

Table II: Recommended prophylaxis regimens according to patient population. See Table III for dose and monitoring recommendations.

Patient subgroups shaded blue are at higher risk of mould infections and yellow are at higher risk of yeast infections

Disease	Specific subgroup	Timing and duration of prophylaxis	Recommended prophylaxis	Alternative if recommended prophylaxis contraindicated	
(1) ALL	NON RELAPSED ALL				
	High Risk (HR) B-cell ALL (including Ph+/like subtypes), or T-cell ALL , or Infantile ALL	<u>Induction</u> Start: at diagnosis, irrespective of ANC Stop: when ANC expected to remain $\geq 0.5 \times 10^9/L$ for at least 7 days AND when high-dose steroids completed	Liposomal amphotericin B three times a week (when on <i>weekly</i> vincristine* or TKI) OR Voriconazole tablets (preferred) or liquid (when not on <i>weekly</i> vincristine or TKI) (*withhold voriconazole the day before, day of, and day after vincristine).	Echinocandin (micafungin or caspofungin)	
		<u>Consolidation & DI</u> Start: when ANC $< 0.5 \times 10^9/L$ Stop: when ANC expected to remain $\geq 0.5 \times 10^9/L$ for at least 7 days			
	Burkitt Leukaemia	All cycles with expected prolonged (>7d) neutropenia. Start: when ANC $< 0.5 \times 10^9/L$ Stop: when ANC expected to remain $\geq 0.5 \times 10^9/L$ for at least 7 days	Echinocandin (micafungin or caspofungin)	Fluconazole	
	Standard Risk B-cell ALL	All subtypes	<u>Induction</u> Routine prophylaxis is not required		
		High Risk subtype	<u>Consolidation & Delayed Intensification</u> Manage as per HR B-cell ALL (Consolidation and DI phases)		
Favourable or Average subtype		<u>Consolidation & Delayed Intensification</u> Routine prophylaxis is not required			

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ANC, absolute neutrophil count; TKI, Tyrosine Kinase Inhibitors; HSCT, Haemopoetic stem cell transplantation; IFI, Invasive fungal infection; GvHD, Graft versus host disease; CAR-T, Chimeric antigen receptor T cell therapy; CRS, Cytokine release syndrome; ICANS, Immune effector cell-associated neurotoxicity syndrome

Disease	Specific subgroup	Timing and duration of prophylaxis	Recommended prophylaxis	Alternative if recommended prophylaxis contraindicated
(1) ALL	RELAPSED ALL			
	Relapsed ALL	<p>Start: at relapse diagnosis with Induction chemotherapy</p> <p>Stop: ANC expected to remain $\geq 0.5 \times 10^9/L$ for at least 7 days and not on high-dose steroids</p>	<p>Liposomal amphotericin B three times a week (when on <i>weekly</i> vincristine* or TKI)</p> <p>OR</p> <p>Voriconazole tablets (preferred) or liquid (when not on <i>weekly</i> vincristine* or TKI)</p> <p>(*withhold voriconazole the day before, day of, and day after vincristine).</p>	Echinocandin (micafungin or caspofungin)
(2) AML	Non relapsed or Infantile AML	<p>Start: at diagnosis (cycle 1/induction) or $ANC < 0.5 \times 10^9/L$ (subsequent cycles)</p> <p>Stop: when ANC expected to remain $\geq 0.5 \times 10^9/L$ for at least 7 days</p>	<p>Posaconazole tablets (including crushed): if ≥ 13 yrs OR ≥ 10 yrs and ≥ 30 kg</p> <p>Alternative: Voriconazole tablets (preferred) or liquid.</p>	<p>Echinocandin (micafungin or caspofungin) (if on TKI OR gemtuzumab)</p> <p>Alternative: Liposomal amphotericin B three times a week</p>
	Relapsed	<p>Start: at relapse diagnosis</p> <p>Stop: continue until HSCT then manage as per (7) Allogenic HSCT</p>		
(3) Other leukaemia	Mixed phenotype acute leukaemia	Manage as per HR B-cell ALL		
	Myelodysplastic syndrome			
	Juvenile myelomonocytic (JMML)	If prolonged (>7 days) neutropenia during <i>induction</i> , consider managing as per High Risk B-Cell ALL		
	Chronic myeloid leukaemia	Routine prophylaxis not required		

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Disease	Specific subgroup	Timing and duration of prophylaxis	Recommended prophylaxis	Alternative if recommended prophylaxis contraindicated
(4) Lymphoma	HR B-cell lymphoblastic lymphoma or T-cell lymphoblastic lymphoma	Manage as per High Risk B-cell ALL		
	SR B-cell lymphoblastic lymphoma	Routine prophylaxis not required.		
	Burkitt leukaemia	Refer to (1) ALL, Burkit leukaemia		
	Burkitt lymphoma	Start: when ANC $<0.5 \times 10^9/L$ and during intensive phases only Stop: when ANC expected to remain $\geq 0.5 \times 10^9/L$ for at least 7 days	Fluconazole	Liposomal amphotericin B three times a week if at home or Echinocandin (micafungin or caspofungin) if in hospital
	Lymphoma other	Routine prophylaxis not required. Consider fluconazole if prolonged (>10 days) neutropenia (ANC $<0.5 \times 10^9/L$)		
(5) Solid tumours	Medulloblastoma	Start: when ANC $<0.5 \times 10^9/L$ or mucositis (Grade 2 or above) Stop: when ANC expected to remain $\geq 0.5 \times 10^9/L$ for at least 7 days	Fluconazole	Echinocandin (micafungin or caspofungin)
	All other solid tumours	Routine prophylaxis not required		
(6) Aplastic anaemia	Severe aplastic anaemia	Start: At diagnosis Stop: when ANC expected to remain $\geq 0.5 \times 10^9/L$ for at least 7 days	Posaconazole tablets (including crushed): if ≥ 13 yrs OR ≥ 10 yrs and ≥ 30 kg Alternative: Voriconazole tablets (preferred) or liquid	Liposomal amphotericin B three times a week

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(7) Allogeneic HSCT	Conditioning and PRE engraftment	No prior IFI	Start: during conditioning phase	Fluconazole (Consider mould-active prophylaxis if heavily pre-treated or cord-HSCT. Discuss with ID)	Echinocandin (micafungin or caspofungin)	
		Prior IFI	Mould-active secondary prophylaxis may be required. Discuss with ID. Note: voriconazole and posaconazole interact with many chemotherapy conditioning agents, liaise with ID and CCC pharmacy for an appropriate alternative through conditioning.			
	POST engraftment	No GVHD	Continue prophylaxis as per pre-engraftment above STOP: from day +75 onwards and CD4 >0.2			
		Severe acute GvHD (steroid dependent or grade II-IV)	Start: at diagnosis of severe or extensive GvHD Stop: individualised (when immunosuppression sufficiently weaned). Discuss ongoing need for prophylaxis when steroids are ≤0.5mg/kg/day prednisolone equivalent.	Posaconazole tablets (including crushed): if ≥13yrs OR ≥10yrs and ≥30kg Alternative: Voriconazole tablets (preferred) or liquid	Liposomal amphotericin B three times a week if at home or Echinocandin (micafungin or caspofungin) if in hospital	
		Extensive chronic GVHD				

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Disease	Specific subgroup	Timing and duration of prophylaxis	Recommended prophylaxis	Alternative if recommended prophylaxis contraindicated
(8) Autologous HSCT	All patients	Start: during conditioning phase Stop: Day +30 and ANC expected to remain $\geq 0.5 \times 10^9/L$ for at least 7 days	Fluconazole	Echinocandin (micafungin or caspofungin)
(9a) CAR-T (B-cell directed)	No prior IFI and not relapsed within 12 months of HSCT	Start: during lymphodepletion Stop: day +30 and ANC expected to remain $\geq 0.5 \times 10^9/L$ for at least 7 days	Fluconazole	Echinocandin (micafungin or caspofungin)
	Any of: Relapsed within 12 months of HSCT, CRS requiring tocilizumab, ICANS requiring high dose steroids.	Start: during lymphodepletion Stop: day +30 and ANC expected to remain $\geq 0.5 \times 10^9/L$ for at least 7 days If prior IFI: discuss duration with ID	Posaconazole tablets (including crushed): if ≥ 13 yrs OR ≥ 10 yrs and ≥ 30 kg Alternative: Voriconazole tablets (preferred) or liquid	Echinocandin (micafungin or caspofungin)
(9a) CAR-T (T-cell directed)	All patients undergoing T-cell directed CAR-T	Start: during lymphodepletion Stop: 6 months and ANC expected to remain $\geq 0.5 \times 10^9/L$ for at least 7 days If prior IFI: discuss duration with ID	Posaconazole tablets (including crushed): if ≥ 13 yrs OR ≥ 10 yrs and ≥ 30 kg Alternative: Voriconazole tablets (preferred) or liquid	Discuss with ID
(10) Hemophagocytic lymphohistiocytosis	Children receiving corticosteroid and either chemotherapy and/or	Start: On commencement of treatment	Voriconazole	Echinocandin (micafungin or caspofungin) (if receiving

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	ruxolitinib and or/emapalumab	Stop: individualised (when immunosuppression sufficiently weaned).		etoposide chemotherapy or ruxolitinib)
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