1.1 Complicated Skin and Skin Structure Infections

Daptomycin for injection is approved for the treatment of skin and skin structure infections (cSSSI) caused by certain susceptible Gram-positive bacteria.

1.2. Bloodstream Infections

Daptomycin for injection is approved for the treatment of certain Gram-positive bloodstream infections (Bacteremia) in adult patients, including those with cSSSI, and in pediatric patients (1 to 17 years of age).

1.3. Left-Sided Infective Endocarditis

Daptomycin for injection is not indicated for the treatment of left-sided infective endocarditis due to viridans streptococci.

1.4. Limitations of Use

Daptomycin for injection is not recommended in pediatric patients younger than 1 year of age due to the risk of myopathy and myoglobinuria. Daptomycin for injection is not indicated for the treatment of left-sided infective endocarditis due to viridans streptococci.

2. DOSAGE FORMS AND STRENGTHS

Daptomycin for injection is a sterile, pale yellow to light brown lyophilized powder for reconstitution in a 500 mg vial. The vial contains 500 mg of daptomycin as the free base in 30 mL as follows:

- 240 mg in 20 mL isopropyl alcohol
- 160 mg in 10 mL water for injection

Each mL of the reconstituted solution contains 10 mg of daptomycin as the free base.

2.1 Administration Instructions

To minimize foaming, AVOID vigorous agitation or shaking of the vial during or after reconstitution. Do not use the vial if it has been frozen. − Reconstitute the vial with the 30 mL of sterile water for injection contained in the vial. − Allow the reconstituted solution to stand for 1 minute before use. − Discard unused portions of the reconstituted solution.

2.2 Dosage in Adult Patients (≥18 Years of Age)

Dosage Regimen in Adults

To treat cSSSI:

- Initial and maintenance dosage: 4 mg/kg once every 24 hours for 7 to 14 days.

To treat Bacteremia:

- Initial dosage: 3.5 to 4 mg/kg given as a single intravenous infusion over 60 minutes, followed by 3.5 to 4 mg/kg once every 24 hours for up to 42 days.

2.3 Dosage in Pediatric Patients (1 to 17 Years of Age) with Complicated Skin and Skin Structure Infections

Pediatric cSSSI Patients

- Initial and maintenance dosage: 5 to 6 mg/kg once every 24 hours for 7 to 14 days.

2.4 Dosage in Pediatric Patients (1 to 17 Years of Age) with Left-Sided Infective Endocarditis

Daptomycin for injection is approved for the treatment of left-sided infective endocarditis in pediatric patients weighing more than 10 kg.

Pediatric Endocarditis Patients

- Initial dosage: 3 mg/kg as a single intravenous infusion over 60 minutes, followed by 2 mg/kg once every 24 hours for up to 42 days.

2.5 Dosage in Pediatric Patients (1 to 17 Years of Age) with Left-Sided Infective Endocarditis

Pediatric Endocarditis Patients

- Initial dosage: 3 mg/kg as a single intravenous infusion over 60 minutes, followed by 2 mg/kg once every 24 hours for up to 42 days.

2.6. Dosage in Patients with Renal Impairment

Daptomycin for injection is not recommended for patients with creatinine clearance (CL Cr) < 30 mL/min who are not receiving dialysis. CL Cr < 10 mL/min is associated with higher occurrences of myopathy. The dosage of daptomycin may need to be reduced in patients with CL Cr ≤ 30 mL/min.

2.7. Dosage in Patients with HMG-CoA Reductase Inhibitors

In patients receiving concomitant therapy with an HMG-CoA reductase inhibitor, daptomycin concentrations may be present at trough to cause interaction. Monitor patients for clinical or laboratory signs of adverse reactions associated with HMG-CoA reductase inhibitors.

2.8. Dosage in Patients with CYP3A4 Inhibitors

In patients receiving concomitant therapy with a potent CYP3A4 inhibitor, daptomycin concentrations may be present at trough to cause interaction. Monitor patients for clinical or laboratory signs of adverse reactions associated with CYP3A4 inhibitors.

2.9. Dosage in Patients with CYP3A4 Inducers

In patients receiving concomitant therapy with a CYP3A4 inducer, daptomycin concentrations may be present at trough to cause interaction. Monitor patients for clinical or laboratory signs of adverse reactions associated with CYP3A4 inducers.

2.10. Dosage in Patients Receiving Concurrent or Recent Prior Therapy with an HMG-CoA Reductase Inhibitor

In patients receiving recent prior or concomitant therapy with an HMG-CoA reductase inhibitor, daptomycin concentrations may be present at trough to cause interaction. Monitor patients for clinical or laboratory signs of adverse reactions associated with HMG-CoA reductase inhibitors.

3. CLINICAL PHARMACOLOGY

3.1 Mechanism of Action

Daptomycin for injection exerts its bactericidal effect by disrupting the bacterial cell membrane, leading to cell lysis and death.

3.2 Pharmacokinetics

Daptomycin is rapidly absorbed following intravenous administration. The terminal half-life is approximately 12 hours. Peak concentrations are achieved within 3 hours. Daptomycin concentrations are not significantly altered by changes in renal function.

3.3 Microbiological Activity

Daptomycin is active against a wide range of Gram-positive bacteria, including Staphylococcus aureus, Enterococcus faecalis, and Streptococcus pyogenes.

3.4 Resistance

Resistance to daptomycin is uncommon and generally associated with reduced uptake of the drug into the bacterial cell or altered function of the target membrane.

4. ADVERSE REACTIONS

4.1 General Adverse Reactions

The most common adverse reactions associated with daptomycin are diarrhea, headache, dizziness, rash, abnormal liver function tests, and myopathy.

4.2 Laboratory Abnormalities

LFT abnormalities can occur, including leukopenia, anemia, and thrombocytopenia.

4.3 Myopathy and Rhabdomyolysis

Myopathy and rhabdomyolysis occur primarily in myeloid malignancies and can be life-threatening. Patients should be monitored for the development of muscle pain or weakness.

4.4 Peripheral Neuropathy

Peripheral neuropathy may occur, especially in patients with diabetes mellitus. Symptoms include numbness, tingling, and weakness.

4.5 C. difficile-Associated Diarrhea

C. difficile-associated diarrhea can occur during daptomycin therapy.

4.6 Other Adverse Reactions

Adverse reactions associated with daptomycin include abdominal pain,anorexia, increased transaminases, and vertigo.

5. DOSAGE FORMS AND STRENGTHS

For Injection: 500 mg daptomycin as a sterile, pale yellow to light brown lyophilized powder for reconstitution in a 500 mg vial.

6. CLINICAL TRIALS

Clinical trials enrolled 1,864 adult patients treated with Daptomycin for injection and 1,416 treated with comparator.

7. ADVERSE REACTIONS

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Adverse reactions associated with daptomycin include abdominal pain, anorexia, increased transaminases, and vertigo.
The primary objective of this study was to assess the safety of Daptomycin for injection. The clinical outcome was evaluated at the Test of Cure visit. The pediatric cSSSI pediatric trial was a single prospective multi-center, randomized, comparative trial. A total of 396 pediatric patients were enrolled in the study, comprising 37 (16%) Definite, 144 (61%) Possible, and 54 (23%) Not Endocarditis. Of the 37 patients with an infection, 25 had definite endocarditis according to the modified Duke criteria. Uncomplicated bacteremia was defined as a patient in a compassionate-use trial and from 7 patients in the comparator arm.

### Table 1: Demographics of Patients Treated with Daptomycin for Injection (N=396)

<table>
<thead>
<tr>
<th>Age Group</th>
<th>N</th>
<th>Mean (SD)</th>
<th>Median</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1 year</td>
<td>N=264</td>
<td>4.9 (1.9)</td>
<td>4.1</td>
<td>1-9</td>
</tr>
<tr>
<td>1-2 years</td>
<td>N=266</td>
<td>5.6 (2.1)</td>
<td>5.4</td>
<td>1-16</td>
</tr>
<tr>
<td>3-6 years</td>
<td>N=120</td>
<td>5.0 (1.9)</td>
<td>4.9</td>
<td>3-6</td>
</tr>
<tr>
<td>7-12 years</td>
<td>N=62</td>
<td>7.2 (1.9)</td>
<td>7.0</td>
<td>6-12</td>
</tr>
</tbody>
</table>

### Table 2: Microbiological Response Rates for Patients Treated with Daptomycin for Injection (N=396)

<table>
<thead>
<tr>
<th>Microorganism</th>
<th>N</th>
<th>Clinical Success</th>
<th>Microbiological Success</th>
<th>Clinical + Microbiological Success</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methicillin-sensitive</td>
<td>N=396</td>
<td>52.6%</td>
<td>63.7%</td>
<td>86.1%</td>
</tr>
<tr>
<td>Methicillin-resistant</td>
<td>N=396</td>
<td>44.3%</td>
<td>53.2%</td>
<td>77.5%</td>
</tr>
</tbody>
</table>

### Table 3: Pharmacokinetic Parameters for Daptomycin for Injection in Pediatric Patients (N=396)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>N</th>
<th>Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AUC (mcg•h/mL)</td>
<td>N=15</td>
<td>12.4 (5.6)</td>
</tr>
<tr>
<td>T1/2 (h)</td>
<td>N=15</td>
<td>1.6 (0.6)</td>
</tr>
<tr>
<td>Cmax (mcg/mL)</td>
<td>N=16</td>
<td>5.9 (3.9)</td>
</tr>
<tr>
<td>Cmin (mcg/mL)</td>
<td>N=16</td>
<td>3.9 (2.1)</td>
</tr>
</tbody>
</table>

### Table 4: Comparison of Daptomycin for Injection and Comparator in Pediatric Patients (N=396)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Comparator</th>
<th>Daptomycin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical Success</td>
<td>49.6%</td>
<td>52.6%</td>
</tr>
<tr>
<td>Microbiological Success</td>
<td>58.1%</td>
<td>63.7%</td>
</tr>
<tr>
<td>Clinical + Microbiological Success</td>
<td>87.7%</td>
<td>90.0%</td>
</tr>
</tbody>
</table>

### Table 5: Comparison of Efficacy and Safety between Daptomycin for Injection and Comparator in Pediatric Patients (N=396)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Comparator</th>
<th>Daptomycin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Efficacy Endpoint</td>
<td>80.9%</td>
<td>86.1%</td>
</tr>
<tr>
<td>Safety Endpoint</td>
<td>92.9%</td>
<td>94.4%</td>
</tr>
</tbody>
</table>

### Table 6: Comparison of Efficacy and Safety between Daptomycin for Injection and Comparator in Pediatric Patients (N=396)

<table>
<thead>
<tr>
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</table>