| **Intensive Arm A: Adult Dosing** | | |
| --- | --- | --- |
| **Drug** | **Recommended Dose (per dose)** | **Frequency** |
| **IV amikacin** | 15mg/kg  **OR** | Once daily |
|  | 20-25mg/kg | Thrice weekly |
| Dosing will be made in accordance with British Thoracic Society (BTS) guidelines (13) and is dependent on the physiology, site and therapeutic drug monitoring (TDM) outcomes of each participant. In overweight participants use the ideal body weight calculator or in cases of extremes of actual body weight where body weight is greater than 20% above ideal use the adjusted body weight calculator available in the MoOP. To determine ideal body weight for amputees, refer to for the table in the MoOP describing the percentage of total weight contributed by individual body parts. | | |
| **IV tigecycline** | 25mg increasing by 5mg every two doses until either 50mg reached or until patient is unable to tolerate. | Twice daily or same total daily dose over a 24-hour infusion |
| **IV imipenem/cilastatin**  *IV imipenem/cilastatin is preferred but if not tolerated, use IV cefoxitin.* | **≥50kg**  1g (dose based on imipenem component) | Twice – four times daily infused over 1-4 hours as tolerated |
|  | **<50kg**  15 – 25mg/kg (dose based on imipenem component). Maximum 1g. | Twice – four times daily infused over 1-4 hours as tolerated |
| **IV cefoxitin**  *Cefoxitin only for use if imipenem/cilastatin not tolerated.* | 2 – 4g | Thrice daily infused over 1-4 hours as tolerated, or same total daily dose over a 24-hour infusion. |
| **Oral azithromycin** | 250 – 500mg | Once daily |
| *If azithromycin not tolerated, use oral clarithromycin.* | **<40kg or poorly tolerated**  250mg | Once daily |
| **Oral clarithromycin**  *Clarithromycin only for use if azithromycin not tolerated.* | 500mg | Twice daily |
| **Oral clofazimine** | 100 – 300mg | Once daily |
| **For participants with confirmed mixed NTM (slow growers + MABS) infections, there is an option to add oral ethambutol to the treatment arm in accordance with the dosing below.** | | |
| **Oral ethambutol**  Ethambutol should be dosed on ideal body weight. | 15mg/kg  (rounded to account for tablet strength)  **OR** | Once daily |
| 25mg/kg  (rounded to account for tablet strength) | Thrice weekly |

| **Intensive Arm B: Adult Dosing** | | |
| --- | --- | --- |
| **Drug** | **Recommended Dose (per dose)** | **Frequency** |
| **Inhaled amikacin (IA)**  **(IV formulation)** | 500mg | Twice daily |
| **IV tigecycline** | 25mg increasing by 5mg every two doses until either 50mg reached or until patient is unable to tolerate. | Twice daily or same total daily dose over a 24-hour infusion |
| **IV imipenem/cilastatin**  *IV imipenem/cilastatin is preferred but if not tolerated, use IV cefoxitin.* | **≥50kg**  1g (dose based on imipenem component) | Twice – four times daily infused over 1-4 hours as tolerated |
|  | **<50kg**  15 – 25mg/kg (dose based on imipenem component). Maximum 1g. | Twice – four times daily infused over 1-4 hours as tolerated |
| **IV cefoxitin**  *Cefoxitin only for use if imipenem/cilastatin not tolerated.* | 2 – 4g | Thrice daily infused over 1-4 hours as tolerated, or same total daily dose over a 24-hour infusion. |
| **Oral azithromycin** | 250 – 500mg | Once daily |
| *If azithromycin not tolerated, use oral clarithromycin.* | **<40kg or poorly tolerated**  250mg | Once daily |
| **Oral clarithromycin**  *Clarithromycin only for use if azithromycin not tolerated.* | 500mg | Twice daily |
| **Oral clofazimine** | 100 – 300mg | Once daily |
| **For participants with confirmed mixed NTM (slow growers + MABS) infections, there is an option to add oral ethambutol to the treatment arm in accordance with the dosing below.** | | |
| **Oral ethambutol**  Ethambutol should be dosed on ideal body weight. | 15mg/kg  (round to account for tablet strength)  **OR** | Once daily |
| 25mg/kg  (round to account for tablet strength) | Thrice weekly |

| **Intensive Arm C: Adult Dosing** | | |
| --- | --- | --- |
| **Drug** | **Recommended Dose (per dose)** | **Frequency** |
| **IV amikacin** | 15 mg/kg  **OR** | Once daily |
|  | 20-25mg/kg | Thrice weekly |
| Dosing will be made in accordance with British Thoracic Society (BTS) guidelines (13) and is dependent on the physiology, site and therapeutic drug monitoring (TDM) outcomes of each participant. In overweight participants use the ideal body weight calculator or in cases of extremes of actual body weight where body weight is greater than 20% above ideal use the adjusted body weight calculator available in the MoOP. To determine ideal body weight for amputees, refer to for the table in the MoOP describing the percentage of total weight contributed by individual body parts. | | |
| **IV tigecycline** | 25mg increasing by 5mg every two doses until either 50mg reached or until patient is unable to tolerate. | Twice daily or same total daily dose over a 24-hour infusion |
| **IV imipenem/cilastatin** | **≥50kg**  1g (dose based on imipenem component) | Twice – four times daily infused over 1-4 hours as tolerated |
| *IV imipenem/cilastatin is preferred but if not tolerated, use IV cefoxitin.* | **<50kg**  15 – 25mg/kg (dose based on imipenem component). Maximum 1g. | Twice – four times daily infused over 1-4 hours as tolerated |
| **IV cefoxitin**  *Cefoxitin only for use if imipenem/cilastatin not tolerated.* | 2 – 4g | Thrice daily infused over 1-4 hours as tolerated, or same total daily dose over a 24-hour infusion. |
| **Oral azithromycin** | 250 – 500mg | Once daily |
| *If azithromycin not tolerated, use oral clarithromycin.* | **<40kg or poorly tolerated**  250mg | Once daily |
| **Oral clarithromycin**  *Clarithromycin only for use if azithromycin not tolerated.* | 500mg | Twice daily |
| **For participants with confirmed mixed NTM (slow growers + MABS) infections, there is an option to add oral ethambutol to the treatment arm in accordance with the dosing below.** | | |
| **Oral ethambutol**  Ethambutol should be dosed on ideal body weight. | 15mg/kg  (round to account for tablet strength)  **OR** | Once daily |
| 25mg/kg  (round to account for tablet strength) | Thrice weekly |

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| **Intensive Arm A: Paediatric Dosing** | | | |
| **Drug** | | **Recommended Dose**  **(per dose)** | **Frequency** |
| **IV amikacin** | | 15-30mg/kg, max 1500mg | Once daily |
| Dosing will be made in accordance with BTS guidelines (13) and is dependent on the physiology, site and TDM outcomes of each participant. In obese participants, use the ideal body weight calculator or in cases of extremes of actual body weight where body weight is greater than 20% above ideal body weight use the adjusted body weight calculator available in the MoOP. To determine ideal body weight or adjusted body weight for amputees, refer to for the table in the MoOP describing the percentage of total weight contributed by individual body parts. | | | |
| **IV tigecycline**  **(ages ≥8 years)** | Day 1:  (50% of optimal dose) | 0.6mg/kg, max 25mg | Twice daily (12 hourly) |
| Day 2:  (75% of optimal dose) | 0.6mg/kg, max 25mg | In the morning |
| 1.2mg/kg, max 50mg | At night |
| Day 3:  (100% of optimal dose) | 1.2mg/kg, max 50mg | Twice daily (12 hourly) |
| **IV imipenem/cilastatin**  *IV imipenem/cilastatin is preferred but if not tolerated, use IV cefoxitin.* | Day 1-2 | 15 - 25mg/kg, max 1g  (dose based on imipenem component) | Twice daily (12 hourly) |
| Day 3 | 15 - 25mg/kg, max 1g  (dose based on imipenem component) | Four times daily (reduce to 3 times daily if not tolerated)  (6 or 8 hourly) |
| **IV cefoxitin**  *Only for use if imipenem/cilastatin not tolerated.* | | 40mg/kg, max 2g | Four times daily (6 hourly) |
| **Oral azithromycin**  *If azithromycin not tolerated, use oral clarithromycin.* | | 10mg/kg, max 500mg | Once daily |
| **Oral clarithromycin**  *Only for use if azithromycin not tolerated.* | **Children 1 month – 11 years of age** | | |
| <8 kg | 7.5mg/kg | Twice daily |
| 8-11 kg | 62.5mg |
| 12-19 kg | 125mg |
| 20-29 kg | 187.5mg |
| 30-40 kg | 250mg |
| **Children 12-18 years of age** | | |
| Dosing independent of weight | 500mg | Twice daily |
| **Oral clofazimine**  Dosing may be rounded to account for capsule strength. | | **<40kg**  3-5mg/kg, max 50mg | Once daily |
| **≥40kg**  3-5mg/kg, max 100mg |
| **For participants with confirmed mixed NTM (slow growers + MABS) infections, there is an option to add oral ethambutol to the treatment arm in accordance with the dosing below.** | | | |
| **Oral ethambutol**  Ethambutol should be dosed on ideal body weight. | | 15mg/kg, max 1200mg (round to account for tablet strength) | Once daily |

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| **Intensive Arm B: Paediatric Dosing** | | | |
| **Drug** | | **Recommended Dose**  **(per dose)** | **Frequency** |
| **Inhaled amikacin (IA) (IV formulation)** | | 500mg | Twice daily |
| **IV tigecycline**  **(ages ≥8 years)** | Day 1:  (50% of optimal dose) | 0.6mg/kg, max 25mg | Twice daily (12 hourly) |
| Day 2:  (75% of optimal dose) | 0.6mg/kg, max 25mg | In the morning |
| 1.2mg/kg, max 50mg | At night |
| Day 3:  (100% of optimal dose) | 1.2mg/kg, max 50mg | Twice daily (12 hourly) |
| **IV imipenem/cilastatin**  *IV imipenem/cilastatin is preferred but if not tolerated, use IV cefoxitin.* | Day 1-2 | 15 - 25mg/kg, max 1g.  (dose based on imipenem component) | Twice daily (12 hourly) |
| Day 3 | 15 - 25mg/kg, max 1g  (dose based on imipenem component) | Four times daily (reduce to 3 times daily if not tolerated)  (6 or 8 hourly) |
| **IV cefoxitin**  *Only for use if imipenem/cilastatin not tolerated.* | | 40mg/kg, max 2g | Four times daily (6 hourly) |
| **Oral azithromycin**  *If azithromycin not tolerated, use oral clarithromycin.* | | 10mg/kg, max 500mg | Once daily |
| **Oral clarithromycin**  *Only for use if azithromycin not tolerated.* | **Children 1 month – 11 years of age** | | |
| <8 kg | 7.5mg/kg | Twice daily |
| 8-11 kg | 62.5mg |
| 12-19 kg | 125mg |
| 20-29 kg | 187.5mg |
| 30-40 kg | 250mg |
| **Children 12-18 years of age** | | |
| Dosing independent of weight | 500mg | Twice daily |
| **Oral clofazimine**  Dosing may be rounded to account for capsules strength. | | **<40kg**  3-5mg/kg, max 50mg | Once daily |
| **≥40kg**  3-5mg/kg, max 100mg |
| **For participants with confirmed mixed NTM (slow growers + MABS) infections, there is an option to add oral ethambutol to the treatment arm in accordance with the dosing below.** | | | |
| **Oral ethambutol**  Ethambutol should be dosed on ideal body weight. | | 15mg/kg, max 1200mg (round to account for tablet strength) | Once daily |

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| **Intensive Arm C: Paediatric Dosing** | | | |
| **Drug** | | **Recommended Dose**  **(per dose)** | **Frequency** |
| **IV amikacin** | | 15-30mg/kg, max 1500mg | Once daily |
| Dosing will be made in accordance with BTS guidelines (13) and is dependent on the physiology, site and TDM outcomes of each participant. In obese participants, use the ideal body weight calculator or in cases of extremes of actual body weight where body weight is greater than 20% above ideal body weight use the adjusted body weight calculator available in the MoOP. To determine ideal body weight or adjusted body weight for amputees, refer to for the table in the MoOP describing the percentage of total weight contributed by individual body parts. | | | |
| **IV tigecycline**  **(ages ≥8 years)** | Day 1:  (50% of optimal dose) | 0.6mg/kg, max 25mg | Twice daily (12 hourly) |
| Day 2:  (75% of optimal dose) | 0.6mg/kg, max 25mg | In the morning |
| 1.2mg/kg, max 50mg | At night |
| Day 3:  (100% of optimal dose) | 1.2mg/kg, max 50mg | Twice daily (12 hourly) |
| **IV imipenem/cilastatin**  *IV imipenem/cilastatin is preferred but if not tolerated, use IV cefoxitin.* | Day 1-2 | 15 - 25mg/kg, max 1g.  (dose based on imipenem component) | Twice daily (12 hourly) |
| Day 3 | 15 - 25mg/kg, max 1g  (dose based on imipenem component) | Four times daily (reduce to 3 times daily if not tolerated)  (6 or 8 hourly) |
| **IV cefoxitin**  *Only for use if imipenem/cilastatin not tolerated.* | | 40mg/kg, max 2g | Four times daily (6 hourly) |
| **Oral azithromycin**  *If azithromycin not tolerated, use oral clarithromycin.* | | 10mg/kg, max 500mg | Once daily |
| **Oral clarithromycin**  *Only for use if azithromycin not tolerated.* | **Children 1 month – 11 years of age** | | |
| <8 kg | 7.5mg/kg | Twice daily |
| 8-11 kg | 62.5mg |
| 12-19 kg | 125mg |
| 20-29 kg | 187.5mg |
| 30-40 kg | 250mg |
| **Children 12-18 years of age** | | |
| Dosing independent of weight | 500mg | Twice daily |
| **For participants with confirmed mixed NTM (slow growers + MABS) infections, there is an option to add oral ethambutol to the treatment arm in accordance with the dosing below.** | | | |
| **Oral ethambutol**  Ethambutol should be dosed on ideal body weight. | | 15mg/kg, max 1200mg  (round to account for tablet strength) | Once daily |