NEWBORN ANTIBIOTIC GUIDELINE

for early and late onset sepsis during birth episode of care

Revised June 2018

NSW GOVERNMENT | CLINICAL EXCELLENCE COMMISSION

Source antibacterial recommendations, Neonatal Medicines Formulary Consensus Group with permission.
http://www.seslhd.health.nsw.gov.au/rhw/Newborn_Care/guidelines_med.asp Accessed on 10 April 2018

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DOCUMENT PURPOSE

The Clinical Excellence Commission's (CEC) *Newborn Antibiotic Guideline for early and late onset sepsis during birth episode of care* aims to guide the prescription and timely administration of antibiotics for **newborns during the birth episode of care.**

Definitions of sepsis[1, 2, 3]

SEPSIS - Early onset

Early-onset sepsis < 72 hours of age is associated with acquisition of microorganisms from the mother. Most common microorganisms associated with early-onset infection include the following:

- Group B Streptococcus (GBS)
- *Escherichia coli*
- *Haemophilus influenzae*
- *Listeria monocytogenes*
- Herpes simplex virus

SEPSIS - Late onset

Late-onset sepsis occurs ≥ 72 hours of age and may also be acquired from the caregiving environment. Organisms that have been implicated in causing late-onset sepsis include the following:

- Group B Streptococcus
- *Escherichia coli*
- *Staphylococcus aureus*
- Other gram negative organisms
- Herpes simplex virus
- Coagulase-negative staphylococci

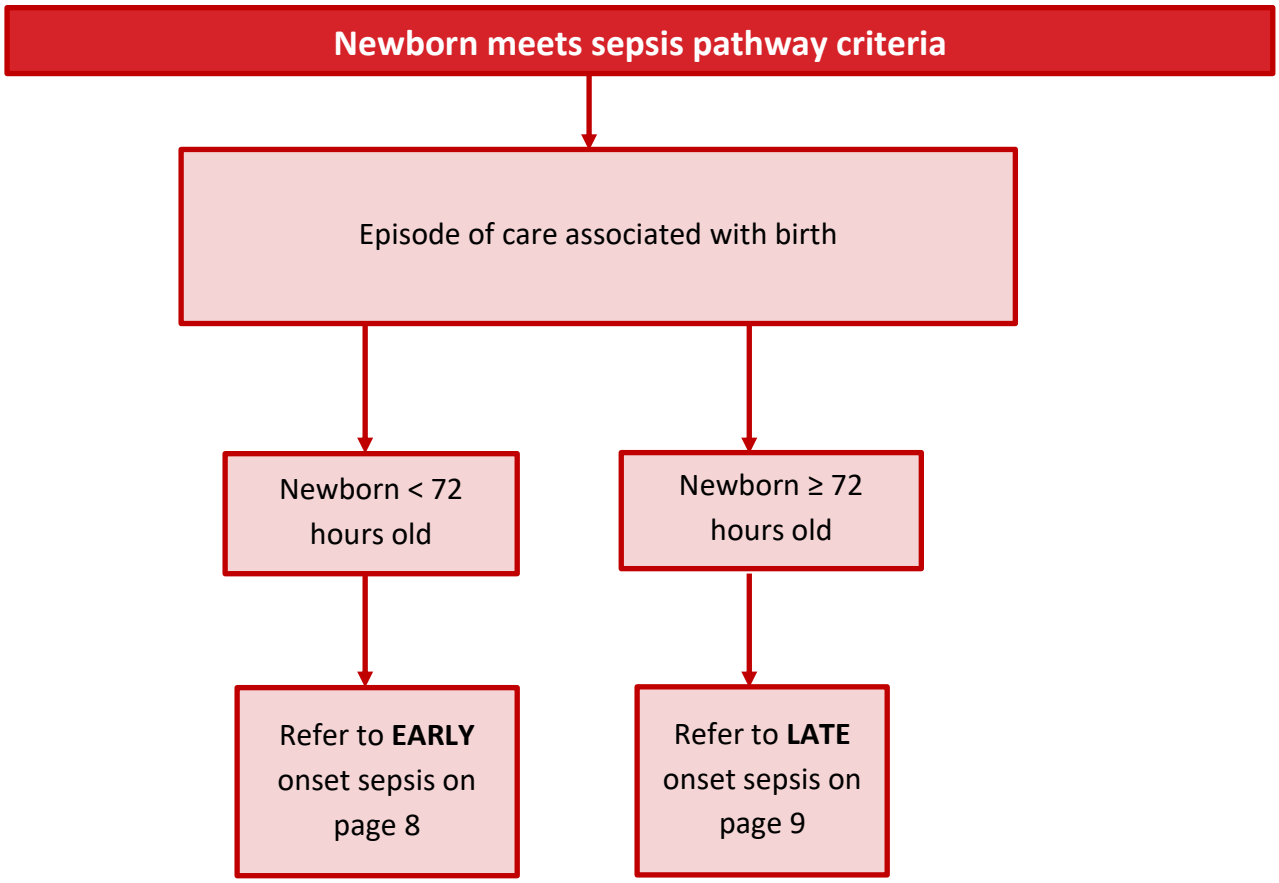
This guideline is not intended for:

- Neonates who present to an Emergency Department after birth → use *Paediatric Antibiotic Guideline for Severe Sepsis and Septic Shock and Unwell Neonates*
- Premature neonates being managed in specialised Neonatal Intensive Care Units (NICUs) with locally-endorsed antibiotic guidelines
- Paediatric patients (29 days – 16 years of age) → use Paediatric Antibiotic Guideline for Severe Sepsis & Septic Shock and Unwell Neonates

IMPORTANT POINTS TO CONSIDER WHEN USING THIS GUIDELINE

- The selection of appropriate antibiotic therapy is complex - this guideline is not intended to cover all possible scenarios
- Prompt administration of antibiotics and resuscitation fluids is vital in the management of the newborn with sepsis. In newborns diagnosed with early or late onset of sepsis, the goal is to commence antibiotic therapy within the first hour
- Obtain at least one set of blood cultures and other clinical specimens (e.g. urine, cerebrospinal fluid, wound swabs) as appropriate **PRIOR TO** antibiotic commencement where possible - do not delay antibiotic administration if a blood culture cannot be obtained or to wait for results of investigations
- If agents listed here are not available in your hospital, consult the Attending Medical Officer and seek expert advice
- Newborn patients must be bare weighed to ensure correct calculation of medication dosing – birth weight is to be used for calculation of medication dosing until the newborn crosses birth weight
- Clinicians must document the indication, drug name, dose, route of administration and review date for antibiotics in the newborn's health care record
- The neonate and antibiotic treatment within 24 and 48 hours or once microbiology results are available and antibiotics continued, changed or ceased as required. Where necessary, discuss with the Paediatrician, Neonatologist or Clinical Microbiologist

NEWBORN ANTIBIOTIC GUIDELINE FOR EARLY AND LATE ONSET SEPSIS DURING BIRTH EPISODE OF CARE
DECISION TREE



Further management:

The newborn with presumed or suspected sepsis must be discussed with a consultant Paediatrician or Neonatologist. If a specialist is not available, call NETS NSW phone **1300 36 2500** for urgent advice.

The newborn must be reviewed by the Attending Medical Officer within 24 - 48 hours of commencing the sepsis pathway and antibiotic therapy, with referral to the infectious diseases and/or clinical microbiology service for specific advice if required. The management plan should be communicated to the Senior Medical Officer, Midwife/Nurse in Charge, and the newborn's family/carers.

Clinicians who are experiencing difficulty in interpreting microbiology results when rationalising antibiotic therapy should contact the designated infectious diseases and/or clinical microbiology service.

INDICATION: EARLY ONSET SEPSIS ASSOCIATED WITH BIRTH (< 72 hours old)	
ROUTE OF ADMINISTRATION	
INTRAVENOUS (IV)	INTRAMUSCULAR (IM) *Should only be used in the short term until IV access established*
benzylpenicillin 60 mg/kg, 12-hourly	benzylpenicillin 60 mg/kg, 12-hourly
PLUS	**PLUS**
gentamicin 5 mg/kg, daily [Note 1]	gentamicin 5 mg/kg, daily [Note 1]
OR	**OR**
ampicillin 50 mg/kg, 12-hourly	ampicillin 50 mg/kg, 12-hourly
PLUS	**PLUS**
gentamicin 5 mg/kg, daily [Note 1]	gentamicin 5 mg/kg, daily [Note 1]
If newborn is severely unwell with suspected or known meningitis **ADD** cefotaxime 50 mg/kg, 8-hourly	***If newborn is severely unwell with suspected or known meningitis*** **ADD** cefotaxime 50 mg/kg, 8-hourly
If Herpes simplex infection is known or suspected **ADD** aciclovir 20 mg/kg, 8-hourly	***If Herpes simplex infection is known or suspected*** **SEEK EXPERT ADVICE**
Note 1: Refer to Neonatal Medicines Formulary Consensus Group http://www.seslhd.health.nsw.gov.au/rhw/Newborn_Care/guidelines_med.asp for ongoing monitoring	

INDICATION: LATE ONSET SEPSIS ASSOCIATED WITH BIRTH (≥72 hours old)

ROUTE OF ADMINISTRATION	
INTRAVENOUS (IV)	INTRAMUSCULAR (IM) *Should only be used in the short term until IV access established*
flucloxacillin 50 mg/kg 0-7 days old, 12-hourly 8-28 days old, 8-hourly	flucloxacillin 50 mg/kg 0-7 days old, 12-hourly 8-28 days old, 8-hourly
PLUS	**PLUS**
gentamicin 5mg/kg, daily	gentamicin 5mg/kg, daily
If newborn has suspected or known meningitis **REPLACE** flucloxacillin with: ampicillin 50 mg/kg 0-7 days old, 12-hourly 8-28 days old, 6-hourly	***If newborn has suspected or known meningitis*** **REPLACE** flucloxacillin with: ampicillin 50 mg/kg 0-7 days old, 12-hourly 8-28 days old, 6-hourly
PLUS	**PLUS**
cefotaxime 50 mg/kg 0-7 days old, 8-hourly 8-28 days old, 6-hourly	cefotaxime 50 mg/kg 0-7 days old, 8 -hourly 8-28 days old, 6-hourly
PLUS	**PLUS**
gentamicin 5 mg/kg, daily [Note 1]	gentamicin 5 mg/kg, daily [Note 1]
If Herpes simplex infection is known or suspected **ADD** aciclovir 20 mg/kg, 8-hourly	***If Herpes simplex infection is known or suspected*** **SEEK EXPERT ADVICE**
If MRSA is known or suspected **ADD** vancomycin 15 mg/kg (maximum single dose, 90 mg) 0-7 days old, 12-hourly 8-28 days old, 8-hourly	***If MRSA is known or suspected*** **SEEK EXPERT ADVICE**
If abdominal sepsis is known or suspected **ADD** metronidazole 15 mg/kg as a loading dose then subsequent doses of: 7.5 mg/kg 0 -7 days old, 8-hourly 7.5 mg/kg 8-28 days old, 6-hourly	**SEEK EXPERT ADVICE**
Note 1: Refer to Neonatal Medicines Formulary Consensus Group http://www.seslhd.health.nsw.gov.au/rhw/Newborn_Care/guidelines_med.asp for ongoing monitoring	

MEDICATION ADMINISTRATION TABLE *Adapted with permission from Neonatal Medicines Formulary Consensus Group*

- From a microbiological perspective, injectable medication **must be prepared immediately prior to administration** using aseptic technique
- Reconstitute antibiotics with sterile water for injection unless stated otherwise in the table below
- Displacement volume is the volume that the powder component of a drug takes up upon reconstitution. It needs to be added to the diluent volume to ensure accuracy when calculating doses that are less than a full vial. Thus the diluent volume recommended in the Product Information (PI) may sometimes differ from the volume recommended in this guideline. The displacement volume provided is an estimate and this may vary between brands. Please check in the Product Information or with the manufacturer

volume of diluent to reconstitute a vial + displacement volume of drug powder = final volume of vial

- If further dilution is required for IV injection or infusion, use sterile sodium chloride 0.9% or sterile glucose 5% unless stated otherwise.
- Where possible use separate dedicated lines for resuscitation fluid and for medications. When injecting antibiotics directly into an IV injection port which has resuscitation fluid running:
  - clamp the infusion fluid line and flush with 0.5 – 1mL sterile sodium chloride 0.9% solution
  - administer antibiotic over the required time
  - flush the line with 0.5 – 1 mL sterile sodium chloride 0.9% solution and recommence resuscitation fluid

Medication	Availability	Reconstitution fluid/volume	Administration	Notes
aciclovir	Vial 250 mg/10 mL	250 mg/10 mL vial: add 40 ml of water for injection to make 5 mg/mL solution	**IV infusion:** over 60 minutes	**DO NOT GIVE INTRAMUSCULARLY** Dose interval adjusted if renal impairment
ampicillin	Vial 500 mg, 1 g	500 mg vial: add 4.7 mL of water for injection to make 100 mg/mL solution 1 g vial: add 9.3 mL of water for injection to make 100 mg/mL solution **IM:** add 1.7 mL of water for injection to the 500 mg vial for reconstitution to make 250 mg/mL solution	**IV infusion:** over 5−10 minutes into the proximal cannula site with a maximum rate of 100 mg/minute	Contraindicated in patients with severe hypersensitivity to penicillins, carbapenems and cephalosporin antibiotics Separate from aminoglycosides by clearing the lines with a flush as ampicillin inactivates them Higher doses should be diluted to 30 mg/mL and infused over 30 minutes In renal impairment the excretion of ampicillin will be delayed. In infants with severe renal impairment it may be necessary to reduce the total daily dose

Medication	Availability	Reconstitution fluid/volume	Administration	Notes
benzylpenicillin	Vial 600 mg	600 mg vial: add 3.6 mL of water for injection to make 150 mg/mL solution	**IV infusion:** over 30 minutes	Contraindicated in patients with severe hypersensitivity to penicillins, carbapenems and cephalosporin antibiotics Separate from aminoglycoside administration by clearing the line with a flush as penicillins inactivate aminoglycosides
		IM: add 1.6 mL water for injection to the 600 mg vial to make 300 mg/mL solution	**IM injection:** inject deep into a large muscle	
cefotaxime	Vial 500 mg, 1 g	500 mg vial: add 4.8 mL of water for injection to make 100 mg/mL solution	**IV injection:** Over 3–5 minutes **IV infusion:** Infuse over 15–30 minutes via syringe driver	Contraindicated in patients with severe hypersensitivity to penicillins, carbapenems and cephalosporin antibiotics
		1 g vial: add 9.6 mL of water to make 100 mg/mL solution		
		IM: add 2 mL of water for injection to the 500 mg powder for reconstitution to make 230 mg/mL solution Vial can be reconstituted with lignocaine 0.5% to reduce pain of injection	**IM injection:** Inject deep into the gluteal muscle	
flucloxacillin	Vial 500 mg, 1 g	500 mg: add 4.6 mL of water for injection to make 100 mg/mL solution 1 g: add 9.3 mL of water for injection to make 100 mg/mL solution Draw up 2.5 mL (250 mg) and add 2.5 mL sodium chloride 0.9% to make a final volume of 5 mL with a concentration of 50 mg/mL	**IV injection:** Slow injection over 3–5 minutes	

Medication	Availability	Reconstitution fluid/volume	Administration	Notes
		IM: 500 mg: add 1.6 mL water for injection or lignocaine 0.5% or 1% to make a final concentration 250mg/1mL 1 g: add 3.3 mL water for injection or lignocaine 0.5% or 1% to 1 g to make a final concentration 250 mg/1mL	**IM injection:** Inject deep into the gluteal muscle	flucloxacillin causes significant pain and irritation with IM use
gentamicin	10 mg/1 mL ampoule – **paediatric strength**	**10 mg/1 mL – paediatric strength:** Add 1 mL (10 mg) of gentamicin to 4 mL sodium chloride 0.9% to make a final volume of 5 mL with a concentration of 2 mg/mL	**IV injection:** Slow infusion over 5 minutes	Gentamicin is inactivated by penicillins and cephalosporins so should not be mixed in the same solution or administered simultaneously Ensure the line is adequately flushed if administered consecutively
	80 mg/2 mL ampoule – **adult strength**	**80 mg/2 mL – adult strength:** Add 1 mL (40 mg) of gentamicin to 19 mL sodium chloride 0.9% to make a final volume of 20 mL with a concentration of 2 mg/mL		
		IM: Reconstitution not required	**IM injection:** administer undiluted	
metronidazole	Infusion bag 500 mg/100mL	Reconstitution not required	**IV infusion:** 20 - 30 minutes. Maximum rate is 25 mg/minute	**DO NOT GIVE INTRAMUSCULARLY**
vancomycin	Vial 500 mg, 1 g	500 mg: add 10 mL of water for injection to make a 50 mg/mL solution Draw up 1 mL (50 mg) of vancomycin and add 9 mL glucose 5% or sodium chloride 0.9% to make a final volume of 10 mL with a final concentration of 5 mg/mL	**IV infusion:** 60 minutes	**DO NOT GIVE INTRAMUSCULARLY** Monitor renal function, full blood count, hearing function and serum vancomycin concentrations Trough level: 10 - 20 mg/L (aim for higher trough level: 15 - 20 mg/L in suspected severe sepsis e.g., MRSA, bone infection, meningitis, endocarditis)

Medication	Availability	Reconstitution fluid/volume	Administration	Notes
vancomycin continued		To prepare 10 mg/mL concentration: Add 10 mL of water for injection to the 500 mg vial to make a 50 mg/mL solution Draw up 2 mL (100 mg) of vancomycin and add 8 mL glucose 5% or sodium chloride 0.9% to make a final volume of 10 mL with a final concentration of 10 mg/mL		Trough concentration should be taken within one hour prior to the 2nd dose for 18 hourly dosing and 4th dose for all other frequencies Check concentration prior to the 4th dose or after any change in dose or frequency. Perform weekly monitoring for prolonged courses More frequent monitoring may be required in renal impairment, those receiving other nephrotoxic drugs or in suspected severe sepsis

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