PENICILLIN G (BENZYLPCNILLIN) 2015

<table>
<thead>
<tr>
<th>Alert</th>
<th>The Antimicrobial Stewardship Team has listed this drug under the following categories: Unrestricted</th>
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</thead>
</table>
| Indication | Empiric treatment of early onset sepsis (in combination with an aminoglycoside)  
Directed treatment of infection to a susceptible bacterium  
Treatment of meningitis to a susceptible bacterium, including GBS (Group B Streptococcus)  
Treatment of congenital syphilis |
| Action | Bactericidal agent which inhibits cell wall synthesis |
| Drug Type | Antibacterial - Penicillin |
| Trade Name | BenPen |
| Presentation | 600 mg vial |
| Maximum Daily Dose | 300 mg/kg/day  
Adjust meningitis doses to comply with maximum daily dose |

### Dosage / Interval

#### Standard infections: 60mg/kg dosing interval as per table below

<table>
<thead>
<tr>
<th>Method</th>
<th>Interval (hours)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Corrected Gestational Age</td>
<td>Age</td>
</tr>
<tr>
<td>&lt; 30 weeks</td>
<td>0-28 days</td>
</tr>
<tr>
<td>&lt; 30 weeks</td>
<td>29+ days</td>
</tr>
<tr>
<td>30-36 weeks</td>
<td>0-14 days</td>
</tr>
<tr>
<td>30-36 weeks</td>
<td>15 + days</td>
</tr>
<tr>
<td>37-44 weeks</td>
<td>0-7 days</td>
</tr>
<tr>
<td>37-44 weeks</td>
<td>8 + days</td>
</tr>
<tr>
<td>≥ 45 weeks</td>
<td>0 +</td>
</tr>
</tbody>
</table>

#### Meningitis: 90mg/kg dosing interval as per table below

<table>
<thead>
<tr>
<th>Method</th>
<th>Interval (hours)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Corrected Gestational Age</td>
<td>Age</td>
</tr>
<tr>
<td>&lt; 37 weeks</td>
<td>0-7 days</td>
</tr>
<tr>
<td>&lt; 37 weeks</td>
<td>8 + days</td>
</tr>
<tr>
<td>≥ 38 weeks</td>
<td>0 +</td>
</tr>
</tbody>
</table>

| Route | IV  
IM (Only if IV route not possible as intramuscular route is painful) |
|-------|------------------------------------------------------------------|
| Preparation/Dilution | Add 3.6mL of water for injection to the 600mg vial to make a 150mg/mL solution.  
**FURTHER DILUTE**  
1mL of penicillin solution (150mg) with 4 mL of water for injection to make a 30mg/mL solution. |
| Administration | IV infusion over 15-30 minutes.  
IV infusion over 30-60 minutes recommended for larger doses (e.g. for meningitis)  
Separate from aminoglycoside administration by clearing the line with a flush as penicillins inactivate aminoglycosides  
IM injection: only if IV route is not possible. |
### Monitoring

Plasma levels are not usually required, however may be useful for infections with high Minimum Inhibitory Concentration (MIC)

- 60mg = 100 000 Units of Penicillin
- 60mg vial contains 0.18mmol Sodium

### Contraindications

Hypersensitivity to Penicillin

### Precautions

Hypersensitivity to Cephalosporins

Significant CNS toxicity including seizures may occur with high doses and rapid infusions

Consider sodium load, especially in renal failure- a dose of 300mg/kg/day provides 0.85mmol/kg/day of sodium

Dose reduction is recommended if significant renal insufficiency

### Drug Interactions

Aminoglycosides including gentamicin should not be mixed with penicillin when both drugs are given parenterally as inactivation occurs. Ensure line is adequately flushed between antibiotics

### Adverse Reactions

Allergy. Note hypersensitivity to penicillin has not been seen in neonates

Bone marrow suppression, granulocytopenia and hepatitis are rare

Significant CNS toxicity including seizures may occur with high doses and rapid infusions

### Compatibility

**Fluids:** Glucose 5% and sodium chloride 0.9%

**Y site:** no information available

### Incompatibility

**Drugs:** Aminoglycosides – amikacin, gentamicin, tobramycin, aminophylline, dobutamine, erythromycin, ganciclovir, haloperidol lactate, heparin sodium, labelatol, metaraminol, noradrenaline, pentamidine, phenobarbitone, phenolbarbitaline, phenolalmine, prochlorperazine, potassium chloride, promethazine, protamine sulfate, suxamethonium, thiopentone, tranexamic acid

### Stability

Administer immediately, discard unused portion of reconstituted solution

### Storage

Room temperature

Protect from light

### Special Comments

CSF penetration is poor even when meninges are inflamed hence larger doses in meningitis

Prescribe in terms of mg rather than units

### Evidence summary

1. Effectiveness: 2 RCT’s comparing penicillin versus ampicillin in the empiric therapy of extremely low-birth weight neonates at risk of early onset sepsis showed similar effectiveness in change of antibiotics at 72 hours and/or 7-day all cause mortality (Level II, Grade B)13, 14

2. Dose: Benzylpenicillin 60 mg/kg/day achieved CSF treponemicidal concentration universally in congenital syphilis in a comparative (non-randomised) study with procaine penicillin 30 mg/kg/day which achieved treponemicidal concentration in 82% of patients (Level III-3, Grade C)15

3. GBS susceptibility: In a recent study16, GBS isolates from pregnant women were found to be uniformly susceptible to penicillin

**Level of evidence**

**Grade of recommendation***

Benzyl Penicillin has similar efficacy to ampicillin in empirical treatment of early onset sepsis in neonate (Level 2, Grade B)

Due to poor CSF penetration of benzyl penicillin, higher minimal bactericidal concentration of GBS in CSF as well as increased inoculum of the bacterium in CSF of neonates with meningitis compared to older infants and children, experts recommend higher dose of Benzyl penicillin in treatment of GBS meningitis (level V recommendation)3,17,18

### References

2. Young TE, Mangum B. Neofax 24th Ed. 2011:80-1
5. UpToDate Reference accessed on www.uptodate.com on 9th July 2014
9. Pediatric Injectable Drugs, 10th edition (The Teddy Bear Book)