### Alert
The Antimicrobial Stewardship Team has listed this drug under the following categories: Unrestricted.

### Indication
- Directed treatment of infection due to a susceptible bacterium.
- Treatment of meningitis due 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 and congenital syphilis:** 60 mg/kg/dose. Dosing interval as per table below

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

**Meningitis:** 90 mg/kg/dose. Dosing interval as per table below

<table>
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<tr>
<th>Method</th>
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</thead>
<tbody>
<tr>
<td>Corrected Gestational Age/Postmenstrual Age</td>
<td>Postnatal Age</td>
</tr>
<tr>
<td>&lt; 37th weeks</td>
<td>0−7 days</td>
</tr>
<tr>
<td>&lt; 37th weeks</td>
<td>8+ days</td>
</tr>
<tr>
<td>≥ 37th weeks</td>
<td>0+ days</td>
</tr>
</tbody>
</table>

### Route
- IV
- IM (only if IV route not possible. IM route can be painful).

### Preparation/Dilution
- IV
  Add 3.6 mL of water for injection to the 600 mg vial to make a 150 mg/mL solution.
  **FURTHER DILUTE**
  Draw up 1 mL (150 mg of penicillin) of solution and add 4 mL of sodium chloride 0.9% to make a final volume of 5mL with a concentration of 30 mg/mL solution.
- IM
  Add 1.6 mL water for injection to the 600 mg vial to make a 300 mg/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.
| **Monitoring** | Plasma concentrations are not usually required, however may be useful for infections with high Minimum Inhibitory Concentration (MIC). |
| **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 300 mg/kg/day provides 0.90 mmol/kg/day of sodium. Dose reduction is recommended in 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%, Glucose 10% and sodium chloride 0.9%
Y site: Amino acid solutions and fat emulsions. |
| **Incompatibility** | Y-site: Aminoglycosides – amikacin, gentamicin, tobramycin; aminophylline, dobutamine, erythromycin, ganciclovir, haloperidol lactate, heparin sodium, labetalol, metaraminol, noradrenaline, pentamidine, phenobarbitone, phenothiazine, potassium chloride, promethazine, protamine, sodium chloride, suxamethonium, thiopentone, tranexamic acid. |
| **Stability** | Administer immediately, discard unused portion of reconstituted solution. |
| **Storage** | Store at 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. 60 mg = 100 000 Units of penicillin. 60 mg vial contains 0.18 mmol sodium. |
| **Evidence summary** | 1. Effectiveness: 2 RCTs 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 study\(^{16}\), GBS isolates from pregnant women were found to be uniformly susceptible to penicillin.
Benzylpenicillin has similar efficacy to ampicillin in empirical treatment of early onset sepsis in neonates (Level 2, Grade B).
Due to poor CSF penetration of benzylpenicillin, 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 benzylpenicillin in treatment of GBS meningitis (level V)\(^{3,17,18}\). |
References

2. Young TE, Mangum B. Neofax 24th Ed. 2011:80–1