Purpose
The purpose of this guideline is to provide recommendations for antibiotics that can be infused via a midline catheter, specifically for those agents commonly started during inpatient admission and intended for outpatient antibiotic therapy (OPAT). This is NOT a comprehensive policy for medication administration via midline during inpatient admission.

Background
Historically, peripherally inserted central catheters (PICC) have been widely used in patients who require long-term central venous access, particularly for those needing courses of outpatient antibiotics.\(^1\,^4\) In recent years, renewed interest has emerged in the use of midline catheters, which, as long peripheral catheters, present reduced risk of infection and venous stenosis when compared to PICCs.\(^2\,^3\,^4\) Additionally, midlines may result in reduced overall costs for IV therapy.\(^2\,^25\) Typically, midlines are inserted in patients who require intravenous medications of between 6 to 14 days of duration, but some devices may be used for longer periods.\(^4\) Midlines are not without drawbacks; compared to other options for IV access, they may have increased rates of mechanical complications and studies differ as to whether rates of associated thrombosis are lower or higher compared to PICCs.\(^1\,^4\,^4\) However, a recent review of 987 articles of midline use demonstrated midlines compare favorably against other types of catheters in terms of failure and infection rates.\(^26\)

Because the tip of a midline does not reside in central circulation, midline catheters cannot be used for continuous vesicant therapy, parenteral nutrition, or infusates with an osmolality greater than 900 mOsm/L.\(^15\) Beyond these current recommendations from the Infusion Nurses Society (INS), however, there is debate about which medications are appropriate for use via midline. Midlines reside less superficially than a peripheral intravenous catheter (PIV), and therefore extravasation injuries may be masked in comparison to a PIV.\(^12\) Prior to 2016, INS considered medications to be inappropriate for peripheral administration if they have a pH outside of the 5-9 range. This standard of practice was removed in 2016 after concern for lack of evidence strongly linking pH to phlebitis risk in literature.\(^14\,^15\)

While INS recommends that each facility should develop guidelines for midline use\(^4\), until recently, literature explicitly referencing use of individual antibiotics infused via midline catheter has been lacking. Michigan Medicine’s historical reference for use of antibiotics via midline has been the pre-2016 INS criteria, as well as a reference sheet provided by Bard, our midline manufacturer. In 2019, several new articles became available with more specific reference to particular antibiotics being safely infused through midlines in an outpatient setting\(^6,^7,^8\). Based on this literature, this guideline provides recommendations for use of specific antibiotics planned to be administered as outpatient therapy via midline catheter.

Key Practice Recommendations
- Antibiotics acceptable for use via midline catheters* (see Exhibit B for evidence-based recommendations):
  - Ertapenem
  - Cefepime
  - Ceftriaxone
  - Daptomycin
  - Meropenem
  - Cefazolin
  - Ceftazidime

Requests to add additional antimicrobials to the included list should be sent to medusepolicy@med.umich.edu for consideration.
Exclusions
  • Absolute exclusion criteria:
    o Known hypersensitivity/allergy to approved antibiotics
    o Prior phlebitis or vein injury to planned antibiotic via peripheral administration
    o Known contraindication to midline such as recent thrombosis within 30 days in same limb as planned midline placement, no available vein or decreased venous flow per assessment by VAST, or a vein preservation strategy.
    o Antibiotics requiring continuous infusion – contraindicated due to potential complications from traction on midline catheter
  • Relative exclusion criteria:
    o Recent infection or occlusion of midline
    o Age <18 years. Clinicians should reference pediatric literature. This guideline did not examine pediatric midline use.
    o History of thrombosis and hypercoagulability
    o Consideration should be made in terms of patient’s anticoagulation status, clot history/timeline/location, and if previously provoked by line placement.
    o Duration of therapy exceeding 14 days

**Providers can further reference the Improve PICC Guidelines for vascular access queries; https://www.improvepicc.com/**

Administration & Monitoring
  • Per Michigan Medicine Nursing Assessment and Care of Venous Access Devices policy Venous Access Devices: Assessment and Care (Venous Access Grid)
  • Per Post-Acute Care Services Midline Catheter Care, Policy Stat ID: 6687848 (pending)

Restrictions
  VAST approval and placement of midline catheter

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Exhibits:
  Nursing Assessment and Care of Venous Access Devices
  Venous Access Grid
  Infection Prevention for Intravenous Peripheral Short Catheters Policy
  Nursing Midline Catheter Removal
  https://www.improvepicc.com/key-guidelines.html
### Exhibit B

<table>
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<tr>
<th>Antibiotic</th>
<th>Evidence &amp; Recommendations</th>
<th>pH</th>
<th>Osmolarity</th>
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</table>
| Ertapenem  | - Used via midline by Dickson et al., no reports of extravasation, necrosis etc.  
- Likely used via midline in Underwood et al. 2019 without apparent serious injury despite 13 extravasation events, cumulative number of OPAT days >200  
- Used via midline in Seo et al 2019, no major complications reported (small number of infiltrations, no extravasations).                                                                 | 7.5<sup>17</sup> | ---         |
| Cefepime   | - Used via midline by Dickson et al., no reports of extravasation, necrosis etc.  
Negative:  
- pH <5                                                                                                           | 4-6<sup>18</sup> | 307        |
| Ceftriaxone | - Used via midline by Dickson et al., no reports of extravasation, necrosis etc.  
- Used via midline in Seo et al 2019, no major complications reported (small number of infiltrations, no extravasations).                                                                 | 6.6-6.7<sup>20</sup> | 270-423    |
| Daptomycin | - Used via midline by Dickson et al., no reports of extravasation, necrosis etc.  
- Likely used via midline in Underwood et al. 2019 without apparent serious injury despite 13 extravasation events, cumulative number of OPAT days >200. Daptomycin was the 4<sup>th</sup> most commonly used antibiotic.  
- Used via midline in Seo et al 2019, but only 2 patients, no major complications reported (small number of infiltrations, no extravasations).  
- No reports of vein injury, phlebitis, extravasation per internal MM safety reports (from 1/1/20-10/19/20)  
Negative:  
- pH <5  
- Keller et al., daptomycin was associated with an increased rate of catheter complications, 4.45 [95% CI: 1.02–19.41]  
- However, use of midlines was low 3% (n=10), as was daptomycin 2.4% (n=8). So don’t actually know if any of the daptomycin-catheter associated complications were in patients who were receiving via midline vs PICC or tunneled CVC. | 4.7<sup>21</sup>-6.8<sup>21,22</sup> | ~323-364<sup>22</sup> |
| Meropenem  | - Used via midline by Dickson et al., no reports of extravasation, necrosis etc.  
- Likely used via midline in Underwood et al. 2019 without apparent serious injury despite 13 extravasation events, cumulative number of OPAT days >200.  
- Low risk per Clark et al 2013.                                                                                         | 7.3-8.3<sup>23</sup> | 300        |
| Cefazolin  | - Used via midline by Dickson et al., no reports of extravasation, necrosis etc.  
- Low risk per Clark et al 2013.                                                                                                                  | 4.5-719     | 270-351    |
| Ceftazidime| - Likely used via midline in Underwood et al. 2019 without apparent serious injury despite 13 extravasation events, cumulative number of OPAT days >200.  
- Low risk per Clark et al 2013.  
- No cases of midline catheter phlebitis per Harwood et al 1992<sup>16</sup> however did not report specifically on ceftazidime, though per the article “95% of patients received IV therapy consisting of tobramycin and ceftazidime” | 5-8<sup>24</sup> | ---         |
References

18. Cefazolin. Package insert. GSK; 2004

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Revision History:

The recommendations in this guide are meant to serve as treatment guidelines for use at Michigan Medicine facilities. If you are an individual experiencing a medical emergency, call 911 immediately. These guidelines should not replace a provider’s professional medical advice based on clinical judgment, or be used in lieu of an Infectious Diseases consultation when necessary. As a result of ongoing research, practice guidelines may from time to time change. The authors of these guidelines have made all attempts to ensure the accuracy based on current information, however, due to ongoing research, users of these guidelines are strongly encouraged to confirm the information contained within them through an independent source.

If obtained from a source other than med.umich.edu/asp, please visit the webpage for the most up-to-date document.