Complicated skin and skin structure infections (Bacteremia) in adult Patients, Including Those with Right-Sided Infective Endocarditis, Caused by Methicillin-Susceptible and Methicillin-Resistant Isolates

### Clinical Trials Experience

### The Bacteremia/Endocarditis Trial

### Adult Patients (Population: ITT)

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>Daptomycin</th>
<th>Comparator (vancomycin)</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacterial sources</td>
<td>37 19%</td>
<td>47 24%</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Bacteremia/Endocarditis</td>
<td>24 12%</td>
<td>19 10%</td>
<td>&gt;0.05</td>
</tr>
</tbody>
</table>

### Pediatric Patients

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>Daptomycin</th>
<th>Comparator</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacterial sources</td>
<td>24 16%</td>
<td>19 16%</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Bacteremia/Endocarditis</td>
<td>17 11%</td>
<td>13 10%</td>
<td>&gt;0.05</td>
</tr>
</tbody>
</table>

### Systemic Effects in Pediatric Patients

### Hypotension

- **1.4**

- **2.4**

- **1.4**

### Vascular Disorders

- **2.5**

### Nervous System Disorders

- **4.1**

### Ear and Labyrinth Disorders

- **5.10**

### ANAHEMOLYTIC RHEUMATOID ARTHRITIS

- **5.7**

### Renal and Urinary Disorders:

- **5.10**

### Respiratory, Thoracic, and Mediastinal Disorders

- **5.10**

### Ear and Labyrinth Disorders

- **5.10**

### Skin and Appendage Disorders

- **5.10**

### Gastrointestinal Disorders

- **5.10**

### Hypersensitivity Reactions

- **5.10**

### Blood and Lymphatic System Disorders

- **5.10**

### Laboratory Changes in Adults

- **5.10**

### Description of Selected Laboratory Changes

- **5.10**

### Adverse Reactions

- **6.1**

### Laboratory Test Interactions

- **7.3**

### Reconstituting Daptomycin for Injection

- **7.3**

### Dilution

- **7.3**

### Administration

- **7.4**

### Table 1: Clinical Success Rate By Route of Administration in Phase 3 CDI Trials In Patients With CAP/ABPs

<table>
<thead>
<tr>
<th>Route of Administration</th>
<th>Clinical Success Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intravenous Injection</td>
<td>80%</td>
</tr>
<tr>
<td>Oral</td>
<td>70%</td>
</tr>
</tbody>
</table>

### Table 2: Clinical Success Rate by Route of Administration in Phase 3 CDI Trials in Patients With C. difficile ASSOCIATED Diarrhea

<table>
<thead>
<tr>
<th>Route of Administration</th>
<th>Clinical Success Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intravenous Injection</td>
<td>85%</td>
</tr>
<tr>
<td>Oral</td>
<td>75%</td>
</tr>
</tbody>
</table>

### Special Populations

- **8.1**

### Pediatric Patients

- **8.6**

### Pregnancy

- **8.6**

- **8.16**

### Nursing Mothers

- **8.6**

### Table 3: Reported Changes in Laboratory Values in Adult Patients

<table>
<thead>
<tr>
<th>Laboratory Parameter</th>
<th>Daptomycin</th>
<th>Comparator</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb</td>
<td>12.1 2.3%</td>
<td>12.3 2.2%</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>WBC</td>
<td>8.9 3.1%</td>
<td>9.1 3.2%</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Platelets</td>
<td>243 52%</td>
<td>242 53%</td>
<td>&gt;0.05</td>
</tr>
</tbody>
</table>

### Recombinant Heparin Analog

- **8.11**

### Table 3: Reported Changes in Laboratory Values in Pediatric Patients

<table>
<thead>
<tr>
<th>Laboratory Parameter</th>
<th>Daptomycin</th>
<th>Comparator</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb</td>
<td>11.9 2.0%</td>
<td>11.8 2.1%</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>WBC</td>
<td>8.3 2.2%</td>
<td>8.4 2.3%</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Platelets</td>
<td>240 52%</td>
<td>239 53%</td>
<td>&gt;0.05</td>
</tr>
</tbody>
</table>

### Safety

- **9.1**

### Adverse Reactions

- **9.1**

### Drug Interactions

- **9.3**

### Monitoring Parameters

- **9.4**

### Adverse Events During Long-Term Therapy

- **9.5**

### Infectious Disease/ Drug Interactions

- **9.6**

### Postmarketing Experience

- **10.1**

### Administration

- **11.1**

### Storage

- **11.2**

###兼ねの入れ替えに伴う医薬品の利用

- **11.3**

### Other Information

- **12.1**

### Use in Specific Populations

- **12.2**

### Pediatric Patients

- **12.6**

### Pregnancy

- **12.6**

### Nursing Mothers

- **12.6**

### Reproduction

- **12.6**

### Carcinogenesis, Mutagenesis, Impairment of Fertility

- **12.7**

### Nonclinical Toxicology

- **12.8**

### Clinical Pharmacology

- **12.9**

### Pharmacokinetics

- **12.10**

### Pharmacodynamics

- **12.11**

### Laboratory Test Interactions

- **12.13**

### Administration

- **12.14**

### Storage

- **12.15**

### Safety

- **12.16**

### Adverse Reactions

- **12.17**

### Drug Interactions

- **12.18**

### Monitoring Parameters

- **12.19**

### Adverse Events During Long-Term Therapy

- **12.20**

### Infectious Disease/ Drug Interactions

- **12.21**

### Postmarketing Experience

- **12.22**

### Administration

- **12.23**

### Storage

- **12.24**

###兼ねの入れ替えに伴う医薬品の利用

- **12.25**

### Other Information

- **12.26**

### Use in Specific Populations

- **12.27**

### Pediatric Patients

- **12.31**

### Pregnancy

- **12.31**

### Nursing Mothers

- **12.31**

### Reproduction

- **12.32**

### Carcinogenesis, Mutagenesis, Impairment of Fertility

- **12.33**

### Nonclinical Toxicology

- **12.34**

### Clinical Pharmacology

- **12.35**

### Pharmacokinetics

- **12.36**

### Pharmacodynamics

- **12.37**

### Laboratory Test Interactions

- **12.39**

### Administration

- **12.40**

### Storage

- **12.41**

### Safety

- **12.42**

### Adverse Reactions

- **12.43**

### Drug Interactions

- **12.44**

### Monitoring Parameters

- **12.45**

### Adverse Events During Long-Term Therapy

- **12.46**

### Infectious Disease/ Drug Interactions

- **12.47**

### Postmarketing Experience

- **12.48**

### Administration

- **12.49**

### Storage

- **12.50**

###兼ねの入れ替えに伴う医薬品の利用

- **12.51**

### Other Information

- **12.52**

### Use in Specific Populations

- **12.53**

### Pediatric Patients

- **12.57**

### Pregnancy

- **12.57**

### Nursing Mothers

- **12.57**

### Reproduction

- **12.58**

### Carcinogenesis, Mutagenesis, Impairment of Fertility

- **12.59**

### Nonclinical Toxicology

- **12.60**

### Clinical Pharmacology

- **12.61**

### Pharmacokinetics

- **12.62**

### Pharmacodynamics

- **12.63**

### Laboratory Test Interactions

- **12.65**

### Administration

- **12.66**

### Storage

- **12.67**

### Safety

- **12.68**

### Adverse Reactions

- **12.69**

### Drug Interactions

- **12.70**

### Monitoring Parameters

- **12.71**

### Adverse Events During Long-Term Therapy

- **12.72**

### Infectious Disease/ Drug Interactions

- **12.73**

### Postmarketing Experience

- **12.74**

### Administration

- **12.75**

### Storage

- **12.76**

###兼ねの入れ替えに伴う医薬品の利用

- **12.77**

### Other Information

- **12.78**
Daptomycin for injection was administered by IV infusion over a 30-minute period. For injection contains daptomycin, a cyclic lipopeptide antibacterial agent derived from Streptomyces roseosporus, the molecular weight is 1620.67. Daptomycin for injection is cleared slowly from the body by hemodialysis (approximately 15% of the administered dose is removed over 48 hours). The use of high-flux dialysis membranes during 4 hours of hemodialysis is not recommended.

### Table 1: Pharmacokinetic Parameters Obtained Following a Single Dose from Patients with Complicated Skin and Skin Structure Infections

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Adult Subjects</th>
<th>Elderly Subjects</th>
<th>Extremely Obese Subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>AUC (mcg·h/mL)</td>
<td>72H</td>
<td>0.9% sodium chloride injection</td>
<td>74H</td>
</tr>
<tr>
<td>CL (mL/min/kg)</td>
<td>8.1</td>
<td>7.9</td>
<td>9.1</td>
</tr>
<tr>
<td>T1/2 (h)</td>
<td>5.8</td>
<td>5.8</td>
<td>7.9</td>
</tr>
<tr>
<td>Tmax (h)</td>
<td>0.102</td>
<td>0.096</td>
<td>0.101</td>
</tr>
</tbody>
</table>

### Table 2: Clinical Success Rates byATING Pathogens in the ERTIT Trials in Adult Patients

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Clinical Success Rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Staphylococcus aureus (including vancomycin-resistant isolates)</td>
<td>94%</td>
</tr>
<tr>
<td>Other Gram-positive cocci</td>
<td>92%</td>
</tr>
<tr>
<td>Methicillin-resistant S. aureus (MRSA)</td>
<td>93%</td>
</tr>
</tbody>
</table>

### Table 3: Common Adverse Reactions in Clinical Trials

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>Rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>34%</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>27%</td>
</tr>
<tr>
<td>Vomiting</td>
<td>12%</td>
</tr>
<tr>
<td>Anorexia</td>
<td>10%</td>
</tr>
</tbody>
</table>

### Table 4: Selected Serious Adverse Reactions

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>Rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thrombosis</td>
<td>5%</td>
</tr>
<tr>
<td>Hemorrhage</td>
<td>4%</td>
</tr>
<tr>
<td>Hypotension</td>
<td>3%</td>
</tr>
</tbody>
</table>

### Table 5: Radiation-Related Adverse Reactions

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>Rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alopecia</td>
<td>30%</td>
</tr>
<tr>
<td>Hair loss</td>
<td>25%</td>
</tr>
<tr>
<td>Nail discoloration</td>
<td>20%</td>
</tr>
</tbody>
</table>

### Table 6: Other Adverse Reactions

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>Rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatigue</td>
<td>20%</td>
</tr>
<tr>
<td>Constipation</td>
<td>15%</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>10%</td>
</tr>
</tbody>
</table>

### Table 7: Selected Laboratory Values

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Baseline</th>
<th>Treatment</th>
<th>Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin</td>
<td>15.0</td>
<td>15.5</td>
<td>0.5</td>
</tr>
<tr>
<td>WBC</td>
<td>8.0</td>
<td>7.0</td>
<td>-1.0</td>
</tr>
<tr>
<td>Platelets</td>
<td>250</td>
<td>230</td>
<td>-20</td>
</tr>
</tbody>
</table>

### Table 8: Summary of Other Pharmacokinetic Parameters

- AUC (mcg·h/mL)
- CL (mL/min/kg)
- T1/2 (h)
- Tmax (h)
- Dose
- Parameters obtained following a single dose from patients with complicated skin and skin structure infections.