Guideline

Fever in a Child with Central Venous Access Device

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Author/custodian	Director, Infection Management and Prevention service (IMPS)		Review date	30/04/2025	
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Applicable to	All Children's Health Queensland staff				
Authorisation	Executive Director Clinical Servi	ces			

Purpose

This guideline provides recommendations for the management of suspected CVAD infection in children; central line associated bloodstream infection (CLABSI).

Scope

This guideline provides information for Children's Health Queensland (CHQ) staff caring for paediatric patients with suspected CVAD associated bloodstream infection in children.

Guideline: Fever in a child with Central Venous Access Device (CVAD)

General Management Principles

- Unexplained fever or suspected CVAD infection (≥38.5°C x1 or ≥38°C x2) in a child with a central venous line always requires medical review, assessment and rapid empiric antibiotics (<u>Figure 1</u>).
- For empiric antibiotic treatment follow flow diagram Figure 1.
- When cultures positive, discuss further management with Infectious Diseases
- Please refer to specific guidelines for the empiric treatment of <u>Febrile Neutropenia</u> (FN), <u>Febrile Non-neutropenia</u> or <u>Fever in child receiving parenteral nutrition</u> (PN)

CVAD infection should be suspected if any of the following are present:

- After flushing CVAD any of the following symptoms:
 - o Fever, rigors, malaise, hypotension, tachycardia
 - o Erythema or pus at exit site or along tunnel tract
- Unexplained febrile illness with signs of haemodynamic compromise in a child with CVAD
- Unexplained fever in children receiving total parenteral nutrition (TPN) via CVAD



Investigations and diagnosing CVL infection

- Bloods:
 - Full blood count (FBC), Electrolytes and Liver function tests (ELFT), C-reactive protein (CRP), blood culture (BC) from each lumen and peripherally if possible or according to unit specific protocols.
 - o Greater than one set of cultures should be collected prior to starting empiric antibiotics when possible.
- Other investigations as clinically indicated: for example. Respiratory viral PCR, chest x-ray (CXR), urine microscopy (MC&S), lumbar puncture, ECHO and if exit site infection, swab MC&S.
- If a catheter suspected to be infected is removed, the tip should be sent for culture.
- Central venous access device (CVAD) tips are NOT routinely cultured in the absence of infection/ symptoms.

If Blood cultures (BC) are negative:

- Patient well with no focus identified, apyrexial for more than 24 hours and at least 2 sets of cultures are negative after 48 hours, stop antibiotics.
- If fevers continue for more than 48 hours; repeat BC and continue antibiotics. If no other source apparent consider CVAD removal.

Line removal for CVAD infections

All CVADs should be removed if no longer required

Consider CVAD removal if "Complicated" (after discussion with the treating consultant):

- Obvious rigors and hypotension after flushing line (rather than awaiting culture results)
- Haemodynamically unstable (Heartrate (HR) score ≥ 2 on Child Early Warning Tool (CEWT), systolic blood pressure (SBP) below age standard on CEWT form, cap refill ≥ 3 seconds)
- Evidence of disseminated infection
- Pus at exit site, erythema along tunnel tract or port abscess
- Positive blood culture persisting 72 hours after starting antibiotics to which the organism is sensitive.
- Difficult to cure organisms are cultured (ie. Infection is difficult to eradicate with line in situ), for example: Candida, other fungi, *Staphylococcus aureus*, *Pseudomonas* aeruginosa, multi-resistant bacterial pathogens, non-tuberculous *Mycobacterium* and *Bacillus cereus*.

Assuming the patient is clinically stable ("<u>Uncomplicated</u>"), with none of the above indications, catheter salvage may be successful with the following organisms:

- Coagulase negative Staphylococci
- Enterococcus including Vancomycin resistant *enterococci* (VRE)
- Gram negative bacilli other than Pseudomonas aeruginosa
- Streptococcus viridans species
- Bacillus spp.(non-cereus)



Systemic antibiotics should be administered through the infected CVAD or Percutaneous inserted central catheter (PICC).

- If only one lumen is infected the systemic antibiotic and lock should be given through this lumen.
- If more than one lumen is infected, the lumen through which the systemic antibiotic is given should be alternated daily whilst the other lumen is antibiotic locked for that day.
- See section 3 below: Antibiotic Lock Therapy

The only exception is when rigors and/or hypotension occur on accessing CVAD/PICC. In this instance CVC should be removed and systemic antibiotics given peripherally if possible.

Catheter salvage may be attempted but is less likely to be successful for:

Bacillus cereus, Staphylococcus aureus, Pseudomonas aeruginosa and Enterobacter spp.

Catheter salvage should NOT be attempted with the following organisms:

- Methicillin resistant Staphylococcus aureus (MRSA)
- Mycobacteria
- Candida species
- Fungi

If CVAD is removed at commencement of treatment:

- Place temporary intravenous access until bacteraemia resolved (more than 48 hours since first negative culture).
- Guidewire exchange could be used if:
 - haemodynamically stable with no evidence of exit site infection and
 - o no other venous access available and after systemic antibiotics given through the line.
 - Daily cultures should then be performed until negative result is obtained.
- If CVAD guidewire exchanged but cultures remain positive after 72 hours of appropriate antibiotic therapy, attempts at salvage should be abandoned and the catheter removed.
- See table 1 and algorithm (figure 1 and 2) for recommended duration antibiotic therapy

Reinsertion of catheter following CVAD-related bacteraemia, should be postponed until:

- Appropriate systemic antibiotic antimicrobial therapy has commenced AND
- The patient is afebrile AND
- There are negative blood cultures (more than 48 hours since first negative culture).
- If time permits, re-insertion of a tunnelled CVC is preferably done after the systemic course of antibiotics has been completed.



If line is NOT removed at commencement of treatment:

- Repeat BC every 24 hours after the institution of treatment until clearance of infection has been documented.
- If BC still positive at 48 to 72 hours either remove line, look for alternate focus or if stable repeat daily until negative.
- Attempt line preservation unless at any point they fulfil the indications above for line removal or have repeated positive cultures.
- Use antibiotic locks in the infected catheter daily or after each dialysis session (see section 3 below: Antibiotic Lock Therapy)
- Consider surveillance blood cultures 5 to 7 days after antibiotics completed.

Antibiotic Lock therapy (ABLT)

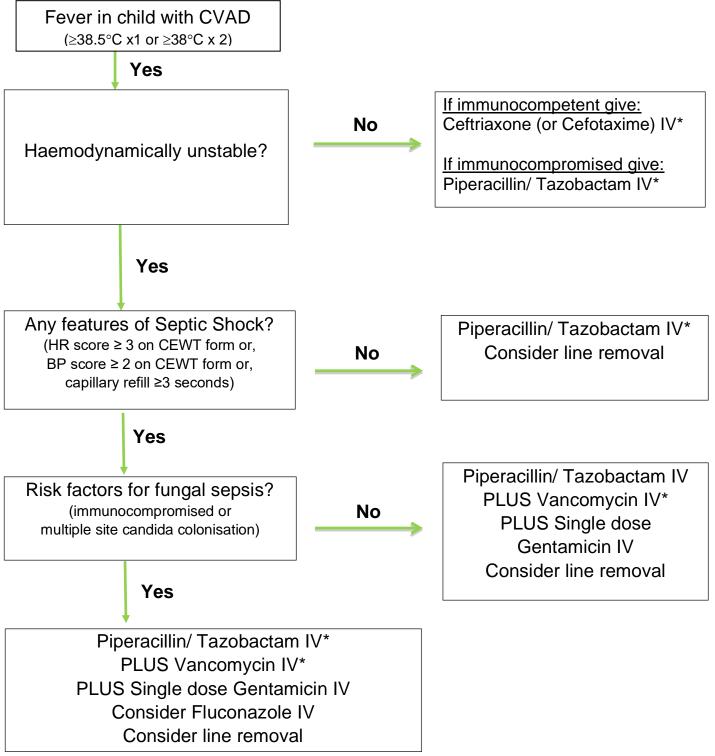
- Antibiotic Lock therapy (ABLT) is indicated for patients with CLABSI involving long-term catheters with no signs of exit site or tunnel infection, where catheter salvage is the goal. ABLT is not appropriate if the incatheter dwell time is less than 6 hours. If dwell time can be 6 hours or more, ABLT should be undertaken for the duration of IV antibiotic systemic therapy.
- ABLT is not required when a BSI is not catheter related.
- ABLT is most commonly undertaken with vancomycin or gentamicin but is feasible with a number of different antibiotics including cefazolin, ciprofloxacin, linezolid, teicoplanin or ampicillin. ID advice and approval required.
 - Gram positive organisms: Vancomycin locks
 - o Gram negative organisms: Gentamicin locks
 - o Minimum dwell time: 6 to 8 hours (to make an impact on biofilm formation)
 - o Maximum dwell time: <u>CHQ-GDL-01065 Antibiotic Lock Therapy for Catheter Related Blood Stream Infections</u>
 - o For preparation and administration advice, <u>CHQ-GDL-01065 Antibiotic Lock Therapy for Catheter Related Blood Stream Infections</u>

Long Term Antiseptic Lock therapy: Taurolidine (1.35%) / citrate (4%) antiseptic locks

- For use in high risk children (more than 10 episodes of catheter related bloodstream infection (CRBSI) per 1000 catheter days (approximately one episode per 3 months), previous life-threatening septic shock or catastrophic implications if that line is lost).
 - ID advice and approval required.
 - Minimum dwell time: 6 to 8 hours (to make an impact on biofilm formation)
 - Maximum dwell time: 28 days
- To be considered for use in children who have had one or more catheter related bloodstream infection (CRBSI) per 1000 catheter days.
- For preparation and administration advice, <u>CHQ-GDL-01060 Use of Taurolidine/Citrate lock solution in the prevention of central venous catheter related bacteraemia</u>



Figure 1. Empiric antibiotic therapy in suspected CVAD infection.



* Notes:

- In a patient known to be colonised with MRSA consider adding vancomycin
- In a patient known to be colonised with VRE, substitute vancomycin with teicoplanin
- In a patient known to be colonised with ESBL, add gentamicin IV to piperacillin/ tazobactam
- In a patient with severe redman syndrome to Vancomycin, substitute vancomycin with teicoplanin



Figure 2. Duration of antibiotic therapy, positive catheter blood culture in child with CVAD.

Notes:

- Duration of antibiotic treatment: Day 1 is from when the first negative culture was obtained.
- For definition of complicated and uncomplicated, see Notes 2 b) and c) above
- If multiple CVAD lumens impacted and line salvage is advised, alternate IV antimicrobial therapy daily via both lumens.
- If antibiotic lock therapy is recommended, note minimum dwell time of 6 to 8 hours for efficacy

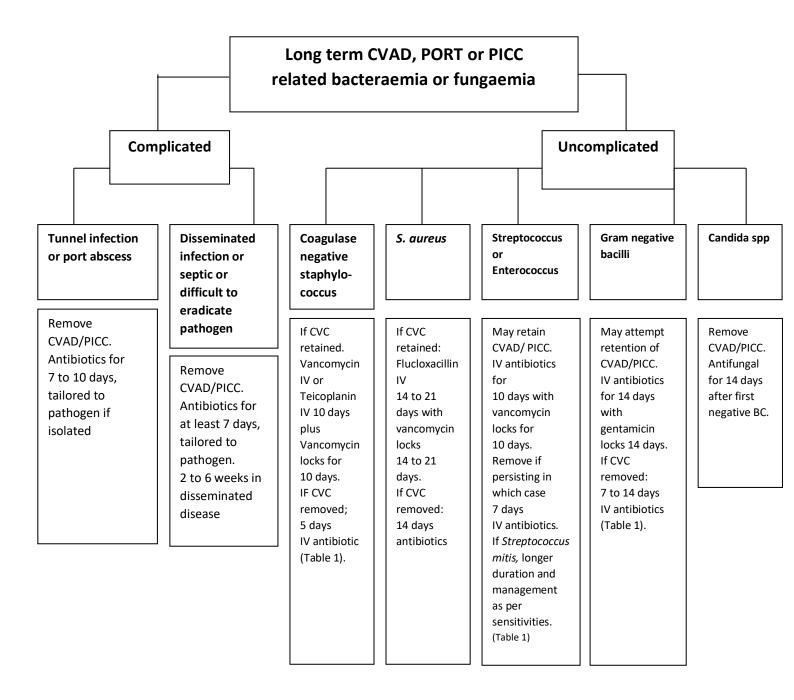




Table 1: Targeted Antibiotic Therapy

(Refer to <u>Table 2</u> for Paediatric Antimicrobial dosing recommendations)

For HITH suitable antibiotics, refer to CHQ AMS website - HITH | Home Intravenous antibiotics |

Antimicrobial Stewardship | CHQ (health.qld.gov.au)

Organism	vardship CHQ (health.qld.gov.au) Complicated	Uncomplicated		
Staphylococcus	CVAD/PICC removed:	CVAD/PICC removed:		
aureus and Staphylococcus Iugdunensis	 Intravenous (IV) antibiotics for 2 weeks from first negative blood culture 4 to 6 weeks IV antibiotics if endocarditis or suppurative thrombophlebitis 	1-2 weeks antibiotics; at least one week via IV route CVAD/PICC retained: Intravenous antibiotics with vancomycin locks for 2 to 3 weeks from first negative blood culture		
	Comments: Strongly consider line removal in these patients. If still febrile or positive blood cultures at 48 hours remove line unless risks of remove outweigh risks of retention. If still febrile at 72 hours, screen for disseminated infection; specifically considering fundoscopy, echocardiogram for endocarditis, bone and joint examination for osted and septic arthritis, abdominal ultrasound for organ micro abscesses. Screening for disseminated infection is not required routinely if rapid resolution of symptoms and fever and no focal signs. Important: ECHO may need to be repeated if fevers or positive cultures persist. Antibiotics: MSSA (Methicillin sensitive S. aureus): Flucloxacillin IV. Alternative for haemod catheters: Cefazolin IV after dialysis. (Teicoplanin IV may be considered for treatm HITH. Discuss with ID team.)			
	MRSA/nmMRSA (Non-multi-resistant Methicillin Resistant <i>Staphylococcus aureus</i>): As per sensitivities. Discuss with ID team.			
Coagulase negative Staphylococcus (CoNS)	CVAD/PICC removed: Vancomycin or Teicoplanin IV or as per sensitivities for 7 days following first negative blood culture	CVAD/PICC removed: Vancomycin/teicoplanin IV or as per sensitivities for 5 days after catheter removal. If not immunocompromised and prompt response, 48 hours may suffice. CVAD/PICC retained: Vancomycin IV or Teicoplanin IV (tailored to sensitivities) for 10 days with vancomycin antibiotic locks for 10 days if possible. Or Vancomycin IV (infusion) for 10 days (no ABLT required) Systemic antibiotics should be administered through the CVAD/PICC.		
	Comments: Most CoNS (coagulase negative staphylococcus) infections are uncomplicated, there is a high success rate with CVAD/PICC salvage using systemic antibiotics and ABLT. Line should be removed if persistently or relapsing positive cultures, haemodynamic instability or disseminated disease (complicated infection). Teicoplanin IV may be considered for treatment via HITH and should be considered if its use facilitates ≥ 6 hour dwell time thus facilitating ABLT. Discuss with ID team.			



Table 1: Targeted Antibiotic Therapy (continued)
(Refer to Table 2 for Paediatric Antimicrobial dosing recommendations)

Organism	Complicated Complicated	Uncomplicated		
Streptococcus	CVAD/PICC removed:	CVAD/PICC removed:		
	IV antibiotic as per sensitivities for 7 to 10 days following first negative blood culture. If S.mitis, IV antibiotics for 10 to 14 days.	IV antibiotic per sensitivities for 7 days after catheter removal; 10 days if S.mitis		
	in G.mas, iv antibiotics for to to 14 days.	CVAD/PICC retained:		
		IV antibiotics (tailored to sensitivities) with vancomycin locks for 10 to 14 days if possible.		
		Systemic antibiotics should be administered through the CVAD/PICC.		
Enterococcus	CVAD/PICC removed:	CVAD/PICC removed:		
	IV antibiotic as per sensitivities for 7 days following first negative blood culture	IV antibiotic per sensitivities for 5 days after catheter removal		
		CVAD/PICC retained:		
		 IV antibiotic with vancomycin antibiotic locks for 10 days if possible . Systemic antibiotics should be administered through the CVAD/PICC. 		
	Comments:			
	Most enterococcus infections are uncomplicated. There is high success rate with CVAD/PICC salvage using systemic antibiotics and ABLT. Line should be removed if persistently or relapsing positive cultures, haemodynamic instability or disseminated disease.			
Bacillus sp.	Where only one BC is positive, with a subsequent negative BC, the significance is uncertain and unlikely to be pathogenic. If systemically well, repeat BC and observe If febrile and no other cause for fever or 2 or more BCs positive, options include: observe and repeat cultures if febrile CVAD/PICC removed: Vancomycin IV or as per sensitivities for 5 days after catheter removal. If not immunocompromised and prompt response, 48 hours may suffice. CVAD/PICC retained: Vancomycin IV or as per sensitivities (administered through the CVAD/PICC) with vancomycin antibiotic locks for 14 days. Although uncommon, true infection of a CVAD/PICC with these organisms can be very difficult to eradicate. If 2 or more BCs are positive, line removal is strongly recommended.			



Table 1: Targeted Antibiotic Therapy (continued) (Refer to Table 2 for Paediatric Antimicrobial dosing recommendations)

Organism	Complicated	Uncomplicated	
Gram negatives	CVAD/PICC removed:	CVC/PICC removed:	
	IV antibiotic per sensitivities for 10 to 14 days	IV antibiotics per sensitivities for	
	following first negative blood culture	7 to 10 days after catheter removal;	
	Consider at least 14 days therapy if Pseudomonas aeruginosa	10 days if immunocompromised	
	T souddinionae deraginioda	CVAD/PICC retained: IV antibiotics per sensitivities with gentamicin antibiotic locks for 14 days. Systemic antibiotics should be administered through the CVAD/PICC.	
	Comments: Increasing experience has indicated success with line retention and systemic antibiotics and ABLT. However, a low threshold for line removal should be maintained, especially where pseudomonas aeruginosa (high biofilm production) is isolated. If still febrile or positive blood cultures at 48 hours remove line unless risks of retention outweigh risk of removal. Line should be removed if persistent or relapsing positive cultures, haemodynamic instability or disseminated disease. If still febrile at 72 hours, screen for disseminated infection specifically considering CXR, fundoscopy, echo cardiogram for endocarditis, abdominal ultrasound for organ micro abscesses, suppurative thrombophlebitis.		
Candida	Removal of catheter recommended in all cases of candida CLABSI. CVAD retention worsens outcomes. Fluconazole IV for 14 days is the treatment of choice for Candida albicans. Intravenous Echinocandin or Liposomal Amphotericin IV may be used in disseminated or persistent disease, or if other candida species isolated, after discussion with ID team. Initial treatment should be IV, with consideration of oral stepdown therapy if rapid clinical and microbiological response.		



Table 2: Paediatric Antimicrobial Dosing Recommendations

Antimicrobial	Dosing recommendations (for paediatric patients over 1 month of age)			
	Normal renal function (CrCl >20mL/min/1.73m2)	Severe renal impairment (CrCl ≤ 20mL/min/1.73m2 or patients receiving haemodialysis)	Haemodialysis Comments	
Amphotericin (Liposomal)	For more information, refer to CHQ-GDL-01075 Antifungal Prophylaxis and Treatment in Paediatric Oncology Patients and other Immunocompromised Children.			
	No dose adjustment in renal impairment/ haemodialysis required. Monitor renal function and potassium levels.			
Ampicillin	50 mg/kg/dose (Max 2 g/dose) IV every 6 hours	50 mg/kg/dose (Max 1 g/dose) IV every 6 hours	Dose after haemodialysis	
Caspofungin	For more information, refer to CHQ-GDL-01075 Antifungal Prophylaxis and Treatment in Paediatric Oncology Patients and other Immunocompromised Children. No dose adjustment in renal impairment/ haemodialysis required.			
Cefazolin	50 mg/kg/dose (Max 2 g/dose) IV every 8 hours	Loading dose: 50mg/kg (Max 2 g) as a single dose, then 25 mg/kg/dose (Max 1 g/dose) IV once daily as maintenance dose	Dose after haemodialysis	
Flucloxacillin	50 mg/kg/dose (Max 2 g/dose) IV every 6 hours	50 mg/kg/dose (Max 1 g/dose) IV every 6 hours	Not dialysed	
Fluconazole	For more information, refer to CHQ-GDL-01075 Antifungal Prophylaxis and Treatment in Paediatric Oncology Patients and other Immunocompromised Children			
	Dose after haemodialysis. TDM - Seek ID advice			
Gentamicin	Refer to CHQ Paediatric Medication guideline – Intravenous Aminoglycoside therapy for dosing and TDM advice			



Table 2: Paediatric Antimicrobial Dosing Recommendations (continued)

Antimicrobial	Dosing recommendations (for paediatric patients over 1 month of age)			
	Normal renal function (CrCl >20mL/min/1.73m2)	Severe renal impairment (CrCl ≤ 20mL/min or patients receiving haemodialysis)	Haemodialysis Comments	
Meropenem	40 mg/kg/dose (Max 2 g/dose) IV every 8 hours	20 mg/kg/dose (Max 1 gram/dose) IV every 8 hours	Dose after haemodialysis	
Micafungin	For more information, refer to CHQ-GDL-01075 Antifungal Prophylaxis and Treatment in Paediatric Oncology Patients and other Immunocompromised Children			
Piperacillin/ Tazobactam	100 mg/kg/dose (Max 4 gram/dose Piperacillin component) IV every 6 hours	100 mg/kg/dose (Max 4 gram/dose Piperacillin component) IV every 12 hours	Dose after haemodialysis	
Teicoplanin	Loading dose: 10 mg/kg (Max 800 mg/dose) IV every 12 hours for 3 doses, Maintenance dose: 10 mg/kg (Max 800 mg) IV once daily	Loading dose: 10 mg/kg (Max 800 mg) IV as a single dose Maintenance dose: 10 mg/kg (Max 400mg) IV every 72 hours	Dose after haemodialysis. TDM - Seek ID advice	
Vancomycin	Refer to CHQ Paediatric Me and TDM advice	edication Guideline – Intravenous	Vancomycin for dosing	



Definition of terms

Term	Definition		
ABLT	Antibiotic lock therapy		
ВС	Blood culture		
CEWT	Child Early Warning Tool		
CHQ	Children's Health Queensland		
CoNS	Coagulase Negative Staphylococcus		
CRBSI	Catheter related blood stream infection		
CrCl	Creatinine clearance		
CRP	C-reactive protein		
CVAD	Central venous access device		
CVC	Central venous catheter		
CVL	Central venous line		
CXR	Chest x-ray		
ELFT	Electrolytes and Liver function tests		
ESBL	Extended spectrum beta-lactamase		
FBC	Full blood count		
ID	Infectious Diseases		
IV	Intravenous		
MC&S	Microscopy		
MRSA	Methicillin resistant Staphylococcus aureus		
MSSA	Methicillin sensitive Staphylococcus aureus		
nmMRSA	Non multi-resistant methicillin resistant Staphylococcus aureus		
PICC	PICC line (Percutaneous Inserted Central Catheter)		
PCR	Polymerase chain reaction		
SBP	Systolic blood pressure		
TDM	Therapeutic drug monitoring		
TPN	Total parenteral nutrition		
VRE	Vancomycin resistant enterococci		



Consultation

Key stakeholders (position and business area) who reviewed this version are:

- Director IMPS, Immunology and Rheumatology
- Paediatric Infection Management Specialist Team (IMPS)
- Paediatric Infection Management Fellows (IMPS)
- Pharmacist Advanced Antimicrobial Stewardship
- Medications Advisory Committee Endorsed 20/07/2023

Related documents

- CHQ-PROC-03455 Management of Compromised Central Venous Access Device (CVAD)
- <u>CHQ-PROC-01052 Parenteral Nutrition emergency management of the child undergoing home</u> parenteral nutrition (PN)
- CHQ-GDL-01249 Management of fever in a Paediatric Oncology Patient: Febrile neutropenia and febrile non- neutropenia
- CHQ-GDL-01066 Empiric Antimicrobial guidelines for Paediatric Intensive care unit (PICU)
- CHQ-GDL-01065 Antibiotic Lock therapy for Catheter related blood stream infections
- CHQ-GDL-01060 Use of Taurolidine/Citrate lock solution in the prevention of central venous catheter related bacteraemia
- Paediatric Medication guideline Intravenous Aminoglycoside therapy
- Paediatric Medication Guideline Intravenous Vancomycin
- CHQ-GDL-01075 Antifungal Prophylaxis and Treatment in Paediatric Oncology Patients and other Immunocompromised Children

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Guideline revision and approval history

Version No.	Modified by	Amendments authorised by	Approved by
1.0	Infectious Diseases Consultant (IMPS)	Medicines Advisory Committee (CHQ)	General Manager Operations
2.0 26/08/2020	Paediatric Infection Management Specialists (IMPS) Pharmacist Advanced – Antimicrobial Stewardship	Medicines Advisory Committee (CHQ) – endorsed 17/09/2020	Executive Director Clinical Services (QCH)
3.0 21/05/2021	Paediatric Infection Management Specialists (IMPS) Pharmacist Advanced – Antimicrobial Stewardship	Director Infection Management and Prevention Services	Divisional Director Medicine
4.0 17/07/2023	Paediatric Infection Management Specialists (IMPS) Pharmacist Advanced – Antimicrobial Stewardship	Director Infection Management and Prevention Services	Executive Director Clinical Services

Keywords	
Accreditation references	

CVAD, central venous access device, infection, antibiotic lock therapy, ABLT, Central line associated bloodstream infection, parenteral nutrition, PN, haemodialysis, 01069 National Safety and Quality Health Service Standards (1-8)

3: Preventing and Controlling Healthcare-Associated Infection,

4: Medication Safety

