<table>
<thead>
<tr>
<th><strong>Guideline/Protocol Title</strong></th>
<th>Expanded Use of Dalbavancin in Patients Undergoing Self-Directed Discharge or Unwilling to Participate with Standard of Care</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Authors</strong></td>
<td>Ryan P. Mynatt, PharmD; Bobbi Jo Stoner, PharmD; Ashley Logan, PharmD; Sami El-Dalati, MD; Michael Young, MD</td>
</tr>
<tr>
<td><strong>Committee Review</strong></td>
<td>Antimicrobial Stewardship Subcommittee, Pharmacy &amp; Therapeutics Committee</td>
</tr>
<tr>
<td><strong>Target Population</strong></td>
<td>Patients with Gram-positive infections including infective endocarditis and/or bone and joint infections who, knowingly, choose to undergo self-directed discharge or otherwise refuse standard of care short-acting antimicrobial therapy.</td>
</tr>
<tr>
<td><strong>Overview</strong></td>
<td>This guideline succinctly outlines treatment related considerations for the transition of patients from inpatient environments to outpatient, patient and/or caregiver methods of medication administration to decrease burden of infusions.</td>
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<tr>
<td><strong>Effective Date</strong></td>
<td>2/28/2022</td>
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<tr>
<td><strong>Revised Date</strong></td>
<td>N/A</td>
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<tr>
<td><strong>Expiration Date</strong></td>
<td>2/28/2024</td>
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<tr>
<td><strong>Schedule for Periodic Review</strong></td>
<td>Every 2 years</td>
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<tr>
<td><strong>Implementation Strategy</strong></td>
<td>Clinical pharmacists will work together to implement this protocol in their respective clinical areas after education and/or orientation by ID/OPAT representatives.</td>
</tr>
<tr>
<td><strong>Education Strategy</strong></td>
<td>Pharmacists will have the guideline emailed to them and it will be posted/shared on CareWeb and the Pharmacy SharePoint sites.</td>
</tr>
<tr>
<td><strong>Primary Outcome (s)</strong></td>
<td>To improve safe, efficient, and effective treatment for severe Gram-Positive infections.</td>
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<tr>
<td><strong>Outcome Assessment Plan</strong></td>
<td>Will review every 2 years for re-assessment.</td>
</tr>
<tr>
<td><strong>Information Technology Needs</strong></td>
<td>N/A</td>
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University of Kentucky Outpatient Parenteral Antimicrobial Therapy (OPAT)
Adult Dalbavancin Expanded Indications Guideline

Purpose:

To provide evidence-based guidelines for the use of dalbavancin, in an expanded protocol, in the treatment of patients who possess barriers to standard of care (SOC) or elect to undergo a self-directed discharge to the outpatient setting who possess a diagnosis of either infective endocarditis, or bone and joint infections. These patients would otherwise require long-term, short-acting intravenous (IV) antimicrobial therapy, and this guideline is not intended to supersede current standard of care, but otherwise serve as an alternative to no treatment.

Background:

Dalbavancin, a synthetic long-acting lipoglycopeptide is approved by the FDA for the treatment of Acute Bacterial Skin and Skin Structure infections (ABSSSI) in both a two, and one-dose regimens. Dalbavancin has activity against numerous Gram-Positives, having demonstrating in-vitro against Streptococcus spp., Enterococcus spp., and both methicillin-susceptible and methicillin-resistant Staphylococcus aureus (MSSA and MRSA). However, data since this drugs approval has demonstrated efficacy in off-labelled, alternative treatment of more invasive diseases such as infective endocarditis and bone and joint infections.

Available literature supporting a 2-dose regimen of dalbavancin include pharmacokinetic modelling studies, which demonstrated sustained concentrations of dalbavancin within bone tissue for up to 8 weeks. Based on these data, a small randomized controlled trial enrolled patients who were randomized to either standard of care (oral or IV therapy) versus dalbavancin for the treatment of osteomyelitis. This study demonstrated comparable efficacy in patients treated with dalbavancin to the standard of care. Subsequent pharmacokinetic analysis further support the two-dose regimen for osteoarticular infections, specifically.

Data related to the treatment of infective endocarditis, while not as comprehensive as above, are promising. These data include large case reports and/or case series that demonstrate high rates of efficacy in patients treated with dalbavancin; however, the doses prescribed varied widely.

Protocol:

Use of this protocol requires approval by an infectious diseases provider, as long as patient meets criteria outlined below.

First Dose Protected:

Dalbavancin is considered a first dose protected antimicrobial and therefore the ID Protected Antimicrobial Review on-call (via EPIC secure chat) should be alerted of this order once an infectious diseases provider has approved, should inpatient administration be required.
# University of Kentucky Outpatient Parenteral Antimicrobial Therapy (OPAT)
## Adult Dalbavancin Expanded Indications Guideline

### Inclusion Criteria (Must meet all three):

**Eligible Infections**
(Common Gram-Positive Pathogens: *Staphylococcus aureus*, *Enterococcus* spp., and *Streptococcus* spp.)

- Infective Endocarditis (native valve)
- Joint Infections (non-Prosthetic)
- Osteomyelitis (non-Prosthetic)

**AND**

- Patient demonstrates intent and/or verbalizes desire for self-directed discharge (SDD)
  
  OR
  
  Verbalizes they do not desire to adhere to standard of care, as would otherwise be recommended

- Received education and/or understands clinical role of dalbavancin in relation to standard of care as well as risks to suboptimal therapy for their infection

*This should be documented within the medical record by the treating/recommending provider*

### Exclusion Criteria:

- Patient has only 1 dalbavancin dose remaining in regimen based on proposed duration of therapy
- Patient does not meet criteria for blood culture clearance
  - Requires at least two sets of negative cultures for two different days (can be non-consecutive)
- New-onset Infectious Central Nervous System events
  - including septic emboli, ischemic or hemorrhagic stroke, or meningitis
- Infection involves any prosthetic material and/or implanted cardiac device (any) not being removed
  - Implantable cardioverter defibrillator (ICD), permanent pacemaker, valve support ring, ventricular assist device (VAD), intravascular graft or other material (excludes stents)
  - Does not include prosthetic or extravascular hardware placed > 60 days before bacteremia (if applicable) which clinically appears uninfected
- Presence of perivalvular abscess
- History of hypersensitivity to dalbavancin or other glycopeptide antimicrobial
- Treatment with EITHER dalbavancin or oritavancin within previous 60 days
- Pregnant and/or nursing females

### Proposed Dosing Regimens Based on Indication

<table>
<thead>
<tr>
<th>Weeks Remaining In Treatment</th>
<th>Bone &amp; Joint Dose</th>
<th>Infective Endocarditis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than 3 Weeks</td>
<td>≥ 30 mL/min</td>
<td>≥ 30 mL/min</td>
</tr>
<tr>
<td></td>
<td>Dalbavancin 1500 mg IV on days 1 and 8</td>
<td>Dalbavancin 1500 mg IV on days 1 and 8</td>
</tr>
<tr>
<td></td>
<td>&lt; 30 mL/min</td>
<td>&lt; 30 mL/min</td>
</tr>
<tr>
<td></td>
<td>Consider Dalbavancin 1500 mg IV on day 1, with 50% reduction in dose on day 8 (750 mg IV)</td>
<td>Consider Dalbavancin 1500 mg on day 1, with 50% reduction in dose on day 8 (750 mg IV)</td>
</tr>
<tr>
<td>≥ 3 Weeks</td>
<td>≥ 30 mL/min</td>
<td>&lt; 30 mL/min</td>
</tr>
<tr>
<td></td>
<td>Dalbavancin 1500 mg IV x 1 dose; then 500 – 1000 mg IV every 7 days (last dose to be 1 week prior to end date)</td>
<td>Dalbavancin 1500 mg IV x 1 dose; then 500 mg IV every 7 days (last dose to be 1 week prior to end date)</td>
</tr>
<tr>
<td></td>
<td>&lt; 30 mL/min</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Consider Dalbavancin 1500 mg on day 1, with 50% reduction in dose on day 8 (750 mg IV)</td>
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</table>
Suggested Workflow:

Dalbavancin therapy oftentimes requires prior authorization for off-labeled indications, and can be associated with significant cost to patients given lack of third-party payer reimbursement. This can result in drug therapy not being affordable once patient is discharged. This possibility should be discussed with the patient to potentially allow for 2-3 day timeframe to ascertain affordability via infusion company.

Orders should be sent via typical discharge process via IV antibiotics order-set to Option Care / Bioscrip via e-scribe with collaboration with site liaisons. Alternative infusion companies or centers will require orders to be sent to them via their preferred referral process. Common patient scenarios are provided below.

Typical Process:

1. Primary service and ID provider(s) determine patient is appropriate for dalbavancin therapy.
2. Patient is educated by infectious diseases provider approving agents use, as above, and is amenable to receiving dalbavancin. Documentation of this interaction performed as above.
   a. [patient unwilling to stay, verbalizes leaving self-directed] First dose can be ordered inpatient, if approved via First-Dose Protected antimicrobial process.
      i. Subsequent doses of dalbavancin should be ordered via e-scribe by discharging team, and sent to Option Care / Bioscrip or other infusion center*.
      ii. If there is concern on patient’s ability to adhere to the second dose appointment schedule given lack of transportation, distance from infusion center, or both, alternative partial oral therapy may be preferred versus incomplete dalbavancin regimen.
   b. [patient willing to stay for insurance third party screening] First dose and subsequent doses should be coordinated via Option Care / Bioscrip or other infusion center*.
      i. If Option Care used, would recommend a notification be sent to site liaisons to facilitate prior authorization process and any other care-related coordination.
   c. Transportation should be confirmed back to infusion pharmacy for second dose. Inability to secure transportation for second dose should prompt discussion about appropriateness of dalbavancin therapy with primary service and infectious diseases.
      i. If transportation requires further facilitation, see suggested pathways below:
         1. Patient will go to Option Care / Bioscrip
            a. If patient resides within 30-40 miles of Lexington Option Care / Bioscrip [2380 Fortune Dr Suite 130, Lexington, KY 40509] recommend facilitation via their staff members and medical transportation.
            b. If patient resides greater than 30-40 miles of Lexington Option Care / Bioscrip, would recommend facilitation of second dose administered via visiting nurse organization, affiliated with Option Care, if possible.
         2. Patient will go to Infusion Center (UK or non-Uk)
            a. Medical transportation should be arranged on a case-by-case basis.

*UK infusion centers require prescription via plan of care; non-Uk infusion centers should have referral materials and prescriptions sent via their institutional specific pathways.
References