Louth: Antimicrobial Guidelines - Louth Hospitals: Antimicrobial Guidelines: Neonatal Antimicrobial IV Monographs

Neonatal - Aciclovir IV

Neonatal - ■Aciclovir IV

Antiviral [1].

MEDICATION SAFETY ISSUES

- Aciclovir may be confused with other antivirals [2]
- Zovirax® may be confused with Zyvox® [2,3]
- Anaphylaxis has been reported very rarely with aciclovir [4].
- Zovirax® may be confused with Zithromax® [2].

USES

- Treatment of herpes simplex and varicella zoster infections [1].
- Under consultant neonatologist and virologist direction, prophylactic IV aciclovir should be considered for neonates whose mothers develop chickenpox 7 days before to 7 days after delivery due to the risk of severe complicated infection despite varicella-zoster immunoglobulin prophylaxis [5].

PRESENTATION

Concentrate for solution for infusion: Aciclovir 250mg/10ml [4].

DOSAGE [1]

Age	Infection	Dose	Frequency	Duration
Neonate	Prophylaxis of chickenpox after delivery	10mg/kg	Every 8 hours	Until blood test confirms absence of virus
Neonate and Child 1 – 3 months	Herpes simplex	20mg/kg	Every 8 hours	14 days (for at least 21 days if CNS involvement, confirm CSF negative for HSV before stopping treatment)
	Herpes zoster	10 – 20 mg/kg	Every 8 hours	At least 7 days (for 10 – 14 days in encephalitis, possibly longer if also immunocompromised)

Renal Impairment : Dose reduction may be required – refer to BNFc and seek advice [1]. Nephrotoxic drugs (e.g. gentamicin, vancomycin) may worsen renal function if used concurrently.

RECONSTITUTION [1,4,6].

In OLOL, aciclovir is available as 250mg/10ml concentrated solution. The vial **must be further diluted** before use. **Dilute** 4ml of the 25mg/ml solution with 16 ml Sodium Chloride 0.9% to a final volume of 20ml.

The resulting solution contains aciclovir 5mg/ml.

ADMINISTRATION

Administer by IV infusion over 1 hour [1,4].

SAMPLE CALCULATION

3.2kg neonate 7 days old with herpes simplex infection. Dose 20mg/kg = 64mg every 8 hours.

Reconstitute aciclovir as above to a solution containing 5mg/ml.

Administer 12.8ml (64mg) by IV infusion over 1 hour.

STORAGE

Store unopened vials at room temperature below 25 ^{o} C. Once diluted, use immediately. Discard any remaining solution [4].

MONITORING

- Maintain adequate hydration, especially with infusion of high doses, or during renal impairment [1,4]
- Monitor for changes in renal function [7], especially when administered concomitantly with nephrotoxic drugs (eg. gentamicin, vancomycin)
- Patients with renal impairment are at increased risk of developing neurological side effects and should be closely monitored for evidence of these effects. Dose reduction is required in patients with renal impairment [1,4].
- Monitor liver function [2].
- Monitor infusion site for phlebitis if administered peripherally [6]
- Monitor neutrophil count at least twice weekly in neonates receiving aciclovir 60 mg/kg/day IV for more than 48 hours [2].

ADVERSE EFFECTS

Nausea, vomiting, abdominal pain, diarrhoea, headache, fatigue, rash, urticaria, pruritus, photosensitivity; *very rarely* hepatitis, jaundice, dyspnoea, neurological reactions (including dizziness, confusion, hallucinations, convulsions, ataxia, dysarthria, and drowsiness), acute renal failure, anaemia, thrombocytopenia, and leucopenia; on *intravenous infusion* , severe local inflammation (sometimes leading to ulceration), and *very rarely* agitation, tremors, psychosis and fever [1].

REFERENCES

1. British Medical Association, Royal Pharmaceutical Society of Great Britain, Royal College of Paediatrics and Child Health, et al. BNF for Children. London: BMJ Group, Pharmaceutical Press and RCPCH Publications Limited; 2020. Available from www.medicinescomplete.com , accessed 16/11/2020.
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Summary of Changes from Previous Versions

Date	Change
Feb 2021: Rev. No. 2	Updated based on Rotunda Aciclovir Monograph Jan 2019. OLOL changes: • Aciclovir 250mg/10ml vials – current brands stocked in OLOL include Baxter and Pfizer. Both are in concentrated solution form and contain 250mg/10ml. Brand name removed from monograph. • References updated.
Aug 2017: Rev. No. 1	Aciclovir Claris® solution for infusion now stocked in OLOL, therefore no need to reconstitute power for solution for infusion.
May 2015	This is the first version of this guideline.

Neonatal - ■Ambisome IV

Neonatal - Ambisome® IV (Liposomal Amphotericin B)

NB. Prescribe by BRAND name only.

Lipid formulation of the antifungal amphotericin B - significantly less toxic than the conventional form [1].

MEDICATION SAFETY ISSUES

- Amphotericin is included on the Institute for Safe Medication Practices (ISMP) List of High-Alert Medications [2]. Mix-ups between different formulations have led to overdoses (sometimes fatal) or underdoses resulting in subtherapeutic treatment [2-4].
- There are two liposomal amphotericin B products available, Ambisome® and Abelcet®. A conventional formulation is also available - Fungizone®. **NB. These preparations are not interchangeable** . **Prescribe Ambisome® by brand name only to avoid confusion** . [1,5]

USES

First-line antifungal for invasive infections [1]. Not licensed for use in infants under one month [1,6].

PRESENTATION

Ambisome® 50mg Powder for Concentrate for Dispersion for Infusion [6]

DOSAGE [1]

Age	Dose	Frequency
Neonate and Child 1 – 3 months	3mg/kg	Every 24 hours

On advice from the Consultant Microbiologist, the dose may be increased to 5mg/kg if required.

RECONSTITUTION [1,6-9]

- Check that the prescription specifies Ambisome® and the product you are using is Ambisome®.
- Ambisome® must be reconstituted with sterile Water for Injection (WFI) and diluted in Glucose 5% **ONLY. AMBISOME® IS INCOMPATIBLE WITH SODIUM CHLORIDE 0.9%.**
- **NB. There are TWO STEPS for reconstitution. BOTH Step 1 and Step 2 below must be followed.**
- **Step 1** : Add 12ml WFI to the 50mg Ambisome® vial and shake vigorously for 30 seconds to completely disperse the drug. The resulting solution contains 4mg/ml.
- **Step 2** : Using the 5 micron filter provided, further dilute 4ml of this solution with 12ml of Glucose 5% to a final volume of 16ml. The resulting solution contains 1mg/ml Ambisome®.
- If the baby is fluid restricted, Ambisome® may be reconstituted to a concentration of 2mg/ml instead.

Contact the Pharmacy Department to order subsequent doses of Ambisome® 1mg/ml reconstituted solution (10ml volume) from external compounding unit if available.

ADMINISTRATION [1,6,10]

- **AMBISOME® IS INCOMPATIBLE WITH SODIUM CHLORIDE 0.9%.**
- Prime the IV line (T-piece) with Glucose 5% before and after administration (or use a separate line).
- Administer by IV infusion - an in-line membrane filter (not less than 1 micron) may be used.
- Administer by IV infusion over 1 hour.
- Monitor vital signs and observe patient for infusion-related reactions.

SAMPLE CALCULATION

3.2kg neonate 9 days old with invasive candida infection. Dose: 3mg/kg = 9.6mg every 24 hours.

Reconstitute and further dilute Ambisome® as above to a solution containing 1mg/ml.

Required dose 9.6mg = 9.6ml. Administer by IV infusion over 1 hour.

STORAGE

Store unopened vials at room temperature below 25 ^{o} C. Once reconstituted, use immediately. [6].

MONITORING [1,7,8]

- Observe patient for infusion reactions during each infusion – a slower rate may reduce reactions.
- Caution if concomitant administration of other nephrotoxic agents.
- Monitor renal function and serum magnesium daily initially, then two to three times weekly

- Monitor liver function and FBC twice weekly
  - **Hypokalaemia is common**
  - **Hypomagnesaemia is common** and may require supplementation
  - Hyponatraemia may occur - ensure adequate hydration.

ADVERSE EFFECTS

Fever and chills/rigors are the most frequent infusion-related reactions [6]. Less frequent infusion-related reactions include chest tightness or pain, dyspnoea, bronchospasm, flushing, tachycardia, hypotension, and musculoskeletal pain. [6]. Other adverse effects include nausea, vomiting, abdominal pain, diarrhoea, cardiovascular effects (including arrhythmias), headache, febrile reactions, electrolyte disturbances (including hypokalaemia and hypomagnesaemia), disturbances in renal function (including renal tubular acidosis), abnormal liver function (discontinue treatment), blood disorders (including anaemia, thrombocytopenia), rash; *less commonly* neurological disorders (including convulsions, peripheral neuropathy, tremor, encephalopathy, hearing loss, diplopia); also reported anorexia, myalgia, arthralgia, toxic epidermal necrolysis, Stevens-Johnson syndrome [1].

REFERENCES

1. British Medical Association, Royal Pharmaceutical Society of Great Britain, Royal College of Paediatrics and Child Health, et al. BNF for Children. London: BMJ Group, Pharmaceutical Press and RCPCH Publications Limited; 2020. Available from www.medicinescomplete.com , accessed 16/11/2020.
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Summary of Changes from Previous Versions

Date	Change
Feb 2021: Rev. No. 1	Updated based on Rotunda Ambisome® Monograph Jan 2019. OLOL changes: References updated.
August 2015	This is the first version of this guideline.

Neonatal - ■Amoxicillin IV and PO

Neonatal - Amoxicillin IV and PO

Amoxicillin is a broad-spectrum penicillin antibiotic which is rapidly bactericidal against certain Gram-positive and Gram-negative organisms [2].

MEDICATION SAFETY ISSUES

- Anaphylaxis and other hypersensitivity reactions have been reported [1].
- Sound alike drugs: Amoxil® may be confused with Augmentin® [3]

USES

Amoxicillin is indicated for the treatment of commonly occurring bacterial infections, in particular it is used to treat listeria and enterococcal infections which are cephalosporin resistant [2].

PRESENTATION

Intravenous: Powder for Solution for injection or infusion: Amoxil® vials 500mg [2]. Generic brands will be supplied when Amoxil® is in short supply.

Oral: Powder for oral suspension Amoxicillin 125mg/5mL [6].

DOSAGE [1]

For susceptible infections including urinary-tract infections, sinusitis; Haemophilus influenzae infections, Listerial meningitis, Group B streptococcal infection, enterococcal endocarditis (in combination with other antibiotics)

Intravenous Infusion

Age	Dose	Frequency	Max Dose
Neonate under 7 days	50mg/kg	Every 12 hours	Dose doubled in meningitis
Neonate 7-28 days	50mg/kg	Every 8 hours	Dose doubled in meningitis
Child 1 to 3 months	50mg/kg	Every 4-6 hours	Max 2g every 4 hours

Oral

Age	Dose	Frequency	Max Dose
Neonate under 7 days	30mg/kg	Every 12 hours	Max per dose 125mg
Neonate 7-28 days	30mg/kg	Every 8 hours	Max per dose 125mg
Child 1 to 3 months	30mg/kg	Every 8 hours	

RECONSTITUTION [1,2,4,5]

Intravenous:

- Reconstitute 500mg vial with 4.6mL Water for Injection (displacement volume = 0.4mL) to give a solution containing amoxicillin 100mg/ml.
- Withdraw the required amount and add to a suitable volume of sodium chloride 0.9% or glucose 5% [1].
- Doses up to 150mg (1.5mL) should be diluted to a total volume of 3mL.
- Doses above 150mg (1.5mL) should be diluted with the same volume of a suitable diluent (e.g. 250mg dose – 2.5mL of amoxicillin solution added to 2.5mL of sodium chloride 0.9% or glucose 5%)
- The solution should be colourless to pale straw in colour (a transient pink colour or slight opalescence may appear during reconstitution) and free from particles.
- If glucose 5% is used to further dilute the reconstituted amoxicillin, the solution should be used within one hour as amoxicillin is less stable in infusions containing carbohydrate [2].

Oral: Follow the reconstitution instructions on the pack.

■

ADMINISTRATION

Intravenous:

- Doses over 30mg/kg must be given by intravenous infusion over 30 - 60 minutes [4].
- If prescribed concurrently with an aminoglycoside, the antibiotics should not be mixed because loss of activity of the aminoglycoside can occur under these conditions. They should preferably be administered at a different site. If this is not possible then the line should be flushed thoroughly with a compatible solution between drugs. [2]

Oral: Give using an appropriate oral/enteral syringe.

SAMPLE CALCULATION

1 day old preterm neonate (0.9kg) with susceptible infection. Amoxicillin 50mg/kg every 12 hours. 50mg x 0.9kg = 45mg every 12 hours. Reconstitute 500mg vial with 4.6mL Water for Injection to give 100mg/mL = 45mg in 0.45mL. Dose below 150mg: dilute to 3mL. Add 0.45mL of the amoxicillin solution to 2.55mL of sodium chloride 0.9%. Infuse at a rate of 0.1mL/min over 30 minutes every 12 hours.

7 day old neonate (3.5kg) with Listerial Meningitis

Amoxicillin: 100mg/kg every 8 hours

100mg x 3.5kg = 350mg every 8 hours

Reconstitute 500mg vial with 4.6mL Water for Injection

500mg in 5mL (displacement value) = 350mg in 3.5mL

Dose above 150mg: dilute with the same volume of a suitable diluent

Add 3.5mL of the amoxicillin solution to 3.5mL of 0.9% Sodium Chloride.

The resulting solution is 7mL

Infuse at a rate of 0.2mL/min over 35 minutes every 8 hours.

STORAGE

Intravenous: Store in original package to protect from moisture/light and keep below 25°C. Use solution immediately following reconstitution [2].

Oral: Dry powder: Do not store above 25°C. Once reconstituted, store in fridge and use within 7 days. [6]

MONITORING

- Renal function should be monitored and doses adjusted in patients with renal impairment [2].
- Maintain adequate hydration and urinary output during high dose administration of amoxicillin in order to reduce the risk of amoxicillin crystalluria [2].
- Monitor for rashes and other skin reactions.

ADVERSE EFFECTS

The main adverse effects seen with amoxicillin administration are diarrhoea, nausea, urticaria, maculopapular rashes, fever, joint pains and angioedema [2].

REFERENCES

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Summary of Changes from Previous Versions

Date	Change
Feb 2021: Rev. No. 1	Updated based on Rotunda Amoxicillin Monograph Mar 2019. Changes to OLOL monograph: • OLOL monograph reworded as required to align with Rotunda monograph • Addition that generic brand IV will be dispensed if Amoxil® brand in short supply • Inclusion of ORAL amoxicillin as per Rotunda monograph in presentation, dose, reconstitution, administration and storage sections. • Note: BNFc does not include a dose of oral amoxicillin for neonates < 7 days. Local decision in Rotunda to include this dose (same as BNFc IV dose for neonates < 7 days). • Reconstitution: Administration volume changed from a convenient volume to 3mL total for doses < 150mg, dilute with equal volume of diluents for doses > 150mg. • Administration: Removed that infusion pumps may be set to one or two decimal places. • Sample calculation: Addition of second calculation example as per Rotunda. • References updated. Removal of reference nos. 5 (Neonatal Formulary 2007), 6 (South Australia Neonatal monograph on Amoxicillin 2014), 7 (OLOL displacement values table) as no longer required. Addition of reference for SPC for oral amoxicillin.
Jan 2015	This is the first version of this guideline. It is based on the Rotunda Hospital Neonatal Monograph for Amoxicillin, Doc. No. 4, Revision No. 0, date of issue 11/8/14. OLOL changes compared to Rotunda monograph: • Dosing – age limit of 3 months for neonatal monograph in OLOL • Reconstitution – removed advice to further dilute 100mg/ml solution unless required for convenience for IV infusion • Administration – removed advice to administer amoxicillin and gentamicin via separate IV lines preferably, included advice to flush line thoroughly before and after administration of each. • Sample calculation – one calculation only, simplified. • Monitoring – added advice to check BNFc and seek advice on dose if renal impairment. • Four references added (numbers 5 to 8).

Neonatal - ■BenzATHINE benzylpenicillin IM

Neonatal - BenzATHINE benzylpenicillin "1,200,000" IM

Tall Man lettering has been used to differentiate benzaTHINE benzylpenicillin and BENZYLpenicillin.

BenzATHINE benzylpenicillin is a prolonged release penicillin antibiotic used for the treatment of infections related to maternal syphilis serology reactive and confirmed positive [1,2].

MEDICATION SAFETY ISSUES

- A fatal neonatal medication error has been reported after confusion between BENZYLpenicillin and benzATHINE benzylpenicillin [3]. A series of errors led to the IV administration of benzaTHINE benzylpenicillin which should only be administered IM. Inadvertent IV administration has resulted in thrombosis, severe neurovascular damage, cardiac arrest and death [4]. **DO NOT GIVE INTRAVENOUSLY.**
- It is essential to use the correct needle size when reconstituting and administering this product to reduce the risk of the patient not receiving the full dose [1].
- Avoid concomitant use with BCG vaccine [5].

USES

Used for the treatment of congenital syphilis in infants during the first month of life [2,6].

PRESENTATION

Benzetacil® "1,200,000" powder for solution for **Intramuscular** injection.

1,200,000 units is equivalent to 900mg of benzATHINE benzylpenicillin.

DOSAGE

Neonatal: Asymptomatic congenital syphilis: **Intramuscular** 50,000 units/kg as a single dose [2,5].

BenzATHINE benzylpenicillin 50,000 units/kg = 37.5 mg/kg [2].

RECONSTITUTION

The reconstituted suspension must be used immediately.

Using a needle size of 20G (available in NICU), reconstitute the Benzetacil® 1,200,000 unit vial with 3mL of the solvent provided to give 1,200,000 units in 3mL (400,000 units per mL).

ADMINISTRATION

The injection should be reconstituted **immediately** before use. The needle may become blocked if injection is not made at a slow, steady rate due to high concentration of suspended material in the product [6].

Administer the correct dose using the reconstituted solution **immediately** via the **intramuscular route using a 20G needle** . Using a smaller diameter needle may lead to blockages and failed injection attempts. Avoid injection into or near an artery or nerve.

Paracetamol for pain relief should be given prior to administration. Oral sucrose should be given for comfort throughout treatment as required.

SAMPLE CALCULATION

Case: 3.28 kg baby with asymptomatic congenital syphilis.

Dose: 50,000 units per kg = 50,000 x 3.28 = 164,000 units.

When reconstituted, **benzATHINE** benzylpenicillin contains 1,200,000 units in 3mL.

Dose =

What you want X Volume it is in

What you have got

= 164,000 units X 3mL

1,200,000 units

= 0.41mL

STORAGE

Use immediately once reconstituted.

MONITORING

BenzATHINE benzylpenicillin is renally excreted. In young infants and patients with renal impairment, excretion is prolonged [6].

ADVERSE EFFECTS

Hypersensitivity reactions may occur [1,4].

REFERENCES

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Summary of Changes from Previous Versions

Date	Change
Feb 2021: Rev. No. 1	Updated based on Rotunda BenzATHINE benzylpenicillin Monograph Nov 2018. Changes to OLOL monograph: • Title of monograph changed from "BenzATHINE penicillin" to "BenzATHINE benzylpenicillin" • OLOL monograph reworded as required to align with Rotunda monograph • Brief introduction reworded to align with Rotunda monograph • Benzetacil® 1,200,000 units stocked in OLOL compared to multiple preparations in Rotunda – adjustments throughout the monograph as required. • Dosage: 50,000 units/kg = 37.5mg/kg is already included in OLOL monograph since 2015. • Reconstitution: Added that 1,200,000 units in 3mL = 400,000 units per mL. • Administration: Added that paracetamol and oral sucrose may be given at the time of administration as per Rotunda. Addition of images of administration as per Rotunda. • Sample calculation format in OLOL monograph (same as 2015 version) is different to sample calculation format in Rotunda. • References updated.
Apr 2015	This is the first version of this guideline. It is based on the Rotunda Hospital Neonatal Monograph for Benzathine penicillin, Doc. No. 1, Revision No. 0, date of issue 10/11/14. Changes in OLOL monograph compared to the Rotunda monograph: • Benzetacil® 1,200,000 units stocked in OLOL compared to 2,400,000 units in Rotunda – adjustments throughout the monograph as required. • Brief intro section for benzathine penicillin simplified. • Dosage: added that 50,000 units/kg = 37.5mg/kg [2]. • Sample calculation format amended.

Neonatal - ■Benzylpenicillin IV

Neonatal - BENZYLpenicillin sodium IV (Penicillin G)

Bactericidal beta-lactamase sensitive penicillin

MEDICATION SAFETY ISSUES

- A fatal neonatal medication error has been reported after confusion between BENZYLpenicillin and benzATHINE benzylpenicillin [1]. A series of errors led to the IV administration of benzATHINE benzylpenicillin which should only be administered IM.
- Anaphylaxis has been rarely reported in neonates after exposure to beta-lactam antibiotics. [2]

USES

Empiric treatment of suspected neonatal sepsis. Treatment of mild to moderately severe infections such as pneumonia and cellulitis, as well as more severe infections such as endocarditis and meningitis due to penicillin susceptible organisms.

PRESENTATION

BENZYLpenicillin is available as Crystapen®. Each vial contains 600mg BENZYLpenicillin sodium.

Doses are expressed in terms of the sodium salt. Each vial contains 1.68 mmol sodium.

DOSAGE [3,4,7]

Dose and frequency of BENZYLpenicillin	Neonatal sepsis (LP not done)	Group B Strep Meningitis [3]	Endocarditis (seek advice, combination therapy may be needed) [4]
Dose			
All ages	50mg/kg	75mg/kg	50mg/kg
Frequency			
Neonate under 7 days	Every 12 hours		-
Neonate 7-28 days	Every 8 hours		-
Child > 28 days	Every 4 - 6 hours		Every 4 hours

Renal Impairment [4]

Dose reduction may be required in renal impairment refer to BNFc and seek advice on assessment of renal function.

RECONSTITUTION [5,7]

Reconstitute the 600mg amp with 5.6mL of water for injection (displacement volume = 0.4mL) to give a solution containing 100mg/mL [5]. May be diluted with sodium chloride 0.9% or glucose 5% if an infusion is required.

ADMINISTRATION

Give by IV infusion over 15 - 30 minutes. Longer administration time is particularly important when using doses of 50mg/kg or greater to avoid CNS toxicity [4].

SAMPLE CALCULATION

2.8kg neonate under 7 days with suspected meningitis. Dose: 75 mg/kg every 12 hours = 210mg every 12 hours. Reconstitute 600mg vial with 5.6mL water for injections = 100mg/mL.

Withdraw 2.1mL of the resultant solution and dilute to an appropriate volume for that baby (e.g. 10mL) with sodium chloride 0.9% or glucose 5% and administer over 15-30 minutes.

STORAGE

Store at room temperature below 25 ^{o} C. Degradation or transformation of BENZYLpenicillin occurs rapidly and may be responsible for sensitisation. Reconstituted solutions should be used immediately [6].

MONITORING

Electrolyte balance, blood counts and renal functions should be monitored if treatment is prolonged (more than 5 days) [7]. Hypernatraemia and hypokalaemia may occur with high doses.

ADVERSE EFFECTS [4]

Hypersensitivity reactions including urticaria, fever, joint pains, rashes, angioedema, anaphylaxis, serum sickness-like reactions; rarely CNS toxicity including convulsions (especially with high doses or in severe renal impairment), interstitial nephritis, haemolytic anaemia, leucopenia, thrombocytopenia and coagulation disorders; also reported diarrhoea (including antibiotic-associated colitis).

REFERENCES

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Summary of Changes from Previous Versions

Date	Change
Feb 2021: Rev. No. 1	Updated based on Rotunda BENZYLpenicillin Sodium Monograph Feb 2019. Changes to OLOL monograph: • Dosage: Section for Child 1 month – 18 years changed to Child > 28 days • Frequency of BENZYLpenicillin sodium for child > 28 days for neonatal sepsis (LP not done) and for Group B Strep Meningitis changed from 4 hourly to 4 to 6 hourly as per BNFc and Rotunda • Administration: Removed information that dose < 50mg/kg can be given as an IV bolus over 3 minutes as this is not relevant – all doses in monograph are at least 50mg/kg. • Sample calculation: Appropriate volume for infusion changed from 5mL to 10mL as per sample calculation in Rotunda. • References updated.
Nov 2014	This is the first version of this guideline. It is based on the Rotunda Hospital Neonatal Monograph for Benzylpenicillin, Doc. No. 2, Revision No. 0, date of issue 19/5/14. There is one change in the OLOL monograph compared to the Rotunda monograph – Administration of 50mg/kg dose of benzylpenicillin as an IV infusion as per BNF for Children 2014. Additional references have also been added to the dosing section (no change to dose).

Neonatal - ■Cef-O-taxime IV

Neonatal - Cef-O-taxime IV

Broad-spectrum third generation bactericidal cephalosporin antibiotic.

MEDICATION SAFETY ISSUES

Confusion with other cephalosporins e.g. Cef-TRI-axone and Cef-UR-oxime.

Should not be used in patients with a known allergy to a cephalosporin.

Individuals who have a hypersensitivity reaction to penicillin may have cross sensitivity to cephalosporins.

USES

Meningitis and severe neonatal infections.

PRESENTATION

Cef-O-taxime 1 g Wockhardt, Claforan® 1g Sanofi.

DOSAGE [1]

Neonates: Meningitis and Severe Infections

Age	Dose	Frequency
Neonate under 7 days	50mg/kg	Every 12 hours
Neonate 7-21 days	50mg/kg	Every 8 hours
>21 days	50mg/kg	Every 6 hours

For less severe infection doses of 25 mg/kg/dose have been used for neonates.

Renal Impairment [1]

Dose reduction may be required in renal impairment refer to BNFc and seek advice on assessment of renal function.

RECONSTITUTION [4,7]

Cef-O-taxime is available as a dry powder containing 1 gram per vial.

To prepare Cef-O-taxime solution 100 mg/mL:

To each vial of Cef-O-taxime add appropriate volume of Water for Injection as per table below and shake well to mix to give Cef-O-taxime 100 mg/mL solution.

This can be further diluted with sodium chloride 0.9% or glucose 5% if required.

Brand	Approx displacement volume	Diluent to be added	Final Concentration
Cef-O-taxime **1g Wockhardt**	0.6mL	9.4mL	100mg/mL
Cef-O-taxime **1g Claforan®**	0.4mL	9.6mL	100mg/mL

ADMINISTRATION

Give by slow IV injection over 3 - 5 minutes or by IV infusion over 20 - 60 minutes [1].

(Rapid IV push < 1 minute has been associated with life threatening arrhythmias) [1].

Should not be mixed in the same syringe with an aminoglycoside – flush IV line well between the administration of cef-O-taxime and an aminoglycoside to avoid formation of precipitate.

SAMPLE CALCULATION

1.3kg neonate 8 days old with suspected meningitis.

Dose: 50mg/kg every 8 hours = 65mg every 8 hours.

Reconstitute 1g vial (Wockhardt) with 9.4mL WFI as per table above to make 100mg/mL solution

Withdraw 0.65mL of the resultant solution and dilute to an appropriate volume for that baby (e.g. 5mL) with sodium chloride 0.9% or glucose 5% and administer over 20-60 minutes.

STORAGE

Store vials in original outer carton at room temperature. Discard remaining reconstituted solution after dose has been given.

MONITORING

Monitor serum creatinine and urea in neonates who are also receiving aminoglycosides and furosemide.

Dosage interval should be increased in babies with severe renal failure (serum creatinine >200 mmol/L).

Monitor for diarrhoea in infants on prolonged therapy.

SIDE EFFECTS

Candidiasis, rash, fever, transient rises in liver transaminase and/or alkaline phosphatase and diarrhoea. Pseudomembranous colitis may rarely occur. Eosinophilia, neutropenia,throbocyropenia and haemolytic anaemia have been reported also – if treatment for longer than 10 days, monitor full blood count. Transient pain may be experienced at the injection site- administration as an infusion will reduce pain.

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Summary of Changes from Previous Versions

Date	Change
Feb 2021: Rev. No. 2	Updated based on Rotunda Cef-O-taxime Monograph Feb 2019. Changes to OLOL monograph: • Dosage: Table reformatted as per updated table in Rotunda monograph • Dosage: Frequency of cef-O-taxime 50mg/kg for patients > 21 days changed from 6 to 8 hourly to 6 hourly as per Rotunda monograph and BNFc. • References updated.
Mar 2018: Rev. No. 1	Displacement value for cef-O-taxime 1g (Wockhardt) updated as per SPC update. Claforan® strength and displacement value updated as 500mg vials no longer stocked in OLOL, 1g vials stocked if needed.
Nov 2014	This is the first version of this guideline. It is based on the Rotunda Hospital Neonatal Monograph for Cefotaxime, Doc. No. 3, Revision No. 0, date of issue 19/5/14. There are four changes in the OLOL monograph compared to the Rotunda monograph: • Insertion of "tallman" lettering to improve medication safety • Presentation of the vials – different brands stocked in OLOL • Reconstitution of the vial – displacement value is brand specific • Sample calculation – reconstitution section

Neonatal - ■Flucloxacillin IV

Neonatal - Flucloxacillin IV

Flucloxacillin is a bactericidal penicillin antibiotic which is effective against staphylococci. Flucloxacillin is acid stable and can be given by mouth where appropriate. [1]

MEDICATION SAFETY ISSUES

- Special caution is essential in the newborn and neonates with renal impairment because of the potential for high serum levels of flucloxacillin due to a reduced rate of renal excretion.[2]
- Risk of kernicterus in jaundiced neonates when high doses given parenterally. [2]

- Cholestatic jaundice and hepatitis may occur very rarely, up to two months after treatment with flucloxacillin has stopped. Administration for more than 2 weeks and increasing age are risk factors. [1]

USES

Infections caused by beta-lactamase-producing staphylococci including otitis externa; as an adjunct in pneumonia, cellulitis and osteomyelitis and in staphylococcal meningitis and endocarditis [1].

PRESENTATION

Powder for solution for injection or infusion: Floxapen® 250mg and 500mg vials [2]

DOSAGE [1,3]

Age	Dose	Frequency	Max Dose
Neonate <7 days	50mg/kg	Every 12 hours	
Neonate 7 – 21 days	50mg/kg	Every 8 hours	
Neonate 21 – 28 days	50mg/kg	Every 6 hours	
Child 1 to 3 months	25mg/kg	Every 6 hours	Max 1g every 6 hours

Dose may be doubled for **severe infections** including osteomyelitis, endocarditis or suspected/confirmed staphylococcal meningitis [3]

RECONSTITUTION [3-6]

- **250mg vial** : Reconstitute 250mg vial with 4.8mL WFI (Displacement volume 0.2mL) to give a final concentration of 50mg/mL.
- **500mg vial** : Reconstitute 500mg vial with 4.7mL WFI (Displacement volume 0.3mL) to give 100mg/mL. **Further dilute** 5mL of this solution with 5mL of Sodium Chloride 0.9% or Glucose 5% (to a final volume of 10mL). The resulting solution contains flucloxacillin 50mg/mL.

ADMINISTRATION

Administer as either a slow IV injection over 3 – 5 minutes **OR** Add the required dose to a suitable volume of diluent (e.g. sodium chloride 0.9% or glucose 5%) and give as an IV infusion over 30 minutes [1,6].

SAMPLE CALCULATION

Two week old preterm neonate (1.1kg) with staphylococcal meningitis.

Dose = 100mg/kg every 8 hours = 110mg every 8 hours.

Reconstitute 250mg vial with 4.8ml WFI to give a concentration of 50mg/mL.

Withdraw 2.2mL (110mg) and give either as a slow IV injection or IV infusion over 30 minutes.

STORAGE

Do not store above 25 ^{o} C. Once reconstituted, the product should be used immediately. [2]

MONITORING [1]

- Monitor liver function and renal function if high doses or prolonged courses.
- Hepatic disorders: Cholestatic jaundice may occur up to 2 months after treatment has stopped. Risk is increased with prolonged courses and increasing age.
- Renal impairment: Dosage reduction not usually required, use normal dose every 8 hours if severe renal impairment.

ADVERSE EFFECTS

Hypersensitivity reactions including urticaria, fever, joint pains, rashes, angioedema, anaphylaxis, serum sickness-like reactions; rarely CNS toxicity including convulsions (especially with high doses or in severe renal impairment), interstitial nephritis, haemolytic anaemia, leucopenia, thrombocytopenia and coagulation disorders; also reported diarrhoea (including antibiotic-associated colitis); also gastro-intestinal disturbances; *very rarely* hepatitis and cholestatic jaundice reported. [1]

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Summary of Changes from Previous Versions

Date	Change
Feb 2021: Rev. No. 1	Updated based on Rotunda Flucloxacillin Monograph Mar 2019. Changes to OLOL monograph: • Monograph reworded to align with Rotunda monograph • Information on ORAL step down options as per Rotunda monograph were NOT added to OLOL monograph – oral switch can be decided if required on a case-by-case basis. • Dosage: Table on dose of IV flucloxacillin reformatted as per updated table in Rotunda monograph. • References updated.
Jan 2015	This is the first version of this guideline. It is based on the Rotunda Hospital Neonatal Monograph for Flucloxacillin, Doc. No. 1, Revision No. 0, date of issue 10/11/14. Changes in OLOL monograph compared to the Rotunda monograph: • Presentation/Reconstitution sections altered as a different brand and two strengths of flucloxacillin stocked in OLOL. • Dose range limited to children up to three months only in OLOL as monograph intended for use in NICU only. • Adverse Effects: full list from BNF for Children included.

Neonatal - ■Fluconazole IV and PO

Neonatal - Fluconazole IV and PO

Triazole antifungal [1].

MEDICATION SAFETY ISSUES

- Fluconazole may be confused with other azole antifungals [2]

USES

- Treatment of susceptible invasive candidal infections and cryptococcal infections [1].
- Prophylaxis of fungal infections in infants <1kg with risk factors for invasive candida such as broad spectrum antimicrobials and NEC. Prophylaxis considered on a case by case basis in patients >1kg with risk factors. **Under Consultant direction** [3,4].

PRESENTATION

Intravenous : Solution for infusion 2mg/ml [5]. Each 200mg bottle contains 15mmol of sodium [1,5].

Oral: Powder for oral suspension.

TREATMENT DOSAGE [1,5]

Age	Dose	Frequency	Duration
Neonate under 14 days	6 – 12 mg/kg	Every 72 hours	Continue according to response (at
Neonate 14 – 28 days	6 – 12 mg/kg	Every 48 hours	least 8 weeks for cryptococcal
Child 1 – 3 months	6 – 12 mg/kg	Every 24 hours	infections)

PROPHYLACTIC DOSAGE: 3mg/kg/dose every 72 hours for 6 weeks by oral or intravenous administration [3,4]

Renal Impairment : Dose reduction may be required – refer to BNFc and seek advice [1].

RECONSTITUTION

Intravenous: Fluconazole solution for infusion is already in liquid form, further dilution is not necessary [1,5].

Oral: For reconstitution of the oral suspension follow the instructions on the pack.

ADMINISTRATION

Fluconazole may be administered either orally or by intravenous infusion, the route being dependent on the clinical state of the patient. On transferring from the intravenous to the oral route, or *vice versa* , there is no need to change the dose [1].

Oral: Shake the bottle before use. Administer using an oral/enteral syringe.

Intravenous: Administer by IV infusion over 30 minutes; do not exceed an infusion rate of 5 – 10 ml/min.[1]

SAMPLE CALCULATION FOR TREATMENT

3.2 kg neonate 9 days old with susceptible candida infection. Dose: 12mg/kg = 38.4mg every 72 hours.

Fluconazole 2mg/ml solution = 38.4mg in 19.2ml. Withdraw 19.2ml and give by IV infusion over 30 min.

SAMPLE CALCULATION FOR PROPHYLAXIS

5 day old, 0.8 kg extremely preterm infant born at 26 weeks gestational age on parenteral nutrition and broad-spectrum antibiotics. Dose (as advised by Consultant): 3 mg/kg = 2.4 mg every 72 hours.

Fluconazole 2mg/ml solution = 2.4 mg in 1.2 ml. Withdraw 1.2 ml and give by IV infusion over 30 min.

STORAGE

Intravenous: Once opened, use immediately. Any unused infusion should be discarded.[5]

Oral: The shelf life of the reconstituted suspension is 28 days. Store below 30°C, do not freeze [6].

MONITORING [4]

- Fluconazole may interact with Erythromycin, Ibuprofen, **Midazolam** , Phenytoin, Zidovudine. This list is not complete. Always check for drug interactions.
- Monitor patient for rash – discontinue fluconazole if bullous lesions or erythema multiforme develop.
- Monitor renal function – dose reduction may be required in renal impairment.
- Monitor liver function – risk of hepatic toxicity.

ADVERSE EFFECTS

The most frequently (>1/10) reported adverse reactions are headache, abdominal pain, diarrhoea, nausea, vomiting, ALT increased, AST increased, ALP increased and rash [5]. Less frequently dyspepsia, taste disturbance, hepatic disorders, angioedema, anaphylaxis, dizziness, seizures, alopecia, pruritus, toxic epidermal necrolysis, Stevens-Johnson syndrome, hyperlipidaemia, leucopenia, thrombocytopenia, and hypokalaemia [1].

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Summary of Changes from Previous Versions

Date	Change
Feb 2021: Rev. No. 1	Updated based on Rotunda Fluconazole Monograph May 2018. Changes to OLOL monograph: • Medication Safety Issues: Removed that Diflucan is similar to Diprivan as not relevant in clinical practice, removed that anaphylaxis has been reported rarely as this is already included in adverse effects section. • Uses: Greater detail on indications for fluconazole prophylaxis added as per Rotunda and references. Remains under direction of Consultant. • Inclusion of ORAL fluconazole as per Rotunda monograph in presentation, dose, reconstitution, administration and storage sections. • Dosage: Prophylaxis dose changed as per Rotunda and references. • Administration: Addition that fluconazole may be given orally or IV, depending on the clinical status of the patient as per Rotunda. • References updated.
May 2015	This is the first version of this guideline.

Neonatal - ■Gentamicin IV

Neonatal - Gentamicin IV

Aminoglycoside antibiotic of choice [1].

MEDICATION SAFETY ISSUES

1. Extended-interval regimen used for neonates – **check dose interval carefully** , **monitor trough levels** .
2. The National Patient Safety Agency (NPSA) issued a patient safety alert in 2010 on the safer use of intravenous gentamicin in neonates [2]. A review of neonatal medication incidents identified that gentamicin was involved in 15% of all reported neonatal medication incidents. The most frequently reported incident (36%) related to administration at the incorrect time.
3. Following reports that some batches of gentamicin sulphate active pharmaceutical ingredient (API) used to manufacture gentamicin may contain higher than expected levels of histamine, which is a residual from the manufacturing process, monitor patients for signs of histamine-related adverse reactions; particular caution is required in patients taking concomitant drugs known to cause histamine release, in children, and in patients with severe renal impairment [1].
4. **Contraindicated in mothers and newborn babies of mothers with Myasthenia Gravis** . Aminoglycosides may impair neuromuscular transmission.
5. **Caution** in babies undergoing therapeutic cooling due to reduced renal function. Seek Consultant advice before prescribing.

USES

Neonatal sepsis and other severe infections when indicated [1].

PRESENTATION

Cidomycin Paediatric® 20mg/2ml ampoules [3].

DOSAGE [1]

Age	Dose	Frequency
Neonate less than 7 days after birth	5mg/kg	Every **36** hours
Neonate more than 7 days after birth	5mg/kg	Every 24 hours

Caution - the main adverse effects of gentamicin (nephrotoxicity and ototoxicity) are dose related. Whenever possible, treatment should not exceed 5 days to minimise risk of toxicity [1].

Renal Impairment : Refer to BNFc and seek advice – change in dosing interval may be required [1].

RECONSTITUTION

The 20mg/2ml vials are already in liquid form. May be further diluted with Sodium Chloride 0.9% or Glucose 5% if required to give a convenient volume for IV infusion [1,4].

ADMINISTRATION

Administer by IV infusion over 30 minutes [1,4].

SAMPLE CALCULATION

3.5kg neonate < 7 days after birth with queried sepsis. Dose 5mg/kg every 36 hours = 17.5mg.

Vial contains 20mg/2ml = 17.5mg/1.75ml. Withdraw 1.75ml from vial and give over 30 minutes.

STORAGE

Store unopened vials at room temperature below 25 ^{o} C. Once reconstituted, use immediately [3]. Discard any unused portions.

MONITORING

- Risk of nephrotoxicity - maintain adequate hydration and monitor renal function closely [1]. Caution if concomitant administration of other nephrotoxic medicines.
- Risk of ototoxicity - review concomitant ototoxic medicines [1]. If furosemide required (potentially ototoxic), separate administration from gentamicin by as long a period as practicable.
- Monitor gentamicin trough levels as directed below.

TROUGH LEVEL MONITORING

- Check trough level immediately before next dose is due.
- Document the date/time of blood sample and the date/time of last dose administered clearly on the laboratory request form. This will allow accurate interpretation of trough level results.

When to check first trough level [5-7]

Neonate Category	First Trough Level	Comment
Normal renal function / No concern regarding renal function (for example, urea and creatinine normal, urine output ≥ 1ml/kg/hour)	Before **3 rd** dose	Give 3 rd dose without waiting for trough level result.
Reduced urine output or uncertainty of adequate renal clearance Examples: • Receiving therapeutic hypothermia • Sepsis-induced renal impairment	Before **2 nd** dose	**Discuss with Consultant Neonatologist** whether to give 2 nd dose or wait for trough level result before giving dose. Risk/benefit decision – treatment of acutely septic neonate versus concern over renal function.
Corrected gestational age < 32 weeks and more than 7 days after birth , prescribed gentamicin every 24 hours	Before **2 nd** dose	Give 2 nd dose without waiting for trough level result. Previously, this patient group received gentamicin every 36 hours, therefore with shortened dosing interval of 24 hours, it is prudent to check trough level pre-2 nd dose.

Interpretation of trough level result [1,7]

Trough	Action
Acceptable: < 2mg/L **(< 1mg/L if more than 3 doses given)**	Continue same gentamicin dose and dose-interval.
High: ≥ 2mg/L (≥ 1mg/L if more than 3 doses given)	Hold next dose. Repeat trough level 12 hours later. If level is due out-of-hours, please contact biochemistry laboratory staff in advance to arrange processing of the result. Wait for trough level result before giving a further dose: • If repeat trough level result in range, restart gentamicin at same dose and extend dosing interval by 12 hours (for example, from 24 to 36 hourly or from 36 to 48 hourly). Reassess dosing interval if renal function improves. • If repeat trough level result is still high, review if gentamicin therapy still required. If so, repeat trough level every 12 to 24 hours until level reported in range. Restart at same dose and extend dosing interval to reflect the time period required to clear the previous dose.

When to check subsequent trough levels

Neonate Category	Subsequent Trough Levels
Reduced urine output or uncertainty of adequate renal clearance	Before every dose or every alternate dose (Consultant decision)
Normal renal function	Before every third dose

ADVERSE EFFECTS

The important adverse effects of the aminoglycosides are nephrotoxicity and irreversible ototoxicity (including vestibular and auditory damage) [1,4]. See BNF for Children [1] or Summary of Product Characteristics [3] for further information on possible adverse effects.

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Summary of Changes from Previous Versions

Date	Change
Feb 2021: Rev. No. 1	Updated based on Rotunda Gentamicin Monograph Feb 2019. Changes to OLOL monograph: • Medication Safety Issues: Additions of point numbers 3,4,5 as per Rotunda • Dosage: Whenever possible, treatment should not exceed 5 days to minimise risk of toxicity – reduced from 7 days as per BNFc/Rotunda monograph to 5 days then review as per practice in LH. • References updated, reference No. 7 added in OLOL.
August 2015	This is the first version of this guideline.

Neonatal - ■Meropenem IV

Neonatal - Meropenem IV

Meropenem is a broad-spectrum carbapenem antibiotic [1]. It is a restricted antimicrobial in LH and should only be prescribed following consultation with the Clinical Microbiologist.

MEDICATION SAFETY ISSUES

- Meropenem is a beta-lactam antibiotic. Avoid if history of immediate hypersensitivity reaction to beta-lactam antibacterials (e.g. penicillins or cephalosporins). Use with caution in patients with sensitivity to beta-lactam antibacterials [2,3].
- Incompatible with Aciclovir, Amphotericin B, Calcium Gluconate, Metronidazole, Sodium Bicarbonate and Zidovudine [1].

USES

Treatment of multi-drug resistant infection caused by certain gram-negative and gram-positive organisms, hospital-acquired septicaemia and meningitis [2]. Not licensed for use in children < 3 months of age [3].

PRESENTATION

Meropenem 500 mg Powder for Solution for Injection or Infusion [6].

DOSAGE [3,4]

Age	Dose	Interval
Neonate <7 days	40mg/kg	Every 12 hours
Neonate 7 – 28 days	40mg/kg	Every 8 hours
Child 1 to 3 months	40mg/kg	Every 8 hours

RECONSTITUTION [3,7]

NB. There are TWO STEPS for reconstitution. BOTH Step 1 and Step 2 below must be followed.

Step 1 : Reconstitute 500mg vial with 9.5mL WFI (Displacement volume 0.5mL) to give 50mg/mL. The displacement value of 0.5mL is for Hikma/Demo/Noridem brands (Fannin) of Meropenem 500mg. Check the displacement value if a different brand is used.

Step 2 : **Further dilute** 4mL of this solution with 6mL sodium chloride 0.9% or glucose 5% to a final volume of 10mL. The resulting solution contains meropenem 20mg/mL.

ADMINISTRATION

Administer as an IV infusion over 30 minutes.

SAMPLE CALCULATION

A 10 day old baby with meningitis weighing 2.3kg. Dose = 40mg/kg = 92mg every 8 hours.

Reconstitue meropenem as above to a solution containing 20mg/mL.

Withdraw 4.6mL (92mg) and administer by IV infusion over 30 minutes.

STORAGE

After reconstitution the solution should be used immediately. The time interval between the beginning of reconstitution and the end of intravenous infusion should not exceed 1 hour [6].

MONITORING

- Monitor renal, hepatic, and hematologic function tests [8].
- Dose reduction may be required in renal impairment – refer to BNFc and seek advice [3].
- Observe for changes in bowel frequency (Pseudomembranous colitis has been reported with the use of meropenem) [4].

ADVERSE EFFECTS

Nausea, vomiting, diarrhoea (antibiotic-associated colitis reported), abdominal pain, disturbances in liver function tests, headache, thrombocythaemia, rash, pruritus; *less commonly* paraesthesia, eosinophilia, thrombocytopenia, leucopenia; *rarely* convulsions; also reported haemolytic anaemia, positive Coombs' test, Stevens-Johnson syndrome, toxic epidermal necrolysis [3].

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Summary of Changes from Previous Versions

Date	Change
Feb 2021: Rev. No. 2	Updated based on Rotunda Meropenem Monograph Mar 2019. Changes to OLOL monograph: • Addition that meropenem is restricted in LH and should only be prescribed following consultation with the clinical microbiologist. • Caution on use in patients with previous reaction to beta-lactams reworded as per current BNFc wording. • Dose for child 1 to 3 months changed from 20 – 40mg/kg to 40mg/kg as per Rotunda monograph. Doses referenced to BNFc also. • References updated.
June 2017: Rev. No. 1	Meropenem Hikma Fannin brand stocked in OLOL. Displacement value changed to 0.5ml and calculation updated.
Jan 2015	This is the first version of this guideline. It is based on the Rotunda Hospital Neonatal Monograph for Meropenem, Doc. No. 1, Revision No. 0, date of issue 10/11/14. Changes in OLOL monograph compared to the Rotunda monograph: • Medication Safety: Do not use if previous severe hypersensitivity reaction to penicillin as per BNF for Children (“severe hypersensitivity” added) • Uses: added that meropenem not licensed for children under 3 months • Dose: added dosing for children 1 to 3 months • Reconstitution: Further dilution added to give a standard concentration of 20mg/mL for all doses. BNF for Children advises 1 – 20mg/mL. • Monitoring: added that dose reduction may be required for renal impairment • Adverse Effects: full list from BNF for Children included.

Neonatal - ■Metronidazole IV

Neonatal - MetroNIDAZOLE IV

Antimicrobial with activity against anaerobic bacteria and protozoa [1].

MEDICATION SAFETY ISSUES

- Anaphylaxis has been reported rarely with metronidazole [2].
- Sound-alike/Look-alike issues: Metronidazole may be confused with metformin, meropenem [3,4].

USES

Infections for which anaerobic cover required, such as Necrotising Enterocolitis (NEC) [1].

PRESENTATION

Metronidazole 5mg/ml Solution for Infusion [2]

DOSAGE [1]

Age	Dose	Frequency
Neonate less than 26 weeks corrected gestational age	Single loading dose 15mg/kg followed after 24 hours by 7.5mg/kg each dose	Every 24 hours
Neonate 26 - 34 weeks corrected gestational age	Single loading dose 15mg/kg followed after 12 hours by 7.5mg/kg each dose	Every 12 hours
Neonate over 34 weeks corrected gestational age	Single loading dose 15mg/kg followed after 8 hours by 7.5mg/kg each dose	Every 8 hours
Child 1 - 2 months	Single loading dose 15mg/kg followed after 8 hours by 7.5mg/kg each dose	Every 8 hours
Child 2 – 3 months	7.5mg/kg (max 500mg)	Every 8 hours

Hepatic Impairment

Dose reduction may be required in hepatic impairment [1]. Refer to BNFc and seek advice on assessment of liver function [1].

RECONSTITUTION

Metronidazole 5mg/ml solution for infusion is already in liquid form. There is no need to further dilute the infusion solution [2,5,6].

ADMINISTRATION

Give by IV infusion over one hour [1,2,5,7].

SAMPLE CALCULATION

2.8kg neonate corrected gestational age 40 weeks with suspected NEC.

Dose 15mg/kg as a single loading dose followed after 8 hours by 7.5mg/kg every 8 hours.

- 15mg/kg = 42mg. Withdraw 8.4ml metronidazole from the bag and give over one hour.
- 7.5mg/kg = 21mg. Withdraw 4.2ml metronidazole from the bag and give over one hour.

STORAGE

Store at room temperature below 25 ^{o} C. Keep container in the outer carton to protect from light. Once infusion solution opened, it must be used immediately. Discard any unused portions. [2,5].

MONITORING

- Monitor liver function tests as dose reduction may be required in hepatic impairment [1].
- Appropriate clinical and laboratory monitoring (especially of full blood count) are advised if administration of metronidazole for more than 10 days is considered necessary [2,5].

ADVERSE EFFECTS

Gastro-intestinal disturbances (including nausea and vomiting), taste disturbances, furred tongue, oral mucositis, anorexia; *very rarely* hepatitis, jaundice, pancreatitis, drowsiness, dizziness, headache, ataxia, psychotic disorders, darkening of urine, thrombocytopenia, pancytopenia, myalgia, arthralgia, visual disturbances, rash, pruritus, and erythema multiforme; on prolonged or intensive therapy peripheral neuropathy, transient epileptiform seizures, and leucopenia; also reported aseptic meningitis, optic neuropathy [1]. Anaphylaxis reported rarely [2].

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Summary of Changes from Previous Versions

Date	Change
Feb 2021: Rev. No. 1	Updated based on Rotunda MetroNIDAZOLE Monograph Jan 2019. Changes to OLOL monograph: • References updated.
August 2015	This is the first version of this guideline.

Neonatal - Piperacillin/Tazobactam IV

Neonatal - Piperacillin/Tazobactam IV

Antipseudomonal **penicillin** with broad spectrum of activity [1].

MEDICATION SAFETY ISSUES

Piperacillin/Tazobactam is a **penicillin** antibiotic – always check for previous hypersensitivity reactions to penicillins, cephalosporins and other allergens before starting therapy [2].

USES

Piperacillin/Tazobactam is a broad spectrum antibiotic. It is not licensed for use in children less than 2 years, however BNFc provides recommended dosing for neonates if required [1]. It should only prescribed in NICU in OLOL following consultation with clinical microbiologist.

PRESENTATION

Powder for solution for infusion. Each 4.5g vial contains 4g piperacillin (as sodium salt) and 0.5g tazobactam (as sodium salt). Each vial of piperacillin/tazobactam 4.5g contains 9.44 mmol of sodium [2].

DOSAGE [1]

Age	Dose	Frequency
Neonate	90mg/kg	Every 8 hours
Child 1 – 3 months	90mg/kg	Every 6 to 8 hours

Renal Impairment : Dose reduction may be required – refer to BNFc and seek advice [1].

RECONSTITUTION

NB. There are TWO STEPS for reconstitution. BOTH Step 1 and Step 2 below must be followed.

Step 1 : Reconstitute 4.5g vial as per table below using the brand specific displacement value and shake until dissolved [2].

Brand	Displacement Volume [2]	Diluent to be added	Final Volume	Final Concentration
Piperacillin/Tazobactam 4.5g **Piperin® Rowex/Sandoz**	3.2mL	16.8mL WFI or NS	20mL	225mg/mL

Step 2 : **Further dilute** 4mL of this solution with 6mL sodium chloride 0.9% or glucose 5% to a final volume of 10mL. The resulting solution contains piperacillin/tazobactam 90mg/mL. [1,3,4]

ADMINISTRATION

Administer by IV infusion over 30 minutes [1-3].

SAMPLE CALCULATION

2.8kg neonate under 7 days. Dose: 90mg/kg every 8 hours = 252mg every 8 hours.

Step 1 : Reconstitute 4.5g vial as per table above to give a concentration of 225mg/mL.

Step 2 : Withdraw 4mL of this solution and further dilute with 6mL sodium chloride 0.9% to a final volume of 10mL. The resulting solution contains 90mg/mL. Withdraw 2.8mL (252mg) and give over 30 minutes.

STORAGE

Store unopened vials at room temperature below 25°C [3,5]. Once reconstituted, use immediately [2].

MONITORING

- Monitor renal function – dose reduction may be required in renal impairment [1].

- Caution - high doses may lead to hypernatraemia owing to the high sodium content of the vials [1].
- Monitor FBC - leucopenia and neutropenia may occur, especially during prolonged therapy [2].
- Periodic liver function tests if treatment prolonged more than 10 days [4,5].

ADVERSE EFFECTS

For all penicillins, common or very common adverse effects include diarrhoea, hypersensitivity, nausea, skin reactions, thrombocytopenia and vomiting [1]. Candida superinfection, insomnia and headache are also common with piperacillin/tazobactam [1,2]. Among the most serious adverse reactions, pseudo-membranous colitis and toxic epidermal necrolysis occur in 1 to 10 patients in 10,000 [2]. Please refer to BNFc or SPC for full information on adverse effects.

REFERENCES

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Summary of Changes from Previous Versions

Date	Change
Feb 2021	This is the first version of this guideline.

Neonatal - ■Vancomycin IV

Vancomycin Hydrochloride

Vancomycin is a bactericidal antibiotic with activity against some aerobic and anaerobic bacteria including multi-resistant staphylococci.

MEDICATION SAFETY ISSUES

- Incompatible with Cephalosporins, Phenobarbital and Piperacillin-tazobactam.[1]
- Red man syndrome: flushing and hypotension if administered too quickly.
- Vancomycin exposure may be associated with hearing impairment in neonates.[2] Concomitant use of other ototoxic medication, e.g. furosemide and loop diuretics, should be avoided if possible.

USES

Drug of choice for serious infections caused by methicillin-resistant staphylococci and penicillin-resistant pneumococci.[1]

PRESENTATION

Vancomycin Hydrochloride 500mg Powder for concentrate for solution for infusion.[3]

DOSAGE [4-6] :

DOSE: 15mg/kg for all ages without renal impairment.

Preterm (<37/40 weeks gestation)		
Weight	**≤7 days of age**	**>7 days of age**
<1.2kg	18 HOURLY	
1.2-2kg	12 HOURLY	
>2kg	12 HOURLY	8 HOURLY

Term (≥ 37/40 weeks gestation)	
≤7 days of age	**>7 days of age ≤ 28 days of age**
12 HOURLY	8 HOURLY
Term >28 days	
6 HOURLY	

If renal impairment, contact Consultant Microbiologist or Pharmacy for advice.

RECONSTITUTION

Warning- reconstitution is a two step process

Step 1 The displacement value for Vancomycin Mylan brand 500mg (stocked in OLOL) is 0.3ml. Add 9.7ml of Water for Injection to a 500mg vial and shake gently to dissolve. The resulting solution contains **50mg/ml vancomycin** .

Step 2 Further dilute 1ml of the reconstituted (50mg/ml) vancomycin solution with 9ml of compatible fluid (e.g. Sodium chloride 0.9%, Glucose 5%). Ensure adequate mixing by inverting the syringe at least 10 times. The resulting solution contains **5mg/ml of vancomycin** .

ADMINISTRATION

Use immediately once reconstituted and diluted. Infuse the prescribed dose over at least 60 minutes.

STORAGE

Do not store above 25 ^{o} C. Use immediately once reconstituted.

MONITORING

Record vancomycin levels and response on the Vancomycin Monitoring Form (see Appendix 1).

Sub-therapeutic levels can result in treatment failure or the emergence of drug resistance.

Toxic or high levels of vancomycin can result in nephrotoxicity and/or ototoxicity. Monitor creatinine and urea at least twice weekly for the duration of treatment. If the patient is on additional nephrotoxic medication (e.g. NSAID's, aciclovir, aminoglycosides, diuretics, omeprazole), monitor renal function more frequently.

Indication	**Target Trough Concentration**
Uncomplicated infections	10 to 20 mg/L
Complicated infections: (e.g. Bacteraemia, endocarditis, osteomyelitis, meningitis, necrotising fasciitis and empyema)	15 to 20 mg/L
Dosing Frequency	**When to take a trough level**
18 HOURLY	Up to ONE HOUR before the 2 nd dose When levels are therapeutic, repeat every 2 days
12 HOURLY	Up to ONE HOUR before the 3rd or 4th dose When levels are therapeutic, repeat every 2 days
8 HOURLY	Up to ONE HOUR before 4th or 5th dose When levels are therapeutic, repeat every 2 days
6 HOURLY	Up to ONE HOUR before 4 th , 5th or 6th dose When levels are therapeutic, repeat every 3 days
In patients with normal renal function, DO NOT withhold the next dose while awaiting the result of the trough level – this may result in the patient being under dosed. If patient has renal impairment, contact Consultant Microbiologist or Pharmacy for advice.	

Vancomycin Targets and Timing of Levels:

Trough Level	Management	Timing of Next Level
Less than 5mg/L	**Preterm & term < 1 month: Increase frequency** 18hours■12hours■8hours>6 hours. For example 18 hours then increase to 12 hourly. **Term >1 month** : Increase by 20%.	Complete 24 hours of new regime before checking next level. Following two consecutive levels within therapeutic range repeat every 2-3 days and monitor renal function. *Complicated infections: Severe infection, reduced sensitivities, bacteraemia, endocarditis, osteomyelitis, meningitis, necrotising fasciitis and empyema
5-9mg/L	Increase by 10%	
10-20mg/L	No change (unless target level is 15-20mg/L for complicated infections* contact micro/ID)	
21-24mg/L	Decrease by 10% & Contact Micro	
≥ 25mg/L	Contact microbiology/ ID or Pharmacy for advice	

SIDE EFFECTS

- Nephrotoxicity and ototoxicity.
- Rash and hypotension (red man syndrome) if given too quickly.
- Phlebitis which can be minimized by slow infusion and dilution of the drug.

SAMPLE CALCULATION

0.86kg neonate 28 weeks corrected gestational age.

Dose: 15mg/kg = 15mg x 0.86kg = 12.9mg

Reconstitute and dilute one 500mg vial of vancomycin following the directions above.

The resulting solution contains 5mg/ml of vancomycin.

5mg in 1ml is equivalent to 1mg in 0.2ml

12.9mg in 2.58ml

Infuse a total volume of 2.58ml at a rate of 2.58ml/hr over 60 minutes.

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Appendix 1: Neonatal Vancomycin Monitoring Form - see hardcopy in NICU folder

Summary of Changes from Previous Versions

Date	Change
Jul 2019	Revision 2 of the Rotunda Neonatal Vancomycin Monograph received with permission (approved in the Rotunda in Dec 2018). Changes from previous version: • Medication Safety Issues: Risk of ototoxicity added. • Dosage: Dose regimen changed based on audits undertaken in the Rotunda Hospital, which found frequent low trough level results with the previous dosing regimen from BNFc. Updated dosing regimen based on American Academy of Paediatrics Red Book 2009. • Monitoring: New addition of Vancomycin Monitoring Form (see Appendix 1). Addition of advice to monitor urea and creatinine at least twice weekly and more frequently if patient on other nephrotoxic medications. • Table of when to take trough levels updated. • Addition of a new table on the management of subsequent doses based on trough level results. • Sample calculation - similar calculation to previous version, neonate weight different. • Side effects - section shortened to the main side effects only. See BNFc for full information. Additional information included in OLOL monograph: • Contact Micro/Pharmacy for advice on dosing regimen if renal impairment. • Added displacement value for vancomycin to reconstitution section. • Contact Micro/Pharmacy for advice on whether to hold dose pending level result if renal impairment.
June 2017	Vancomycin Flynn brand now stocked in OLOL. Displacement value of 500mg vial now 0.4ml. Monograph updated to reflect this.
Jan 2015	This is the first version of this guideline. It is based on the Rotunda Hospital Neonatal Monograph for Vancomycin, Doc. No. 1, Revision No. 0, date of issue 10/11/14. Changes in OLOL monograph compared to the Rotunda monograph: • Medication Safety: further detail on "red man" syndrome from BNFc. • Dose: added to check BNFc and seek advice on dose if patient has renal impairment. • Reconstitution: option to further dilute 2ml of 50mg/ml with 18ml of diluent if high dose • Monitoring: added to contact Consultant Neonatologist if trough level out of range, hold if > 20mg/L. • Adverse Effects: full list from BNF for Children included.