

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

### COG Supportive Care Endorsed Guidelines

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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 |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------|
| <b>ALLOGENEIC HSCT</b>                                                                                                                                                                                                                                                                                                                 |                                                    |
| <ul style="list-style-type: none"> <li>For children 1 month to &lt;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</li> </ul>                                                                    | Strong recommendation, High quality evidence       |
| <ul style="list-style-type: none"> <li>For the above children where fluconazole is contraindicated, administer an echinocandin as an alternative to fluconazole</li> </ul>                                                                                                                                                             | Strong recommendation, Moderate quality evidence   |
| <b>ALLOGENEIC HSCT WITH ACUTE GRADE II–IV GVHD OR CHRONIC EXTENSIVE GVHD</b>                                                                                                                                                                                                                                                           |                                                    |
| <ul style="list-style-type: none"> <li>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</li> </ul>                 | Weak recommendation<br>Moderate quality evidence   |
| <ul style="list-style-type: none"> <li>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</li> </ul>                                                                                                                   | Weak recommendation<br>Low quality evidence        |
| <ul style="list-style-type: none"> <li>For children 1 month to &lt;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</li> </ul> | Weak recommendation<br>Low quality evidence        |
| <b>AUTOLOGOUS HSCT WITH ANTICIPATED NEUTROPENIA &gt;7 DAYS</b>                                                                                                                                                                                                                                                                         |                                                    |
| <ul style="list-style-type: none"> <li>For children 1 month to &lt;19 years of age undergoing autologous HSCT with anticipated neutropenia for &gt;7 days, administer fluconazole 6–12 mg/kg/day (maximum 400 mg/day) IV/PO from the start of conditioning until engraftment</li> </ul>                                                | Strong recommendation<br>Moderate quality evidence |

| RECOMMENDATIONS                                                                                                                                                                                                                                                                          | Strength of Recommendation and Quality of Evidence |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------|
| <b>PATIENTS WITH AML/MDS</b>                                                                                                                                                                                                                                                             |                                                    |
| <ul style="list-style-type: none"> <li>For children 1 month to &lt;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</li> </ul>                                                               | Strong recommendation<br>Moderate quality evidence |
| <ul style="list-style-type: none"> <li>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</li> </ul> | Weak recommendation<br>Moderate quality evidence   |
| <b>FOR OTHER PATIENTS WITH MALIGNANCY WITH ANTICIPATED NEUTROPENIA &gt;7 DAYS</b>                                                                                                                                                                                                        |                                                    |
| <ul style="list-style-type: none"> <li>The panel suggests that antifungal prophylaxis not be given routinely to children with malignancy and neutropenia anticipated to persist for &gt;7 days, outside of patients undergoing HSCT or those with AML/MDS</li> </ul>                     | Weak recommendation<br>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:

|                              |                                                                                                                                                                            |
|------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Strong Recommendation</b> | When using GRADE, panels make strong recommendations when they are confident that the desirable effects of adherence to a recommendation outweigh the undesirable effects. |
| <b>Weak Recommendation</b>   | 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

|                         |                                                                                                                                              |
|-------------------------|----------------------------------------------------------------------------------------------------------------------------------------------|
| <b>High Quality</b>     | Further research is very unlikely to change our confidence in the estimate of effect                                                         |
| <b>Moderate Quality</b> | Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate               |
| <b>Low Quality</b>      | 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 |
| <b>Very Low Quality</b> | 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.