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

Indication
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 and congenital syphilis: 60 mg/kg/dose. Dosing interval as per table below

<table>
<thead>
<tr>
<th>Method</th>
<th>Corrected Gestational Age/Postmenstrual Age</th>
<th>Postnatal Age</th>
<th>Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;30&lt;sup&gt;th&lt;/sup&gt; weeks</td>
<td>0-28 days</td>
<td>12 hourly</td>
</tr>
<tr>
<td></td>
<td>&lt;30&lt;sup&gt;th&lt;/sup&gt; weeks</td>
<td>29+ days</td>
<td>8 hourly</td>
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<tr>
<td></td>
<td>30&lt;sup&gt;th&lt;/sup&gt;-36&lt;sup&gt;th&lt;/sup&gt; weeks</td>
<td>0-14 days</td>
<td>12 hourly</td>
</tr>
<tr>
<td></td>
<td>30&lt;sup&gt;th&lt;/sup&gt;-36&lt;sup&gt;th&lt;/sup&gt; weeks</td>
<td>15+ days</td>
<td>8 hourly</td>
</tr>
<tr>
<td></td>
<td>37&lt;sup&gt;th&lt;/sup&gt;-44&lt;sup&gt;th&lt;/sup&gt; weeks</td>
<td>0-7 days</td>
<td>12 hourly</td>
</tr>
<tr>
<td></td>
<td>37&lt;sup&gt;th&lt;/sup&gt;-44&lt;sup&gt;th&lt;/sup&gt; weeks</td>
<td>8+ days</td>
<td>8 hourly</td>
</tr>
<tr>
<td></td>
<td>≥45&lt;sup&gt;th&lt;/sup&gt; weeks</td>
<td>0+ days</td>
<td>6 hourly</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Method</th>
<th>Corrected Gestational Age/Postmenstrual Age</th>
<th>Postnatal Age</th>
<th>Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;37&lt;sup&gt;th&lt;/sup&gt; weeks</td>
<td>0-7 days</td>
<td>12 hourly</td>
</tr>
<tr>
<td></td>
<td>&lt;37&lt;sup&gt;th&lt;/sup&gt; weeks</td>
<td>8+ days</td>
<td>8 hourly</td>
</tr>
<tr>
<td></td>
<td>≥37&lt;sup&gt;th&lt;/sup&gt; weeks</td>
<td>0+ days</td>
<td>8 hourly</td>
</tr>
</tbody>
</table>

Route
IV
IM (Only if IV route not possible as intramuscular route is painful)

Preparation/Dilution
IV
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.
IM
Add 1.6mL water for injection to the 600mg vial to make a 300mg/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.
**Benzylpenicillin (Penicillin G)**

**Monitoring**

- Plasma levels 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 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, labetalol, metaraminol, noradrenaline, pentamidine, phenobarbital, phenotolamine, procainemycin, potassium chloride, promethazine, protamine sulfate, suxamethonium, thiopentone, tranexam acid.

**Stability**

- Administer immediately, discard unused portion of reconstituted solution

**Storage**

- Store in 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
- 60mg = 100 000 Units of Penicillin
- 60mg vial contains 0.18mmol 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.

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).\(^{1,17,18}\)
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)