO is suggested as an alternative to posaconazole	Weak recommendation Low quality evidence
• For children 1 month to <13 years of age undergoing allogeneic HSCT with acute Grade II–IV or chronic extensive GVHD, fluconazole 6–12 mg/kg/day (maximum 400 mg/day) IV/PO from GVHD diagnosis until resolution of acute Grade II–IV GVHD or chronic extensive GVHD is suggested	Weak recommendation Low quality evidence
AUTOLOGOUS HSCT WITH ANTICIPATED NEUTROPENIA >7 DAYS	
• For children 1 month to <19 years of age undergoing autologous HSCT with anticipated neutropenia for >7 days, administer fluconazole 6–12 mg/kg/day (maximum 400 mg/day) IV/PO from the start of conditioning until engraftment	Strong recommendation Moderate quality evidence

RECOMMENDATIONS	Strength of Recommendation and Quality of Evidence
PATIENTS WITH AML/MDS	
• For children 1 month to <19 years of age with AML or MDS, administer fluconazole 6–12 mg/kg/day (maximum 400 mg/day) IV/PO during chemotherapy-associated neutropenia	Strong recommendation Moderate quality evidence
• For children 13 years of age or older with AML or MDS, posaconazole 200 mg PO TID is suggested as an alternative to fluconazole in centers where there is a high local incidence of mold infections or if fluconazole is not available	Weak recommendation Moderate quality evidence
FOR OTHER PATIENTS WITH MALIGNANCY WITH ANTICIPATED NEUTROPENIA >7 DAYS	
• The panel suggests that antifungal prophylaxis not be given routinely to children with malignancy and neutropenia anticipated to persist for >7 days, outside of patients undergoing HSCT or those with AML/MDS	Weak recommendation Moderate quality evidence

HSCT, hematopoietic stem cell transplant; GVHD, graft-versus-host-disease; AML, acute myeloid leukemia; MDS, myelodysplastic syndrome.

Appendix 1: GRADE

Strength of Recommendations:

Strong Recommendation	When using GRADE, panels make strong recommendations when they are confident that the desirable effects of adherence to a recommendation outweigh the undesirable effects.
Weak Recommendation	Weak recommendations indicate that the desirable effects of adherence to a recommendation probably outweigh the undesirable effects, but the panel is less confident.

Strength of Recommendations Determinants:

Factor	Comment
Balance between desirable and undesirable effects	The larger the difference between the desirable and undesirable effects, the higher the likelihood that a strong recommendation is warranted. The narrower the gradient, the higher the likelihood that a weak recommendation is warranted
Quality of evidence	The higher the quality of evidence, the higher the likelihood that a strong recommendation is warranted
Values and preferences	The more values and preferences vary, or the greater the uncertainty in values and preferences, the higher the likelihood that a weak recommendation is warranted
Costs (resource allocation)	The higher the costs of an intervention—that is, the greater the resources consumed—the lower the likelihood that a strong recommendation is warranted

Quality of Evidence

High Quality	Further research is very unlikely to change our confidence in the estimate of effect
Moderate Quality	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate
Low Quality	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate
Very Low Quality	Any estimate of effect is very uncertain

Guyatt, G.H., et al., *GRADE: an emerging consensus on rating quality of evidence and strength of recommendations.* BMJ, 2008; 336: 924-926.
Guyatt, G.H., et al., *GRADE: going from evidence to recommendations.* BMJ, 2008; 336: 1049-1051.