Paediatric Drug Dosage Adjustments in Patients with Renal Impairment or on Renal Replacement Therapies for use on the Intensive Care and Renal Units
Introduction

When adjusting drug doses for patients with renal impairment or on renal replacement therapies, drug doses should be adjusted taking into account all of the following:

- the usual mechanism of clearance of the drug
- the degree of renal failure
- the potential nephrotoxicity of the drug
- the degree of removal of the drug by renal replacement therapies, and
- the severity of the condition being treated.

Limitations of this guideline

1. Wherever possible, drug doses as per the British National Formulary for Children have been used, however in some instances antibiotic doses and references as per GOSH local guidelines have been utilised.

2. GFR has been used as a substitute for CrCL and for eGFR. The variations in local assays may make these difficult to determine and interpret.

3. Differentiations between the different modalities of haemofiltration (CVVH, CVVHD, CVVHDF) have not been specified.

4. Supplementary doses for patients undergoing haemofiltration for non-renal reasons (such as drug overdose) have not been specified.

Notes regarding dose adjustment in PICU patients undergoing haemofiltration

1. It is important to determine the indication for which the patient is being filtered. Not all patients that are haemofiltered have severe renal impairment – for example patients may undergo haemofiltration because of drug overdose, for reasons of fluid overload, or for removal of high levels of ammonia, lactate or other toxins. In these cases it may be inappropriate to reduce drug doses where renal textbooks say for CVVH to dose as per GFR of <10ml/minute; dosing as per normal renal function may be more appropriate. Remember to check the patient’s degree of residual kidney function before recommending any drug dose reductions.

2. In patients with septic shock, the risk of mortality from sepsis may often outweigh any risk of toxicity or further kidney damage from antibiotic accumulation, in which case initial drug dosing may be more aggressive than the usual recommended dose reductions. It should always be discussed with the consultant looking after the patient and a senior pharmacist who specialises in CVVH before any dosage reductions are recommended in any patient with sepsis.
3. For drugs for which CVVH dosage adjustment information is not available, it may be useful to consider the properties of the drug in order to determine whether it is likely that the drug will be removed by the filter or not, as listed below.

4. It is important to remember that once the patient is stabilised on haemofiltration, the patient's urea and creatinine may begin to return back to within the normal range. This does not imply that all other drugs will be also be cleared, or that the patient can be treated as having normal renal function; the filter will remove urea and creatinine because of their small molecular weight and because they are water soluble molecules, so serum creatinine and urea values cannot be used to determine a patient's renal function once they are undergoing haemofiltration.

Drugs properties to consider in order to determine likelihood of drug removal by haemofiltration

The following drug properties are required in order for a drug to be removed by haemofiltration:

- Low molecular weight (< 10000 daltons)
- Low volume of distribution (< 1L/kg)
- High degree of water solubility
- Low degree of protein binding

Small, water soluble molecules with low volume of distribution and low protein binding are more likely to be removed by the filter; however it is important to remember that there are other factors such as stearic hindrance at the membrane site which may affect drug clearance and which may be difficult to predict.
Drug: **ACICLOVIR**

**Usual route of clearance:** Aciclovir is predominantly renally cleared (75-80% excreted unchanged in the urine)\(^1,2\) by glomerular filtration and tubular secretion.\(^3\) There is only one significant metabolite, which accounts for 10-15% of the dose excreted in the urine.\(^1,4\)

**Pharmacokinetic parameters:**
- **Protein binding:** 9-33\(^%\),\(^1,3,4\)
- **Molecular Wt:** 225.20 daltons\(^5\)
- **Vd:**
  - Adults: 0.7 L/kg\(^6\)
  - Children: 1.01 ± 0.28\(^2\)
- **Half-life (t½):**
  - Adults: approximately 3 hours\(^1\)
  - Children 1-12 years old: 2-3 hours\(^7\)
  - Neonates: approximately 4 hours\(^1,7\)
- **t½ in renal imp:** Approximately 20 hours\(^1,3,4\)

| Normal dose: (meningo-encephalitis): |  
|<3 months: | 20mg/kg iv every 8 hours\(^6,9\) |
| >3 months-12 yrs: | 500mg/m\(^2\) iv every 8 hours\(^8\) |
| >12 years: | 10mg/kg iv every 8 hours\(^8\) |

**Dose adjustment in renal impairment:**
- **GFR 25-50ml/min:** Give normal dose iv every 12 hours\(^1,4,6,8,10\)
- **GFR 10-25ml/min:** Give normal dose iv every 24 hours\(^1,4,6,8,10\)
- **GFR <10ml/min:** Give half the normal dose iv every 24 hours\(^6,11\)

**Dose adjustment in HD:**
- Dialysed.\(^9\) HD removes approximately 60% of a dose.\(^7\)
- Give half the normal dose iv every 24 hours\(^1,4,10,11,12\) administered after dialysis session.\(^7,12\)

**Dose adjustment in PD:** Not dialysed.\(^9\)

**Intraperitoneal dose:** No information

**Dose adjustment in CVVH:**
- Filtered. Give normal dose iv every 24 hours.\(^2,6\)
- Increase to every 12 hours\(^7,12\) if severe infection eg herpes encephalitis.

**Notes:**
Nephrotic – decrease risk by infusing over one hour and ensuring patient is well hydrated.\(^1,8\) Polyuric renal failure may occur with high dose therapy, especially when administered with concurrent nephrotoxic drugs. This generally responds rapidly to hydration and reduction/withdrawal of aciclovir.\(^9\)
The risk of neurological toxicity is increased in renal impairment.\(^6,7\)

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Monograph checked by: Sue Patey (Renal Senior Specialist Pharmacist) and Dr Quen Mok (Consultant Paediatric Intensivist)
Date of last review: 16/12/10

References:
4. Summary of Product Characteristics: EMC/Package Insert, Last updated: 20/05/08 Manufacturer: Wockhardt UK Ltd
7. Lexi-comp online accessed via www.crlonline.com, accessed 16/12/10
10. Guy’s, St Thomas’ and Lewisham Hospitals Trust. Paediatric Formulary, 8th edn. London, UK, 2010

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Approved by: Drugs & Therapeutics Committee
Date document created: November 2011
Date of interim review: May 2014 Reviewed by: Venetia Horn (PICU Senior Pharmacist) Checked by: Vani Suri (NICU Pharmacist)
Date for next review: September 2014
Version: 3

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**Drug:** AMIKACIN

<table>
<thead>
<tr>
<th>Usual route of clearance:</th>
<th>94-98% of a dose of amikacin is excreted in the urine unchanged within 24 hours,(^1,^2) primarily by glomerular filtration.(^3)</th>
</tr>
</thead>
</table>
| Pharmacokinetic parameters: | **Protein binding:** <20\(^%\)\(^3\)
  **Molecular Wt:** 585.60 daltons\(^4\)
  **Vd:**
    - Adults: 0.22-0.29 L/kg\(^5\)
    - Paediatrics: 0.2-0.7 L/kg\(^6\)
    - Adults: 2-3 hours\(^1,^3\)
  **Half-life (t½):**
    - Adolescents: 1.5 ± 1 hour\(^2\)
    - Children: 1.6-2.5 hours\(^2\)
  **t½ in renal imp:**
    - Term neonates >7 days old: 4-5 hours\(^1,^2\)
    - Pre-term neonates 1-3 days old: 7-8 hours\(^1,^2\)
    - 17-150 hours\(^5\) |
| Normal dose: | <2kg <4wks of life: 10mg/kg iv every 24 hours\(^7\)
  <2kg >4wks of life: 15mg/kg iv every 24 hours\(^7\)
  >2kg <4wks of life: 15mg/kg iv every 24 hours\(^7\)
  Prophylaxis:
    - Cystic fibrosis: 10mg/kg iv every 12 hours for 3 doses (use ideal body weight)\(^7\)
    - All other patients: 30mg/kg (max 1.5g) iv every 24 hours\(^7\)
    - 20mg/kg (max 1.5g) iv every 24 hours (use ideal body weight)\(^7\) |
| Dose adjustment in renal impairment: | Give 10mg/kg iv, take trough level after 24 hours, and hold dose until trough level is available. Adjust dosage interval according to serum levels – aim to keep trough <10mg/L and peak 20-30mg/L.\(^7\) |
| Dose adjustment in HD: | Dialysed.\(^1,^2,^5\) Give 10mg/kg iv, take trough level after 24 hours, and hold dose until trough level is available. Adjust dosage interval according to serum levels – aim to keep trough <10mg/L and peak 20-30mg/L.\(^8\) |
| Dose adjustment in PD: | Dialysed.\(^1,^2,^5\) Give 10mg/kg iv, take trough level after 24 hours, and hold dose until trough level is available. Adjust dosage interval according to serum levels – aim to keep trough <10mg/L and peak 20-30mg/L.\(^8\) |
| Intraperitoneal dose: | Loading dose: 25mg/L, maintenance dose: 12mg/L\(^9\) |
| Dose adjustment in CVVH: | Give 10mg/kg iv, take trough level after 24 hours, and hold dose until trough level is available. Adjust dosage interval according to serum levels\(^10\) – aim to keep trough <10mg/L and peak 20-30mg/L.\(^8\) |
| Notes: | Peak levels are only required for doses <20mg/kg.\(^7\)
Repeat levels daily in renal impairment or if on any form of dialysis or haemofiltration.\(^7\)
Take care not to underdose; ensure that a therapeutic peak level is maintained. |

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Date of last review: 16/12/10

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**References:**
3. Summary of Product Characteristics: EMC/Package Insert, Last updated: 03/02/09 Manufacturer: Hospira UK Ltd

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Version: 3
7. Gt Ormond St Hospital for Children NHS Trust Antibiotic Policy Amikacin Guidelines V2.0 Feb 2008
8. Gt Ormond St Hospital for Children NHS Trust - Local Practice as at December 2010
**Drug:** AMPHOTERICIN LIPOSOMAL (AMBISOME)

**Usual route of clearance:** 2-5% of a dose is excreted unchanged in the urine.\(^1\)

The excretion of liposomal amphotericin has not been studied and the metabolic pathways are unknown, however due to the size of the liposomes the degree of glomerular filtration and renal elimination is very low.\(^6\)

Liposomal amphotericin exhibits nonlinear kinetics (an increase in dose may result in a greater than proportional increase in serum concentration).\(^3\)

**Pharmacokinetic parameters:**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protein binding</td>
<td>90%(^{1,4})</td>
</tr>
<tr>
<td>Molecular Wt.</td>
<td>924.08 daltons(^5)</td>
</tr>
<tr>
<td>Vd</td>
<td>Adults: 0.1-0.44 L/kg(^1)</td>
</tr>
<tr>
<td></td>
<td>Adults: 6.3-10.7 hours(^1)</td>
</tr>
<tr>
<td>Half-life (t½)</td>
<td>Unchanged(^1)</td>
</tr>
<tr>
<td>t½ in renal imp.</td>
<td>Unchanged(^1)</td>
</tr>
</tbody>
</table>

**Normal dose:**

**Prophylaxis:** 1mg/kg iv every 24 hours\(^8\)

3-5mg/kg iv every 24 hours\(^6\)

Give test dose of 100mcg/kg (max 1mg) over 10 minutes prior to first dose, followed by the rest of the dose one hour later if no reaction.\(^6\)

**Treatment:**

**Dose adjustment in renal impairment:**

<table>
<thead>
<tr>
<th>GFR 20-50ml/min</th>
<th>No dosage adjustment required - give normal dose(^{1,7,9})</th>
</tr>
</thead>
<tbody>
<tr>
<td>GFR 10-20ml/min</td>
<td>No dosage adjustment required - give normal dose(^{1,7,9})</td>
</tr>
<tr>
<td>GFR &lt;10ml/min</td>
<td>No dosage adjustment required - give normal dose(^{1,7,9})</td>
</tr>
</tbody>
</table>

**Dose adjustment in HD:**

Not dialysed.\(^7\) No dosage adjustment required - give normal dose, administered after dialysis session.\(^1,2\)

**Dose adjustment in PD:**

Not dialysed.\(^7\) No dosage adjustment required - give normal dose.\(^2,9\)

**Intraperitoneal dose:**

No information

**Dose adjustment in CVVH:**

Not filtered but no dosage adjustment required - give normal dose.\(^1,9\)

Administer into the venous return of the of the filtration circuit as liposomal preparations may increase the risk of the filter clotting.\(^1,9\)

**Notes:**

Liposomal amphotericin is less nephrotoxic than conventional amphotericin, due to the size of the liposomes preventing interaction of amphotericin B with the cells of the distal tubules.\(^1,2,6\)

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**References:**

2. Summary of Product Characteristics: EMC/Packge Insert, Last updated: 21/05/09 Manufacturer: Gilead Sciences Ltd
3. Lexi-comp online accessed via [www.crlonline.com](http://www.crlonline.com), accessed 16/12/10
7. Guy’s, St Thomas’ and Lewisham Hospitals Trust. Paediatric Formulary, 8th edn. London, UK, 2010

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<table>
<thead>
<tr>
<th>Drug:</th>
<th>AMPICILLIN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Usual route of clearance:</td>
<td>Ampicillin is excreted mainly in the bile and urine; 60-80% is excreted unchanged in the urine.</td>
</tr>
</tbody>
</table>

**Pharmacokinetic parameters:**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protein binding</td>
<td>17-20%&lt;sup&gt;3&lt;/sup&gt;</td>
</tr>
<tr>
<td>Molecular Wt.</td>
<td>349.40 daltons&lt;sup&gt;5&lt;/sup&gt;</td>
</tr>
</tbody>
</table>
| Vd | Adults: 0.17-0.31 L/kg<sup>2</sup>  
Paediatrics: 0.32 L/kg<sup>3</sup> |
| Half-life (t½): | Adults: 1-2 hours<sup>4</sup>  
Children: 1-1.8 hours<sup>4</sup>  
Neonates 8-14 days old: 2.8 hours<sup>4</sup>  
Neonates 2-7 days old: 4 hours<sup>4</sup> |
| t½ in renal imp: | 7-20 hours<sup>2</sup> |

**Normal dose:**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Dose</th>
</tr>
</thead>
</table>
| Meningitis, enterococcal & Group B streptococcal infection: | ≤ 1 week of life and ≤ 2 kg: 50 mg/kg iv 12 hourly<sup>8</sup>  
> 1 week of life and ≤ 2 kg: 50 mg/kg iv 8 hourly<sup>6</sup>  
≤ 1 week of life and > 2 kg: 50 mg/kg iv 8 hourly<sup>6</sup>  
> 1 week of life and > 2 kg: 50 mg/kg (max 2 g)<sup>7</sup> iv 6 hourly<sup>6</sup> |
| Highly suspected/confirmed listeria meningitis: | ≤ 1 week of life: 50 mg/kg 6 hourly<sup>4,8</sup>  
> 1 week of life: 50 mg/kg (max 2 g)<sup>7</sup> 4 hourly<sup>4,8</sup> |

**Dose adjustment in renal impairment:**

| GFR 20-50 ml/min: | No dosage adjustment required - give normal dose<sup>2</sup> |
| GFR 10-20 ml/min: | Give normal dose every 6-12 hours<sup>3,4</sup> |
| GFR <10 ml/min: | Give normal dose every 12 hours<sup>3,4</sup> |

**Dose adjustment in HD:**

| Dialysed, approximately 40% of a dose is removed by HD.<sup>4,9</sup> |
| Give normal dose every 12 hours, administered after dialysis session.<sup>9</sup> |

**Dose adjustment in PD:**

| Not dialysed. Give normal dose every 12 hours.<sup>9</sup> |

**Intraperitoneal dose:**

| 125 mg/L<sup>10</sup> |

**Dose adjustment in CVVH:**

| Filtered, give normal dose every 6<sup>8</sup> to 8<sup>3</sup> hours |

**Notes:**

The neonatal dose for meningitis and Group B streptococcal infection is lower than that specified in the BNF-C, as it is Trust policy that ampicillin is always used in combination with cefotaxime for empirical treatment of suspected meningitis. If being used as monotherapy, the dose should always be discussed with microbiology/infectious diseases.

For monotherapy of highly suspected/confirmed listeria meningitis, the dose has been extrapolated from that used in Lexi-comp for Group B streptococcal meningitis. Again, these patients should be discussed with microbiology/infectious diseases.

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**References:**

Manufacturer: Essential Generics
4. Lexi-comp online accessed via [www.crilonline.com](http://www.crilonline.com), accessed 16/12/10

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© Gt Ormond St Hospital for Children Foundation Trust. While all care has been taken in the preparation of this guide, no responsibility will be taken by the authors for the drug doses, which should always be confirmed independently by the prescriber.
8. Gt Ormond St Hospital for Children NHS Trust Antibiotic Policy Neonatal Antibiotic Doses V3.0 November 2010
**Drug:** BENZYLPPENICILLIN

**Usual route of clearance:** 60-90% of a dose is excreted by renal elimination, 10% of which is by glomerular filtration and 90% of which is by tubular secretion.\(^1\)

10-30% of a dose is metabolised in the liver to penicilloic acid.\(^2\)

Biliary excretion accounts for only a minor fraction of the dose.\(^1\)

**Pharmacokinetic parameters:**

| Protein binding: | 60%\(^1,3\) |
| Molecular Wt: | 334.39 daltons\(^4\) |
| Vd: | Adults: 0.3-0.42 L/kg\(^3\) |
| | Adults: 30 minutes\(^1,3,5\) |
| Half-life (t½): | Infants and Children: 0.5-1.2 hours\(^2\) |
| | Neonates >14 days old: 0.9-1.9 hours\(^2\) |
| | Neonates 7-13 days old: 1.2-2.2 hours\(^2\) |
| | Neonates < 6 days old: 3.2-3.4 hours\(^2\) |
| | 10 hours\(^3\) |

**Normal dose:**

- **Meningitis, meningococcal disease:**
  - <4 weeks: 50mg/kg iv every 12 hours\(^5\)
  - >4 weeks: 50mg/kg (max 2.4g) iv every 8 hours\(^6\)

- **Bacterial endocarditis, treatment or prevention of neonatal group B streptococcus infection, NEC, other severe infection:**
  - <1 week of life: 25mg/kg iv every 8 hours\(^6\)
  - 1-4 weeks of life: 50mg/kg iv every 8 hours\(^6\)
  - >4 weeks of life: 50mg/kg (max 2.4g) iv every 4-6 hours\(^6\)

- **Mild-moderate infection:**
  - <1 week of life: 25mg/kg iv every 12 hours\(^6\)
  - 1-4 weeks of life: 25mg/kg iv every 8 hours\(^6\)
  - >4 weeks of life: 25mg/kg iv every 6 hours\(^6\)

**Dose adjustment in renal impairment:**

| GFR 10-50ml/min: | Give normal dose q8-12h\(^2,6,7\) |
| GFR <10ml/min: | Give normal dose q12h\(^2,6,7\) |

Maximum adult dose in severe renal impairment is 4.8g/day\(^3\)

**Dose adjustment in HD:** Dialysed.\(^3\) Give normal dose every 12 hours, administered after dialysis.\(^3,8\)

**Dose adjustment in PD:** Dialysed.\(^3\) Give normal dose every 12 hours (or 50% of dose at same frequency).\(^3,7,8\)

**Intraperitoneal dose:** No information

**Dose adjustment in CVVH:** Give normal dose every 8\(^2,7,8\) to 12 hours\(^3,7\)

**Notes:**

- Increased incidence of neurotoxicity (seizures) with benzylpenicillin in renal impairment.\(^3,6\)
- Further dose reductions are required if advanced hepatic impairment is associated with severe renal failure.\(^1\) — discuss with pharmacy.

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References:
1. Summary of Product Characteristics: EMC/Package Insert, Last updated: 16/09/08 Manufacturer: Genus Pharmaceuticals
2. Lexi-comp online accessed via www.crlonline.com, accessed 16/12/10

Written by: Rachelle Booth (PICU Senior Specialist Pharmacist)
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Approved by: Drugs & Therapeutics Committee
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Date for next review: September 2014
Version: 3
7. Guy's, St Thomas' and Lewisham Hospitals Trust. Paediatric Formulary, 8th edn. London, UK, 2010
<table>
<thead>
<tr>
<th>Drug:</th>
<th>CASPOFUNGIN</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Usual route of clearance:</strong></td>
<td>Caspofungin undergoes spontaneous degradation to an open-ring compound. Further metabolism involves peptide hydrolysis and N-acetylation in the liver. Distribution is the dominant mechanism affecting plasma clearance, with a short alpha phase of distribution, followed by a beta phase with a half-life of 9-11 hours, then a terminal gamma phase with a half-life of 45 hours. 35% of a dose is excreted in faeces primarily as metabolites and 41% of a dose is excreted in urine primarily as metabolites. Only 1.4% of a dose is excreted unchanged in the urine. Caspofungin exhibits non-linear pharmacokinetics.</td>
</tr>
<tr>
<td><strong>Pharmacokinetic parameters:</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Protein binding:</strong></td>
<td>92.4-96.5%</td>
</tr>
<tr>
<td><strong>Molecular Wt:</strong></td>
<td>1093.31 daltons</td>
</tr>
<tr>
<td><strong>Vd:</strong></td>
<td>Unknown</td>
</tr>
<tr>
<td><strong>Half-life (t½):</strong></td>
<td>Adults: 12-15 days, Beta phase half-life is 32% to 43% lower in paediatric patients than in adult patients. Increased but not significantly.</td>
</tr>
<tr>
<td><strong>t½ in renal imp:</strong></td>
<td>No information</td>
</tr>
<tr>
<td><strong>Normal dose:</strong></td>
<td>1-3 months: 25mg/m² iv every 24 hours²,³,⁵ 50mg/m² iv every 24 hours⁵ 70mg/m² (max 70mg) iv on Day 1, then 50mg/m² (max 70mg) iv every 24 hours. May be increased to 70mg/m² (max 70mg) every 24 hours if lower dose is tolerated but there is an inadequate response.</td>
</tr>
<tr>
<td><strong>Dose adjustment in renal impairment:</strong></td>
<td>GFR 20-50ml/min: No dosage adjustment required - give normal dose¹,³,⁵,⁶,⁷ GFR 10-20ml/min: No dosage adjustment required - give normal dose¹,³,⁵,⁶,⁷ GFR &lt;10ml/min: No dosage adjustment required - give normal dose¹,³,⁵,⁶,⁷</td>
</tr>
<tr>
<td><strong>Dose adjustment in HD:</strong></td>
<td>No dialysed.²,³,⁶ No dosage adjustment required - give normal dose¹,²,³,⁶,⁷</td>
</tr>
<tr>
<td><strong>Dose adjustment in PD:</strong></td>
<td>No dialysed.²,³ No dosage adjustment required - give normal dose¹,²,³,⁶,⁷</td>
</tr>
<tr>
<td><strong>Intraperitoneal dose:</strong></td>
<td>No information</td>
</tr>
<tr>
<td><strong>Dose adjustment in CVVH:</strong></td>
<td>Unlikely to be removed by haemofiltration due to high degree of protein binding. No dosage adjustment required - give normal dose²,³,⁶,⁷</td>
</tr>
<tr>
<td><strong>Notes:</strong></td>
<td>Adverse effects include renal failure although this is uncommon. Dose reduction is required in patients with moderate hepatic impairment – reduce dose by 30%.</td>
</tr>
</tbody>
</table>

References:
1. Summary of Product Characteristics: EMC/Package Insert, Last updated: 20/07/09 Manufacturer: Merck Sharpe and Dohme Ltd
3. Lexi-comp online accessed via www.crlonline.com, accessed 16/12/10

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Checked by: Sue Patey (Renal Senior Specialist Pharmacist) and Dr Quen Mok (Consultant Paediatric Intensivist)  
Date of last review: 24/05/11
<table>
<thead>
<tr>
<th>Drug:</th>
<th>CEFOTAXIME</th>
</tr>
</thead>
<tbody>
<tr>
<td>Usual route of clearance:</td>
<td>Cefotaxime is partially metabolised prior to excretion. Elimination is predominantly by renal excretion; approximately 60% of a dose is excreted unchanged in the urine, while approximately 24% is excreted as the microbiologically active metabolite desacetyl-cefotaxime.¹ ² ³</td>
</tr>
</tbody>
</table>
| Pharmacokinetic parameters: | **Protein binding:** 40%⁴  
**Molecular Wt:** 455.47 daltons⁵  
**Vd:** Adults: 0.15-0.55 L/kg⁶  
**Half-life (t½):** Adults: 0.9-1.14 hours; metabolite 1.3 hours¹  
**t½ in renal imp:** Children: 1.5 hours³  
Neonates 1-4 weeks old: 2 hours³  
Full-term neonates <1 week old: 2-3.4 hours³  
Premature neonates <1 week old: 5-6 hours³  
Adults: 2.5 hours; metabolite approximately 10 hours⁴ |
| Normal dose: | Meningitis:  
<1 week of life: 50mg/kg iv every 12 hours⁷  
1-3 weeks of life: 50mg/kg iv every 8 hours⁷  
>3 weeks of life: 50mg/kg iv (max 3g) every 6 hours⁷  |
| Dose adjustment in renal impairment: | No dosage adjustment required - give normal dose⁴  
No dosage adjustment required - give normal dose⁴  
Give 1x normal dose initially, then give half the normal dose and keep the frequency the same¹ ⁷ ⁹ |
| Dose adjustment in HD: | Dialysed.⁴ ⁹ Give 1x normal dose initially, then give half the normal dose and keep the frequency the same⁴  |
| Dose adjustment in PD: | Not dialysed.⁴ Give 1x normal dose initially, then give half the normal dose and keep the frequency the same⁴  |
| Intraperitoneal dose: | Loading dose 500mg/L then maintenance 125¹¹ to 250mg/L¹⁰  |
| Dose adjustment in CVVH: | >3 weeks of life: give normal dose every 8 hours⁵  |
| Notes: | Administration of high-dose cephalosporins in patients with renal impairment may result in encephalopathy (decreased consciousness, dyskinesias, convulsions).¹  
Because of extra-renal elimination, it is only necessary to decrease the dose in severe renal failure where GFR<5ml/min.¹ ⁷ ⁹  
Reduce dose further if the patient has concomitant hepatic and renal failure⁴ – discuss with pharmacy. |

**References:**
1. Summary of Product Characteristics: EMC/Package Insert, Last updated: 15/08/07  
3. Lexi-comp online accessed via www.cronline.com, accessed 16/12/10  

**Written by:** Rachelle Booth (PICU Senior Specialist Pharmacist)  
**Checked by:** Sue Patey (Renal Senior Specialist Pharmacist) and Dr Quen Mok (Consultant Paediatric Intensivist)  
**Approved by:** Drugs & Therapeutics Committee  
**Date document created:** November 2011  
**Date of interim review:** May 2014  
**Reviewed by:** Venetia Horn (PICU Senior Pharmacist)  
**Checked by:** Vani Suri (NICU Pharmacist)  
**Date for next review:** September 2014  
**Version:** 3

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**Drug:** CEFTAZIDIME

<table>
<thead>
<tr>
<th>Usual route of clearance:</th>
<th>80-90% of a dose of ceftazidime is excreted unchanged in the urine by glomerular filtration. Less than 1% of a dose is excreted via the bile.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pharmacokinetic parameters:</td>
<td>Protein binding:</td>
</tr>
<tr>
<td></td>
<td>Molecular Wt: 546.58 daltons</td>
</tr>
<tr>
<td></td>
<td>Adults: 0.28-0.4 L/kg</td>
</tr>
<tr>
<td></td>
<td>Paediatrics: 1.043 L/kg</td>
</tr>
<tr>
<td></td>
<td>Adults: 1.8-2.2 hours</td>
</tr>
<tr>
<td></td>
<td>Neonates: 5.4-8.8 hours</td>
</tr>
<tr>
<td></td>
<td>13-25 hours</td>
</tr>
<tr>
<td>Normal dose:</td>
<td>&lt;1 week of life: 25mg/kg iv every 24 hours, double in severe infection</td>
</tr>
<tr>
<td></td>
<td>1-3 weeks of life: 25mg/kg iv every 12 hours, double in severe infection</td>
</tr>
<tr>
<td></td>
<td>&gt;3 weeks of life: 25mg/kg iv every 8 hours, double in severe infection (max 2g every 8 hours, cystic fibrosis max 3g every 8 hours)</td>
</tr>
<tr>
<td>Dose adjustment in renal impairment:</td>
<td>GFR 30-50ml/min: Give 1x normal dose initially, followed by 50-100% of normal dose every 12 hours</td>
</tr>
<tr>
<td></td>
<td>GFR 15-30ml/min: Give 1x normal dose initially, followed by 50-100% of normal dose every 24 hours</td>
</tr>
<tr>
<td></td>
<td>GFR 5-15ml/min: Give 1x normal dose initially, followed by 25-50% of normal dose every 24 hours</td>
</tr>
<tr>
<td></td>
<td>GFR &lt;5ml/min: Give 1x normal dose initially, followed by 25-50% of normal dose every 48 hours</td>
</tr>
<tr>
<td>Dose adjustment in HD:</td>
<td>Dialysed. Give 1x normal dose initially, followed by 50% of the normal dose every 24 hours, administered after dialysis</td>
</tr>
<tr>
<td>Dose adjustment in PD:</td>
<td>Dialysed. Give 50% of the normal dose every 24 hours</td>
</tr>
<tr>
<td>Intraperitoneal dose:</td>
<td>Loading dose: 250mg/L, maintenance dose: 125mg/L</td>
</tr>
<tr>
<td>Dose adjustment in CVVH:</td>
<td>Give 50-100% of normal dose every 12 hours</td>
</tr>
<tr>
<td>Notes:</td>
<td>There have been reports of neurological sequelae including tremor, myoclonia, convulsions, encephalopathy, and coma in patients with renal impairment in whom the dose of ceftazidime has not been appropriately reduced.</td>
</tr>
</tbody>
</table>

**References:**

1. Summary of Product Characteristics: EMC/Packaging Insert, Last updated: 21/12/09 Manufacturer: Sandoz Ltd
2. Summary of Product Characteristics: EMC/Packaging Insert, Last updated: 12/08/09 Manufacturer: GlaxoSmithKline UK
3. Lexi-comp online accessed via www.crlonline.com, accessed 16/12/10
<table>
<thead>
<tr>
<th>Drug:</th>
<th>CEFTRIAXONE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Usual route of clearance:</td>
<td>Ceftriaxone is eliminated mainly as unchanged drug, with approximately 60% of a dose being excreted in the urine, almost exclusively by glomerular filtration. The remainder of the dose is excreted via the biliary and intestinal tracts.</td>
</tr>
<tr>
<td>Pharmacokinetic parameters:</td>
<td></td>
</tr>
<tr>
<td>Protein binding:</td>
<td></td>
</tr>
<tr>
<td>Molecular Wt:</td>
<td>554.58 daltons</td>
</tr>
<tr>
<td>Vd:</td>
<td>454.58 daltons</td>
</tr>
<tr>
<td>Half-life (t½):</td>
<td>1-3</td>
</tr>
<tr>
<td>t½ in renal imp:</td>
<td>1-3</td>
</tr>
<tr>
<td>Normal dose:</td>
<td>Meningitis:</td>
</tr>
<tr>
<td>Dose adjustment in renal impairment:</td>
<td>GFR 20-50ml/min:</td>
</tr>
<tr>
<td></td>
<td>GFR 10-20ml/min:</td>
</tr>
<tr>
<td></td>
<td>GFR &lt;10ml/min:</td>
</tr>
<tr>
<td>Dose adjustment in HD:</td>
<td>Not dialysed. Give 50mg/kg (max 2g) every 24 hours</td>
</tr>
<tr>
<td>Dose adjustment in PD:</td>
<td>Not dialysed. Give 50mg/kg (max 2g) every 24 hours</td>
</tr>
<tr>
<td>Intraperitoneal dose:</td>
<td>Loading dose: 250mg/L; maintenance dose: 125mg/L</td>
</tr>
<tr>
<td>Dose adjustment in CVVH:</td>
<td>No dosage adjustment required - give normal dose (unless concomitant hepatic impairment, see below)</td>
</tr>
<tr>
<td>Notes:</td>
<td>In patients with renal or hepatic dysfunction, the pharmacokinetics of ceftriaxone are only minimally altered and the half-life only slightly increased; if renal function alone is impaired then biliary excretion is increased, if liver function alone is impaired then renal elimination is increased. If both renal and hepatic function are impaired then dosage adjustment will be necessary – discuss with pharmacy. The policy on the intensive care units is to change patients admitted on ceftriaxone to cefotaxime at the earliest convenient time, due to the risk of ceftriaxone and calcium interactions, as per the MHRA Drug Safety Bulletin Oct 2009.</td>
</tr>
</tbody>
</table>

References:
1. Summary of Product Characteristics: EMC/Package Insert, Last updated: 13/01/10  Manufacturer: Wockhardt UK Ltd
2. Lexi-comp online accessed via www.crtonline.com, accessed 16/12/10
10. MHRA Drug Safety Update October 2009

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Checked by: Sue Patey (Renal Senior Specialist Pharmacist) and Dr Quen Mok (Consultant Paediatric Intensivist)
Approved by: Drugs & Therapeutics Committee
Date document created: November 2011
Date of interim review: May 2014 Reviewed by: Venetia Horn (PICU Senior Pharmacist) Checked by: Vani Suri (NICU Pharmacist)
Date for next review: September 2014
Version: 3

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# Cidofovir

<table>
<thead>
<tr>
<th>Drug</th>
<th>CIDOFOVIR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Usual route of clearance:</td>
<td>The major route of elimination of cidofovir is by renal excretion of unchanged drug via glomerular filtration and tubular secretion. 80-100% of a dose is excreted unchanged in the urine within 24 hours. No metabolites have been detected in the serum or urine of patients receiving cidofovir.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Pharmacokinetic parameters:</th>
<th>Protein binding: Molecular Wt: Vd: Half-life (t½): t½ in renal imp:</th>
<th>&lt;10% 279.19 daltons Adults: 0.388 ± 0.125 L/kg Adults: 2.2 hours Adults: 16-25 hours</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal dose:</td>
<td>Adenovirus, CMV:</td>
<td>5mg/kg iv once per week for two weeks (induction), then 5mg/kg iv every two weeks (maintenance) Administer with concomitant hyperhydration and probenecid in order to minimise potential nephrotoxicity.</td>
</tr>
</tbody>
</table>

| Dose adjustment in renal impairment: | GFR >55ml/min: GFR 10-55ml/min: GFR <10ml/min: | No dosage adjustment required - give normal dose 1mg/kg iv three times per week for two weeks (induction), then 1mg/kg iv every two weeks (maintenance) 0.5mg/kg iv once per week for two weeks (induction), then 0.5mg/kg iv every two weeks (maintenance) |

| Dose adjustment in HD: | Dialysed. Give 2mg/kg iv once per week for two weeks (induction), then 2mg/kg iv every two weeks (maintenance). Administer dose 2 hours before dialysis session to benefit from peak concentration without having delayed clearance. High-flux HD has been shown to reduce serum concentrations of cidofovir by 52% ± 11%. |

<table>
<thead>
<tr>
<th>Dose adjustment in PD:</th>
<th>Not dialysed. Give 0.5mg/kg iv once per week for two weeks (induction), then 0.5mg/kg iv every two weeks (maintenance)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intraperitoneal dose:</td>
<td>No information</td>
</tr>
<tr>
<td>Dose adjustment in CVVH:</td>
<td>Give 2mg/kg iv weekly for two weeks (induction), then 2mg/kg iv every two weeks (maintenance).</td>
</tr>
</tbody>
</table>

| Notes: | The manufacturers state that renal insufficiency or proteinuria >100mg/dL is a contraindication for the use of cidofovir. Dose-dependent nephrotoxicity is the major dose-limiting toxicity related to cidofovir administration. Constant serum levels of cidofovir are not required as it is the intracellular levels which provide antiviral effect. Probencid is unlikely to be effective in patients with GFR<30ml/minute. Patients on CAPD or HD should not receive hyperhydration or probenecid as the risk of fluid overload and probenecid adverse effects does not outweigh the benefit of administering these medications. |

---

**References:**

5. Lexi-comp online accessed via www.crlonline.com, accessed 29/12/10

Written by: Rachelle Booth (PICU Senior Specialist Pharmacist)
Checked by: Sue Patey (Renal Senior Specialist Pharmacist) and Dr Quen Mok (Consultant Paediatric Intensivist)
Approved by: Drugs & Therapeutics Committee
Date document created: November 2011
Date of interim review: May 2014 Reviewed by: Venetia Horn (PICU Senior Pharmacist) Checked by: Vani Suri (NICU Pharmacist)
Date for next review: September 2014
Version: 3

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<table>
<thead>
<tr>
<th>Drug:</th>
<th>CIPROFLOXACIN</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Usual route of Clearance:</strong></td>
<td>Ciprofloxacin and its active metabolites are eliminated primarily by the kidney, with approximately 40-70% of a dose being excreted unchanged in the urine. Non-renal clearance of ciprofloxacin is mainly due to active trans-intestinal secretion and metabolism, with approximately 1% of a dose eliminated via the biliary route.</td>
</tr>
<tr>
<td><strong>Pharmacokinetic parameters:</strong></td>
<td>PB: 20-40%&lt;sup&gt;1,3&lt;/sup&gt;&lt;br&gt;Mol Wt: 331.34 daltons&lt;sup&gt;4&lt;/sup&gt;&lt;br&gt;Vd: Adults: 2-3 L/kg&lt;sup&gt;1,2&lt;/sup&gt;&lt;br&gt;t½: Adults: 3-5 hours&lt;sup&gt;5&lt;/sup&gt;&lt;br&gt;t½ in renal imp: Paediatrics: 4-5 hours&lt;sup&gt;2&lt;/sup&gt;</td>
</tr>
<tr>
<td><strong>Normal dose (severe GI or respiratory tract infection):</strong></td>
<td>&lt;4 weeks of life: iv: 10mg/kg every 12 hours&lt;sup&gt;6,7&lt;/sup&gt;&lt;br&gt;po/ng: 15mg/kg every 12 hours&lt;sup&gt;6&lt;/sup&gt; &gt;4 weeks – 18yrs (including patients with cystic fibrosis): iv: 10mg/kg (max 400mg) every 8 hours&lt;sup&gt;6&lt;/sup&gt;&lt;br&gt;po/ng: 20mg/kg (max 750mg) every 12 hours&lt;sup&gt;6&lt;/sup&gt;</td>
</tr>
<tr>
<td><strong>Dose adjustment in renal impairment:</strong></td>
<td>GFR 30-50ml/min: No dosage adjustment required – give normal dose.&lt;sup&gt;1&lt;/sup&gt; GFR 10-30ml/min: Give 50&lt;sup&gt;2&lt;/sup&gt;-100&lt;sup&gt;1&lt;/sup&gt;% of the normal dose iv/po/ng every 12 hours&lt;sup&gt;1&lt;/sup&gt; GFR &lt;10ml/min: Give 50% of the normal dose iv/po/ng every 12 hours&lt;sup&gt;1,3,8&lt;/sup&gt;</td>
</tr>
<tr>
<td><strong>Dose adjustment in HD:</strong></td>
<td>&lt;10% removed by dialysis.&lt;sup&gt;9&lt;/sup&gt; Give 50% of the normal dose iv/po/ng every 12 hours&lt;sup&gt;3,8&lt;/sup&gt; administered after dialysis session OR give 100% of the normal dose iv/po/ng every 24 hours, administered after dialysis session&lt;sup&gt;2,9&lt;/sup&gt;</td>
</tr>
<tr>
<td><strong>Dose adjustment in PD:</strong></td>
<td>&lt;10% removed by dialysis.&lt;sup&gt;9&lt;/sup&gt; Give 100% of the normal dose iv/po/ng every 24 hours&lt;sup&gt;9&lt;/sup&gt;</td>
</tr>
<tr>
<td><strong>Intraperitoneal dose:</strong></td>
<td>25-100mg/L&lt;sup&gt;1&lt;/sup&gt;</td>
</tr>
<tr>
<td><strong>Dose adjustment in CVVH:</strong></td>
<td>Give 75&lt;sup&gt;4&lt;/sup&gt;-100%&lt;sup&gt;1,3,6,9&lt;/sup&gt; of the dose iv/po/ng every 12 hours</td>
</tr>
<tr>
<td><strong>Notes:</strong></td>
<td>Licensed for children over 1 year for specific indications.&lt;sup&gt;2&lt;/sup&gt; The bioavailability of the oral suspension is 70-80%.&lt;sup&gt;1,2&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

**References:**
2. Summary of Product Characteristics: EMC/Package Insert, Last updated: 12/11/08 Manufacturer: Bayer PLC

Written by: Rachelle Booth (PICU Senior Specialist Pharmacist)
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Approved by: Drugs & Therapeutics Committee
Date document created: November 2011
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Date for next review: September 2014
Version: 3

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### CLARITHROMYCIN

**Usual route of clearance:** Clarithromycin undergoes first-pass metabolism to form a microbiologically-active metabolite (14-hydroxyclarithromycin). Bioavailability of the active metabolite is reduced following iv administration. Approximately 33% of clarithromycin and 11% of the active metabolite is excreted unchanged in the urine.

Elimination of clarithromycin appears to follow non-linear pharmacokinetics, possibly due to saturable metabolism.

**Pharmacokinetic parameters:**

<table>
<thead>
<tr>
<th>Protein binding:</th>
<th>Molecular Wt:</th>
<th>Vd:</th>
</tr>
</thead>
<tbody>
<tr>
<td>80%³</td>
<td>747.95 daltons⁴</td>
<td>Adults: 2-4 L/kg³</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Adults: 3-7 hours³</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Prolonged²,³</td>
</tr>
</tbody>
</table>

**Normal dose:**

| <4 weeks of life: | iv: 7.5mg/kg every 12 hours³ |
|                  | po/ng: 7.5mg/kg every 12 hours⁶ |
| >4 weeks - 12ys: | iv: 7.5mg/kg (max 500mg) every 12 hours²,⁶,⁷ |
|                  | po/ng: <8kg: 7.5mg/kg every 12 hours; >8kg: dose band as per BNF-C⁶ |
| 12-18 years:     | iv: 500mg every 12 hours⁶ |
|                  | po/ng: 250-500mg every 12 hours⁶ |

**Dose adjustment in renal impairment:**

| GFR 30-50ml/min: | No dosage adjustment required - give normal dose¹,²,³,⁶,⁸,¹⁰ |
| GFR <30ml/min:   | Give 50% of normal dose iv/po/ng every 12 hours¹,²,³,⁶,⁷,⁸ |

**Dose adjustment in HD:**

| Dialysed:³ | po/ng: no dosage adjustment required - give normal dose³ |
|            | iv: give 50¹⁰-100%⁴ of dose every 24 hours⁴ after dialysis session⁸ |

**Dose adjustment in PD:**

| Unknown dialysability.³ | po/ng: no dosage adjustment required - give normal dose³ |
|                        | iv: give 50¹⁰-100%⁴ of dose every 24 hours⁴ |

**Intraperitoneal dose:**

| No information |

**Dose adjustment in CVVH:**

| po/ng: no dosage adjustment required - give normal dose³ |
| iv: give 50-100%⁴ of dose every 12 hours³ |

**Notes:**

- Vomiting may occur in patients with severe renal impairment receiving high doses.³
- Patients with hepatic impairment alone do not usually require a dosage adjustment as renal clearance of clarithromycin is increased in these patients,² however a dosage reduction will be required if patient has both renal and hepatic impairment, dose as per GFR <30ml/min.²

---

**References:**

1. Summary of Product Characteristics: EMC/Package Insert, Last updated: 08/01/10 Manufacturer: Abbott Laboratories Ltd
7. Guy's, St Thomas' and Lewisham Hospitals Trust. Paediatric Formulary, 8th edn. London, UK, 2010
8. Lexi-comp online accessed via www.cfronline.com, accessed 23/05/11

**Written by:** Rachelle Booth (PICU Senior Specialist Pharmacist)
**Checked by:** Sue Patey (Renal Senior Specialist Pharmacist) and Dr Quen Mok (Consultant Paediatric Intensivist)
**Date of last review:** 14/10/11

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<table>
<thead>
<tr>
<th>Drug:</th>
<th>CLINDAMYCIN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Usual route of clearance:</td>
<td>Clindamycin phosphate is biologically inactive and is hydrolysed to clindamycin, which undergoes metabolism to both active and inactive metabolites. High concentrations occur in bile. Approximately 10% is excreted in the urine as active drug or metabolites, approximately 4% is excreted in the faeces and the remainder is excreted as inactive metabolites.</td>
</tr>
<tr>
<td>Pharmacokinetic parameters:</td>
<td></td>
</tr>
<tr>
<td>Protein binding:</td>
<td>&gt;90%</td>
</tr>
<tr>
<td>Molecular Wt:</td>
<td>424.98 daltons</td>
</tr>
<tr>
<td>Vd: Adults: 0.6-1.2 L/kg, Adults and children: 2-3 hours, Infants 1month–1 year: 3 hours, Term neonates: 3.6 hours, Pre-term neonates: 8.7 hours</td>
<td></td>
</tr>
<tr>
<td>Half-life (t½):</td>
<td>t½ in renal imp: Adults: 3-5 hours</td>
</tr>
<tr>
<td>Normal dose:</td>
<td>&lt;2 weeks of life: 5mg/kg iv every 8 hours (may increase to 6 hourly if hepatic function is normal), 2-4 weeks of life: 5mg/kg iv every 8 hours, &gt;4 weeks - 12 yrs: Mild-moderate infection: 3.75-6.25mg/kg iv every 6 hours, Severe infection: 10mg/kg (max 1.2g) iv every 6 hours, 12-18 years: Mild-moderate infection: 150-675mg iv every 6 hours (or total daily dose may be given in 3 divided doses), Severe infection: up to 1.2g iv every 6 hours</td>
</tr>
<tr>
<td>Dose adjustment in renal impairment:</td>
<td>GFR 20-50ml/min: No dosage adjustment required - give normal dose, GFR 10-20ml/min: No dosage adjustment required - give normal dose, GFR &lt;10ml/min: No dosage adjustment required - give normal dose</td>
</tr>
<tr>
<td>Dose adjustment in HD:</td>
<td>Not dialysed, No dosage adjustment required - give normal dose</td>
</tr>
<tr>
<td>Dose adjustment in PD:</td>
<td>Not dialysed, No dosage adjustment required - give normal dose</td>
</tr>
<tr>
<td>Intraperitoneal dose:</td>
<td>Loading dose: 300mg/L, maintenance dose: 150mg/L</td>
</tr>
<tr>
<td>Dose adjustment in CVVH:</td>
<td>No dosage adjustment required - give normal dose</td>
</tr>
<tr>
<td>Notes:</td>
<td>Monograph written by: Rachelle Booth (PICU Senior Specialist Pharmacist) Monograph checked by: Sue Patey (Renal Senior Specialist Pharmacist) and Dr Quen Mok (Consultant Paediatric Intensivist) Date of interim review and update: 13/09/13, Updated by: Rachelle Booth, Checked by: Venetia Horn (NICU Specialist Pharmacist)</td>
</tr>
</tbody>
</table>

References:
1. Summary of Product Characteristics: EMC/Packaging Insert, Last updated: 08/09/09, Manufacturer: Pharmacia Ltd
4. Lexi-comp online accessed via www.crlonline.com, accessed 15/02/11

Written by: Rachelle Booth (PICU Senior Specialist Pharmacist) Checked by: Sue Patey (Renal Senior Specialist Pharmacist) and Dr Quen Mok (Consultant Paediatric Intensivist) Approved by: Drugs & Therapeutics Committee Date document created: November 2011 Date of interim review: May 2014 Reviewed by: Venetia Horn (PICU Senior Pharmacist) Checked by: Vani Suri (NICU Pharmacist) Date for next review: September 2014 Version: 3

© Gt Ormond St Hospital for Children Foundation Trust. While all care has been taken in the preparation of this guide, no responsibility will be taken by the authors for the drug doses, which should always be confirmed independently by the prescriber.
**Drug:** CO-AMOXICLAV (AMOXICILLIN+CLAVULANIC ACID)

**Usual route of clearance:**
The pharmacokinetics of amoxicillin and clavulanic acid are similar. Amoxicillin is largely excreted through the kidneys (52 ± 15% in unchanged form within 7 hours) with a small fraction excreted in the bile. Clavulanic acid is 50-70% metabolised, with approximately 40% eliminated via the kidneys, primarily by glomerular filtration, of which 18-38% is in the unchanged form. 

**Pharmacokinetic parameters:**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Protein binding</th>
<th>Molecular Wt:</th>
<th>Vd:</th>
<th>Half-life (t½):</th>
<th>t½ in renal imp:</th>
</tr>
</thead>
<tbody>
<tr>
<td>amoxicillin</td>
<td>~17-20%</td>
<td>365.40 daltons</td>
<td>Adult: ~0.3-0.4 L/kg</td>
<td>Adults: ~1 hour</td>
<td>Adults: 6 hours if CrCl 10-30ml/min and 10-15 hours in anuric patients, 2.6 hours if CrCl 20-70ml/min and 3-4 hours in anuric patients</td>
</tr>
<tr>
<td>clavulanic acid</td>
<td>~22-30%</td>
<td>199.16 daltons</td>
<td>Adult: ~0.2 L/kg</td>
<td>Children 2-15 years: 1.2 hours</td>
<td>Adults: 2.6 hours if CrCl 20-70ml/min and 3-4 hours in anuric patients</td>
</tr>
</tbody>
</table>

**Normal dose:**

**Intravenous:**
- <1 week of life & pre-term babies: 30mg/kg iv every 12 hours
- >1wk of life-3mths: 30mg/kg iv every 8 hours
- >3mths-18 yrs: 30mg/kg iv (max 1.2g) every 8 hours (increased to every 6 hours in severe infections)

**Enteral:**
- <4 weeks of life: 0.25ml/kg of 125/31 suspension every 8 hours
- >4 weeks - 1 year:
  - 1-6 years: 5ml of 125/31 suspension every 8 hours or 0.25ml/kg of 125/31 suspension every 8 hours (dose doubled in severe infection)
  - 6-12 years: 5ml of 250/62 suspension every 8 hours or 0.15ml/kg of 250/62 suspension every 8 hours (dose doubled in severe infection)
  - 12-18 years: One 250/125 strength tablet every 8 hours, increase in severe infection to one 500/125 strength tablet every 8 hours

**Dose adjustment in renal impairment:**

- GFR 30-50ml/min: No dosage adjustment required - give normal dose
- GFR 10-30ml/min: iv: Use normal initial dose, followed by 50% of dose every 12 hours
  po/ng: give normal dose every 12 hrs
- GFR <10ml/min: iv: Use normal initial dose, followed by 50% of dose every 24 hours
  po/ng: give 100% of the normal mild/moderate infection dose every 12 hours
| **Dose adjustment in HD:** | iv: give normal initial dose, followed by 50% of dose every 24 hours<sup>5</sup>  
| po/ng: give 50% of normal dose every 12 hrs<sup>10</sup> |
| **Dose adjustment in PD:** | iv: give normal initial dose, followed by 50% of dose every 24 hours<sup>4</sup>  
| po/ng: give 50% of normal dose every 12 hrs<sup>10</sup> |
| **Intraperitoneal dose:** | No information |
| **Dose adjustment in CVVH:** | iv: Use normal initial dose, followed by 50% of dose every 12 hours<sup>5</sup>  
| po/ng: give normal dose every 12 hours<sup>5</sup> |

**Notes:**

Monograph written by: Rachelle Booth (PICU Senior Specialist Pharmacist)  
Monograph checked by: Sue Patey (Renal Senior Specialist Pharmacist) and Dr Quen Mok (Consultant Paediatric Intensivist)  
Date of last review: 14/10/11

**References:**

1. Summary of Product Characteristics: EMC/Package Insert, Last updated: 11/07/07  
Manufacturer: GlaxoSmithKline UK

2. Summary of Product Characteristics: EMC/Package Insert, Last updated: 25/09/07  
Manufacturer: Wockhardt UK Ltd


### Drug: CO-TRIMOXAZOLE (TRIMETHOPRIM + SULFAMETHOXAZOLE)

#### Usual route of clearance:
- **Trimethoprim:** principal route of excretion is renal with approximately 50% of a dose excreted unchanged in the urine within 24 hours.\(^1\)
- **Sulfamethoxazole:** principal route of excretion is renal with approximately 15-30% excreted unchanged in the urine.\(^1\)
- Both trimethoprim and sulfamethoxazole undergo hepatic metabolism.\(^2\)

#### Pharmacokinetic parameters:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Trimethoprim</th>
<th>Sulfamethoxazole</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Protein binding:</strong></td>
<td>~50%(^1)</td>
<td>~66%(^1)</td>
</tr>
<tr>
<td><strong>Molecular Wt:</strong></td>
<td>290.32 daltons(^3)</td>
<td>253.28 daltons(^3)</td>
</tr>
<tr>
<td><strong>Vd:</strong></td>
<td>Adults: 1.0-2.2 L/kg(^4)</td>
<td>Adults: 0.28-0.38 L/kg(^4)</td>
</tr>
<tr>
<td><strong>Half-life (t(\frac{1}{2}):</strong></td>
<td>Adults: 8.6-17 hours(^1)</td>
<td>Children 1-10 years old: 5.5 hours(^1)</td>
</tr>
<tr>
<td></td>
<td>Infants &lt;1 year old: 7.7 hours(^2)</td>
<td>Adults: 12.9-51 hours(^1)</td>
</tr>
<tr>
<td><strong>t(\frac{1}{2}) in renal imp:</strong></td>
<td>5.5 hours(^2)</td>
<td>No change in the t(\frac{1}{2}) of sulfamethoxazole in renal impairment but the t(\frac{1}{2}) of the major metabolite is increased when CrCl &lt;25ml/min.(^1)</td>
</tr>
</tbody>
</table>

#### Normal dose:

<table>
<thead>
<tr>
<th>Condition</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment of PCP:</td>
<td>&gt;4 weeks of life: 60mg/kg every 12 hours iv/po/ng for 14-21 days, total daily dose may alternatively be given in 3-4 divided doses(^5)</td>
</tr>
<tr>
<td>Stenotrophomonas</td>
<td>&gt;4 weeks of life: 45mg/kg every 12 hours iv/po/ng(^6)</td>
</tr>
<tr>
<td>maltophilia:</td>
<td>See individual protocols as prophylactic regimens vary.</td>
</tr>
<tr>
<td>Prophylaxis:</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

#### Dose adjustment in renal impairment:

| GFR >30ml/min:          | No dosage adjustment required - give normal dose\(^1,4,5\) |
| GFR 15-30ml/min:        | Give 50% of normal dose.\(^1,4,5\) |
| GFR <15ml/min:          | If treating PCP, give normal dose for 3 days then give 50% of normal dose ie 30mg/kg iv/po/ng every 12 hours.\(^4,7\) |
|                         | Give 50% of normal iv/po/ng dose (no loading dose).\(^4,7,8,9\) |

#### Dose adjustment in HD:
- Dialysed.\(^9\) Give 50% of normal iv/po/ng dose.\(^4,7,8\)

#### Dose adjustment in PD:
- Not dialysed.\(^4,7\) Give 50% of normal iv/po/ng dose.\(^4,8\)

#### Intraperitoneal dose:
- 480mg/L\(^10\)

#### Dose adjustment in CVVH:
- Give 50% of normal iv/po/ng dose.\(^7\) |
- If treating PCP, give normal dose for 3 days then give 50% of normal dose ie 30mg/kg iv/po/ng every 12 hours.\(^4,8\)

#### Notes:

Monograph written by: Rachelle Booth (PICU Senior Specialist Pharmacist)
Monograph checked by: Sue Patey (Renal Senior Specialist Pharmacist) and Dr Quen Mok (Consultant Paediatric Intensivist)
Date of last review: 20/09/11
References:
1. Summary of Product Characteristics: EMC/Package Insert, Last updated: 31/07/09  Manufacturer: GlaxoSmithKline UK
6. Personal communication from GOSH microbiologist James Soothill 28/01/10 (local policy)
7. Guy’s, St Thomas’ and Lewisham Hospitals Trust. Paediatric Formulary, 8th edn. London, UK, 2010

Written by: Rachelle Booth (PICU Senior Specialist Pharmacist)
Checked by: Sue Patey (Renal Senior Specialist Pharmacist) and Dr Quen Mok (Consultant Paediatric Intensivist)
Approved by: Drugs & Therapeutics Committee
Date document created: November 2011
Date of interim review: May 2014 Reviewed by: Venetia Horn (PICU Senior Pharmacist) Checked by: Vani Suri (NICU Pharmacist)
Date for next review: September 2014
Version: 3

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<table>
<thead>
<tr>
<th>Drug:</th>
<th>COLISTIMETHATE (COLISTIN)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Usual route of clearance:</td>
<td>Colistimethate is predominantly renally cleared with 80% of a dose recovered unchanged in the urine at 24 hours.(^1,2) Colistimethate does not undergo biliary excretion.(^1) The remainder of the dose is thought to be inactivated in the tissues however the mechanism for this is unknown.(^1) The pharmacokinetics of colistimethate in children appears to be similar to that of adults.(^1)</td>
</tr>
<tr>
<td>Pharmacokinetic parameters:</td>
<td>Protein binding: Low(^1) Molecular Wt: 1749.82 daltons(^3) Vd: Adults: 0.09-0.34 L/kg(^2) Half-life (t½): Adults: 1.5(^1,2)-8 hours(^2) t½ in renal imp: Adults: 13-20 hours(^2)</td>
</tr>
<tr>
<td>Normal dose:</td>
<td>Cystic fibrosis: 1 month - 18 years old and &lt;60kg: 25000 units/kg iv every 8 hours(^4) &gt;60kg: 2 million units iv every 8 hours(^4)</td>
</tr>
<tr>
<td>Dose adjustment in renal impairment:</td>
<td>GFR 20-50ml/min: No dosage adjustment required - give normal dose(^1) GFR 10-20ml/min: Give 50% of normal dose iv every 12-18 hours(^1,2) GFR &lt;10ml/min: Give 50% of normal dose iv every 18-24 hours(^1,2)</td>
</tr>
<tr>
<td>Dose adjustment in HD:</td>
<td>Not dialysed.(^2) Give 50% of normal dose iv every 18-24 hours(^2)</td>
</tr>
<tr>
<td>Dose adjustment in PD:</td>
<td>Dialysed.(^2) Give 50% of normal dose iv every 18-24 hours(^2)</td>
</tr>
<tr>
<td>Intraperitoneal dose:</td>
<td>No information</td>
</tr>
<tr>
<td>Dose adjustment in CVVH:</td>
<td>Give 50% of normal dose iv every 18-24 hours(^5)</td>
</tr>
<tr>
<td>Notes:</td>
<td>Serum levels should be monitored in children with renal impairment; peak concentrations (30 minutes after the end of the infusion) should be maintained between 10-15mg/L (125-200units/ml).(^4)</td>
</tr>
</tbody>
</table>

Monograph written by: Rachelle Booth (PICU Senior Specialist Pharmacist)
Monograph checked by: Sue Patey (Renal Senior Specialist Pharmacist) and Dr Quen Mok (Consultant Paediatric Intensivist)
Date of last review: 20/09/11

References:
1. Summary of Product Characteristics: EMC/Package Insert, Last updated: 08/01/10 Manufacturer: Forest laboratories UK Ltd
5. Local practice at GOSH as at 24/02/10
### Drug: **ERYTHROMYCIN**

**Usual route of clearance:** Erythromycin is metabolised principally by demethylation in the liver and excreted in the bile. Approximately 12-15% is excreted in the active form in the urine.

**Pharmacokinetic parameters:**
- **Protein binding:**
- **Molecular Wt:** 70-95%[^4]
- **Vd:** 733.93 daltons[^5]
- **Half-life (t½):** Adults: 0.6-1.2 L/kg[^4]
- **t½ in renal imp:** Adults: ~2 hours[^2]
- **t½ in renal imp:** Adults: 4-7 hours in severe renal impairment[^2,^4]

**Normal dose:**
- **Gastric stasis:**
- **Chest infection:** 3mg/kg po/ng every 6 hours (all ages)[^6,^8]
- **Meningitis:** 12.5mg/kg (max 1g) iv every 6 hours (all ages)[^6,^7,^8]

**Dose adjustment in renal impairment:**
- **GFR 20-50ml/min:** No dosage adjustment required - give normal dose[^4,^6,^9]
- **GFR 10-20ml/min:** No dosage adjustment required - give normal dose[^4,^6,^9]
- **GFR <10ml/min:** Give 50-75% of normal total daily dose[^4], max 1.5g in 24 hours[^10]

**Dose adjustment in HD:** Not dialysed.[^4] Give 50-75% of normal dose every 6 hours;[^4] max 1.5g in 24 hours[^10]

**Dose adjustment in PD:** Not dialysed.[^4] Give 50-75% of normal dose every 6 hours;[^4] max 1.5g in 24 hours[^10]

**Intraperitoneal dose:** No information

**Dose adjustment in CVVH:** No dosage adjustment required - give normal dose[^4,^9,^11], max 1.5g in 24 hours[^10] unless treating meningoencephalitis – discuss with pharmacist

**Notes:**
- Despite being predominantly hepatically metabolised, toxicity (ototoxicity) has been seen in patients with severe renal impairment.[^8]
- The iv route should always be used if treating meningoencephalitis.
- Erythromycin may markedly elevate levels of other hepatically metabolised drugs such as ciclosporin and tacrolimus[^12] – ensure erythromycin drug interactions are always checked with the pharmacist.

---

**References:**
2. Summary of Product Characteristics: EMC/Package Insert, Last updated: 30/01/09 Manufacturer: Hospira UK Ltd
8. Guy's, St Thomas' and Lewisham Hospitals Trust. Paediatric Formulary, 8th edn. London, UK, 2010

---

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**Drug:** FLUCLOXACILLIN

**Usual route of clearance:** Flucloxacillin is metabolised to a limited extent and the metabolites are excreted in the urine by glomerular filtration and renal tubular secretion. Approximately 60-76% of a dose is recovered in the urine within 8 hours. Only small amounts are excreted in the bile.

**Pharmacokinetic parameters:**

<table>
<thead>
<tr>
<th>Protein binding:</th>
<th>Molecular Wt:</th>
<th>Vd:</th>
<th>Half-life (t½):</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- Adults: 1 hour
- Neonates: prolonged

**t½ in renal imp:**

- Adults: 2.25-2.9 hours

**Normal dose:**

<table>
<thead>
<tr>
<th>&lt;7 days of life:</th>
<th>7-21 days of life:</th>
<th>21-28 days of life:</th>
<th>&gt;4 weeks of life-18 years:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infection due to β-lactamase-producing <em>Staphylococci</em></td>
<td>Infection due to β-lactamase-producing <em>Staphylococci</em></td>
<td>Infection due to β-lactamase-producing <em>Staphylococci</em></td>
<td>Infection due to β-lactamase-producing <em>Staphylococci</em></td>
</tr>
<tr>
<td>25mg/kg iv every 12 hours, double dose in severe infection</td>
<td>25mg/kg iv every 8 hours, double dose in severe infection</td>
<td>25mg/kg iv every 6 hours, double dose in severe infection</td>
<td>12.5-25mg/kg (max 1g) iv every 6 hours, double dose in severe infection</td>
</tr>
<tr>
<td>Meningitis, osteomyelitis: 50-100mg/kg iv every 12 hours</td>
<td>Meningitis, osteomyelitis: 50-100mg/kg iv every 8 hours</td>
<td>Meningitis, osteomyelitis: 50-100mg/kg iv every 6 hours</td>
<td>Meningitis, osteomyelitis: 50mg/kg (max 2g) iv every 6 hours</td>
</tr>
</tbody>
</table>

**Dose adjustment in renal impairment:**

- GFR 20-50ml/min: No dosage adjustment required - give normal dose
- GFR 10-20ml/min: No dosage adjustment required - give normal dose
- GFR <10ml/min: Give normal dose iv every 8 hours

**Dose adjustment in HD:** Not dialysed. Give normal dose iv every 8 hours

**Dose adjustment in PD:** Not dialysed. Give normal dose iv every 8 hours

**Intraperitoneal dose:** No information

**Dose adjustment in CVVH:** Not filtered. Give normal dose iv every 8 hours

**Notes:**

Monograph written by: Rachelle Booth (PICU Senior Specialist Pharmacist)
Monograph checked by: Sue Patey (Renal Senior Specialist Pharmacist) and Dr Quen Mok (Consultant Paediatric Intensivist)
Date of last review: 20/09/11

**References:**

1. Summary of Product Characteristics: EMC/Package Insert, Last updated: 29/06/09 Manufacturer: Wockhardt UK Ltd

Written by: Rachelle Booth (PICU Senior Specialist Pharmacist)
Checked by: Sue Patey (Renal Senior Specialist Pharmacist) and Dr Quen Mok (Consultant Paediatric Intensivist)
Approved by: Drugs & Therapeutics Committee
Date document created: November 2011
Date of interim review: May 2014 Reviewed by: Venetia Horn (PICU Senior Pharmacist) Checked by: Vani Suri (NICU Pharmacist)
Date for next review: September 2014
Version: 3

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5. Guy’s, St Thomas’ and Lewisham Hospitals Trust. Paediatric Formulary, 8th edn. London, UK, 2010
6. Local practice at GOSH as at 24/02/10
Drug: **FLUCONAZOLE**

<table>
<thead>
<tr>
<th>Usual route of clearance:</th>
<th>Fluconazole is predominantly renally cleared, with approximately 80% of a dose excreted unchanged in the urine. There is no evidence of circulating metabolites.¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pharmacokinetic parameters:</td>
<td><strong>Protein binding:</strong></td>
</tr>
<tr>
<td><strong>Molecular Wt:</strong></td>
<td>306.27 daltons⁴</td>
</tr>
<tr>
<td><strong>Vd:</strong></td>
<td>0.65-0.7 L/kg⁵ &lt;br&gt;Paediatrics: 0.95 ± 0.39 L/kg²</td>
</tr>
<tr>
<td><strong>Half-life (t½):</strong></td>
<td>Adults: 30 hours³,⁵ &lt;br&gt;Paediatrics: 15-25 hours³ &lt;br&gt;Adults: 98 hours³</td>
</tr>
<tr>
<td><strong>t½ in renal imp:</strong></td>
<td>Adults: 30 hours³,⁵ &lt;br&gt;Paediatrics: 15-25 hours³ &lt;br&gt;Adults: 98 hours³</td>
</tr>
<tr>
<td>Normal dose:</td>
<td><strong>Prophylaxis:</strong></td>
</tr>
<tr>
<td><strong>Treatment of invasive infection:</strong></td>
<td>&lt;2 weeks of life: 6-12mg/kg every 72 hours po/iv²,⁷ &lt;br&gt;2-4 weeks of life: 6-12mg/kg every 48 hours po/iv² &lt;br&gt;4 weeks of life: 6-12mg/kg (max 800mg) every 24 hours po/iv²</td>
</tr>
<tr>
<td>Dose adjustment in renal impairment:</td>
<td>GFR &gt;50ml/min:</td>
</tr>
<tr>
<td><strong>GFR &lt;50ml/min:</strong></td>
<td>Give 1x normal dose initially, followed by 50% of the normal dose¹,⁷,⁹</td>
</tr>
<tr>
<td>Dose adjustment in HD:</td>
<td>Dialysed.³,⁵,⁷ Give 50% of the normal dose daily,⁵ or give 100% of the dose three times a week, administered after dialysis session³,⁹,¹⁰,¹¹</td>
</tr>
<tr>
<td>Dose adjustment in PD:</td>
<td>Dialysed.³,⁵ Give 50% of the normal dose daily³,⁵,¹⁰</td>
</tr>
<tr>
<td>Intraperitoneal dose:</td>
<td>Not recommended¹²</td>
</tr>
<tr>
<td>Dose adjustment in CVVH:</td>
<td>Filtered.⁵ No dosage adjustment required,¹⁰ but give upper range of normal dose.²</td>
</tr>
</tbody>
</table>

Notes:

Monograph written by: Rachelle Booth (PICU Senior Specialist Pharmacist) <br>Monograph checked by: Sue Patey (Renal Senior Specialist Pharmacist) and Dr Quen Mok (Consultant Paediatric Intensivist) <br>Date of interim review and update: 11/09/13, Updated by: Rachelle Booth, Checked by: Venetia Horn (NICU Specialist Pharmacist)

References:

**Drug:** GANCICLOVIR

**Usual route of clearance:** The major route of elimination is renal excretion of unchanged drug by glomerular filtration and active tubular secretion\(^1\) (approximately 80-100% of a dose is excreted unchanged).\(^2,3\)

**Pharmacokinetic parameters:**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protein binding</td>
<td>1-2%(^2,4,6)</td>
</tr>
<tr>
<td>Molecular Wt:</td>
<td>255.23(^7)</td>
</tr>
<tr>
<td>Vd:</td>
<td>Adults: 0.54-0.87 L/kg(^2)</td>
</tr>
<tr>
<td></td>
<td>Paediatrics: 0.64 ± 0.22 L/kg(^3,3)</td>
</tr>
<tr>
<td>Half-life (t(\frac{1}{2}))</td>
<td>Adults: 2.73 ± 1.29 – 3.98 ± 1.78 hours(^4)</td>
</tr>
<tr>
<td></td>
<td>Children: 2.49 ± 0.57 hours(^4)</td>
</tr>
<tr>
<td></td>
<td>Neonates and infants up to 49 days old: 2.4 hours(^3)</td>
</tr>
<tr>
<td></td>
<td>Adults: 2.9-28.5 hours(^1)</td>
</tr>
<tr>
<td>t(\frac{1}{2}) in renal imp:</td>
<td>1-2%(^2,4,6)</td>
</tr>
</tbody>
</table>

**Normal dose:** CMV, VZV: >4 weeks of life: 5mg/kg iv every 12 hours\(^6,8\)

**Dose adjustment in renal impairment:**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose (mg/kg iv every 12 hours)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;70</td>
<td>5</td>
</tr>
<tr>
<td>50-70</td>
<td>2.5</td>
</tr>
<tr>
<td>25-50</td>
<td>2.5</td>
</tr>
<tr>
<td>10-25</td>
<td>1.25</td>
</tr>
<tr>
<td>&lt;10</td>
<td>1.25</td>
</tr>
</tbody>
</table>

**Dose adjustment in HD:** Dialysed.\(^3\) Approximately 40-50% is removed by a four-hour dialysis session.\(^3\)

**Dose adjustment in PD:** Give 1.25mg/kg iv every 24 hours\(^6,9\)

**Intraperitoneal dose:** No information

**Dose adjustment in CVVH:** 2.5mg/kg iv every 24 hours\(^4,9,10\)

**Notes:** Nephrotoxic. Monitor for signs of myelosuppression.

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**References:**
1. Summary of Product Characteristics: EMC/Package Insert, Last updated: 21/04/06 Manufacturer: Roche Products Ltd
3. Lexi-comp online accessed via www.crlonline.com, accessed 16/12/10

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Drug: GENTAMICIN

Usual route of clearance: Gentamicin does not undergo metabolism and is 90% excreted unchanged in the urine by glomerular filtration. Small amounts of gentamicin appear in the bile.

Pharmacokinetic parameters:

- **Protein binding:**
  - Molecular Wt: 463.97 daltons
  - Adults: 0.31 L/kg
  - Adolescents: 0.3 ± 0.1 L/kg
  - Children: 0.35 ± 0.15 L/kg
  - Infants: 0.4 ± 0.1 L/kg
  - Neonates: 0.45 ± 0.1 L/kg
- **Molecular Wt:**
  - Adults: 0.3 L/kg
  - Adolescents: 0.3 ± 0.1 L/kg
  - Children: 0.35 ± 0.15 L/kg
  - Infants: 0.4 ± 0.1 L/kg
  - Neonates: 0.45 ± 0.1 L/kg
- **Vd:**
  - Adults: 0.31 L/kg
  - Adolescents: 0.3 ± 0.1 L/kg
  - Children: 0.35 ± 0.15 L/kg
  - Infants: 0.4 ± 0.1 L/kg
  - Neonates: 0.45 ± 0.1 L/kg
- **Half-life (t½):**
  - Adults: 2-3 hours
  - Adolescents: 1.5 ± 1 hour
  - Children: 2 ± 1 hour
  - Infants: 4 ± 1 hour
  - Neonates: 7-28 days: 3-6 hours
  - Neonates <7 days: 3-11.5 hours

- **Prolonged t½ in renal imp:**
  - Adults: 0-30%
  - Adolescents: 0-30%
  - Children: 0-30%

Normal dose:

- **Neonate <32wks postmenstrual age:**
  - Neonate ≥ 32wks postmenstrual age:
  - Cystic fibrosis:
  - All other patients >4 weeks of life:

Dose adjustment in renal impairment:

- GFR 30-70ml/min:
  - 3-5mg/kg iv
  - 2-3mg/kg iv
  - 2mg/kg iv
- GFR 10-30ml/min:
  - Take trough level after 24 hours, and hold next dose until trough level is available.
  - Adjust dosage interval according to serum levels aim to keep trough <1mg/L and peak 5-10mg/L.
- GFR <10ml/min:
  - 3-2mg/kg iv

Dose adjustment in HD:

- Dialysed: Give 2mg/kg iv, take trough level after 24 hours, and hold next dose until trough level is available. Adjust dosage interval according to serum levels aim to keep trough <1mg/L and peak 5-10mg/L.

Dose adjustment in PD:

- Dialysed: Give 2mg/kg iv, take trough level after 24 hours, and hold next dose until trough level is available. Adjust dosage interval according to serum levels aim to keep trough <1mg/L and peak 5-10mg/L.

Intraperitoneal dose:

- Loading dose 8mg/L, maintenance dose 4mg/L

Dose adjustment in CVVH:

- Give 4-5mg/kg iv, take trough level after 24 hours, and hold until trough level is available. Adjust dosage interval according to serum levels aim to keep trough <1mg/L and peak 5-10mg/L.

Notes:

- Peak levels are only required for doses <7mg/kg.
- Repeat levels daily in renal impairment or if on any form of dialysis/haemofiltration.
- Take care not to underdose; ensure that a therapeutic peak level is maintained.
- The above regimens are not suitable for patients with endocarditis; discuss with pharmacist.

Monograph written by: Rachelle Booth (PICU Senior Specialist Pharmacist)
Monograph checked by: Sue Patey (Renal Senior Specialist Pharmacist) and Dr Quen Mok (Consultant Paediatric Intensivist)
Date of last review: 06/06/11

Written by: Rachelle Booth (PICU Senior Specialist Pharmacist)
Checked by: Sue Patey (Renal Senior Specialist Pharmacist) and Dr Quen Mok (Consultant Paediatric Intensivist)
Approved by: Drugs & Therapeutics Committee
Date document created: November 2011
Date of interim review: May 2014
Reviewed by: Venetia Horn (PICU Senior Pharmacist)
Checked by: Vani Suri (NICU Pharmacist)
Date for next review: September 2014
Version: 3

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References:
2. Summary of Product Characteristics: EMC/Package Insert, Last updated: 28/04/09, Manufacturer: Hospira UK Ltd
5. Lexi-comp online accessed via www.crilonline.com, accessed 06/06/11
7. Summary of Product Characteristics: EMC/Package Insert, Last updated: 24/09/08, Manufacturer: Winthrop Pharmaceuticals Ltd
8. Summary of Product Characteristics: EMC/Package Insert, Last updated: 27/05/09, Manufacturer: Amdipharm

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**Drug:** IMIPENEM + CILASTATIN

**Usual route of clearance:**
Cilastatin is an enzyme inhibitor which blocks the metabolism of imipenem in the kidney, increasing the plasma concentration, AUC, and urinary concentration of imipenem.\(^1,2\)

When imipenem and cilastatin are administered concurrently in a 1:1 ratio approximately 50-70% of the imipenem dose and 75% of the cilastatin dose is excreted unchanged in the urine within 10 hours by both glomerular filtration and tubular secretion.\(^2\)

Imipenem also undergoes a degree of non-renal metabolism with approximately 20-30% of an imipenem dose undergoing hydrolysis of the beta-lactam ring to form a microbiologically inactive metabolite.\(^2\)

Approximately 12% of a dose of cilastatin undergoes metabolism in the kidneys to N-acetylcilastatin; the remaining metabolic pathways of cilastatin are unknown.\(^6\)

Less than 1% of an imipenem dose and less than 2% of a cilastatin dose are excreted in the faeces.\(^2\)

**Pharmacokinetic parameters:**

| Protein binding | imipenem: 13-21%\(^2,3\) | cilastatin: ~40%\(^2,3,4\) |
| Molecular Wt: | imipenem: 299.35 daltons\(^5\) | cilastatin: 358.45 daltons\(^5\) |
| Vd: | imipenem: Adults: 0.23 L/kg\(^4\)  
Paediatrics: 0.5 L/kg\(^4\)  
Neonates 1-8 days old: 0.251-0.418 L/kg\(^4\)  
| | cilastatin: Adults: 0.2 L/kg\(^4\)  
Paediatrics: 0.4 L/kg\(^2\)  
| Half-life (t\(^1/2\): | imipenem: Children aged 2-12 years: 1.1-1.3 hours\(^2\)  
Neonates 1-10 days old: 1.5-2.6 hours\(^2\)  
| | cilastatin: Adults: 0.83-1.1 hours\(^2\)  
Neonates: 3.1-8.8 hours\(^2\)  
| t\(^1/2\) in renal imp: | imipenem: Adults: 2.1-3.7 hours\(^2\)  
| | cilastatin: Adults: 2.5-17 hours\(^6\)  
| Normal dose: | <1 week of life: 20mg/kg iv every 12 hours\(^6,7\)  
1-3 weeks of life: 20mg/kg iv every 8 hours\(^6,7\)  
3 weeks - 3 months: 20mg/kg iv every 6 hours\(^6,7\)  
3 months - 18 yrs: <40kg: 15mg/kg (max 500mg) iv every 6 hours\(^6\)  
>40kg: 250-500mg iv every 6 hours; \(^6\) less sensitive organisms 12.5mg/kg (max 1g) iv every 6 hours\(^6\)  
| Cystic fibrosis: | See doses in BNF-C\(^6\) |

**Dose adjustment in renal impairment:**

| GFR 30-70ml/min: | >4 weeks of life: Give 80-100% of dose every 8 hours\(^4\)  
| GFR 20-30ml/min: | >4 weeks of life: Give 80-100% of dose every 12 hours\(^4\)  
| GFR <20ml/min: | >4 weeks of life: Give 30-50% of dose every 12 hours\(^4\)  
| GFR <5ml/min: | Do not start imipenem/cilastatin unless haemodialysis or haemofiltration is to be started within 48 hours\(^1\)  

**Dose adjustment in HD:**
Give normal dose iv every 12 hours, administered after dialysis session

**Dose adjustment in PD:**
Give 50% of the normal dose every 24 hours\(^9\)

**Intraperitoneal dose:**
Loading dose: 500mg/L, maintenance dose: 200mg/L\(^8,9\)

**Dose adjustment in CVVH:**
Give 80-100% of normal dose iv every 8-12 hours\(^4\)

---

**Written by:** Rachelle Booth (PICU Senior Specialist Pharmacist)
**Checked by:** Sue Patey (Renal Senior Specialist Pharmacist) and Dr Quen Mok (Consultant Paediatric Intensivist)
**Approved by:** Drugs & Therapeutics Committee
**Date document created:** November 2011
**Date of interim review:** May 2014
**Reviewed by:** Venetia Horn (PICU Senior Pharmacist)  
**Checked by:** Vani Suri (NICU Pharmacist)
**Date for next review:** September 2014
**Version:** 3

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Notes: Increased risk of convulsions when imipenem/cilastatin is used in patients with renal impairment\(^\text{10}\) (it may be more appropriate to change treatment to meropenem).

References:
1. Summary of Product Characteristics: EMC/Package Insert, Last updated: 05/03/09 Manufacturer: Merck Sharp & Dohme Limited
3. Lexi-comp online accessed via www.cronline.com, accessed 06/06/11

Written by: Rachelle Booth (PICU Senior Specialist Pharmacist)
Checked by: Sue Patey (Renal Senior Specialist Pharmacist) and Dr Quen Mok (Consultant Paediatric Intensivist)
Date of last review: 06/06/11

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### Drug:
**LINEZOLID**

| **Usual route of clearance:** | The (s)-linezolid enantiomer is biologically active and is primarily metabolised by oxidation to form two inactive metabolites; the predominant metabolite is thought to be formed by a non-enzymatic process. Non-renal clearance accounts for approximately 65% of the total clearance of linezolid. |
| **Pharmacokinetic parameters:** | **Protein binding:** | Approximately 31%<sup>1,2,3,4</sup>  
337.35 daltons<sup>4</sup>  
**Molecular Wt:** |  
**Vd:** | Adults: 0.6 L/kg<sup>3</sup>  
Paediatrics: 0.73 ± 0.18 L/kg<sup>4</sup>  
**Half-life (t½):** | Preterm neonates <7 days of life: 5.6 hours<sup>1</sup>  
Full-term neonates <7 days of life: 3 hours<sup>1</sup>  
Neonates 7-28 days of life: 1.5 hours<sup>1</sup>  
Infants >28 days to 2 months: 1.8 hours<sup>1</sup>  
Children 3 months to 11 years: 2.9 hours<sup>1</sup>  
Adolescents 12–17 years: 3.1 hours<sup>1</sup>  
**t½ in renal imp:** | Unchanged<sup>9</sup>  
**Normal dose:** | <1 week of life: | 10mg/kg iv/po/ng every 12 hours<sup>1,5,6,7</sup> increase to every 8 hours if poor response<sup>9</sup>  
>1 week – 12 yrs: | 10mg/kg (max 600mg) iv/po/ng every 8 hours<sup>1,5,6,7</sup>  
>12 years: | 600mg iv/po/ng every 12 hours<sup>1,5,6,7</sup> |
| **Dose adjustment in renal impairment:** | GFR 20-50ml/min: | No dosage adjustment required - give normal dose<sup>2,3,8,9</sup>  
GFR 10-20ml/min: | No dosage adjustment required - give normal dose<sup>2,3,8,9</sup>  
GFR <10ml/min: | No dosage adjustment required - give normal dose<sup>2,3,8,9</sup>  
| **Dose adjustment in HD:** | Dialysed. No dosage adjustment required - give normal dose, administered after dialysis session<sup>2,3,4</sup>  
| **Dose adjustment in PD:** | Likely to be dialysed. No dosage adjustment required - give normal dose<sup>3</sup>  
| **Intraperitoneal dose:** | No information  
| **Dose adjustment in CVVH:** | No dosage adjustment required - give normal dose<sup>3,4,9,10</sup>  
| **Notes:** | While no dosage adjustment is required in renal impairment, note that the metabolites may accumulate if the estimated GFR is <30ml/min/1.73m<sup>2</sup>, and that these metabolites may have NAOI activity. Patients with severe renal impairment may have 10-fold increases in serum levels of the inactive metabolites, the clinical significance of which is unknown. As linezolid is metabolised by a non-enzymatic process, impairment of hepatic function is not expected to significantly alter its metabolism. |

**References:**
2. Summary of Product Characteristics: EMC/Package Insert, Last updated: 14/10/09 Manufacturer: Pharmacia
7. Guy’s, St Thomas’ and Lewisham Hospitals Trust. Paediatric Formulary, 8th edn. London, UK, 2010

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**Date of last review:** 29/07/11
## Meropenem

**Drug:** MEROPENEM

### Usual route of clearance:

Approximately 70% of a dose is excreted unchanged in the urine over 12 hours. The only metabolite of meropenem is microbiologically inactive.

### Pharmacokinetic parameters:

- **Protein binding:**
  - Approximately 2%<sup>1,2,3</sup>
  - 383.46 daltons<sup>4</sup>
- **Molecular Wt:**
  - 335.46 daltons
- **Vd:**
  - Adults: 0.35 L/kg<sup>2</sup>
  - Children: 0.43 ± 0.06 L/kg<sup>3</sup>
- **Half-life (t½):**
  - Adults: 1 hour<sup>1,2</sup>
  - Children <2 years: 1.5-2.3 hours
  - Adults: 6-13.7 hours<sup>2</sup>
- **t½ in renal imp:**
  - Approximately 2%<sup>1,2,3</sup>

### Normal dose:

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;7 days</td>
<td>20mg/kg (severe infection/meningitis 40mg/kg) iv every 12 hours&lt;sup&gt;5,6,7&lt;/sup&gt;</td>
</tr>
<tr>
<td>7-28 days</td>
<td>20mg/kg (severe infection/meningitis 40mg/kg) iv every 8 hours&lt;sup&gt;5,6,7&lt;/sup&gt;</td>
</tr>
<tr>
<td>1 month-12 years and &lt;50kg</td>
<td>10-20mg/kg (severe infection/meningitis 40mg/kg) iv every 8 hours (up to max 6g/day)&lt;sup&gt;6&lt;/sup&gt;</td>
</tr>
<tr>
<td>12-18 years or &gt;50kg</td>
<td>0.5-1g (severe infection/meningitis 2g) iv every 8 hours&lt;sup&gt;6&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

### Dose adjustment in renal impairment:

| GFR 20-50ml/min | Give normal dose iv every 12 hours<sup>1,6,7,8</sup> |
| GFR 10-20ml/min | Give 50% of dose iv every 12 hours<sup>1,6,7,8</sup> |
| GFR <10ml/min   | Give 50% of dose iv every 24 hours<sup>1,6,7,8,9,10</sup> |

### Dose adjustment in HD:

Dialysed.<sup>2,7</sup> Give 50% of dose iv every 24 hours, administered after dialysis session<sup>1,8,10</sup>

### Dose adjustment in PD:

Dialysed.<sup>2,7</sup> Give 50% of dose iv every 24 hours<sup>7,9,10</sup>

### Intraperitoneal dose:

100mg/L<sup>2</sup>

### Dose adjustment in CVVH:

Give 100% of normal dose every 12 hours<sup>2,10</sup> or every 8 hours<sup>1</sup> depending upon severity of infection (eg for meningitis) – discuss with pharmacist.

### Notes:

Meropenem has less potential to induce seizures than imipenem.<sup>2</sup>

Licensed for children over 3 months old.<sup>6</sup>

---

**References:**

7. Guy's, St Thomas' and Lewisham Hospitals Trust. Paediatric Formulary, 8th edn. London, UK, 2010
<table>
<thead>
<tr>
<th>Drug:</th>
<th>METRONIDAZOLE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Usual route of clearance:</td>
<td>Metronidazole is predominantly metabolised by hepatic oxidation. Approximately 10% to 20% of a dose is excreted in the urine as unchanged drug.</td>
</tr>
</tbody>
</table>

### Pharmacokinetic parameters:

<table>
<thead>
<tr>
<th>Protein binding:</th>
<th>Molar binding:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vd:</td>
<td></td>
</tr>
<tr>
<td>Half-life (t½):</td>
<td></td>
</tr>
<tr>
<td>t½ in renal imp:</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>GFR 20-50ml/min:</th>
<th>Dose adjustment required - give normal dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>GFR 10-20ml/min:</td>
<td></td>
</tr>
<tr>
<td>GFR &lt;10ml/min:</td>
<td></td>
</tr>
</tbody>
</table>

### Normal dose:

- **<4 weeks of life:**
  - 7.5mg/kg iv/po/ng every 12 hours
  - 7.5mg/kg (max 400mg) po/ng every 8 hours
  - 7.5mg/kg (max 500mg) iv every 8 hours

- **>4 weeks of life:**
  - No dosage adjustment required

### Dose adjustment in renal impairment:

- **Dialysed:**
  - No dosage adjustment required
  - give normal dose

### Dose adjustment in HD:

- **Dialysed:**
  - No dosage adjustment required
  - give normal dose

### Dose adjustment in PD:

- **Dialysed:**
  - No dosage adjustment required
  - give normal dose

### Intraperitoneal dose:

- No information

### Dose adjustment in CVVH:

- No dosage adjustment required
  - give normal dose

### Notes:

- Although the elimination half-life is unchanged in the presence of renal impairment, the clearance of the metabolites is reduced, the significance of which is unknown.
- The incidence of gastrointestinal and vestibular toxicity is increased in patients on metronidazole with renal impairment.
- A 50% to 67% decrease in dosage is required in patients with hepatic impairment.

---

**References:**

10. Guy’s, St Thomas’ and Lewisham Hospitals Trust. Paediatric Formulary, 8th edn. London, UK, 2010

**Written by:** Rachelle Booth (PICU Senior Specialist Pharmacist)
**Checked by:** Sue Patey (Renal Senior Specialist Pharmacist) and Dr Quen Mok (Consultant Paediatric Intensivist)
**Approved by:** Drugs & Therapeutics Committee

**Date document created:** November 2011
**Date of interim review:** May 2014
**Reviewed by:** Venetia Horn (PICU Senior Pharmacist) **Checked by:** Vani Suri (NICU Pharmacist)
**Date for next review:** September 2014
**Version:** 3

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Drug: **MICAFUNGIN**

**Usual route of clearance:** Micafungin exhibits linear pharmacokinetics.\(^1\) Elimination of micafungin is primarily non-renal,\(^1\) with micafungin undergoing hepatic metabolism and then excretion in the faeces.\(^2\) Less than 1% of a dose is eliminated renally.\(^3\)

<table>
<thead>
<tr>
<th>Pharmacokinetic parameters:</th>
<th>PB: &gt;99%(^1,2,3,4,5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mol Wt:</td>
<td>1292.3 daltons(^4)</td>
</tr>
<tr>
<td>Vd:</td>
<td>Adults: 18-19L(^1) or 0.39 ± 0.11 L/kg(^3)</td>
</tr>
<tr>
<td></td>
<td>Children 9-17 years: 0.28 ± 0.09 L/kg(^3)</td>
</tr>
<tr>
<td></td>
<td>Children 2-8 years: 0.35 ± 0.18 L/kg(^3)</td>
</tr>
<tr>
<td></td>
<td>Neonates: 0.34-0.76 L/kg(^3)</td>
</tr>
<tr>
<td>t(^{1/2}):</td>
<td>Adults: 10-17 hours(^1)</td>
</tr>
<tr>
<td></td>
<td>Children 9-17 years: 13.3 ± 4.3 hours(^3)</td>
</tr>
<tr>
<td></td>
<td>Children 2-8 years: 11.6 ± 2.8 hours(^3)</td>
</tr>
<tr>
<td></td>
<td>Neonates: 6.7 ± 2.2 hours(^3)</td>
</tr>
</tbody>
</table>

**t\(^{1/2}\) in renal imp:** No information

**Normal dose:**

- <4 weeks of life: 2mg/kg iv once daily, increased to 4mg/kg iv once daily if inadequate response.\(^6\)
- >4 wks and <40kg: 2mg/kg iv once daily, increased to 4mg/kg iv once daily (max 200mg) if inadequate response.\(^6\)
- >40kg: 100mg iv once daily (increased to 200mg/kg iv once daily if inadequate response).\(^1,6\)

**Dose adjustment in renal impairment:**

- GFR 20-50ml/min: No dosage adjustment required - give normal dose\(^1,2,3,5\)
- GFR 10-20ml/min: No dosage adjustment required - give normal dose\(^1,2,3,5\)
- GFR <10ml/min: No dosage adjustment required - give normal dose\(^1,2,3,5\)

**Dose adjustment in HD:** Not dialysed.\(^2,3\) No dosage adjustment required - give normal dose\(^5\)

**Dose adjustment in PD:** Not dialysed.\(^2,3\) No dosage adjustment required - give normal dose\(^5\)

**Intraperitoneal dose:** No information

**Dose adjustment in CVVH:** Unlikely to be filtered. No dosage adjustment required - give normal dose\(^5\)

**Notes:**

Mean values of clearance in younger children (2 – 11 years) are approximately 1.3-fold greater than those in older children (12 – 17 years). Older children exhibit mean clearance values similar to those adults. Mean clearance in premature infants (gestational age approximately 26 weeks) is approximately 5-fold greater than in adults.\(^1\) While no dosage adjustment is required in renal impairment, micafungin should be used with caution, as it may cause a further deterioration in renal function.\(^6\)

No adjustment needed in mild-to-moderate hepatic impairment; the effect of severe hepatic impairment on micafungin pharmacokinetics has not been studied.\(^3\)

---

**References:**

1. Summary of Product Characteristics: EMC/Package Insert, Last updated: 03/12/09 Manufacturer: Astellas Pharma Ltd
3. Lexi-comp online accessed via [www.crlonline.com](http://www.crlonline.com), accessed 16/12/10

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**Drug:** OSELTAMIVIR

**Usual Route of Clearance:** Oseltamivir is predominantly eliminated by conversion to oseltamivir carboxylate, an active metabolite, by liver esterases. The active metabolite is then eliminated entirely by renal excretion. Less than 20% of an oral dose is excreted in the faeces.

**Pharmacokinetic parameters:**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protein binding</td>
<td>42% (oseltamivir carboxylate: 3%)</td>
</tr>
<tr>
<td>Molecular Wt.</td>
<td>312.40 daltons</td>
</tr>
<tr>
<td>Vd</td>
<td>Adults: 0.3-0.4 L/kg</td>
</tr>
<tr>
<td>Half-life (t½)</td>
<td>Adults: 1-3 hours, (oseltamivir carboxylate: 6-10 hours)</td>
</tr>
<tr>
<td>t½ in renal imp.</td>
<td>Adults: &gt;20 hours</td>
</tr>
</tbody>
</table>

**Normal dose:**

**Treatment:**

Dose is given twice daily for 5 days or as clinically indicated.

- Premature neonate (<38 weeks postmenstrual age):
  - 1mg/kg orally twice daily
- 0-1 month: 2mg/kg orally twice daily
- 1-3 months: 2.5mg/kg orally twice daily
- 3 months-1 year: 3mg/kg orally twice daily

- Age 1-13 years and:
  - 10-15kg: 30mg orally twice daily
  - >15-23kg: 45mg orally twice daily
  - >23-40kg: 60mg orally twice daily
  - >40kg: 75mg orally twice daily

**Prophylaxis:**

Dose is given once daily for 10 days.

- Premature neonate (<38 weeks postmenstrual age):
  - 1mg/kg orally twice daily
- 0-1 month: 2mg/kg orally once daily
- 1-3 months: 2.5mg/kg orally once daily
- 3 months-1 year: 3mg/kg orally once daily

- Age 1-13 years and:
  - 10-15kg: 30mg orally once daily
  - >15-23kg: 45mg orally once daily
  - >23-40kg: 60mg orally once daily
  - >40kg: 75mg orally once daily

**Dose adjustment in renal impairment:**

- GFR >30ml/min: Give normal dose
- GFR 10-30ml/min: Treatment: give 100% of the normal dose every 24 hrs
- GFR <10ml/min: Treatment: give 50% of the normal dose as a single stat dose (for longer courses, maximum 10 days)

**Dose adjustment in HD:**

- Treatment: give 50% of the normal dose after each dialysis session
- Prophylaxis: give 50% of the normal dose after each dialysis session

**Dose adjustment in PD:**

- Treatment: give 50% of the normal dose as a single dose once a week, after dialysate exchange
- Prophylaxis: give 50% of the normal dose as a single stat dose. A second dose may be given after one week

**Dose adjustment in CVVH:**

- Treatment: give 100% of the normal dose every 24 hours
- Prophylaxis: give 100% of the normal dose every 48 hours

**Notes:**

The use of oseltamivir in patients with CrCl<10ml/min and for patients...
receiving renal replacement therapy is not recommended by the manufacturer and there is no definitive dose guidance. Patients must be monitored closely for efficacy, adverse effects and signs of toxicity. Gastrointestinal side effects and dizziness are more common in renal impairment. See Trust Guidelines and discuss all use of oseltamivir with microbiology.

References:
7. Gt Ormond St Hospital for Children NHS Trust Oseltamivir Treatment and Prophylaxis in Renal Impairment – Paediatric Nephrology Guideline July 2009, developed in conjunction with RCPCH, BAPN, UKRPG & Dept of Health Guidelines.
# Piperacillin + Tazobactam

**Drug:** Piperacillin + Tazobactam

**Usual route of clearance:** Piperacillin is excreted rapidly as unchanged drug, with 68% of the administered dose appearing in the urine. Tazobactam is metabolised to a single inactive metabolite, with 80% of a dose appearing in the urine unchanged and the remainder as the inactive metabolite. Both piperacillin and tazobactam are eliminated by the kidney via glomerular filtration and tubular secretion. There is also some biliary excretion of piperacillin, tazobactam, and the desethyl piperacillin metabolite.

**Pharmacokinetic parameters:**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Piperacillin</th>
<th>Tazobactam</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protein binding</td>
<td>20-30%</td>
<td>20-30%</td>
</tr>
<tr>
<td>Molecular Wt</td>
<td>515.55 daltons</td>
<td>300.29 daltons</td>
</tr>
<tr>
<td>Vd</td>
<td>Adults: 0.18-0.3 L/kg, Paediatrics: 0.21 ± 0.1 L/kg</td>
<td>Adults: 0.18-0.33 L/kg, Paediatrics: 0.35 ± 0.1 L/kg</td>
</tr>
<tr>
<td>Half-life (t½)</td>
<td>Adults: 0.7-1.2 hours, Children 2-12 years: 0.7 hours, Children 6-12 years: 0.9 hours, Children 2-5 years: 0.8 hours</td>
<td>Adults: 4-6 hours, Children: 7 hours</td>
</tr>
</tbody>
</table>

**Normal dose:**

<table>
<thead>
<tr>
<th>Age</th>
<th>Piperacillin</th>
<th>Tazobactam</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1 month</td>
<td>90mg/kg iv every 8 hours</td>
<td>90mg/kg iv every 6 hours</td>
</tr>
<tr>
<td>&gt;1 month &amp; &lt;10.49kg</td>
<td>1080mg iv every 6 hours</td>
<td>1440mg iv every 6 hours</td>
</tr>
<tr>
<td>10.5-13.9kg</td>
<td>1890mg iv every 6 hours</td>
<td>2520mg iv every 6 hours</td>
</tr>
<tr>
<td>14.0-17.9kg</td>
<td>2330 mg iv every 6 hours</td>
<td>4500mg iv every 6 hours</td>
</tr>
<tr>
<td>18.0-24.9kg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>25.0-32.9kg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>33.0-43.9kg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;44kg</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Dose adjustment in renal impairment:**

| GFR 40-80ml/min | | |
| GFR 20-39ml/min | | |
| GFR <20ml/min | | |

**Dose Adjustment in HD:**

| Dialysed | >1 month old and <50kg: 45mg/kg iv every 8 hours | >50kg: 4500mg iv every 12 hours and supplementary dose of 2250mg iv post dialysis on dialysis days (haemodialysis removes 30-50% of piperacillin in 4 hours) |

**Dose Adjustment in PD:**

| Not dialysed | >1 month old: decrease frequency to every 12 hours |

**Intraperitoneal dose:**

| 250mg/L |

**Notes:** Licensed for children over 2 years old

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**Checked by:** Sue Patey (Renal Senior Specialist Pharmacist) and Quen Mok (Consultant Paediatric Intensivist)
**Approved by:** Drugs & Therapeutics Committee
**Date document created:** November 2011
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**Checked by:** Vani Suri (NICU Specialist Pharmacist)
**Date for next review:** September 2014
**Version:** 3

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References:
1. Summary of Product Characteristics: EMC/Package Insert, Last updated: 22/06/09  Manufacturer: Wockhardt UK Ltd
2. Summary of Product Characteristics: EMC/Package Insert, Last updated: 01/04/09  Manufacturer: Hospira UK Ltd
4. Summary of Product Characteristics: EMC/Package Insert, Last updated: 02/02/10  Manufacturer: Sandoz Ltd
9. Gt Ormond St Hospital for Children NHS Trust Antibiotic Policy - Piperacillin + Tazobactam Dose Banding, V4, February 2013
10. Guy's, St Thomas' and Lewisham Hospitals Trust. Paediatric Formulary, 8th edn. London, UK, 2010

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Approved by: Drugs & Therapeutics Committee
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## Drug: RIBAVIRIN

### Usual route of clearance:
Ribavirin is metabolised principally to deribosylated ribavirin (1,2,4-triazole-3-carboxamide), which is thought to probably occur in the liver. This metabolite has a similar activity to the parent drug.\(^1\)
Ribavirin also undergoes phosphorylation in erythrocytes.\(^1\)
Ribavirin is excreted primarily in the urine, with a small amount also fecally excreted.\(^1\)

### Pharmacokinetic parameters:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protein binding</td>
<td>Negligible(^2)</td>
</tr>
<tr>
<td>Molecular Wt</td>
<td>244.2 daltons(^3)</td>
</tr>
<tr>
<td>Vd</td>
<td>Paediatrics (after single iv dose only): 7.7 ± 5.1 L/kg(^2)</td>
</tr>
<tr>
<td></td>
<td>Paediatrics (after single iv dose only): 18.6 ± 10.2 hours(^2)</td>
</tr>
<tr>
<td>Half-life (t(1/2))</td>
<td>Likely to be increased(^2)</td>
</tr>
<tr>
<td>t(1/2) in renal imp</td>
<td></td>
</tr>
</tbody>
</table>

### Normal dose:

<table>
<thead>
<tr>
<th>Virus/Agent</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>RSV / Paraflu / Adenovirus</td>
<td>&gt;1 month old: 33mg/kg iv as a single dose, then 16mg/kg iv every 6 hours for 4 days, followed by 8mg/kg iv every 8 hours for 3 days then review(^4,5)</td>
</tr>
</tbody>
</table>

### Dose adjustment in renal impairment:

| GFR 30-50ml/min:             | iv: no dosage adjustment required - give normal dose\(^3,5\) |
| GFR 10-30ml/min:             | iv: no dosage adjustment required (but see notes below)\(^3,5\) |
| GFR <10ml/min:               | iv: no dosage adjustment required (but see notes below)\(^3,5\) |

### Dose adjustment in HD:
Not dialysed.\(^3\) iv: no dosage adjustment required (but see notes below)\(^3\)

### Dose adjustment in PD:
Unlikely to be dialysed.\(^3\) iv: no dosage adjustment required (but see notes below)\(^3\)

### Intraperitoneal dose:
No information

### Dose adjustment in CVVH:
iv: no dosage adjustment required - give normal dose (but see notes below)\(^3\)
enteral: avoid if GFR<50ml/min\(^3,5,6\)

### Notes:
Caution should be used if iv ribavirin is prescribed in patients with GFR <30ml/minute.\(^5\)
While the normal dosage regimen may be prescribed, patients should be closely monitored for signs of toxicity such as anaemia.\(^2,3\)
There is no experience of iv ribavirin use in patients with end-stage renal disease or on renal replacement therapies.\(^3\)
The manufacturer recommends that the oral preparation should be avoided in patients with GFR<50ml/min or on haemodialysis.\(^3,5,6\)

---

**References:**

2. Investigational Drug Brochure: Virazole (Ribavirin USP) Injection 100mg/ml IND 9076, 4\(^{th}\) Edition; August 2004. Manufacturer: Valeant Pharmaceuticals International
4. Guy's, St Thomas' and Lewisham Hospitals Trust. Paediatric Formulary, 8\(^{th}\) edn. London, UK, 2010
<table>
<thead>
<tr>
<th>Drug:</th>
<th>RIFAMPICIN</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Usual route of clearance:</strong></td>
<td>Rifampicin is rapidly eliminated in the bile and undergoes enterohepatic recirculation, during which it undergoes progressive deacetylation to an active metabolite. Nearly all the drug in the bile is in this form within approximately 6 hours. Intestinal reabsorption is reduced by deacetylation, therefore facilitating elimination. Up to 30% of a dose is excreted in the urine, with about half of this being unchanged drug.</td>
</tr>
</tbody>
</table>
| **Pharmacokinetic parameters:** | Protein binding: ~80%<sup>1,2,3,4</sup>  
Molecular Wt: 822.9 daltons<sup>2</sup>  
Vd: Adults: 0.64-0.66 L/kg<sup>2</sup>  
Paediatrics: ~2-3 hours<sup>1</sup>  
Half-life (t½): Adults: ~1-3.8 hours<sup>5</sup>  
t½ in renal imp: Possibly increased<sup>5</sup>  
 | |
| **Normal dose:** | <4 weeks of life: 5-10mg/kg (meningitis 10mg/kg) iv/po/ng every 12 hours<sup>5</sup>  
1-12 months: 5-10mg/kg (meningitis 10mg/kg) iv/po/ng every 12 hours<sup>6</sup>  
1-18 years: 10mg/kg (max 600mg) iv/po/ng every 12 hours<sup>6</sup>  
 | |
| **Dose adjustment in renal impairment:** | GFR 20-50ml/min: No dosage adjustment required - give normal dose<sup>2,3,7</sup> but use with caution if dose is above 10mg/kg daily<sup>6</sup>  
GFR 10-20ml/min: No dosage adjustment required - give normal dose<sup>2,3,7</sup> but use with caution if dose is above 10mg/kg daily<sup>6</sup>  
GFR <10ml/min: Give 50-100% of normal dose<sup>2,8</sup> but use with caution if dose is above 10mg/kg daily<sup>6</sup>  
 | |
| **Dose adjustment in HD:** | Not dialysed.<sup>2,3</sup> Give 50-100% of normal dose iv/po/ng<sup>2,5,8</sup>  
 | |
| **Dose adjustment in PD:** | Not dialysed.<sup>2</sup> Give 50-100% of normal dose iv/po/ng<sup>2,5,8</sup>  
 | |
| **Intraperitoneal dose:** | No information  
 | |
| **Dose adjustment in CVVH:** | No dosage adjustment required - give normal dose<sup>2,3</sup>  
 | |
| **Notes:** | Renal dysfunction has been noted with rifampicin.<sup>1,2</sup>  
Rifampicin is excreted into PD fluid causing an orange-yellow colour.<sup>2</sup>  
If patient has impaired hepatic function, avoid or do not exceed 8mg/kg iv/po daily.<sup>6,9</sup>  
 | |

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Monograph checked by: Sue Patey (Renal Senior Specialist Pharmacist) and Dr Quen Mok (Consultant Paediatric Intensivist)  
Date of last review: 20/09/11  

References:  
4. Lexi-comp online accessed via www.crlonline.com, accessed 16/12/10  

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Approved by: Drugs & Therapeutics Committee  
Date document created: November 2011  
Date of interim review: May 2014  
Reviewed by: Venetia Horn (PICU Senior Pharmacist)  
Checked by: Vani Suri (NICU Pharmacist)  
Date for next review: September 2014  
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<table>
<thead>
<tr>
<th>Drug:</th>
<th>TEICOPLANIN</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Usual route of clearance:</strong></td>
<td>Greater than 97% of a dose of teicoplanin is excreted unchanged, predominantly in the urine.¹,² No metabolites of teicoplanin have been identified.¹</td>
</tr>
<tr>
<td><strong>Pharmacokinetic parameters:</strong></td>
<td><strong>Protein binding:</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Molecular Wt:</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Vd:</strong></td>
</tr>
<tr>
<td></td>
<td><strong>t½ in renal imp:</strong></td>
</tr>
<tr>
<td><strong>Normal dose:</strong></td>
<td>&lt;4 weeks of life:</td>
</tr>
<tr>
<td></td>
<td>&gt;4 weeks of life:</td>
</tr>
<tr>
<td><strong>Dose adjustment in renal impairment:</strong></td>
<td>GFR 40-60ml/min:</td>
</tr>
<tr>
<td></td>
<td>GFR &lt;40ml/min:</td>
</tr>
<tr>
<td><strong>Dose adjustment in HD:</strong></td>
<td>Not dialysed.² Give normal regimen for the first three days, then reduce dose on Day 4 to one third of the dose once daily or give 100% of the dose every third day.¹,²,⁴,⁷</td>
</tr>
<tr>
<td><strong>Dose adjustment in PD:</strong></td>
<td>Not dialysed.² Give normal regimen for the first three days, then reduce dose on Day 4 to one third of the dose once daily or give 100% of the dose every third day.²,⁷</td>
</tr>
<tr>
<td><strong>Intraperitoneal dose:</strong></td>
<td>Give 10mg/kg (max 400mg) IV stat dose, then 20mg/L per bag for 7 days, then 20mg/L per alternate bag for 7 days, then 20mg/L per night-bag only for 7 days²</td>
</tr>
<tr>
<td><strong>Dose adjustment in CVVH:</strong></td>
<td>Give normal regimen for the first three days, then reduce dose on Day 4 to one third of the dose once daily or give 100% of the dose every third day.⁷</td>
</tr>
<tr>
<td><strong>Notes:</strong></td>
<td>Due to the long half-life of the drug, dose reduction is not required until the 4th day of treatment.⁴</td>
</tr>
</tbody>
</table>

Monograph written by: Rachelle Booth (PICU Senior Specialist Pharmacist)
Monograph checked by: Sue Patey (Renal Senior Specialist Pharmacist) and Dr Quen Mok (Consultant Paediatric Intensivist)
Date of interim review and update: 13/09/13, Updated by: Rachelle Booth, Checked by: Venetia Horn (NICU Specialist Pharmacist)

References:
1. Summary of Product Characteristics: EMC/Package Insert, Last updated: 06/01/09 Manufacturer: sanofi-aventis
4. Guy’s, St Thomas' and Lewisham Hospitals Trust. Paediatric Formulary, 8th edn. London, UK, 2010
**TICARCILLIN + CLAVULANIC ACID**

**Usual route of clearance:** The major route of elimination for both ticarcillin and clavulanic acid is renal excretion.\(^1\) Approximately 60-77% of a dose of ticarcillin and 30-45% of clavulanic acid is excreted unchanged in the urine within 6 hours.\(^2,3\) The metabolic fate of clavulanic acid has not been completely elucidated.\(^3\)

**Pharmacokinetic parameters:**

<table>
<thead>
<tr>
<th>Protein binding:</th>
<th>ticarcillin: Approximately 45-60%(^2,3)</th>
<th>clavulanic acid: Approximately 22-30%(^3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular Wt:</td>
<td>ticarcillin: 384.43 daltons(^4)</td>
<td>clavulanic acid: 199.16 daltons(^4)</td>
</tr>
<tr>
<td>Vd:</td>
<td>ticarcillin: Adults: ~0.17 L/kg(^3)</td>
<td>Paediatrics: 0.22 L/kg(^2,5)</td>
</tr>
<tr>
<td></td>
<td>clavulanic acid: Adults: ~0.315-0.342 L/kg(^3)</td>
<td>Paediatrics: 0.4 L/kg(^2,5)</td>
</tr>
<tr>
<td>Half-life (t½):</td>
<td>ticarcillin: Adults: 1.1-1.2 hours(^3,5)</td>
<td>Children: 1.1 hours(^5)</td>
</tr>
<tr>
<td></td>
<td>clavulanic acid: Adults: 1.1-1.5 hours(^3,5)</td>
<td>Children: 0.9 hours(^5)</td>
</tr>
</tbody>
</table>

**t½ in renal imp:**

| ticarcillin: | Adults: 4.9 hours if CrCl = 11-37ml/min\(^3\) | Adults: 8.5 hours if CrCl <8ml/min\(^3\) |
| clavulanic acid: | Adults: 2.3 hours if CrCl = 11-37ml/min\(^3\) | Adults: 2.9 hours if CrCl <8ml/min\(^3\) |

**Normal dose:**

| Pre-term neonates: | <2kg: 80mg/kg iv every 12 hours\(^1,6\) | >2kg: 80mg/kg iv every 8 hours, increase to every 6 hours in severe infections\(^1,6\) |
| Term neonates: | 80mg/kg iv every 8 hours, increase to every 6 hours in severe infections\(^1,6\) | 80mg/kg (max 3.2g) iv every 8 hours, increase to every 6 hours in severe infections\(^1,6\) |
| >4 wks and <40kg: | 3.2g iv every 6-8 hours, increase to every 4 hours in severe infections\(^6\) |
| >4 wks and >40kg: | 3.2g iv every 6-8 hours, increase to every 4 hours in severe infections\(^6\) |

**Dose adjustment in renal impairment:**

| GFR 30-60ml/min: | >2kg: Give normal dose but reduce frequency to every 8 hours\(^2,6,7\) |
| GFR 10-30ml/min: | >2kg: Give 50%\(^1,6,9\)-100%\(^2,8\) of normal dose every 8 hours\(^2,6,8\) |
| GFR <10ml/min: | >2kg: Give 50%\(^1,6,9\)-100%\(^2,8\) of normal dose every 12 hours\(^2,6,8,9\) |

**Dose adjustment in HD:**

Dialysed:

5,7 Give 50%\(^1,6,9\)-100%\(^2,8\) of normal dose and reduce frequency to every 12 hours\(^1,8,9\)

**Dose adjustment in PD:**

Not dialysed:

7 Give 50%\(^1\)-100%\(^8,9\) of normal dose and reduce frequency to every 12 hours\(^1,8\)

**Intraperitoneal dose:**

No information

**Dose adjustment in CVVH:**

Give 100% of normal dose but consider reducing frequency to every 8 hours\(^2,8\) depending on the severity of the infection.

**Notes:**

If patient has concomitant hepatic impairment then dose should be reduced to every 24 hours\(^8\)

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Date of last review: 14/06/11

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### Drug: VANCOMYCIN

**Usual route of clearance:** At least 75% of a vancomycin dose is excreted in the urine by glomerular filtration within 24 hours.\(^1,2\)

<table>
<thead>
<tr>
<th>Pharmacokinetic parameters:</th>
<th>Protein binding:</th>
<th>Molecular Wt:</th>
<th>Vd:</th>
<th>Half-life (t½):</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>At least 75% of a vancomycin dose is excreted in the urine by glomerular filtration within 24 hours.(^1,2)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1449.25 daltons(^5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Adults: 0.39-0.97 L/kg(^1)</td>
<td>Paediatrics: 0.4-0.75 L/kg (inversely related to age)(^6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Children 2.5-11 years: 5.6 hours(^2)</td>
<td>Infants 1-12 months: 4.1 hours(^2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Term neonates: 6.7 hours(^2)</td>
<td>Adults: 32.3-146.7 hours(^2)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Normal dose:</th>
<th>&lt;2kg &lt;4ks of life:</th>
<th>15mg/kg iv, frequency dependent upon levels(^7)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&gt;2kg &lt;4wks of life:</td>
<td>15mg/kg iv every 12 hours(^7)</td>
</tr>
<tr>
<td></td>
<td>&gt;2kg &gt;4wks of life:</td>
<td>15mg/kg iv every 8 hours(^7)</td>
</tr>
<tr>
<td></td>
<td>Central nervous system infection: 15mg/kg iv every 6 hours(^5,7) (NB Maximum total daily dose is 2g)(^8)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Dose adjustment in renal impairment:</th>
<th>GFR 10-50ml/min:</th>
<th>Give 10mg/kg iv every 12 hours, take trough level after 12 hours, give the next dose, and adjust regimen if necessary in order to maintain serum trough level between 5-10mg/L.(^7)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>GFR &lt;10ml/min:</td>
<td>Give 10mg/kg iv every 24 hours, take trough level after 24 hours and hold dose until the serum trough level is between 5-10mg/L.(^7)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Dose adjustment in HD:</th>
<th>Minimally removed by HD.(^2,9) Give 10mg/kg(^3) iv as determined by serum levels.(^3) Hold dose until the serum level is between 5-10mg/L.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dose adjustment in PD:</td>
<td>Minimally removed by PD.(^2,9) Give 10mg/kg(^3) iv as determined by serum levels.(^3) Hold dose until the serum level is between 5-10mg/L.</td>
</tr>
</tbody>
</table>

| Intraperitoneal dose: | 12.5-25mg/L\(^9\) |

<table>
<thead>
<tr>
<th>Dose adjustment in CVVH:</th>
<th>Substantially removed by haemofiltration.(^2) Give 10mg/kg(^3) iv every 12 hours, take trough level after 12 hours, give, and adjust regimen if necessary in order to maintain serum trough level between 5-10mg/L.</th>
</tr>
</thead>
</table>

**Notes:** Repeat levels daily in renal impairment or if on any form of dialysis/haemofiltration. Take care not to underdose; ensure that the trough level is maintained above 5mg/L otherwise treatment will be subtherapeutic. For patients with normal renal function, aim for trough levels 5-15mg/L.\(^7\) For patients with central nervous system infection, aim for trough levels 10-15mg/L.\(^7\)

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**References:**
4. Lexi-comp online accessed via [www.crffline.com](http://www.crffline.com), accessed 15/06/11

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**Drug:** VORICONAZOLE  

**Usual route of clearance:** Voriconazole is metabolised by the cytochrome P450 2C19, 2C9 and 3A4 isoenzymes and exhibits non-linear pharmacokinetics due to its saturable metabolism. Less than 2% of a dose is excreted unchanged in the urine. Inter-individual variability of pharmacokinetics is high.

**Pharmacokinetic parameters:**
- **Protein binding:** 58%[^1-3]
- **Molecular Wt:** 349.31 daltons[^5]
- **Vd:** Adults: ~4.6 L/kg[^1,2,3]
- **Half-life (t½):** Variable and dose-dependent due to saturable metabolism[^1]
- **t½ in renal imp:** Variable and dose-dependent due to saturable metabolism[^1]

**Normal dose:**
- **<2 years old:** iv/po/ng: Loading dose of 6mg/kg every 12 hours for two doses, followed by 4mg/kg every 12 hours[^6]
- **2-14 years old and <50kg:**
  - iv: Loading dose of 9mg/kg every 12 hours for two doses, followed by 8mg/kg every 12 hours[^1], for a maximum of 6 months[^7]. If response is inadequate, the iv dose may be increased by 1mg/kg steps. If treatment is not tolerated, dose may be reduced by 1mg/kg steps.[^1]
  - po/ng: 9mg/kg (max 350mg) every 12 hours.[^1] If response is inadequate, the enteral dose may be increased by 1mg/kg steps, or by 50mg steps if the patient is on 350mg. If treatment is not tolerated, dose may be reduced by 1mg/kg steps, or by 50mg steps if the patient is on 350mg.[^3]
- **12-14 years old and ≥ 50kg, or >15 years old:**
  - iv: Loading dose of 6mg/kg every 12 hours for two doses, followed by 4mg/kg every 12 hours[^1], for a maximum of 6 months[^7]
  - po/ng: <40kg: Loading dose of 200mg every 12 hours for 2 doses, followed by 100mg every 12 hours.[^1] If response is inadequate, dose may be increased to 150mg every 12 hours.[^1]
  - po/ng: >40kg: Loading dose of 400mg every 12 hours for 2 doses, followed by 200mg every 12 hours.[^1] If response is inadequate, dose may be increased to 300mg every 12 hours.[^1]

**Dose adjustment in renal impairment:**
- **GFR <50ml/min:** po/ng: no dosage adjustment required - give normal dose[^1,2,4,7]
  - iv: No dosage adjustment required - give normal dose.[^3,4,7] however iv use is not recommended[^2,4,8] therefore only use if benefit outweighs risk (see notes below).

**Dose adjustment in HD:** Dialysed.[^3] No dosage adjustment required - give normal dose.[^3,4,7] however iv use is not recommended[^4,8] therefore only use if benefit outweighs risk (see notes below).

**Dose adjustment in PD:** Probably dialysed.[^3] No dosage adjustment required - give normal dose.[^3,4,7] however iv use is not recommended[^4,8] therefore only use if benefit outweighs risk (see notes below).

---

[^1]: Written by: Rachelle Booth (PICU Senior Specialist Pharmacist)  
[^2]: Checked by: Sue Patey (Renal Senior Specialist Pharmacist) and Dr Quen Mok (Consultant Paediatric Intensivist)  
[^3]: Approved by: Drugs & Therapeutics Committee  
[^4]: Date document created: November 2011  
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[^6]: Reviewed by: Venetia Horn (PICU Senior Pharmacist)  
[^7]: Checked by: Vani Suri (NICU Pharmacist)  
[^8]: Date for next review: September 2014  
[^9]: Version: 3  

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<table>
<thead>
<tr>
<th>Intra</th>
<th>intraperitoneal dose:</th>
<th>No information</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dose adjustment in CVVH:</td>
<td>No dosage adjustment required - give normal dose, however iv use is not recommended therefore only use if benefit outweighs risk (see notes below)</td>
<td></td>
</tr>
<tr>
<td>Notes:</td>
<td>In patients with GFR &lt;50ml/minute, the oral route is preferred, as accumulation of the iv vehicle sulphobutylether beta cyclodextrin sodium (SBECD) occurs, therefore the iv route should only be used if the risk-benefit justifies its use. Voriconazole may cause acute renal failure.</td>
<td></td>
</tr>
</tbody>
</table>

Monograph written by: Rachelle Booth (PICU Senior Specialist Pharmacist)
Monograph checked by: Sue Patey (Renal Senior Specialist Pharmacist) and Dr Quen Mok (Consultant Paediatric Intensivist)
Date of last review: 19/04/12

References:
1. Summary of Product Characteristics: EMC/Packag Insert, Last updated: 29/02/12. Manufacturer: Pfizer Ltd
2. Lexi-comp online accessed via www.crlonline.com, accessed 06/06/11
6. Gt Ormond St Hospital for Children NHS Trust Prescribing Guidelines for Individual Medicines – Voriconazole for prophylaxis and treatment of fungal infections v5.0 December 2011

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