Note: This is Online Appendix 1 of Chibabhai V, Bekker A, Black M, et al. Appropriate use of colistin in neonates, infants and children: Interim guidance. S Afr J Infect Dis. 2023;38(1), a555. https://doi.org/10.4102/sajid.v38i1.555

# Online Appendix 1: Appendix A and B

## Appendix A: Practical considerations for administering colistin in neonates, infants and children

Taken from: "Colistin administration in paediatrics; Prof Helena Rabie, Adrie Bekker, Dr Christel du Buisson, Dr Veshni Pillay-Fuentes Lorente and Prof Eric Decloedt; Stellenbosch University Therapeutics Bulletin; November 2021"

**Follow the steps below in conjunction with the Table A1:**

**Step 1**: Decide how many vials are needed by assessing the dose prescribed (#1 and #2 in the table)

**Step 2**: Add 2 mL sterile water for injection into each of the 1 MU colistin (CMS) vial and gently shake each vial until the powder has completely dissolved.

**Step 3**: Choose the appropriate syringe. If you are using 1-5 vials to dose the patient, draw up the colistin into a 10 mL syringe. If you are using 6 or more vials to dose, draw up all the colistin into a 20 mL syringe (# 3 in the table).

**Step 4**: If you are using a 10ml syringe draw further sterile water for injection into the 10 mL syringe as per the table below (#4 in the table).

NOTE: If more than one vial is used, add 2 mL sterile water for injection into each vial. Draw up the colistin from all the required vials using the same 10 mL syringe (if □ 5 vials required) or a 20mL syringe (if > 5 vials required). Use the table below to reconstitute the mixture.

**Step 5**: Calculate the volume to be injected by dividing the dose in IU by the concentration i.e. the amount of colistin per mL (#5 and #6).

**Step 7**: Use the port closest to the patient and administer the required dose as a slow bolus injection over 5-10 minutes.

**Step 8**: Once the slow bolus injection is completed, flush the canula with 2 mL sterile water for injection.

**Step 9**: Discard all "left over" medication.

# Appendix B: Assessing acute kidney injury during administration of colistin

(Adapted from: "Assessing acute kidney injury during administration of nephrotoxic drugs; Prof Helena Rabie, Adrie Bekker, Dr Christel du Buisson, Dr Veshni Pillay-Fuentes Lorente and Prof Eric Decloedt; Stellenbosch University Therapeutics Bulletin; November 2021)

Definition of acute kidney injury (AKI): AKI is a decrease in glomerular filtration rate (GFR), that is manifested by an elevation in serum creatinine (S-Cr) from baseline, and/or a reduction in urine output. AKI is staged according to the Kidney Disease: Improving Global Outcomes (KDIGO) as per Table B1

- Risk factors for colistin associated nephrotoxicity include:
    - Acute-severe illness
    - Nephrotoxin exposure (e.g. NSAIDS, antibiotics, furosemide, contrast, etc)
    - Comorbidities (e.g. sickle cell vaso-occlusive crisis, congenital heart disease)

- Assessing renal function
    - Urine output is VERY important. It reflects perfusion and function, and where AKI is suspected should preferably be monitored and where necessary with a with a catheter.
    - Review S-Cr but remember the following caveats
        - S-Cr reflects GFR in individuals at steady state with stable kidney function.
        - Affected by several factors.
        - Increases to s-Cr is often a delayed
        - S-Cr does not accurately reflect the GFR in a patient whose kidney function is changing.
        - In neonates initial s-Cr reflect maternal s-Cr

Table B1: KDIGO Classification of renal dysfunction in neonates and children and suggested actions

| Stage | **Child** | | **Neonate** | | General Recommendations | Specific Recommendation |
|---|---|---|---|---|---|---|
| | s-Cr | Urine output | s-Cr | Urine output | | |
| 1 | 1.5–1.9 times baseline# in 7 days OR 26.5 µmol/L increase within 48 h | < 0.5 mL/kg/h over 6–12 h | 1.5–1.9 Times baseline* in 7 days OR 26.5 µmol/L increase within 48 h | > 0.5 and ≤ 1 mL/kg/h over 24 h | • Optimize volume status, and blood pressure<br>• Avoid nephrotoxic agents<br>• Monitor colistin levels if possible<br>• Measure urine output<br>• Repeat s-Cr in 24 hours | |
| 2 | ↑2.0–2.9 times baseline# | < 0.5 mL/kg/h over ≥ 12 h | 2.0–2.9 times baseline* | >0.3 and ≤ 0.5 | | • Discuss dosing with Nephrology/Clinical Pharmacology/ID |

| | | | | | | |
|---|---|---|---|---|---|---|
| | | | | mL/kg/h over 24 h | | |
| 3 | ≥ 3.0 times baseline# OR s-Cr ≥ 353.6 µmol/L OR initiation of renal replacement therapy OR decrease in eGFR to < 35 mL/min/1.73 $m^2$ | < 0.3 mL/kg/h ≥ 24 h OR anuria for ≥ 12 h | ≥ 3.0 times baseline* OR increase in serum creatinine to ≥ 221 µmol/L OR initiation of renal replacement therapy | ≤ 0.3 mL/kg/h over 24 h | | • Actively switch away from nephrotoxic agent if possible<br>• Calculate eGFR<br>• Adjust dose of all agents where necessary<br>• Discuss dosing with Nephrology/Clinical Pharmacology/ID |
| • Estimated glomerular filtration rate (eGFR) is calculated using the Bedside Schwartz formula.<br>• #Baseline creatine in children = lowest previous value or if none is available, calculate backward using an eGFR of 100–120 mL/min/1.73 m2, assuming that previous kidney function was normal.<br>• *Baseline creatine in infants > 3 days < 1 month = lowest previous s-Cr AND not more than 95$^{th}$ percentile for gestation and age.<br>• GFR (mL/min/1.73 $m^2$) = (0.41 3* Height in cm) / (Creatinine in umol/l * 0.0113)<br>http://nephron.com/bedside_peds_nic.cgi | | | | | | |

Table B2: Estimated glomerular filtration rate (eGFR) normal values for infants > 1 month children

| Age | Serum creatinine (µmol/L) | Estimated glomerular filtration rate (eGFR) (mL/min/1.73 m 2 ) |
|---|---|---|
| 1 month | 18 to 35 | 48 (28–68) |
| 2 months | | 58(30–86) |
| 6 months | | 77(41-103) |
| 9 months | | 103(49-157) |
| 12 months | | 115(65-160) |
| 1-10 years | 27 to 62 | 127(89-165) |
| 10 years | 44 to 88 | 85 - 150 |

Table B3: Creatinine reference ranges for neonates and infants

| **Gestational age (weeks)** | **Serum Creatinine (µmol/L)** | | | |
|---|---|---|---|---|
| | Birth | 48 hours | 7 days | 14 days |
| 27-29 | 77 ±12 | 116 ± 40 | 84 ± 32 | 72 ± 32 |
| 30-32 | 65 ±4 | 104 ± 38 | 83 ± 41 | 69 ± 32 |
| 33-35 | 73 ±6 | 93 ± 39 | 68 ± 44 | 55 ± 36 |
| >36 | 65 ±5 | 75 ± 38 | 50 ± 36 | 38 ± 20 |