Impact of restriction criteria on optimal ertapenem use in a community health system

Curtis Stump PharmD

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Impact of Restriction Criteria on Optimal Ertapenem Use in a Community Health System

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Parkview Health

The speaker has no actual or potential conflict of interest in relation to this presentation.
Background

- Ertapenem is a convenient option for empiric treatment and surgical prophylaxis
  - More costly than suitable alternatives

- Parkview implemented ertapenem restriction in November 2020 as a departmental improvement initiative

<table>
<thead>
<tr>
<th>Standard cost of therapy per day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ertapenem</td>
</tr>
<tr>
<td>Meropenem</td>
</tr>
<tr>
<td>Levofloxacin + metronidazole</td>
</tr>
<tr>
<td>Ceftriaxone + metronidazole</td>
</tr>
<tr>
<td>Piperacillin-tazobactam</td>
</tr>
<tr>
<td>Cefepime + metronidazole</td>
</tr>
</tbody>
</table>
Restriction Process

- **October 13, 2020**: P&T approved restriction
- **October 26, 2020**: Integration of restriction into EPIC
- **November 12, 2020**: Restriction went live
- **November 18, 2020**: Ertapenem removed from preferences/quick lists
- **December 4, 2020**: Replaced ertapenem order with new order panel within order sets
Ertapenem Restriction Criteria

- Inpatient orders for ertapenem will only be accepted for patients who meet the following criteria:
  - **Empiric therapy:**
    - Documented history of infection with ESBL-producing bacteria at any anatomical site within the past twelve months
    - Necrotizing pancreatitis confirmed by imaging
    - Severe community acquired pneumonia without Pseudomonal risk in patients with a severe penicillin or cephalosporin allergy
    - Colorectal surgery prophylaxis in patients with documented severe penicillin or cephalosporin allergy
Inpatient orders for ertapenem will only be accepted for patients who meet the following criteria:

- **Definitive therapy:**
  - Treatment of infection caused by ESBL-producing bacteria
  - Treatment of infection caused by *Enterobacter* species, *Klebsiella* aerogenes, *Citrobacter* species, *Morganella* species or *Serratia* species
  - Inpatient orders placed by an Infectious Diseases physician for patients who will be discharged on ertapenem for outpatient **parenteral** antimicrobial therapy
Study Purpose & Rationale

- Evaluate the implementation of ertapenem restriction
- Identify the main indications of ertapenem use within the health system
- Assess the potential for cost savings
Methods - Overview

Pre-implementation period
May 1, 2020 – November 1, 2020

Post-implementation period
December 1, 2020 – June 1, 2021

Implementation of restriction criteria
November 12, 2020
Inclusion/Exclusion Criteria

**Inclusion**
- Receiving at least one dose of ertapenem during hospitalization as empiric or definitive therapy

**Exclusion**
- Outpatient infusions for ertapenem

**Study Definitions**

<table>
<thead>
<tr>
<th>Type</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Empiric</td>
<td>Ertapenem use before relevant cultures have resulted, or as prophylaxis for surgery</td>
</tr>
<tr>
<td>Definitive</td>
<td>Ertapenem initiated after relevant culture results available</td>
</tr>
</tbody>
</table>
Outcomes

- **Primary outcome:**
  - Percent change of ertapenem orders considered optimal before and after implementation of restriction criteria
    - **Optimal use:** Matching an indication listed in the restriction criteria

- **Secondary outcomes:**
  - Percent change of ertapenem orders considered optimal for empiric and definitive therapy
  - Indications of any suboptimal use after implementation
  - Selected antibiotic use (ertapenem, levofloxacin, and meropenem)
  - Cost reduction estimate analysis
Patient Inclusion

Pre-Implementation

1,955 Encounters Screened

1,289 Encounters Excluded
Outpatient Infusions

667 Encounters
250 Randomized

174 Empiric
76 Definitive

Post-Implementation

642 Encounters Screened

452 Encounters Excluded
Outpatient Infusions

190 Encounters

37 Empiric
153 Definitive
Baseline Characteristics

<table>
<thead>
<tr>
<th>Characteristic, mean (± SD or %)</th>
<th>Pre-Implementation (n = 250)</th>
<th>Post-Implementation (n = 190)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age 51.9 (± 21.3)</td>
<td>60.9 (± 16.2)</td>
<td></td>
</tr>
<tr>
<td>Male (n, %) 126 (50.4%)</td>
<td>89 (46.8%)</td>
<td></td>
</tr>
<tr>
<td>Doses of ertapenem per encounter</td>
<td>3 (± 4.9)</td>
<td>3.6 (± 3.9)</td>
</tr>
<tr>
<td>Length of stay in days 5.5 (± 8.2)</td>
<td>9.1 (± 9.0)</td>
<td></td>
</tr>
<tr>
<td>Severe allergies (n, %) Penicillin</td>
<td>52 (20.8%)</td>
<td>20 (10.5%)</td>
</tr>
<tr>
<td>Cephalosporin</td>
<td>21 (8.4%)</td>
<td>6 (3.2%)</td>
</tr>
<tr>
<td>Indication</td>
<td>Pre-Implementation (n = 250)</td>
<td>Post-Implementation (n = 190)</td>
</tr>
<tr>
<td>------------------------------------------------</td>
<td>------------------------------</td>
<td>------------------------------</td>
</tr>
<tr>
<td>Intraabdominal infection</td>
<td>68 (27.2%)</td>
<td>29 (15.3%)</td>
</tr>
<tr>
<td>Appendicitis</td>
<td>45 (18.0%)</td>
<td>4 (2.1%)</td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>34 (13.6%)</td>
<td>39 (20.5%)</td>
</tr>
<tr>
<td>Surgical prophylaxis (primarily colorectal)</td>
<td>27 (10.8%)</td>
<td>6 (3.2%)</td>
</tr>
<tr>
<td>Bloodstream infection</td>
<td>23 (9.2%)</td>
<td>23 (12.1%)</td>
</tr>
<tr>
<td>Skin or soft tissue infection</td>
<td>19 (7.6%)</td>
<td>11 (5.8%)</td>
</tr>
<tr>
<td>Bone or joint infection</td>
<td>15 (6.0%)</td>
<td>51 (26.8%)</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>7 (2.8%)</td>
<td>11 (5.8%)</td>
</tr>
<tr>
<td>Other</td>
<td>12 (4.8%)</td>
<td>16 (8.4%)</td>
</tr>
</tbody>
</table>

*Other indications include infective endocarditis, empyema, fever of unknown etiology, etc.*
Impact of Restriction Criteria

667 encounters (1,974 total doses)

Implementation of restriction

190 encounters (676 total doses)
Primary Outcome – Optimal Use

Pre-Implementation (n=250)

- Optimal: 74.0%
- Suboptimal: 26.0%

Post-Implementation (n=190)

- Optimal: 82.6%
- Suboptimal: 17.4%

Percent difference: 56.6%

P < 0.001
Secondary Outcome – Empiric and Definitive Therapy

Empiric
Percent difference: 29.4%
P < 0.001

Definitive
Percent difference: 21.7%
P < 0.001
## Suboptimal Indications Post-Implementation

<table>
<thead>
<tr>
<th>Suboptimal Empiric Indication (n=24)</th>
<th>Number of encounters, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bone or joint infection</td>
<td>7 (29.1%)</td>
</tr>
<tr>
<td>Appendicitis</td>
<td>4 (16.7%)</td>
</tr>
<tr>
<td>Intraabdominal infection</td>
<td>4 (16.7%)</td>
</tr>
<tr>
<td>Surgical prophylaxis</td>
<td>3 (12.5%)</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>2 (8.3%)</td>
</tr>
<tr>
<td>Infective endocarditis</td>
<td>1 (4.2%)</td>
</tr>
<tr>
<td>Fever</td>
<td>1 (4.2%)</td>
</tr>
<tr>
<td>Lung abscess or empyema</td>
<td>1 (4.2%)</td>
</tr>
<tr>
<td>Skin or soft tissue infection</td>
<td>1 (4.2%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Suboptimal Definitive Indication (n=9)</th>
<th>Number of encounters, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intraabdominal infection</td>
<td>5 (55.6%)</td>
</tr>
<tr>
<td>Bone or joint infection</td>
<td>2 (22.2%)</td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>2 (22.2%)</td>
</tr>
</tbody>
</table>
Secondary Outcome – Antibiotic Usage

Days of therapy per 1,000 patient days


- Ertapenem
- Meropenem
- Levofloxacin
# Secondary Outcome – Cost Reduction Estimate

<table>
<thead>
<tr>
<th></th>
<th>Total days of therapy</th>
<th>Difference in days of therapy</th>
<th>Cost of ertapenem</th>
<th>Cost of levofloxacin + metronidazole*</th>
<th>Cost of meropenem**</th>
<th>Range of cost savings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-implementation</td>
<td>1,974</td>
<td>1,298</td>
<td>$73,376</td>
<td>$8,437</td>
<td>$22,417</td>
<td>$50,959 – $64,939</td>
</tr>
<tr>
<td>Post-implementation</td>
<td>676</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*The least expensive alternative to ertapenem on Parkview formulary  
**The most expensive alternative to meropenem on Parkview formulary
Discussion

- Decreased ertapenem use overall
  - No sustained increase in meropenem or levofloxacin

- Major improvement in optimal orders after implementation
  - Decreased use for intrabdominal infections and appendicitis

- Estimated cost savings up to $64,000
Future Direction

- Update current restriction criteria to address unique clinical situations found during study time frame
  - Address continuation of ertapenem from OPAT on admission
  - Clarify appropriate definition of colorectal surgery prophylaxis

- Pharmacist education to ensure compliance with policy

- Develop manuscript and seek publication
  - Serve as a guide for other institutions
  - Share challenges encountered
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