Therapeutics Bulletin

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PAEDIATRIC COLISTIN DOSING

KEY POINTS TO REMEMBER:

» Loading doses must be administered to all patients initiated on colistin.

» Maintenance doses must be adjusted in patients with renal impairment.

» All patients on colistin must have frequent renal function monitoring.

Paediatric colistin dosing

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Colistin, also known as polymyxin E, is available as an intravenous preparation, colistimethate sodium (CMS). CMS is a prodrug that is hydrolyzed in plasma to active colistin.[1] Colistin exerts its antimicrobial activity by strongly interacting with phospholipids within the cell membrane and causes disruption of the cell membrane structure and integrity.[1]

What are the indications and antibiotic policy for prescribing colistin?

A decision to commence colistin should be made in consultation with Infectious Diseases (ID) and every patient must be discussed on the antimicrobial stewardship rounds. Every colistin prescription requires a Section 21 application and an ID specialist or microbiologist authorization and/or signature.

Table 1: Colistin dosing recommendations in paediatrics

Patient categories	Loading dose		Maintenance dose		Dosing interval
	CBA mg/kg	IU	CBA mg/kg	IU	hours
Neonates to children < 12 years and weighing < 60 kg*	4	118 000 IU/kg	2.5	74 000 IU/kg	12
Adolescents ≥ 12 years and weighing ≥ 60 kg	-	9 000 000 IU (NOT per kg)	-	5 000 000 IU (NOT per kg)	12

CBA – Colistin Base Activity, IU – International Units
* Patients < 12 years old and weighing ≥ 60 kg must be discussed with the *Clinical Pharmacologist on call* for dosing recommendations.

FIGURE 1:

Process to follow when prescribing and monitoring colistin

- ¥ Special populations include patients with renal impairment, obese or critically ill patients.
- # Colistin excretion is dependent on renal elimination, and a creatinine concentration is imperative
- + Creatinine concentration to be done if the patient does not have a baseline creatinine prior to colistin commencement or if the patient has renal impairment.
- * The Clinical Pharmacologist on call can be contacted via Switchboard



Patient with indication for colistin:

Obtain authorisation for colistin use from Infectious Diseases consultant or Microbiology



Administer loading dose followed by maintenance doses as per *Table 1*.

For dosing in special populations¥ consult *Clinical Pharmacologist on call*



Take blood for creatinine concentration#

Send blood to the NHLS for a creatinine concentration initially, and periodically thereafter+



Contact the *Clinical Pharmacologist on call** for advice on dosing and dose adjustment, as needed

How should colistin be dosed?

The pharmacokinetic/pharmacodynamic parameters related to colistin efficacy is area-under-the-concentration-time-curve (AUC)/Minimum inhibitory concentration (MIC). For isolates with an MIC ≤ 2 mcg/mL, an $AUC_{0\text{-}24}$ of 50 mg.h/L is considered acceptable to achieve adequate efficacy. This is extrapolated from adult data since there is a lack of data in the paediatric population. In the absence of a loading dose colistin exposures are inadequate.[2–4] Hence, to achieve optimal colistin exposures, a loading dose is recommended. Table 1 represents proposed colistin dosing in the paediatric population at Tygerberg Hospital .

How should colistin be monitored?

Therapeutic drug monitoring of colistin is not routine due to assay complexities. Nephrotoxicity is associated with colistin use. Regular monitoring of renal function is mandatory. Patients with renal impairment require dose adjustments. Refer to document on Acute Kidney Injury and Antimicrobials for further information on assessment of acute kidney injury. For colistin dose adjustments in patients with renal impairment consult the *Clinical Pharmacologist on call*.

How should colistin be administered?

CMS is available as a powdered solution. Each CMS vial contains 1 million international unit (IU) which constitutes approximately 34 mg colistin base activity, or 80 mg CMS. The contents of the vial can be reconstituted and administered as a slow bolus injection over 5 – 10 minutes.[5] Refer to the *Colistin administration in paediatrics* for a practical, stepwise approach to colistin administration in paediatric wards.

References

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