INDICATION AND USAGE
DALVANCE® (dalbavancin) for injection is indicated for the treatment of adult patients with acute bacterial skin and skin structure infections (ABSSSI) caused by susceptible isolates of the following Gram-positive microorganisms:

- Staphylococcus aureus (including methicillin-susceptible and methicillin-resistant strains),
- Streptococcus pyogenes, Streptococcus agalactiae,
- Streptococcus dysgalactiae, Streptococcus anginosus group (including S. anginosus, S. intermedius, S. constellatus) and Enterococcus faecalis (vancomycin-susceptible strains).

To reduce the development of drug-resistant bacteria and maintain the effectiveness of DALVANCE and other antibacterial agents, DALVANCE should be used only to treat infections that are proven or strongly suspected to be caused by susceptible bacteria.

IMPORTANT SAFETY INFORMATION
Contraindications
DALVANCE is contraindicated in patients with known hypersensitivity to dalbavancin.

Please see additional Important Safety Information on page 12.
Please also see enclosed full Prescribing Information.
INTRODUCTION

The DALVANCE® (dalbavancin) for injection CODING AND BILLING REFERENCE GUIDE has been developed to help healthcare providers and billing staff understand third-party reimbursement for DALVANCE (dalbavancin). Specifically, this guide presents general information on coverage, coding, payment and claims submission for DALVANCE to third-party payors. As such, the information contained in this guide is intended to provide a general understanding of the reimbursement process and is not intended to assist healthcare providers in obtaining reimbursement for any specific claim. Additional information about coding, billing, and coverage of DALVANCE can be obtained through DALVANCE CONNECTS™, a single source of services designed to simplify access to therapy with DALVANCE, at: 1.855.387.2824, Monday through Friday excluding holidays, 8 AM to 8 PM ET, or visit the website: www.DALVANCE.com for additional support, including prescribing information.

COVERAGE for DALVANCE

Third-party payors (eg, commercial insurers, Medicare, Medicaid, etc.) cover DALVANCE (dalbavancin) for its approved U.S. Food and Drug Administration indications (see Indication on front cover of this guide). Coverage and benefits, however, may vary depending upon a patient’s insurer or specific insurance plan or “product” (ie, HMO, PPO, Indemnity, other) offered by a payor.

When reviewing claims for DALVANCE, third-party payors will first determine if the reported service is covered under their coverage policies or contract. Most payors cover drug infusions as part of their core medical benefits according to indications. In some cases, payors will look for evidence supporting the medical necessity of therapy. This evidence may sometimes include:

- Prescribing information
- A physician’s statement or letter of medical necessity
- Information about the patient’s medical condition and history

There are other general administrative policies that may also affect coverage of therapy with DALVANCE. For example, payors may consider the following:

A Prior Authorization may be required by the patient’s insurance plan

Many commercial plans and Medicaid require that non-emergency services be preapproved through a Prior Authorization process prior to the administration of DALVANCE. Failure to obtain appropriate Prior Authorization can result in nonpayment by the plan. Medicare does not require a Prior Authorization for services, regardless of setting.

The patient’s health plan may restrict coverage of the therapy when provided in certain settings

Payors may have site-specific coverage rules that restrict provision of infused antibiotics. For example, Medicare may restrict coverage for infused therapies in the home setting under Medicare Part B.

Payors contract with providers to deliver services to the plan’s members

Contracted healthcare providers are thus “participating” or within that plan’s network (“in-network”), requiring the billing healthcare provider to abide by the contract charge structure when providing care for that plan’s members.

CODING for DALVANCE

It is important to accurately and fully complete claim forms for the therapy, whether the claim is submitted by physician offices or infusion centers using the CMS-1500 claim form or by hospital outpatient departments using the UB-04 claim form. This section identifies procedure and supply codes that are likely to be most relevant to healthcare provider claims for therapy with DALVANCE. Please note that healthcare providers are responsible for selecting appropriate codes for any particular claim based on the patient’s condition and the items and services that are furnished. Contact your local payor with regard to local payment and policies. The Table on the following page summarizes the relevant codes for DALVANCE claims.

Please see Important Safety Information on page 12.
Please also see enclosed full Prescribing Information.
When coding and billing for DALVANCE (dalbavancin) and drug administration services, providers may also need to accurately calculate billing units for the dosage amount used.

The HCPCS code for DALVANCE (dalbavancin) is J0875, described as: “Injection, dalbavancin, 5 mg.” Thus, each 5 mg dose of dalbavancin equals one billing unit. It is important to understand that when billing for DALVANCE, each 500 mg vial of drug represents 100 units of J0875.

<table>
<thead>
<tr>
<th>Number of 500 mg vials of DALVANCE</th>
<th>Number of mg</th>
<th>Number of billing units based on J0875 (5 mg dalbavancin per unit)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>500</td>
<td>100</td>
</tr>
<tr>
<td>2</td>
<td>1000</td>
<td>200</td>
</tr>
</tbody>
</table>

**DALVANCE Billing Units**

When coding and billing for DALVANCE (dalbavancin) and drug administration services, providers may also need to accurately calculate billing units for the dosage amount used.

The HCPCS code for DALVANCE (dalbavancin) is J0875, described as: “Injection, dalbavancin, 5 mg.” Thus, each 5 mg dose of dalbavancin equals one billing unit. It is important to understand that when billing for DALVANCE, each 500 mg vial of drug represents 100 units of J0875.

Medicare, most commercial insurers, and most Medicaid agencies require healthcare providers to use Healthcare Common Procedure Coding System (HCPCS) codes (known as “J-Codes”) to identify infused drugs on claims forms. HCPCS codes have a 5-character alphanumeric format.

A new and permanent J-code has been issued for DALVANCE (dalbavancin) for Injection effective January 1, 2016:

**J0875**
Injection, dalbavancin, 5 mg

The J0875 permanent J-code replaces Miscellaneous J-codes (J3490 or J3590) and C-9443 that have been used to bill for DALVANCE prior to 2016.

Some commercial payors and the majority of Medicaid fee-for-service programs require a National Drug Code (NDC) for billing in addition to, or instead of, an HCPCS code, for physicians and other service providers as well.

Although the FDA uses a 10-digit format when registering NDCs, payors usually recognize and often require an 11-digit NDC format on claim forms for billing purposes. It is important to confirm with your payor which NDC format they require. Guidelines for reporting the NDC in the appropriate format, quantity, and unit of measure vary by state and by payor, and should be reviewed prior to submitting the claim.

The 10-digit NDC and 11-digit alternative NDC formats for DALVANCE 500 mg dalbavancin, single-use vial are:

- 10-digit NDC format: 57970-100-01
- 11-digit NDC format: 57970-0100-01
<table>
<thead>
<tr>
<th>Code Set</th>
<th>Setting of Care</th>
<th>Description and Code</th>
<th></th>
</tr>
</thead>
</table>
| **CPT codes used to report IV infusion** | • Physician office  
• Free-standing infusion center  
• Hospital outpatient department  
• Hospital outpatient provider-based clinic  
• Hospital inpatient | Services in physician offices, infusion centers, and hospital departments are reported on claims forms using the Current Procedural Terminology (CPT), 4th Edition, coding system. The CPT code most commonly associated with the administration of DALVANCE® is:  
96365 Intravenous infusion for therapy, prophylaxis, or diagnosis (specify substance or drug); initial, up to 1 hour  
NOTE: The medical record documented start and stop time of IV infusion must be >15 minutes. |
| **Revenue Codes**            | • Varies                                             | Many payors require use of American Hospital Association (AHA) revenue codes to bill for services provided in hospital outpatient departments. Revenue codes consist of a leading zero followed by three other digits and are used on claim forms to assign costs to broad categories of hospital revenue centers.  
The revenue codes that are commonly used with DALVANCE (dalbavancin) are:  
• 0250 Pharmacy, drugs not requiring detailed coding (used for claims to many non-Medicare payors)  
• 0510 Clinic  
• 0636 Pharmacy, drugs requiring detailed coding with HCPCS code (suggested for Medicare and sometimes required for other payors to obtain pass-through payment for drugs)  
When AHA revenue code 0636 is used to identify DALVANCE, hospital outpatient departments should also record HCPCS code J0875.  
It is important to review your major payor contracts and their billing manuals to determine the appropriate revenue codes to link to the HCPCS and CPT codes that represent the outpatient hospital services, procedures, and products. |
| **ICD-10-CM Codes**          | • All healthcare settings                             | International Classification of Diseases, 10th edition, Clinical Modification (ICD-10-CM) is a detailed and specific diagnosis coding system developed by the Centers for Disease Control and Prevention (CDC) for use in all U.S. healthcare treatment settings. More detailed than ICD-9-CM, ICD-10 has been in use in a number of other countries for over a decade. It is intended to enhance accurate payment for services and assist with evaluating medical processes and outcomes. Diagnosis coding under ICD-10-CM uses 3–7 alpha and numeric digits and full code titles, but the format is very much the same as ICD-9. ICD-10 does not impact outpatient hospital or physician practice coding for supplies and services using HCPCS and CPT codes.  
The compliance date for implementation of ICD-10-CM is October 1, 2015, for all Health Insurance Portability and Accountability Act (HIPAA)-covered entities. ICD-10-CM will replace International Classification of Diseases, 9th Edition, Clinical Modification (ICD-9-CM) Diagnosis Codes in all healthcare settings for diagnosis reporting with dates of service, or dates of discharge for inpatients, that occur on or after October 1, 2015. |

Please see Important Safety Information on page 12.  
Please also see enclosed full Prescribing Information.
## DALVANCE (dalbavancin) Coding Summary

<table>
<thead>
<tr>
<th>Type of Claim Information</th>
<th>Type of Code</th>
<th>Code</th>
<th>Description</th>
<th>Location on CMS-1500 Form</th>
<th>Location on UB-04 Form</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cellulitis</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>L03.011-L03.019</td>
<td>Cellulitis of finger</td>
<td>Item 21</td>
<td>Form Locator 67</td>
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<tr>
<td></td>
<td></td>
<td>L03.031-L03.039</td>
<td>Cellulitis of toe</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>L03.111-L03.119</td>
<td>Cellulitis of other parts of limb</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>L03.211</td>
<td>Cellulitis of face</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>L03.221</td>
<td>Cellulitis of neck</td>
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<tr>
<td></td>
<td></td>
<td>L03.311-L03.319</td>
<td>Cellulitis of trunk</td>
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<td></td>
<td>L03.811-L03.818</td>
<td>Cellulitis of other sites</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>L03.90</td>
<td>Cellulitis, unspecified</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Methicillin-resistant Staphylococcus aureus</td>
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<td>A49.02</td>
<td>Methicillin-resistant Staphylococcus aureus infection, unspecified site</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>B95.62</td>
<td>Methicillin-resistant Staphylococcus aureus infection as the cause of diseases classified elsewhere</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Staphylococcus</td>
<td></td>
<td>A41.01-A41.2</td>
<td>Sepsis due to Staphylococcus</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>A49.01</td>
<td>Methicillin-susceptible Staphylococcus aureus infection, unspecified site</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>A49.02</td>
<td>Methicillin-resistant Staphylococcus aureus infection, unspecified site</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>B95.61-B95.8</td>
<td>Staphylococcus aureus as the cause of diseases classified elsewhere</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Streptococcus</td>
<td></td>
<td>A40.0-A40.9</td>
<td>Streptococcal sepsis</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>A49.1</td>
<td>Streptococcal infection, unspecified site</td>
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<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>B95.01-B95.1, B95.3-B95.8</td>
<td>Streptococcus</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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Call DALVANCE CONNECTS™ toll-free at 1.855.387.2824 for more information on ICD-10-CM, International Classification of Diseases, 10th Revision, Clinical Modification codes. THIS IS NOT AN ALL-INCLUSIVE LIST; CONSULT WITH PAYOR TO OBTAIN SPECIFIC COVERAGE POLICIES AND REQUIREMENTS FOR COVERED INDICATIONS.
### DALVANCE® (dalbavancin) Coding Summary

<table>
<thead>
<tr>
<th>Type of Claim Information</th>
<th>Type of Code</th>
<th>Code</th>
<th>Description</th>
<th>Location on CMS-1500 Form</th>
<th>Location on UB-04 Form</th>
</tr>
</thead>
<tbody>
<tr>
<td>Procedures, Services and Supplies</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CPT</td>
<td>96365</td>
<td>Intravenous infusion for therapy, prophylaxis, or diagnosis (specify substance or drug); initial, up to 1 hour</td>
<td>Item 24D</td>
<td>Form Locator 44</td>
<td></td>
</tr>
<tr>
<td>AHA Revenue Codes</td>
<td>0250</td>
<td>Pharmacy, drugs not requiring detailed coding (used for claims to many non-Medicare payors)</td>
<td>N/A</td>
<td>Form Locator 42 and 43</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0510</td>
<td>Clinic visit</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0636</td>
<td>Pharmacy, with detailed coding (requires HCPCS code)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DALVANCE</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medicare HCPCS</td>
<td>J0875</td>
<td>Injection, dalbavancin, 5 mg</td>
<td>Item 24/D</td>
<td>Form Locator 44 or Electronic Comment Field</td>
<td></td>
</tr>
<tr>
<td>NDC (11 digit)</td>
<td>57970-0100-01</td>
<td>500 mg dalbavancin, single-use vial</td>
<td>Shaded area above 24D or Item 24A or Item 19</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### 2016 Physician Office Sample Claim Form: CMS-1500

1. Item 19—Some payors may ask providers to specify DALVANCE (dalbavancin) dosage and NDC code while others may require alternative product codes (e.g., Medicaid claims). Please consult with your local payors or contact DALVANCE CONNECTS™ toll-free at 1.855.387.2824 to confirm payor-specific coding requirements.

2. Item 21—Indicate diagnosis/diagnoses using appropriate ICD-10-CM codes effective October 1, 2015.

3. Item 24D—Indicate appropriate CPT and HCPCS codes as required.

4. Use of evaluation and management codes requires documentation of medically appropriate services performed on the same day as the infusion. Medicare requires the use of modifier 25 when reporting a significant, separately identifiable E/M service by the same physician, on the same day of the infusion procedure.

5. Item 24E—Refer to the diagnosis for this service (see box 21). Enter only one diagnosis pointer per line.

6. Item 24G—5-mg units (100 units of J0875 = a single 500-mg vial of dalbavancin).

Please see Important Safety Information on page 12.
Please also see enclosed full Prescribing Information.
This document is provided for your guidance only. Please call DALVANCE CONNECTS™ at 1.855.387.2824 to verify coding and claim information for specific payors.

**Box 19 Additional Information:** Enter the appropriate drug-identifying information as required by payor; eg, brand and generic drug name, National Drug Code (NDC) 11-digit format, dosage, method of administration, etc. Note: Additional information may also be sent via attachment electronically or other format as allowed by payor.

**Box 21 Diagnosis:** Enter the appropriate diagnosis code; eg, ICD-10-CM: 041.12 for MRSA. Final code depends on medical record documentation. Note: Other diagnosis codes may apply.

**Box 21 ICD Indicator:** Identify the type of ICD diagnosis code used; eg, enter a “0” for ICD-10-CM.

**Box 23 Prior Authorization:** Enter the payor authorization number as obtained prior to services rendered.

**Box 24D Procedures/Services/Supplies:** Enter the appropriate CPT/HCPCS codes and modifiers; eg, - Drug: J0875 for DALVANCE - Administration: 96365 for IV infusion

**Box 24E Diagnosis Pointer:** Enter the letter (A-J) that corresponds to the diagnosis in Box 21.
# 2015 HOPD Sample Claim Form: UB-04

<table>
<thead>
<tr>
<th></th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Locator Box 42—List revenue codes in ascending order.</td>
</tr>
<tr>
<td>2</td>
<td>Locator Box 43—Describe procedure (eg, IV therapy, clinic visit).</td>
</tr>
<tr>
<td>3</td>
<td>Use of E/M codes requires documentation of medically appropriate services performed on the same day as the infusion.</td>
</tr>
<tr>
<td>4</td>
<td>Locator Box 44—Indicate appropriate CPT and HCPCS codes and modifiers if required.</td>
</tr>
<tr>
<td>5</td>
<td>Locator Box 46—5 mg units (100 units of J0875 = a single 500 mg vial of dalbavancin).</td>
</tr>
<tr>
<td>6</td>
<td>Locator Box 47—Indicate total charges.</td>
</tr>
<tr>
<td>7</td>
<td>Locator Box 67—Indicate diagnosis using appropriate ICD-10-CM codes effective October 1, 2015.</td>
</tr>
</tbody>
</table>

Please see Important Safety Information on page 12.
Please also see enclosed full Prescribing Information.
### Field 42-43: Enter the appropriate revenue code and description corresponding to the HCPCS code in Field 44; eg:
- 0636 for DALVANCE
- 0510 for IV infusion administered in the clinic

### Field 44: Enter appropriate CPT/HCPCS codes and modifiers; eg:
- Drug: J0875 for DALVANCE (for Medicare)
- Administration: 96365 for drug administration

### Field 46: Enter appropriate number of units of service; eg, J0875 1 unit equals 5 mg. Therefore a 500 mg injection would be 100 units (500 mg/5 mg = 100 units)

### Note: Some payors may provide alternative guidance

### Field 66: Identify the type of ICD diagnosis code used; eg, enter a “0” for ICD-10-CM

### Fields 67 and 67A-67Q: Enter the appropriate diagnosis code. Final code may depend on medical record documentation

### Note: Other diagnosis codes may apply

### Field 74: Enter principal ICD-10-CM procedure code; eg, 99.29 for IV infusion

### Field 80: Enter the appropriate drug-identifying information as required by payor; eg, brand and generic drug name, National Drug Code (NDC) 11-digit format, dosage, method of administration, etc; when using J0875, Medicare will no longer require this information

### Note: Additional information may also be sent via attachment electronically or other format as allowed by payor
Checklist for Accurate Billing

To proactively prevent denials and underpayments, it may be helpful to perform a prebilling review prior to submitting any claim to a payor. The following may be considered:

✓ Has insurance been verified?
✓ Is this a covered service?
✓ Were the specific payor requirements followed?
✓ Was a Prior Authorization needed and obtained?
✓ If applicable, is the referral authorized?
✓ Is medical necessity documented?
✓ Is all of the required information included on the claim?
✓ Are the correct codes (diagnosis, CPT, and HCPCS) reported?
✓ Are the billed units accurate and consistent with the J code descriptor?
✓ If a separate and distinct E/M service was provided, is it identified with modifier 25?

Appeals

The most common reasons for denials or underpayment of claims include:

• Omission of any information that clarifies medical necessity (eg, relevant diagnosis codes)
• Inaccurately reporting the billable units of drug; note that DALVANCE® (dalbavancin) is reported in 5 mg units
• Use of incorrect CPT or HCPCS codes; note that DALVANCE has a new and permanent HCPCS code: J0875, effective January 1, 2016
• Failure to follow payor-specific requirements for providing this therapy, including referrals and Prior Authorization
• Lack of proper and complete documentation
• Omission of special coding requirements (eg, the NDC number or required modifiers)
• In certain cases, omission of a physician letter/statement of medical necessity

Different payors provide different appeals rights depending upon the level of appeal for the denied claim (eg, first appeal, second appeal). In the event of a claim denial, be sure to resubmit your claim. Most well-documented follow-up submissions are successful.

Please see Important Safety Information on page 12.
Please also see enclosed full Prescribing Information.
For additional information regarding coding, coverage, and reimbursement policies or claim denials for DALVANCE (dalbavancin), call DALVANCE CONNECTSM, a single source of services designed to simplify access to therapy with DALVANCE, at: 1.855.387.2824, Monday through Friday excluding holidays, 8 AM to 8 PM ET.

The information in this guide is provided to assist you in understanding the reimbursement process. It is intended to help providers in accurately obtaining reimbursement for healthcare services. It is not intended to increase or maximize reimbursement by any payor. We strongly suggest that you consult your payor organization with regard to local reimbursement policies. This document is presented for informational purposes only and is not intended to provide reimbursement or legal advice. Laws, regulations, and policies concerning reimbursement are complex and updated frequently. While Allergan plc has made an effort to be current as of the issue date of this document, the information may not be as current or comprehensive when you view it. Please consult with your reimbursement specialist for any reimbursement or billing questions. Similarly, all Current Procedural Terminology (CPT®) & Healthcare Common Procedure Coding System (HCPCS) billing codes are supplied for informational purposes only and represent no statement, promise, or guarantee by Allergan plc that these codes will be appropriate or that reimbursement will be made.

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IMPORTANT SAFETY INFORMATION (continued)

Warnings and Precautions

Hypersensitivity Reactions
Serious hypersensitivity (anaphylactic) and skin reactions have been reported with glycopeptide antibacterial agents, including DALVANCE®. Exercise caution in patients with known hypersensitivity to glycopeptides due to the possibility of cross-sensitivity. If an allergic reaction occurs, treatment with DALVANCE should be discontinued.

Infusion-related Reactions
Rapid intravenous infusion of DALVANCE can cause reactions, including flushing of the upper body, urticaria, pruritus, and rash.

Hepatic Effects
ALT elevations with DALVANCE treatment were reported in clinical trials.

Clostridium difficile-associated Diarrhea
Clostridium difficile-associated diarrhea (CDAD) has been reported with nearly all systemic antibacterial agents, including DALVANCE, with severity ranging from mild diarrhea to fatal colitis. Evaluate if diarrhea occurs.

Development of Drug-resistant Bacteria
Prescribing DALVANCE in the absence of a proven or strongly suspected bacterial infection is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.

Adverse Reactions
The most common adverse reactions in patients treated with DALVANCE were nausea (4.7%), headache (3.8%), and diarrhea (3.4%).

Use in Specific Populations

• There have been no adequate and well-controlled studies with DALVANCE in pregnant or nursing women. DALVANCE should only be used if the potential benefit justifies the potential risk in these populations.

• In patients with renal impairment whose known creatinine clearance is less than 30 mL/min and who are not receiving regularly scheduled hemodialysis, the recommended regimen of DALVANCE is 1125 mg, administered as a single dose, or 750 mg followed one week later by 375 mg. No dosage adjustment is recommended for patients receiving regularly scheduled hemodialysis, and DALVANCE can be administered without regard to the timing of hemodialysis.

• Caution should be exercised when prescribing DALVANCE to patients with moderate or severe hepatic impairment (Child-Pugh Class B or C) as no data are available to determine the appropriate dosing in these patients.

Please see full Indication and additional Important Safety Information on front cover.

Please see enclosed full Prescribing Information.
HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use DALVANCE® safely and effectively. See full prescribing information for DALVANCE.

DALVANCE (dalbavancin) for injection, for intravenous use
Initial U.S. Approval: 2014

1 INDICATIONS AND USAGE
1.1 Acute Bacterial Skin and Skin Structure Infections

DALVANCE® (dalbavancin) for injection is indicated for the treatment of adult patients with acute bacterial skin and skin structure infections (ABSSSI), caused by susceptible isolates of the following Gram-positive microorganisms: Staphylococcus aureus (including methicillin-susceptible and methicillin-resistant strains), Streptococcus pyogenes, Streptococcus agalactiae, Streptococcus dysgalactiae, Streptococcus anginosus group (including S. anginosus, S. intermedius, S. constellatus) and Enterococcus faecalis (vancomycin susceptible strains).

1.2 Usage

To reduce the development of drug-resistant bacteria and maintain the effectiveness of DALVANCE and other antibacterial drugs, DALVANCE should be used only to treat infections that are proven or strongly suspected to be caused by susceptible bacteria. (1.2)

2 DOSAGE AND ADMINISTRATION

2.1 Recommended Dosage Regimen

The recommended dosage regimen of DALVANCE in patients with normal renal function is 1500 mg, administered either as a single dose, or 1000 mg followed one week later by 500 mg. DALVANCE should be administered over 30 minutes by intravenous infusion [see Dosage and Administration (2.3)].

2.2 Dosage in Patients with Renal Impairment

In patients with renal impairment whose known creatinine clearance is less than 30 mL/min and who are not receiving regularly scheduled hemodialysis, the recommended regimen of DALVANCE is 1125 mg, administered as a single dose, or 750 mg followed one week later by 375 mg [see Use in Specific Populations (8.5), Clinical Pharmacology (12.3)].

2.3 Preparation and Administration

DALVANCE (dalbavancin) for injection must be reconstituted with either Sterile Water for Injection, USP, or 5% Dextrose Injection, USP, and subsequently diluted only with 5% Dextrose Injection, USP, to a final concentration of 1 mg/mL to 5 mg/mL.

3 DOSAGE FORMS AND STRENGTHS

DALVANCE for injection, for intravenous use, is supplied as a lyophilized powder for reconstitution. The single dose vial contains dalbavancin 1500 mg. The two-dose vial contains dalbavancin 1000 mg and dalbavancin 500 mg.

4 CONTRAINDICATIONS

Hypersensitivity to dalbavancin

5 WARNINGS AND PRECAUTIONS

Serious hypersensitivity (anaphylactic) and skin reactions have been reported with glycopeptide antibacterial agents, including DALVANCE; exercise caution in patients with known hypersensitivity to glycopeptides. (5.1)

6 ADVERSE REACTIONS

The most common adverse reactions in patients treated with DALVANCE were nausea (4.7%), headache (3.8%), and diarrhea (3.4%). (6.1)

7 DRUG INTERACTIONS

7.1 Drug-Laboratory Test Interactions

To reduce the development of drug-resistant bacteria and maintain the effectiveness of DALVANCE and other antibacterial drugs, DALVANCE should be used only to treat infections that are proven or strongly suspected to be caused by susceptible bacteria. (1.2)

7.2 Drug-Drug Interactions

Dosage adjustment is required in patients whose creatinine clearance is less than 30 mL/min and who are not receiving regularly scheduled hemodialysis. (2.2, 8.6)

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

8.2 Lactation

8.4 Pediatric Use

8.5 Geriatric Use

8.6 Renal Impairment

8.7 Hepatic Impairment

10 OVERDOSAGE

11 DESCRIPTION

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

12.2 Pharmacodynamics

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13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

13.2 Animal Toxicology and/or Pharmacology

14 CLINICAL STUDIES

15 REFERENCES

16 HOW SUPPLIED/STORAGE AND HANDLING

17 PATIENT COUNSELING INFORMATION

*Sections or subsections omitted from the full prescribing information are not listed

DOSAGE FORMS AND STRENGTHS

For injection: 500 mg of lyophilized powder in a vial for reconstitution (3)

CONTRAINDICATIONS

WARNINGS AND PRECAUTIONS

RECENT MAJOR CHANGES

INDICATIONS AND USAGE

DALVANCE is indicated for acute bacterial skin and skin structure infections (ABSSSI) caused by designated susceptible strains of Gram-positive microorganisms. (1.1)

To reduce the development of drug-resistant bacteria and maintain the effectiveness of DALVANCE and other antibacterial drugs, DALVANCE should be used only to treat infections that are proven or strongly suspected to be caused by susceptible bacteria. (1.2)

Dosage and Administration (2)

Dosage in patients with normal or impaired renal function (2.1, 2.2):

<table>
<thead>
<tr>
<th>Estimated CrCl</th>
<th>Single Dose Regimen</th>
<th>Two-Dose Regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 30 mL/min or on regular hemodialysis</td>
<td>1500 mg</td>
<td>1000 mg followed one week later by 500 mg</td>
</tr>
<tr>
<td>&lt; 30 mL/min and not on regular hemodialysis</td>
<td>1125 mg</td>
<td>750 mg followed one week later by 375 mg</td>
</tr>
</tbody>
</table>

• Administer by intravenous infusion over 30 minutes (2.1, 2.3)

• See Full Prescribing Information for instructions on reconstitution of lyophilized powder and preparation of injection (2.3).

FULL PRESCRIBING INFORMATION: CONTENTS*

1 INDICATIONS AND USAGE

1.1 Acute Bacterial Skin and Skin Structure Infections

1.2 Usage

2 DOSAGE AND ADMINISTRATION

2.1 Recommended Dosage Regimen

2.2 Dosage in Patients with Renal Impairment

2.3 Preparation and Administration

3 DOSAGE FORMS AND STRENGTHS

4 CONTRAINDICATIONS

5 WARNINGS AND PRECAUTIONS

5.1 Hypersensitivity Reactions

5.2 Infusion-Related Reactions

5.3 Hepatic Effects

5.4 Clostridium difficile-Associated Diarrhea

5.5 Development of Drug-Resistant Bacteria

6 ADVERSE REACTIONS

6.1 Clinical Trials Experience

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8 USE IN SPECIFIC POPULATIONS

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15 REFERENCES

16 HOW SUPPLIED/STORAGE AND HANDLING

17 PATIENT COUNSELING INFORMATION

Revised 01/2016
Reconstitution: DALVANCE must be reconstituted under aseptic conditions, using 25 mL of either Sterile Water for Injection, USP, or 5% Dextrose Injection, USP, for each 500 mg vial. To avoid foaming, alternate between gentle swirling and inversion of the vial until its contents are completely dissolved. Do not shake. The reconstituted vial contains 20 mg/mL dalbavancin as a clear, colorless to yellow solution. Reconstituted vials may be stored either refrigerated at 2 to 8 °C (36 to 46 °F), or at controlled room temperature 20 to 25 °C (68 to 77 °F). Do not freeze.

Dilution: Aseptically transfer the required dose of reconstituted dalbavancin solution from the vial(s) to an intravenous bag or bottle containing 5% Dextrose Injection, USP. The diluted solution must have a final dalbavancin concentration of 1 mg/mL to 5 mg/mL. Discard any unused portion of the reconstituted solution.

Once diluted into an intravenous bag or bottle as described above, DALVANCE may be stored either refrigerated at 2 to 8 °C (36 to 46 °F) or at a controlled room temperature of 20 to 25 °C (68 to 77 °F). Do not freeze.

The total time from reconstitution to dilution to administration should not exceed 48 hours.

Like all parenteral drug products, diluted DALVANCE should be inspected visually for particulate matter prior to infusion. If particulate matter is identified, do not use.

Administration: After reconstitution and dilution, DALVANCE is to be administered via intravenous infusion, using a total infusion time of 30 minutes.

Do not co-infuse DALVANCE with other medications or electrolytes. Saline-based infusion solutions may cause precipitation and should not be used. The compatibility of reconstituted DALVANCE with intravenous medications, additives, or substances other than 5% Dextrose Injection, USP has not been established.

If a common intravenous line is being used to administer other drugs in addition to DALVANCE, the line should be flushed before and after each DALVANCE infusion with 5% Dextrose Injection, USP.

3 DOSAGE FORMS AND STRENGTHS

DALVANCE is supplied in clear glass vials containing sterile powder (white/off-white to pale yellow) equivalent to 500 mg of dalbavancin.

4 CONTRAINDICATIONS

DALVANCE is contraindicated in patients with known hypersensitivity to dalbavancin. No data are available on cross-reactivity between dalbavancin and other glycopeptides, including vancomycin.

5 WARNINGS AND PRECAUTIONS

5.1 Hypersensitivity Reactions

Serious hypersensitivity (anaphylactic) and skin reactions have been reported in patients treated with DALVANCE. If an allergic reaction occurs, treatment with DALVANCE should be discontinued. Before using DALVANCE, inquire carefully about previous hypersensitivity reactions to glycopeptides, and due to the possibility of cross-sensitivity, exercise caution in patients with a history of glycopeptide allergy [see Patient Counseling Information (17)].

5.2 Infusion-Related Reactions

DALVANCE is administered via intravenous infusion, using a total infusion time of 30 minutes to minimize the risk of infusion-related reactions. Rapid intravenous infusions of DALVANCE can cause reactions that resemble "Red-Man Syndrome," including flushing of the upper body, urticaria, pruritus, and/or rash. Stopping or slowing the infusion may result in cessation of these reactions.

5.3 Hepatic Effects

In Phase 2 and 3 clinical trials, more DALVANCE than comparator-treated subjects with normal baseline transaminase levels post-baseline alanine aminotransferase (ALT) elevation greater than 3 times the upper limit of normal (ULN) Overall, abnormalities in liver tests (ALT, AST, bilirubin) were reported with similar frequency in the DALVANCE and comparator arms [see Adverse Reactions (6.1)].

5.4 Clostridium difficile-Associated Diarrhea

Clostridium difficile-associated diarrhea (CDAD) has been reported in users of nearly all systemic antibacterial drugs, including DALVANCE, with severity ranging from mild diarrhea to fatal colitis. Treatment with antibacterial agents may alter the normal flora of the colon, and may permit overgrowth of C. difficile.

C. difficile produces toxins A and B which contribute to the development of CDAD. Hypertoxin-producing strains of C. difficile cause increased morbidity and mortality, as these infections can be refractory to antibacterial therapy and may require colectomy. CDAD must be considered in all patients who present with diarrhea following antibacterial use. Careful medical history is necessary because CDAD has been reported to occur more than 2 months after the administration of antibacterial agents.

If CDAD is suspected or confirmed, ongoing antibacterial use not directed against C. difficile should be discontinued, if possible. Appropriate measures such as fluid and electrolyte management, protein supplementation, antibacterial treatment of C. difficile, and surgical evaluation should be instituted as clinically indicated.

5.5 Development of Drug-Resistant Bacteria

Prescribing DALVANCE in the absence of a proven or strongly suspected bacterial infection is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.

6 ADVERSE REACTIONS

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in clinical trials of DALVANCE cannot be directly compared to rates in the clinical trials of another drug and may not reflect rates observed in practice.

Adverse reactions were evaluated for 2473 patients treated with DALVANCE: 1778 patients were treated with DALVANCE in seven Phase 2/3 trials comparing DALVANCE to comparator antibacterial drugs and 695 patients were treated with DALVANCE in one Phase 3 trial comparing DALVANCE single and two-dose regimens. A causal relationship between study drug and adverse reactions was not always established. The median age of patients treated with DALVANCE was 48 years, ranging between 16 and 93 years. Patients treated with DALVANCE were predominantly male (59.5%) and White (61.2%).

Serious Adverse Reactions and Adverse Reactions Leading to Discontinuation

Serious adverse reactions occurred in 121/2473 (4.9%) of patients treated with any regimen of DALVANCE. In the Phase 2/3 trials comparing DALVANCE to comparator, serious adverse reactions occurred in 108/1778 (6.1%) of patients in the DALVANCE group and 80/1224 (6.5%) of patients in the comparator group. In a Phase 3 trial comparing DALVANCE single and two-dose regimens, serious adverse reactions occurred in 7/349 (2.0%) of patients in the DALVANCE single dose group and 5/346 (1.4%) of patients in the DALVANCE two-dose group. DALVANCE was discontinued due to an adverse reaction in 64/2473 (2.6%) patients treated with any regimen of DALVANCE. In the Phase 2/3 trials comparing DALVANCE to comparator, DALVANCE was discontinued due to an adverse reaction in 53/1778 (3.0%) of patients in the DALVANCE group and 35/1224 (2.9%) of patients in the comparator group. In a Phase 3 trial comparing DALVANCE single and two-dose regimens, DALVANCE was discontinued due to an adverse reaction in 6/349 (1.7%) of patients in the DALVANCE single-dose group and 5/346 (1.4%) of patients in the DALVANCE two-dose group.

Most Common Adverse Reactions

The most common adverse reactions in patients treated with DALVANCE were nausea (4.7%), headache (3.8%), and diarrhea (3.4%). The median duration of adverse reactions was 3.0 days in patients treated with DALVANCE. In the Phase 2/3 trials comparing DALVANCE to comparator, the median duration of adverse reactions was 3.0 days for patients in the DALVANCE group and 4.0 days in patients in the comparator group. In a Phase 3 trial comparing DALVANCE single and two-dose regimens, the median duration of adverse reactions was 3.0 days for patients in the DALVANCE single and two-dose group.

Table 2 lists selected adverse reactions occurring in ≥2% of patients treated with DALVANCE in Phase 2/3 clinical trials.

<table>
<thead>
<tr>
<th>Adverse Reactions</th>
<th>DALVANCE (N = 1778)</th>
<th>Comparator* (N = 1224)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>98 (5.5)</td>
<td>78 (6.4)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>50 (2.8)</td>
<td>37 (3)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>79 (4.4)</td>
<td>72 (5.9)</td>
</tr>
<tr>
<td>Headache</td>
<td>83 (4.7)</td>
<td>59 (4.8)</td>
</tr>
<tr>
<td>Rash</td>
<td>48 (2.7)</td>
<td>30 (2.4)</td>
</tr>
<tr>
<td>Pruritus</td>
<td>38 (2.1)</td>
<td>41 (3.3)</td>
</tr>
</tbody>
</table>

* Comparators included linezolid, ceftaroline, cefepime, and vancomycin.

In the Phase 3 trial comparing the single and two-dose regimen of DALVANCE, the adverse reaction that occurred in ≥2% or more of patients treated with DALVANCE was nausea (3.4% in the DALVANCE single dose group and 2% in the DALVANCE two-dose group).

The following selected adverse reactions were reported in DALVANCE-treated patients at a rate of less than 2% in these clinical trials:

**Blood and lymphatic system disorders:** anemia, hemorrhagic anemia, leucopenia, neutropenia, thrombocytopenia, petechiae, epistaxis, lymphopenia, thrombocytosis

**Gastrointestinal disorders:** gastrointestinal hemorrhage, melena, hemorrhage, abdominal pain

**General disorders and administration site conditions:** infusion-related reactions

**Hepatobiliary disorders:** hepatic toxicity

**Immune system disorders:** anaphylactic reaction

**Infections and infestations:** Clostridium difficile- colitis, oral candidiasis, vulvovaginal mycotic infection

**Investigations:** hepatic transaminases increased, blood alkaline phosphatase increased, international normalized ratio increased, blood lactate dehydrogenase increased, gamma-glutamyl transferase increased

**Metabolism and nutrition disorders:** hypoglycemia

**Nervous system disorders:** dizziness

**Respiratory, thoracic and mediastinal disorders:** bronchospasm

**Skin and subcutaneous tissue disorders:** rash, pruritus, urticaria

**Vascular disorders:** flushing, phlebitis, wound hemorrhage, spontaneous hematoma
8.1 Pregnancy

**Risk Summary**
There have been no adequate and well-controlled studies with DALVANCE in pregnant women. DALVANCE should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

No treatment-related malformations or embryo-fetal toxicity were observed in pregnant rats or rabbits at clinically relevant exposures of dalbavancin. Treatment of pregnant rats with dalbavancin at 3.5 times the human dose on an exposure basis during early embryonic development and from implantation to the end of lactation resulted in delayed fetal maturation and increased fetal loss, respectively (see Data).

The background risk of major birth defects and miscarriage for the indicated population is unknown. However, the background risk in the U.S. general population of major birth defects and miscarriage is 2 to 4% and of miscarriage is 15 to 20% of clinically recognized pregnancies.

**Data**

*Animal Data*
No evidence of embryo or fetal toxicity was found in the rat or rabbit at a dose of 15 mg/kg/day (1.2 and 0.7 times the human dose on an exposure basis, respectively). Delayed fetal maturation was observed in the rat at a dose of 45 mg/kg/day (3.5 times the human dose on an exposure basis).

In a rat prenatal and postnatal development study, increased embryo lethality and increased offspring deaths during the first week post-partum were observed at a dose of 45 mg/kg/day (3.5 times the human dose on an exposure basis).

**8.2 Lactation**

**Risk Summary**
It is not known whether dalbavancin or its metabolite is excreted in human milk; therefore, caution should be exercised when DALVANCE is administered to a nursing woman.

The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for DALVANCE and any potential adverse effects on the breastfed child from DALVANCE or from the underlying maternal condition.

**Data**

*Animal Data*
Dalbavancin is excreted in the milk of lactating rats.

**8.4 Pediatric Use**
Safety and efficacy in pediatric patients have not been established.

**8.5 Geriatric Use**
Of the 2473 patients treated with DALVANCE in Phase 2 and 3 clinical trials, 403 patients (16.5%) were 65 years of age or older. The efficacy and tolerability of DALVANCE were similar to comparator regardless of age. The pharmacokinetics of DALVANCE was not significantly altered with age; therefore, no dosage adjustment is necessary based on age alone.

DALVANCE is substantially excreted by the kidney, and the risk of adverse reactions may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection in this age group.

**8.6 Renal Impairment**
In patients with renal impairment whose known creatinine clearance is less than 30 mL/min and who are not receiving regularly scheduled hemodialysis, the recommended regimen for DALVANCE is 1125 mg, administered as a single dose, or 750 mg followed one week later by 375 mg. No dosage adjustment is recommended for patients receiving regularly scheduled hemodialysis, and DALVANCE can be administered without regard to the timing of hemodialysis (see Dosage and Administration (2.2), Clinical Pharmacology (12.3)).

**8.7 Hepatic Impairment**
No dosage adjustment of DALVANCE is recommended for patients with mild hepatic impairment (Child-Pugh Class A). Caution should be exercised when prescribing DALVANCE to patients with moderate or severe hepatic impairment (Child-Pugh Class B or C) as no data are available to determine the appropriate dosing in these patients (see Clinical Pharmacology (12.3)).

10 OVERDOSE

Specific information is not available on the treatment of overdose with DALVANCE, as dose-limiting toxicity has not been observed in clinical studies. In Phase 1 studies, healthy volunteers have been administered cumulative doses of up to 4500 mg over a period of up to 8 weeks, with no signs of toxicity or laboratory results of clinical concern.

Treatment of overdose with DALVANCE should consist of observation and general supportive measures. Although no information is available specifically regarding the use of hemodialysis to treat overdose, in a Phase 1 study in patients with renal impairment less than 6% of the recommended dalbavancin dose was removed (see Clinical Pharmacology (12.3)).

11 DESCRIPTION

DALVANCE (dalbavancin) for injection is a lipoglycopeptide synthesized from a fermentation product of Nonomuraea species.

Dalbavancin is a mixture of five species. The component B₂ is the major component of dalbavancin. The homologs share the same core structure and differ in the fatty acid side chain of the N-acylaminoglucuronic acid moiety (R₃) structure and/or the presence of an additional methyl group (R₄) on the terminal amino group (shown in the Figure 1 and Table 3 below).

**Figure 1. Dalbavancin Structural Formula**

![Dalbavancin Structural Formula](image)

**Table 3. Substitution Patterns for Dalbavancin API Homologs**

<table>
<thead>
<tr>
<th>Dalbavancin</th>
<th>R₁</th>
<th>R₂</th>
<th>Molecular Formula</th>
<th>Molecular Weight*</th>
</tr>
</thead>
<tbody>
<tr>
<td>A₀</td>
<td>CH(CH₃)₂</td>
<td>H</td>
<td>C₉H₁₉N₂O₂Cl₂ · 1.6 HCl</td>
<td>1802.7</td>
</tr>
<tr>
<td>A₁</td>
<td>CH₂CH₂CH₂</td>
<td>H</td>
<td>C₁₀H₂₁N₂O₂Cl₂ · 1.6 HCl</td>
<td>1802.7</td>
</tr>
<tr>
<td>B₀</td>
<td>CH₂CH₂CH₂</td>
<td>H</td>
<td>C₁₀H₂₁N₂O₂Cl₂ · 1.6 HCl</td>
<td>1816.7</td>
</tr>
<tr>
<td>B₁</td>
<td>CH₂CH₂CH₂</td>
<td>H</td>
<td>C₁₀H₂₁N₂O₂Cl₂ · 1.6 HCl</td>
<td>1816.7</td>
</tr>
<tr>
<td>B₂</td>
<td>CH₂CH₂CH₂</td>
<td>CH</td>
<td>C₁₀H₂₂N₂O₂Cl₂ · 1.6 HCl</td>
<td>1830.7</td>
</tr>
</tbody>
</table>

*Anhydrous free base


DALVANCE is supplied in clear glass vials as a sterile, lyophilized, preservative-free, white to off-white to pale yellow solid. Each vial contains dalbavancin HCl equivalent to 500 mg of dalbavancin as the free base, plus lactose monohydrate (129 mg) and mannitol (159 mg) as excipients. Sodium hydroxide or hydrochloric acid may be added to adjust the pH at the time of manufacture. The powder is to be reconstituted and further diluted for IV infusion (see Dosage and Administration (2.3), How Supplied/Storage and Handling (16)).
Dalbavancin is an antibiotic drug [see Microbiology (12.4)].

12.2 Pharmacodynamics

The antibacterial activity of dalbavancin appears to be best correlated with the ratio of area under the concentration-time curve to minimal inhibitory concentration (AUC/MIC) for Staphylococcus aureus based on animal models of infection. An exposure-response analysis of a single study in patients with complicated skin and skin structure infections supports the two-dose regimen [see Dosage and Administration (2.1), Clinical Pharmacology (12.3)].

Cardiac Electrophysiology: In a randomized, positive- and placebo-controlled, thorough QT/QTc study, 200 healthy subjects received dalbavancin 1000 mg IV, dalbavancin 1500 mg IV, oral moxifloxacin 400 mg, or placebo. Neither dalbavancin 1000 mg nor dalbavancin 1500 mg had any clinically relevant adverse effect on cardiac repolarization.

12.3 Pharmacokinetics

Dalbavancin pharmacokinetic parameters have been characterized in healthy subjects, patients, and specific populations. Pharmacokinetic parameters following administration of single intravenous 1000 mg and 1500 mg doses were as shown in Table 4. The pharmacokinetics of dalbavancin can be described using a three-compartment model.

Table 4. Dalbavancin Pharmacokinetic Parameters in Healthy Subjects

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Single 1000 mg Dose</th>
<th>Single 1500 mg Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>C&lt;sub&gt;max&lt;/sub&gt; (µg/mL)</td>
<td>297 (13.9)&lt;sup&gt;1&lt;/sup&gt;</td>
<td>423 (13.2)&lt;sup&gt;1&lt;/sup&gt;</td>
</tr>
<tr>
<td>AUC&lt;sub&gt;0-336&lt;/sub&gt; (µg•h/L)</td>
<td>3185 (12.8)&lt;sup&gt;1&lt;/sup&gt;</td>
<td>4837 (13.7)&lt;sup&gt;1&lt;/sup&gt;</td>
</tr>
<tr>
<td>AUC&lt;sub&gt;0-144&lt;/sub&gt; (µg•h/L)</td>
<td>11160 (41.1)&lt;sup&gt;1&lt;/sup&gt;</td>
<td>ND</td>
</tr>
<tr>
<td>AUC&lt;sub&gt;0-56&lt;/sub&gt; (µg•h/L)</td>
<td>23443 (40.9)&lt;sup&gt;1&lt;/sup&gt;</td>
<td>ND</td>
</tr>
<tr>
<td>Terminal t&lt;sub&gt;1/2&lt;/sub&gt; (h)</td>
<td>346 (16.5)&lt;sup&gt;2,3&lt;/sup&gt;</td>
<td>ND</td>
</tr>
<tr>
<td>CL (L/h)</td>
<td>0.0515 (46.8)&lt;sup&gt;2&lt;/sup&gt;</td>
<td>ND</td>
</tr>
</tbody>
</table>

<sup>1</sup> Data from 50 healthy subjects.
<sup>2</sup> Data from 12 healthy subjects.
<sup>3</sup> Based upon population pharmacokinetic analyses of data from patients, the effective half-life is approximately 8.5 days (204 hours).

All values are presented as mean (± coefficient of variation)

In healthy subjects, dalbavancin AUC<sub>0-144</sub> and C<sub>max</sub> both increased proportionally to dose following single IV dalbavancin doses ranging from 140 mg to 1500 mg, indicating linear pharmacokinetics.

The mean plasma concentration-time profile for dalbavancin following the recommended two-dose regimen of 1000 mg followed one week later by 500 mg is shown in Figure 2.

![Figure 2. Mean (± standard deviation) dalbavancin plasma concentrations versus time in healthy subjects (n=10) following IV administration over 30 minutes of 1000 mg dalbavancin (Day 1) and 500 mg dalbavancin (Day 8).](image)

No apparent accumulation of dalbavancin was observed following multiple IV infusions administered once weekly for up to eight weeks, with 1000 mg on Day 1 followed by up to seven weekly 500 mg doses, in healthy adults with normal renal function.

Distribution: Dalbavancin is reversibly bound to human plasma proteins, primarily to albumin. The plasma protein binding of dalbavancin is approximately 93% and is not altered as a function of drug concentration, renal impairment, or hepatic impairment. The mean concentrations of dalbavancin achieved in skin blister fluid remain above 30 µg/mL up to 7 days (approximately 146 hours) post dose, following 1000 mg IV dalbavancin. The mean ratio of the AUC<sub>0-144</sub> in skin blister fluid/AUC<sub>0-144</sub> in plasma is 0.80 (range 0.44 to 0.64).

Metabolism: In vitro studies using human microsomal enzymes and hepatocytes indicate that dalbavancin is not a substrate, inhibitor, or inducer of CYP450 isoenzymes. A minor metabolite of dalbavancin (hydroxy-dalbavancin) has been observed in the urine of healthy subjects. Quantifiable concentrations of the hydroxy-dalbavancin metabolite have not been observed in human plasma (lower limit of quantification = 0.4 µg/mL) [see Drug Interactions (7.2)].

12.4 Microbiology

Mechanism of Action

Dalbavancin, a semisynthetic lipoglycopeptide, interferes with cell wall synthesis by binding to the D-alanyl-D-alanine terminus of the stem pentapeptide in nascent cell wall peptidoglycan, thus preventing cross-linking. Dalbavancin is bactericidal in vitro against Staphylococcus aureus and Streptococcus pyogenes at concentrations similar to those sustained throughout treatment in humans treated according to the recommended dosage regimen.

Mechanism of Resistance

The development of bacterial isolates resistant to dalbavancin has not been observed, either in vitro, in studies using serial passage, or in animal infection experiments.

Interaction with Other Antimicrobials

When tested in vitro, dalbavancin demonstrated synergistic interactions with oxacillin and did not demonstrate antagonistic or synergistic interactions with any of the following antibacterial agents of various classes: gentamicin, vancomycin, levofloxacin, clindamycin, quinupristin/dalfopristin, linezolid, aztreonam, rifampin or daptomycin. The clinical significance of these in vitro findings is unknown.

Dalbavancin has been shown to be active against the following microorganisms, both in vitro and in clinical infections [see Indications and Usage (1)].

Excretion: Following administration of a single 1000 mg dose in healthy subjects, 20% of the dose was excreted in feces through 70 days post dose. An average of 33% of the administered dalbavancin dose was excreted in urine as unchanged dalbavancin and approximately 12% of the administered dose was excreted in urine as the metabolite hydroxy-dalbavancin through 42 days post dose.

Specific Populations

Renal Impairment: The pharmacokinetics of dalbavancin were evaluated in 28 subjects with varying degrees of renal impairment and in 15 matched control subjects with normal renal function.

Following a single dose of 500 mg or 1000 mg dalbavancin, the mean plasma clearance (CL<sub>D</sub>) was reduced 11%, 35%, and 47% in subjects with mild (CL<sub>D</sub> 50 to 79 mL/min), moderate (CL<sub>D</sub> 30 to 49 mL/min), and severe (CL<sub>D</sub> less than 30 mL/min), renal impairment, respectively, compared to subjects with normal renal function. The clinical significance of the decrease in mean plasma CL<sub>D</sub> and the associated increase in AUC<sub>D</sub> is noted in these pharmacokinetic studies of dalbavancin in subjects with severe renal impairment has not been established [see Dosage and Administration (2.2), Use in Specific Populations (8.6)].

No dosage adjustment is necessary for patients with CL<sub>D</sub> greater than 30 mL/min or patients receiving hemodialysis. The recommended regimen for dalbavancin in patients with severe renal impairment who are not receiving regularly scheduled hemodialysis is 1125 mg, administered as a single dose, or 750 mg followed one week later by 375 mg.

Dalbavancin pharmacokinetic parameters in subjects with end-stage renal disease receiving regularly scheduled hemodialysis (three times/week) are similar to those observed in subjects with mild to moderate renal impairment, and less than 6% of an administered dose is removed after three hours of hemodialysis. Therefore, no dosage adjustment is recommended for patients receiving regularly scheduled hemodialysis, and dalbavancin may be administered without regard to the timing of hemodialysis in such patients [see Dosage and Administration (2.1), Overdosage (10)].

Hepatic Impairment: The pharmacokinetics of dalbavancin were evaluated in 17 subjects with mild, moderate, or severe hepatic impairment (Child-Pugh class A, B, or C) and compared to those in nine matched healthy subjects with normal hepatic function. The mean AUC<sub>0-380</sub> was unchanged in subjects with mild hepatic impairment compared to subjects with normal hepatic function; however, the mean AUC<sub>0-144</sub> decreased 28% and 51% in subjects with moderate and severe hepatic impairment respectively, compared to subjects with normal hepatic function. The clinical significance of the decreased AUC<sub>0-380</sub> in subjects with moderate and severe hepatic function is unknown.

No dosage adjustment is recommended for patients with mild hepatic impairment. Caution should be exercised when prescribing dalbavancin to patients with moderate or severe hepatic impairment as no data are available to determine the appropriate dosing.

Gender: Clinically significant gender-related differences in dalbavancin pharmacokinetics have not been observed either in healthy subjects or in patients with infections. No dosage adjustment is recommended based on gender.

Geriatric Patients: Clinically significant age-related differences in dalbavancin pharmacokinetics have not been observed in patients with infections. No dosage adjustment is recommended based solely on age.

Pediatric Patients: The pharmacokinetics of dalbavancin in pediatric populations <12 years of age have not been established.

Drug Interactions

Nonclinical studies demonstrated that dalbavancin is not a substrate, inhibitor, or inducer of CYP450 isoenzymes. In a population pharmacokinetic analysis, dalbavancin pharmacokinetics were not affected by co-administration with known CYP450 substrates, inducers or inhibitors, nor by individual medications including acetaminophen, aztreonam, fentanyl, metronidazole, furosemide, proton pump inhibitors (omeprazole, esomeprazole, pantoprazole, lanoprazole), midazolam, and simvastatin.
Gram-positive bacteria
Staphylococcus aureus (including methicillin-resistant isolates)
Streptococcus pyogenes
Streptococcus agalactiae
Streptococcus dysgalactiae
Streptococcus anginosus group (including S. anginosus, S. intermedius, S. constellatus)
Enterococcus faecalis (vancomycin-susceptible isolates only)

The following in vitro data are available, but their clinical significance is unknown. In addition, at least 90% of organisms in the following bacteria exhibit an in vitro minimum inhibitory concentration (MIC) less than or equal to the dalbavancin susceptible breakpoint of 0.25 mcg/mL. However, the safety and efficacy of dalbavancin in treating clinical infections due to these bacteria have not been established in adequate well-controlled clinical trials.

Gram-positive bacteria
Enterococcus faecium (vancomycin-susceptible isolates only)

Susceptibility Test Methods
When available, the clinical microbiology laboratory should provide the results of in vitro susceptibility test results for antimicrobial drug products used in resident hospitals to the physician as periodic reports that describe the susceptibility profile of nosocomial and community-acquired pathogens. These reports should aid the physician in selecting an antibiotic drug for treatment.

Dilution Techniques
Quantitative methods are used to determine minimum inhibitory concentrations (MICs). These MICs provide estimates of the susceptibility of bacteria to antimicrobial compounds. The MICs should be determined using a standardized test method.1,2 When determining dalbavancin MICs, polysorbate-80 (P-80), should be added at a final concentration of 0.002% to freshly prepared or frozen microtiter trays. The MIC values should be interpreted according to the criteria provided in Table 5.

Diffusion Techniques
Dalbavancin disks for diffusion susceptibility testing are not available. Disk diffusion is not a reliable method for determining the in vitro activity of dalbavancin.

Table 5. Susceptibility Test Interpretive Criteria for Dalbavancin

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>MIC (mcg/mL)</th>
<th>Zone Diameter (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Staphylococcus aureus (including methicillin-resistant isolates)</td>
<td>≤ 0.25</td>
<td>-- -- -- -- -- --</td>
</tr>
<tr>
<td>Streptococcus pyogenes, Streptococcus agalactiae, and Streptococcus dysgalactiae, and Streptococcus anginosus group</td>
<td>≤ 0.25</td>
<td>-- -- -- -- -- --</td>
</tr>
<tr>
<td>Enterococcus faecalis (vancomycin-susceptible isolates only)</td>
<td>≤ 0.25</td>
<td>-- -- -- -- -- --</td>
</tr>
</tbody>
</table>

1 The current absence of data on resistant isolates precludes defining any category other than “Susceptible”. Isolates yielding test results other than “Susceptible” should be retested, and if the result is confirmed, the isolate should be submitted to a reference laboratory for additional testing.

A report of “Susceptible” indicates that the antibiotic agent is likely to inhibit growth of the pathogen if the antibiotic compound reaches the concentrations at the infection site necessary to inhibit growth of the pathogen.

Quality Control
Standardized susceptibility test procedures require the use of laboratory controls to monitor and ensure the accuracy and precision of supplies and reagents used in the assay, and the techniques of the individuals performing the test.1 Standard dalbavancin powder should provide the following range of MIC values noted in Table 6.

Table 6. Acceptable MIC Quality Control Ranges for Dalbavancin

<table>
<thead>
<tr>
<th>Quality Control Strain</th>
<th>MIC Range (µg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Staphylococcus aureus ATCC® 29213</td>
<td>0.03-0.12</td>
</tr>
<tr>
<td>Streptococcus pneumonia ATCC® 49619†</td>
<td>0.008-0.03</td>
</tr>
<tr>
<td>Enterococcus faecalis ATCC® 29212</td>
<td>0.03-0.12</td>
</tr>
</tbody>
</table>

† This organism may be used for validation of susceptibility test results when testing Streptococcus species other than S. pneumoniae.

13 NONCLINICAL TOXICOLOGY
13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
Long-term studies in animals to determine the carcinogenic potential of dalbavancin have not been conducted.

Dalbavancin was not genotoxic in a bacterial reverse mutation (Ames) assay, a mammalian HGPRT gene mutation assay, an in vitro chromosome aberration assay in Chinese Hamster Ovary cells, or an in vivo mouse micronucleus assay.

Impaired fertility in the rat was not observed at a dose of 15 mg/kg/day (1.2 times the human dose on an exposure basis). Reductions in male and female fertility and increased embryo resorptions occurred at a dose of 45 mg/kg/day (3.5 times the human dose on an exposure basis), at which signs of parental toxicity were also observed.

13.2 Animal Toxicology and/or Pharmacology

Increases in serum levels of liver enzymes (ALT, AST), associated with microscopic findings in the liver were noted in toxicology studies in rats and dogs where dalbavancin was administered daily for 28 to 90 days. Hepatoxic necrosis was observed in dogs dosed at ≥ 10 mg/kg/day for longer than 2 months, i.e., at approximately 5 to 7 times the expected human dose on an exposure basis. Histioctic vacuolation and hepatocyte necrosis were observed in rats dosed daily at 40 and 80 mg/kg/day, respectively, for 4 weeks, (approximately 3 and 6 times the expected human dose on an exposure basis, respectively). In addition, renal toxicity characterized by increases in serum BUN and creatinine and microscopic kidney findings was observed in rats and dogs at doses to 5 times the expected human dose on an exposure basis. The relation of these findings in the animal toxicology studies after 28 and 90 consecutive days of dosing to the indicated clinical dosing of 2 doses 7 days apart are unclear.

14 CLINICAL STUDIES

Acute Bacterial Skin and Skin Structure Infections: DALVANCE Two-dose Regimen (1000 mg Day 1; 500 mg Day 8)

Adult patients with ABSSSI were enrolled in two Phase 3, randomized, double-blind, double-dummy clinical trials of similar design (Trial 1 and Trial 2). The Intent-to-Treat (ITT) population included 1,312 randomized patients. Patients were treated for two weeks with either a two-dose regimen of intravenous DALVANCE (1000 mg followed one week later by 500 mg) or intravenous vancomycin (1000 mg or 15 mg/kg every 12 hours, with the option to switch to oral linezolid after 3 days). DALVANCE-treated patients with creatinine clearance of less than 30 mL/min received 755 mg followed one week later by 375 mg. Approximately 5% of patients also received a protocol-specified empiric course of treatment with intravenous aminoglycosides for coverage of Gram-negative pathogens.

The specific infections in these trials included cellulitis (approximately 50% of patients across treatment groups), major abscess (approximately 30%), and wound infection (approximately 20%). The median lesion area at baseline was 341 cm². In addition to local signs and symptoms of infection, patients were also required to have at least one systemic sign of disease at baseline, defined as temperature ≥ 38°C or higher (approximately 85% of patients), white blood cell count greater than 12,000 cells/mm³ (approximately 40%), or 10% or more band forms on white blood cell differential (approximately 23%). Across both trials, 59% of patients were from Eastern Europe and 36% of patients were from North America. Approximately 89% of patients were Caucasian and 58% were males. The mean age was 50 years and the mean body mass index was 29.1 kg/m².

The primary endpoint of these two ABSSSI trials was the clinical response rate where responders were defined as patients who had no increase from baseline in lesion area 48 to 72 hours after initiation of therapy, and had a temperature consistently at or below 37.5°C upon repeated measurement. Table 7 summarizes overall clinical response rates in these two ABSSSI trials using the pre-specified primary efficacy endpoint in the ITT population.

Table 7. Clinical Response Rates in ABSSSI Trials at 48-72 Hours after Initiation of Therapy

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>DALVANCE n/N (%)</th>
<th>Vancomycin/Linezolid n/N (%)</th>
<th>Difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Staphylococcus aureus (including methicillin-resistant isolates)</td>
<td>240/288 (83.3)</td>
<td>233/285 (81.8)</td>
<td>1.5 (-4.6, 7.9)</td>
</tr>
<tr>
<td>Streptococcus pyogenes, Streptococcus agalactiae, and Streptococcus dysgalactiae, and Streptococcus anginosus group</td>
<td>285/371 (76.8)</td>
<td>286/368 (78.3)</td>
<td>1.5 (-7.4, 4.6)</td>
</tr>
</tbody>
</table>

1 There were 7 patients who did not receive treatment and were counted as non-responders: 6 DALVANCE patients (3 in each trial) and one vancomycin/linezolid patient in Trial 2.

2 Patients who died or used non-study antibacterial therapy or had missing measurements were classified as non-responders.

3 The 95% Confidence Interval (CI) is computed using the Miettinen and Nurminen approach, stratified by baseline fever status.

A key secondary endpoint in these two ABSSSI trials evaluated the percentage of ITT patients achieving a 20% or greater reduction in lesion area from baseline at 48-72 hours after initiation of therapy. Table 8 summarizes the findings for this endpoint in these two ABSSSI trials.

Table 8. Patients in ABSSSI Trials with Reduction in Lesion Area of 20% or Greater at 48-72 Hours after Initiation of Therapy

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>DALVANCE n/N (%)</th>
<th>Vancomycin/Linezolid n/N (%)</th>
<th>Difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Staphylococcus aureus (including methicillin-resistant isolates)</td>
<td>259/288 (89.9)</td>
<td>259/285 (90.9)</td>
<td>-1.0 (-5.7, 4.0)</td>
</tr>
<tr>
<td>Streptococcus pyogenes, Streptococcus agalactiae, and Streptococcus dysgalactiae, and Streptococcus anginosus group</td>
<td>325/371 (87.6)</td>
<td>316/366 (85.9)</td>
<td>-1.3 (-3.2, 6.7)</td>
</tr>
</tbody>
</table>

1 There were 7 patients (as described in Table 7) who did not receive treatment and were counted as non-responders.

2 Patients who died or used non-study antibacterial therapy or had missing measurements were classified as non-responders.

3 The 95% CI is computed using the Miettinen and Nurminen approach, stratified by baseline fever status.

Another secondary endpoint in these two ABSSSI trials was the clinical success rate assessed at a follow-up visit occurring between Days 26 to 30. Clinical Success at this visit was defined as having a decrease in lesion size (both length and width measurements), a temperature of 37.6°C or lower, and meeting pre-specified criteria for local signs: purulent discharge and swelling/induration & tenderness to palpation absent or mild.

Other signs and symptoms of infection were also noted, including improvement in muscle/joint pain and improvement in baseline fever status.
Table 10 shows outcomes in patients with an identified baseline pathogen, using pooled data from Trials 1 and 2 in the microbiological ITT (microITT) population. The outcomes shown in the table are clinical response rates at 48 to 72 hours and clinical success rates at follow-up (Day 26 to 30), as defined above.

Table 10. Outcomes by Baseline Pathogen (Trial 1, 2; MicroITT)$^1$

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>DALVANCE, n/N (%)</th>
<th>Comparator, n/N (%)</th>
<th>Difference (95% CI)$^2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Staphylococcus aureus</td>
<td>212/256 (83.0)</td>
<td>202/250 (80.8)</td>
<td>-2.2% (-5.1, 0.7)</td>
</tr>
<tr>
<td>Methicillin-susceptible</td>
<td>124/152 (81.6)</td>
<td>123/151 (81.5)</td>
<td>-0.1% (-5.0, 4.8)</td>
</tr>
<tr>
<td>Methicillin-resistant</td>
<td>105/129 (81.1)</td>
<td>105/129 (81.1)</td>
<td>0.0% (-5.0, 5.0)</td>
</tr>
<tr>
<td>Streptococcus pyogenes</td>
<td>124/152 (81.6)</td>
<td>123/151 (81.5)</td>
<td>-0.1% (-5.0, 4.8)</td>
</tr>
<tr>
<td>Streptococcus agalactiae</td>
<td>113/142 (80.0)</td>
<td>110/140 (78.6)</td>
<td>-1.4% (-5.0, 2.2)</td>
</tr>
<tr>
<td>Streptococcus anginosus</td>
<td>113/142 (80.0)</td>
<td>110/140 (78.6)</td>
<td>-1.4% (-5.0, 2.2)</td>
</tr>
<tr>
<td>Enterococcus faecalis</td>
<td>113/142 (80.0)</td>
<td>110/140 (78.6)</td>
<td>-1.4% (-5.0, 2.2)</td>
</tr>
</tbody>
</table>

All DALVANCE dosing regimens in Trials 1 and 2 consisted of two doses.

1 There were 2 patients in the DALVANCE arm with methicillin-susceptible S. aureus at baseline who did not receive treatment and were counted as non-responders/failures.

2 Early Responders are patients who had no increase from baseline in lesion area 48 to 72 hours after initiation of therapy, and had a temperature consistently at or below 37.6°C upon repeated measurement.

DALVANCE 1500 mg Single Dose Regimen

Adult patients with ABSSSI were enrolled in a Phase 3, double-blind, clinical trial. The ITT population included 688 patients who were randomized to DALVANCE treatment with either a single 1500 mg dose or a two-dose regimen of 1000 mg followed one week later by 500 mg (Trial 3). Patients with creatinine clearance less than 30 mL/min had their dose adjusted (Section 2.2). Approximately 5% of patients also received a protocol-specified empiric course of treatment with intravenous aztreonam for coverage of Gram-negative pathogens. The specific population included 698 patients who were randomized to DALVANCE treatment with either a single 1500 mg dose or a two-dose regimen of 1000 mg followed one week later by 500 mg (Trial 3). Patients with creatinine clearance less than 30 mL/min had their dose adjusted (Section 2.2). Approximately 5% of patients also received a protocol-specified empiric course of treatment with intravenous aztreonam for coverage of Gram-negative pathogens. The specific population included 698 patients who were randomized to DALVANCE treatment with either a single 1500 mg dose or a two-dose regimen of 1000 mg followed one week later by 500 mg (Trial 3). Patients with creatinine clearance less than 30 mL/min had their dose adjusted (Section 2.2).

The primary endpoint in this ABSSSI trial was the clinical response rate where responders were defined as patients who had at least a 20% decrease from baseline in lesion area 48 to 72 hours after randomization without receiving any rescue antibacterial therapy. The secondary endpoint was the clinical success rate at a follow-up visit occurring between Days 26 and 30, with clinical success defined as having at least a 90% decrease from baseline in lesion area, a temperature of 37.6°C or lower, and meeting pre-specified criteria for local signs: purulent discharge and drainage absent or mild and improved from baseline (for patients with wound infections), heat/warmth and fluctuance absent, swelling/induration and tenderness to palpation absent or mild. Table 11 summarizes results for these two endpoints in the ITT population. Note that there are insufficient historical data to establish the magnitude of drug effect for antibacterial drugs compared with placebo at the follow-up visit. Therefore, comparisons between treatment groups based on clinical success rates at this visit cannot be utilized to establish non-inferiority.

Table 11. Primary and Secondary Efficacy Results in ABSSSI Patients (Trial 3)$^3$

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>DALVANCE, n/N (%)</th>
<th>Comparator, n/N (%)</th>
<th>Difference (95% CI)$^3$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Staphylococcus aureus</td>
<td>212/256 (83.0)</td>
<td>202/250 (80.8)</td>
<td>-2.2% (-5.1, 0.7)</td>
</tr>
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<td>Methicillin-susceptible</td>
<td>124/152 (81.6)</td>
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<td>-0.1% (-5.0, 4.8)</td>
</tr>
<tr>
<td>Methicillin-resistant</td>
<td>105/129 (81.1)</td>
<td>105/129 (81.1)</td>
<td>0.0% (-5.0, 5.0)</td>
</tr>
<tr>
<td>Streptococcus pyogenes</td>
<td>124/152 (81.6)</td>
<td>123/151 (81.5)</td>
<td>-0.1% (-5.0, 4.8)</td>
</tr>
<tr>
<td>Streptococcus agalactiae</td>
<td>113/142 (80.0)</td>
<td>110/140 (78.6)</td>
<td>-1.4% (-5.0, 2.2)</td>
</tr>
<tr>
<td>Streptococcus anginosus</td>
<td>113/142 (80.0)</td>
<td>110/140 (78.6)</td>
<td>-1.4% (-5.0, 2.2)</td>
</tr>
<tr>
<td>Enterococcus faecalis</td>
<td>113/142 (80.0)</td>
<td>110/140 (78.6)</td>
<td>-1.4% (-5.0, 2.2)</td>
</tr>
</tbody>
</table>

1 There were 3 patients in the two-dose group who did not receive treatment and were counted as non-responders.

2 Patients who died or used non-study antibacterial therapy or had missing measurements were classified as non-responders.

3 The 95% Confidence Interval (CI) is computed using the Miettinen and Nurminen approach, stratified by baseline fever status.

In Trials 1, 2, and 3, all patients had blood cultures obtained at baseline. A total of 40 ABSSSI patients who received DALVANCE had bacteremia at baseline caused by one or more of the following bacteria: 26 S. aureus (21 MSSA and 5 MRSA), 6 S. agalactiae, 7 S. pyogenes, 2 S. anginosus group, and 1 E. faecalis. In patients who received DALVANCE, a total of 24/40 (60%) were clinical responders at 48-72 hours and 32/40 (80%) were clinical successes at Day 26 to 30.

15 REFERENCES


2. CLSI. Performance Standards for Antimicrobial Susceptibility Testing; Twenty-Fifth Informational Supplement. CLSI document M100-S25 Clinical and Laboratory Standards Institute, 950 West Valley Road, Suite 2500, Wayne, Pennsylvania 19087, USA, 2015.

16 HOW SUPPLIED/STORAGE AND HANDLING

DALVANCE (dalbavancin) for injection is supplied in the following packaging configuration: 500 mg/vial: package of 1 (NDC 57970-100-01)

Unconjugated DALVANCE (dalbavancin) for injection should be stored at 25°C (77°F); excursions permitted to 15 to 30°C (59 to 86°F) [see USP Controlled Room Temperature].

17 PATIENT COUNSELING INFORMATION

Patients should be advised that allergic reactions, including serious allergic reactions, could occur, and that serious allergic reactions require immediate treatment. Patients should inform their healthcare provider about any previous hypersensitivity reactions to DALVANCE, or other glycopeptides.

Patients should be counseled that antibacterial drugs including DALVANCE should only be used to treat bacterial infections. They do not treat viral infections (e.g., the common cold). When DALVANCE is prescribed to treat a bacterial infection, patients should be told that although it is common to feel better early in the course of therapy, the medication should be taken exactly as directed. Skipping doses or not completing the full course of therapy may (1) decrease the effectiveness of treatment, and (2) increase the likelihood that bacteria will develop resistance and will not be treatable by DALVANCE and other antibacterial drugs in the future.

Patients should be advised that diarrhea is a common problem caused by antibacterial drugs and usually resolves when the drug is discontinued. Sometimes, frequent watery or bloody diarrhea may occur and may be a sign of a more serious intestinal infection. If severe watery or bloody diarrhea develops, patients should contact their healthcare provider.

Manufactured for: Durata Therapeutics U.S. Limited.
Paripsy, NJ 07054


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