Clinical Excellence Commission

# Sepsis NEONATAL First Dose

## Empirical Parenteral Antibiotic Guideline v2

The Clinical Excellence Commission (CEC) Sepsis Neonatal Empirical Parenteral Antibiotic Guideline aims to guide the prescription and timely administration of the **FIRST DOSE** of antibiotics for **neonatal patients** (less than one month of age) who re-present after going home and have a diagnosis of sepsis.

Antibiotics can be administered via umbilical or intraosseous access when peripheral intravenous access is not available. Prior to gaining intraosseous access in the neonate, consideration must be given as to whether the umbilical vein is still accessible. If in doubt please refer to local neonatologist or NETS NSW. Intramuscular antibiotics should only be used FOR SHORT TERM if unable to obtain intravenous, umbilical or intraosseous access.

The guideline is based on MIMS, 2011[1] and the Therapeutic Guidelines: Antibiotic version 14, 2010[2]. Some doses may vary from Therapeutic Guidelines as they are under review. The CEC guideline incorporates best available evidence and expert opinion[3,4,5] and is intended to provide an accessible resource which can be adapted to suit individual facility preferences as required.

**Prompt administration of antibiotics and resuscitation fluids is vital in the management of the neonate at risk of, or with, sepsis. The goal is to commence antibiotic therapy within the first hour of the recognition of the risk of sepsis.** Neonates at risk of sepsis may develop irretrievable septic syndromes if antibiotics are delayed.

**This is a guideline for the FIRST DOSE of antibiotics after which clinicians should seek local assistance and examine results of tests to inform ongoing directed therapy**.

**Sepsis in neonates** is often described as early-onset or late-onset. Neonates with early-onset sepsis may have antenatal risk factors of positive group B streptococcus colonisation of the maternal vagina, premature or prolonged rupture of membranes, unexplained premature labour and/or peri-partum maternal fever. Sepsis in the neonate often presents with subtle signs which may include dusky episodes, pallor, temperature instability (fever or hypothermia), poor feeding, sleepiness, low blood glucose, milky or bilious vomits or early onset respiratory distress before becoming a fulminant, systemic illness. This is why a low index of suspicion should be maintained and treatment instituted where **two or more** of the above risk factors or signs are present prior to fulminant disease.

Late-onset disease is described as occurring after 48 hours of age. Term infants with late-onset sepsis may have a history of obstetric complications but this is less characteristic. It is important to note that many septic newborns have no apparent antenatal or obstetric risk factors.

### Use Table 1 when there is no obvious source of infection

### Use Table 2 when the source of infection is suspected or known





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| Table 1: NEONATAL antibiotic prescribing when NO OBVIOUS SOURCE OF INFECTION | | | |
|---|---|---|---|
| | **FIRST DOSE empirical intravenous (IV) or intraosseous (IO) antibiotic regimen**<br><br>**Less than 7 days age** | **FIRST DOSE empirical intravenous (IV) or intraosseous (IO) antibiotic regimen**<br><br>**7-28 days age** | **FIRST DOSE empirical intramuscular (IM) antibiotic regimen** |
| **Sepsis or suspected sepsis, with NO OBVIOUS SOURCE of infection**<br><br>See Table 3 for common infecting bacteria | **cefotaxime** 50mg/kg/dose IV/IO, 12-hourly<br>***PLUS***<br>**gentamicin 5 MINUTE PUSH** 5mg/kg/dose IV/IO, 24-hourly<br>***PLUS***<br>**ampicillin** 50mg/kg/dose IV/IO, 8-hourly<br>***PLUS***<br>**aciclovir** 20mg/kg/dose IV/IO 8-hourly | **cefotaxime** 50mg/kg/dose IV/IO, 8-hourly<br>***PLUS***<br>**gentamicin 5 MINUTE PUSH** 5mg/kg/dose IV/IO, 24-hourly<br>***PLUS***<br>**ampicillin** 50mg/kg/dose IV/IO, 6-hourly<br>***PLUS***<br>**aciclovir** 20mg/kg/dose IV/IO 8-hourly | **cefotaxime** 50mg/kg/dose IM, 12-hourly (age < 7 days)<br>**OR**<br>8-hourly (age 7-28 days)<br>***PLUS***<br>**gentamicin** 5mg/kg/dose IM, 24-hourly<br>***PLUS***<br>**ampicillin** 50mg/kg/dose IM, 8-hourly (age < 7 days)<br>**OR**<br>6–hourly (age 7-28 days)<br><br>**aciclovir** CANNOT be given intramuscularly |

**Intramuscular (IM) administration** indicated ONLY FOR SHORT TERM USE if unable to obtain intravenous, umbilical or intraosseous access.

### Notes for Table 1:

- If renal failure is present, dosages and intervals of antibiotics may need to be adjusted especially for vancomycin, gentamicin and penicillin drugs.
- All antibiotic dosing in neonates relates to birth weight. Where scales are available the baby should be bare weighed. If no scales available the weight can be estimated by the paediatrician or neonatologist. When in doubt call **NETS 1300 36 2500** for adequate dosing and management.
- Obtain 1mL of blood for blood culture (aerobic bottle) **before** administering antibiotics if possible (0.5mL absolute minimum for blood culture).
- Obtain other clinical specimens as appropriate but **do not delay administration of antibiotics** or wait for results of investigations.
- **All neonates with presumed or suspected sepsis should be discussed with a consultant Paediatrician or Neonatologist. If not available call NETS NSW phone 1300 36 2500 for urgent advice.**
- **Always obtain expert advice about further investigation and treatment if blood culture or CSF cultures become positive.**



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## Table 2: NEONATAL antibiotic prescribing when SOURCE OF INFECTION IS SUSPECTED OR KNOWN

Notes – see numbers in table text below:

1. Consider aciclovir if severe sepsis, pneumonia, meningitis, seizures, hepatitis or if skin vesicles or ulceration present.
2. Consider adding clindamycin if high risk for community acquired MRSA.
3. Add vancomycin if severe sepsis 15mg/kg/dose 12 hourly (less than 7 days age) or 8 hourly (7-28 days age).

| Apparent source of sepsis | FIRST DOSE empirical intravenous (IV) or intraosseous (IO) antibiotic regimen<br><br>Less than 7 days age | FIRST DOSE empirical intravenous (IV) or intraosseous (IO) antibiotic regimen<br><br>7-28 days age | FIRST DOSE empirical intramuscular (IM) antibiotic regimen |
|---|---|---|---|
| **Meningitis / encephalitis** | **cefotaxime** 50mg/kg/dose IV/IO, 12-hourly<br>***PLUS***<br>**ampicillin** 50mg/kg/dose IV/IO, 8-hourly<br>***PLUS***<br>**aciclovir** 20mg/kg/dose IV/IO 8-hourly | **cefotaxime** 50mg/kg/dose IV/IO, 8-hourly<br>***PLUS***<br>**ampicillin** 50mg/kg/dose IV/IO, 6-hourly<br>***PLUS***<br>**aciclovir** 20mg/kg/dose IV/IO 8-hourly | **cefotaxime** 50mg/kg/dose IM, 8 or 12-hourly<br>***PLUS***<br>**ampicillin** 50mg/kg/dose IM, 8-hourly (age < 7 days)<br>***OR***<br>6-hourly (age 7-28 days)<br><br>**acyclovir** CANNOT be given intramuscularly |
| **Pneumonia**<br><br>*Refer to note (1) above* | **benzylpenicillin** 60mg/kg/dose IV/IO, 12-hourly<br>***PLUS***<br>**gentamicin 5 MINUTE PUSH** 5mg/kg/dose IV/IO, 24-hourly<br>***PLUS***<br>**azithromycin** 10mg/kg/dose IV/IO, 24-hourly (if considering chlamydia or pertussis) | **benzylpenicillin** 60mg/kg/dose IV/IO, 6-hourly<br>***PLUS***<br>**gentamicin 5 MINUTE PUSH** 5mg/kg/dose IV/IO, 24-hourly<br>***PLUS***<br>**azithromycin** 10mg/kg/dose IV/IO, 24-hourly (if considering chlamydia or pertussis) | **benzylpenicillin** 60mg/kg/dose IM, 12-hourly (age < 7 days)<br>**OR**<br>6-hourly (age 7-28 days)<br>***PLUS***<br>**gentamicin 5 MINUTE PUSH** 5mg/kg/dose IM, 24-hourly<br><br>**azithromycin** CANNOT be given intramuscularly |
| **Urinary tract infection** | **ampicillin** 50mg/kg/dose IV/IO, 8-hourly<br>***PLUS***<br>**gentamicin 5 MINUTE PUSH** 5mg/kg/dose IV/IO, 24-hourly | **ampicillin** 50mg/kg/dose IV/IO, 6-hourly<br>***PLUS***<br>**gentamicin 5 MINUTE PUSH** 5mg/kg/dose IV/IO, 24-hourly | **ampicillin** 50mg/kg/dose IM, 8-hourly (age < 7 days)<br>**OR**<br>6-hourly (age 7-28 days)<br>***PLUS***<br>**gentamicin** 5mg/kg/dose IM, 24-hourly |



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| Table 2: NEONATAL antibiotic prescribing SOURCE OF INFECTION IS SUSPECTED OR KNOWN (cont.) | | | |
|---|---|---|---|
| **Apparent source of sepsis** | **FIRST DOSE empirical intravenous (IV) or intraosseous (IO) antibiotic regimen**<br><br>**Less than 7 days age** | **FIRST DOSE empirical intravenous (IV) or intraosseous (IO) antibiotic regimen**<br><br>**7-28 days age** | **FIRST DOSE empirical intramuscular (IM) antibiotic regimen** |
| **Cellulitis or omphalitis**<br><br>*Refer to notes (2),(3) above* | **flucloxacillin** 50mg/kg/dose IV/IO, 12-hourly | **flucloxacillin** 50mg/kg/dose IV/IO, 6-hourly | **flucloxacillin** 50mg/kg/dose IM, 12-hourly (age< 7 days)<br>**OR**<br>6-hourly (age 7-28 days) |
| **Osteomyelitis/septic arthritis**<br><br>*Refer to notes (2)(3)* | **flucloxacillin** 50mg/kg/dose IV/IO, 12-hourly | **flucloxacillin** 50mg/kg/dose IV/IO, 6-hourly | **flucloxacillin** 50mg/kg/dose IM, 12-hourly (age< 7 days)<br>**OR**<br>6-hourly (age 7-28 days) |
| **Intra-abdominal infection** | **gentamicin 5 MINUTE PUSH** 5mg/kg/dose IV/IO, 24-hourly<br>***PLUS***<br>**ampicillin** 50mg/kg/dose IV/IO, 8-hourly<br>***PLUS***<br>**metronidazole** 15mg/kg as a loading dose then 7.5mg/kg/dose 12-hourly.<br>This is given 12 hours after the loading dose. | **gentamicin 5 MINUTE PUSH** 5mg/kg/dose IV/IO, 24-hourly<br>***PLUS***<br>**ampicillin** 50mg/kg/dose IV/IO, 6-hourly<br>***PLUS***<br>**metronidazole** 15mg/kg/dose IV/IO 12-hourly | **gentamicin** 5mg/kg/dose IM, 24-hourly<br>***PLUS***<br>**ampicillin** 50mg/kg/dose IM, 8-hourly (age < 7 days)<br>**OR**<br>6-hourly (age 7-28 days)<br>***PLUS***<br>**clindamycin** 5mg/kg/dose 8-hourly (age < 7 days)<br>**OR**<br>6-hourly (age 7-28 days) |



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| Table 3: Antibiotics that treat common infecting bacteria | |
|---|---|
| **Drug** | **Susceptible bacteria** |
| aciclovir | Herpes simplex type 1, herpes simplex type 2 and varicella zoster viruses |
| ampicillin | Group A and B streptococci, Listeria monocytogenes, penicillin SENSITIVE Staphylococcus aureus, E coli*, Proteus mirabilis* |
| azithromycin | *Chlamydia trachomatis* |
| benzyl penicillin (penicillin g) | Group A and B streptococci, pneumococcus, meningococcus Listeria monocytogenes, , penicillin SENSITIVE Staphylococcus aureus |
| cefotaxime | Group A and B streptococci, pneumococcus, meningococcus, methicillin SENSITIVE Staphylococcus aureus, E coli, Klebsiella, Proteus mirabilis. Note: Good CNS penetration. |
| clindamycin | *Staphylococcus aureus**, Group A streptococcus* (*Streptococcus pyogenes*)* *Streptococcus pneumoniae** (pneumococcus) and anaerobes |
| flucloxacillin | Methicillin SENSITIVE Staphylococcus aureus, group A and B streptococci |
| gentamicin | Enterobacteriaceae (e.g. E coli, Klebsiella, Proteus, Enterobacter, Serratia, Morganella, Hafnia species) and Pseudomonas aeruginosa. Note: Poor CNS penetration. |
| metronidazole (flagyl) | Anaerobic gram negative bacteria including *Bacteroides fragilis*. |

* = if sensitive

**Footnote:** This table provides information about common infecting bacteria and their probable sensitivities. This is not an exhaustive list further information can be obtained from a microbiologist or infectious diseases physician. Final sensitivities are dependent on laboratory testing.

## Table 4: NEONATAL antibiotic administration

- Administer the antibiotic which takes the least time to inject or infuse, in the order provided.
- Reconstitute antibiotics with sterile water for injection (WFI) unless stated otherwise.
- If further dilution is required for IV injection or infusion, use sterile sodium chloride 0.9% or sterile glucose 5% unless stated otherwise.
- To avoid drug incompatibility without delaying fluid administration, flush the IV line with 0.5mL sterile sodium chloride 0.9% before and after the antibiotic injection/infusion.
- When injecting antibiotics directly into an IV injection port which has resuscitation fluid (0.9% sodium chloride) running:
  - clamp the infusion fluid line
  - administer antibiotic over the required time
  - recommence resuscitation fluid (0.9% sodium chloride)

| Antibiotic | Presentation | Reconstitution volume / fluid for intravenous (IV), umbilical or intraosseous administration | Final volume for IV, umbilical or intraosseous administration | Minimum IV, umbilical or intraosseous administration time | Intramuscular (IM) administration | Notes |
|---|---|---|---|---|---|---|
| **ampicillin** | Vial 1g | 10mL WFI | 10 - 20mL | 3 – 5 minutes | Reconstitute 1g vial with 1.5mL WFI and administer intramuscularly | Penicillin class antibiotic. |
| **aciclovir** | 250mg/10mL Vial | 50mL WFI | 250mg/50mL or 5mg/mL | 60 minutes | Do NOT give intramuscularly | Dose interval adjusted if renal impairment |
| **azithromycin** | Vial 500mg | 4.8mL WFI | 100mg/mL | 60 minutes | Do NOT give intramuscularly | Concentration must be 1 or 2 mg/mL to avoid local infusion site reaction. Rare reports of prolonged QT interval. |
| **benzylpenicillin** | Vials | | 300mg/1mL | 15 minutes | For 600mg vial: Add 1.6mL WFI = 300mg/mL and administer intramuscularly | Penicillin class antibiotic. |
| | 600mg | 2mL WFI | | | | |
| | 1.2g | 4mL WFI | | | For 1.2g vial: Add 3.2mL WFI = 300mg/mL and administer intramuscularly | |




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**Table 4: NEONATAL antibiotic administration (cont.)**

| Antibiotic | Presentation | Reconstitution volume / fluid for intravenous (IV), umbilical or intraosseous administration | Final volume for IV, umbilical or intraosseous administration | Minimum IV, umbilical or intraosseous administration time | Intramuscular (IM) administration | Notes |
|---|---|---|---|---|---|---|
| **cefotaxime** | Vial 500mg | 5 mL WFI | 100mg/mL | 3 minutes | Reconstitute with lignocaine 0.5-1% or WFI to a final concentration of 330mg/mL and administer intramuscularly. | Cephalosporin class antibiotic. |
| | Vial 1g | 10 mL WFI | 100mg/mL | 3 minutes | | |
| **clindamycin** | Ampoule: 300mg/2mL 600mg/4mL | Dilute 0.5 mL from vial with 35 mL 0.9% saline | 75 mg / 25mL solution. 1.67 mL = 5mg | 1 hour | If giving intramuscularly do NOT dilute | **FRIDGE ITEM: Kept at 2-8°C** Check product is clear of any crystals before administration. |
| **flucloxacillin** | Vial 500mg | Add 4.6mL WFI; then add 20mLs 0.9% sodium chloride | 20mg/mL | 10 minutes | Administer undiluted intramuscularly | Check product is clear of any crystals prior to administration. Penicillin class antibiotic. |
| | Vial 1g | 9.3mL WFI. Further reconstitution required: 1ml of reconstituted solution with 4mls WFI | 20mg/mL | 10 minutes | | |
| **gentamicin** | Ampoule 10mg/1mL | Dilute 10mg ampoule to 5mL with WFI | 2mg/mL | 5 minutes | Administer undiluted intramuscularly | Administration via a 5 MINUTE PUSH is safe and will deliver rapid therapy.[7, 8] IV gentamicin is inactivated by IV cephalosporins and penicillins. Flush line before giving gentamicin to prevent inactivation. Monitor levels for ongoing dosing. |




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| Table 4: NEONATAL antibiotic administration (cont.) | | | | | | |
|---|---|---|---|---|---|---|
| **Antibiotic** | **Presentation** | **Reconstitution volume / fluid for intravenous (IV), umbilical or intraosseous administration** | **Final volume for IV, umbilical or intraosseous administration** | **Minimum IV, umbilical or intraosseous administration time** | **Intramuscular (IM) administration** | **Notes** |
| **metronidazole** | Infusion bag 500mg/100mL | Not required | 500mg/100mL | 15 minutes | Do NOT give intramuscularly | |
| **vancomycin** | 500 mg<br><br>1000 mg | 500 mg dilute with 10 mL WFI or<br><br>1000 mg dilute with 20 ml WFI<br><br>Dilute 2 mL of above with 8 mL WFI | 10mg/mL | 1 hour | Do NOT give intramuscularly | Infusion related effects are common. Baby may flush red in "red man syndrome". In this instance decrease infusion rate, check dosing and monitor closely. Serum Levels required for ongoing dosing. |

**References**

1. MIMS (2011) http://nsw.mimsmobile.com.au.acs.hcn.com.au/?acc=36422
2. Antibiotic Expert Group. *Therapeutic Guidelines: Antibiotic. Version 14*. Melbourne: Therapeutic Guidelines Limited; 2010. Accessed through *eTG complete* (via CIAP).
3. Burridge N (ed). *Australian Injectable* Drugs Handbook (4th ed*)*. The Society of Hospital Pharmacists Australia; 2008.
4. Rossi S (ed). *Australian Medicines Handbook*. Chapter 5. Adelaide: Australian Medicines Handbook; 2011.
5. Paediatric Sepsis Reference Group, Clinical Excellence Commission.
6. Robinson RF. Nahata MC. Safety of Intravenous Bolus Administration of Gentamicin in Pediatric Patients. Annals of Pharmacotherapy. 35(11): 1327-31, 2001 Nov
7. Bromiker R. Adelman C. Ared I. Shapiro M. Levi H. Safety of Gentamicin Administered by Intravenous Bolus in the Nursery. Clinical Pediatrics. 433-435, 1999 Jul
8. Wade KC and Benjamin Jr DK (2011). Clinical pharmacology of anti-infective drugs in Infectious Diseases of the fetus and newborn Infant. Pp1160-1211.7th Edition Eds Remington JS, Klein JO Wilson CB, Nizet V, Maldonado YA. Elsevier Saunders Philadelphia USA

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