Antimicrobial Stewardship Strategy: Formulary review/streamlining

Formulary review and streamlining involves limiting the number of antimicrobials available to the minimum needed for effective treatment, while eliminating agents with duplicate spectrums of activity.¹

Description

This is an overview and not intended to be an all-inclusive summary. As a general principle, patients must be monitored by the health care team after changes to therapy resulting from recommendations made by the antimicrobial stewardship team.

Institutions are encouraged to review and streamline the number and choice of antimicrobials they have available for use. This is also referred to as a “closed formulary.”

This strategy entails limiting the number of antimicrobials available on the institutional drug formulary to the minimum needed for effective treatment, while eliminating agents with duplicate spectrums of activity.¹ It usually involves selecting one or two representative antimicrobials from each class, rather than carrying all choices (e.g., identifying one first- and second-generation cephalosporin, one or two echinocandins). Agents are assessed based on therapeutic efficacy, safety, indications, potential for development of resistance, pharmacokinetics and cost, usually by a pharmacy and therapeutics committee or a similar group. Need and frequency of use are also considered: for example, smaller institutions may not require agents that are usually reserved for more complicated infections or resistant organisms (e.g., voriconazole, colistin, tigecycline), although these could be made available on a nonformulary basis for specific cases when justified.

Formulary review and streamlining also includes identifying and implementing restrictions for specific antimicrobial agents (see Formulary restriction).

The use of auto-substitutions (see Formulary automatic substitution/therapeutic interchange policies) may facilitate the management of some nonformulary drug requests; others must be addressed on a case-by-
case basis. Frequent requests for the same agent may prompt a review of the agent for addition to the formulary. Formularies may be specific for an institution, a group of institutions or a region.

Advantages

- One of the core strategies recommended in the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America guidelines.
- Considered an effective strategy for controlling antimicrobial use.
- Shown to reduce the costs of targeted antimicrobials and decrease the use of antimicrobials that are unavailable or restricted.
- May help with specific resistance issues in an institution, since resistance patterns can mirror usage patterns.
- Functions with minimal staff resources once established.
- Can be done without adversely affecting clinical outcomes.
- Minimal threat to physician autonomy.

Disadvantages

- Requires initial organized effort and buy-in from physicians, pharmacists, microbiology laboratory personnel and administration to streamline the formulary.
- Unclear if this is effective at reducing overall antimicrobial resistance.
- May direct (inappropriate) use to another antimicrobial agent that is available and unrestricted.
- May not be effective if there is a way for prescribers to circumvent the process and obtain nonformulary antimicrobials.

Requirements

- Process for reviewing requests to add new/alternate agents.
- Mechanism to contact prescribers when nonformulary antimicrobials are ordered and review one-time requests.

Associated Metrics

- Effectiveness of formulary streamlining with institutional costs of antimicrobials and/or drug utilization (drug class or individual agent).
- Resistance rates if a particular agent is removed from or added to formulary (note that it may take years to see measurable changes in resistance rates).

References

Limited formulary antibiotics to the minimum number required for effective treatment, eliminated duplication within antibiotic classes, taking into consideration susceptibility patterns of nosocomial pathogens.

Successfully reduced costs and reduced use of specific antibiotics.


Additional Useful References

Select articles to provide supplemental information and insight into the strategy described and/or examples of how the strategy was applied; not a comprehensive reference list. URLs are provided when materials are freely available on the Internet.

  
  Removed ciprofloxacin from an emergency department formulary.
  
  Reduced rate of ciprofloxacin use for cystitis from 6.3 per cent to 3.4 per cent without an increase in the rate of pyelonephritis.

Samples/Examples (updated June 2016)

- Example: Halton Healthcare - Hospital Formulary Anti-infective Agents (includes therapeutic interchanges and restriction criteria)

These documents have been generously shared by various health care institutions to help others develop and build their antimicrobial stewardship programs. We recommend crediting an institution when adopting a specific tool/form/pathway in its original form.

Examples that contain clinical or therapeutic recommendations may not necessarily be consistent with published guidelines, or be appropriate or directly applicable to other institutions. All examples should be considered in the context of the institution’s population, setting and local antibiogram.

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Links with Other Strategies

- Formulary automatic substitution/therapeutic interchange policies
- Formulary restriction
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Citation


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For further information


Email: asp@oahpp.ca

Public Health Ontario acknowledges the financial support of the Ontario Government
Example: Halton Healthcare - Hospital Formulary Anti-infective Agents (includes therapeutic interchanges and restriction criteria)

**Hospital Formulary**

<table>
<thead>
<tr>
<th>8:00</th>
<th>Anti-Infective Agents</th>
</tr>
</thead>
<tbody>
<tr>
<td>8:12</td>
<td>Antibacterials</td>
</tr>
<tr>
<td>8:12:02</td>
<td>Aminoglycosides</td>
</tr>
</tbody>
</table>

**Gentamicin**  Garamycin®
- Injection 60mg/50ml, 80mg/50ml, 100mg/100ml, 120mg/100ml in NS premixed bags
- Injection 60mg/2ml, 40mg/ml 20ml vial

**GENTAMICIN**
General use is not restricted, but any use beyond 7 days requires pharmacist/Infectious Diseases review

<table>
<thead>
<tr>
<th>Drug Ordered:</th>
<th>Drug Supplied:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gentamicin injection</td>
<td>Tobramycin injection (same dose and frequency)</td>
</tr>
</tbody>
</table>

**Tobramycin PF**
(Preservative Free)
- Injection 80mg/2ml

**Streptomycin sulphate**
- Injection 1000 mg vial

**STREPTOMYCIN RESERVED INDICATIONS:**
- Part of combination therapy of active tuberculosis (second-line)
- Brucellosis
- Plague
- Tularemia
- Infectious Disease Service consultation is recommended

**Amikacin**
- Injection 500mg/2ml

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Example: Halton Healthcare - Hospital Formulary Anti-infective Agents (includes therapeutic interchanges and restriction criteria) (continued)

### Cephalexin
Capsule 500mg

<table>
<thead>
<tr>
<th>CEPHALEXIN Therapeutic Interchange</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Drug Ordered</strong></td>
</tr>
<tr>
<td>Cephalexin 250-500mg tablets</td>
</tr>
<tr>
<td>any frequency</td>
</tr>
<tr>
<td><strong>Drug Supplied</strong></td>
</tr>
<tr>
<td>Cefadroxil 500 mg po</td>
</tr>
<tr>
<td>q12h</td>
</tr>
<tr>
<td><strong>Exception:</strong></td>
</tr>
<tr>
<td>no substitution for Cephalexin suspension</td>
</tr>
<tr>
<td>Cephalexin 750mg–1 g tablets</td>
</tr>
<tr>
<td>any frequency</td>
</tr>
<tr>
<td><strong>Drug Supplied</strong></td>
</tr>
<tr>
<td>Cefadroxil 1 g po</td>
</tr>
<tr>
<td>q12h</td>
</tr>
<tr>
<td><strong>Exception:</strong></td>
</tr>
<tr>
<td>no substitution for Cephalexin suspension</td>
</tr>
</tbody>
</table>

### Cefazolin sodium
Arice®, Kefzol®
Injection 1 g vial, 500mg vial
1 g/50ml, 2 g/100ml NS premixed bags

<table>
<thead>
<tr>
<th>CEFAZOLIN Therapeutic Interchange</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Drug Ordered</strong></td>
</tr>
<tr>
<td>Cefazolin IV any dose prescribed</td>
</tr>
<tr>
<td>more frequent than q8h, ADULT only</td>
</tr>
<tr>
<td><strong>Drug Supplied</strong></td>
</tr>
<tr>
<td>Cefazolin same dose IV q8h</td>
</tr>
</tbody>
</table>

### Cephalexin
Keflex®
Liquid 250mg/5mL

### Cefoxitin
Injection 1 g
Injection 2 g

### Cefprozil
Cefzil®
Liquid 250 mg/5 mL
Halton Healthcare Hospital Formulary
Date of last revision: September 2015

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### Example: Halton Healthcare - Hospital Formulary Anti-infective Agents (includes therapeutic interchanges and restriction criteria) (continued)

#### Dose Equivalency Table for Cefuroxime Oral Suspension and Cefaclor Oral Suspension
**Interchange to Cefprozil Oral Suspension**

<table>
<thead>
<tr>
<th>Indication</th>
<th>If Cefuroxime (Ceftin) Oral Suspension Ordered</th>
<th>If Cefaclor (Cefclor) Oral Suspension Ordered</th>
<th>Give Cefprozil (Cefzil) Oral Suspension</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin/soft tissue</td>
<td>15mg/kg q12h</td>
<td>10mg/kg q12h</td>
<td>20mg/kg q24h</td>
</tr>
<tr>
<td>Otitis</td>
<td>15mg/kg q12h</td>
<td>20mg/kg q12h</td>
<td>15mg/kg q12h</td>
</tr>
<tr>
<td>Upper respiratory tract (pharyngitis/tonsillitis)</td>
<td>10mg/kg q12h</td>
<td>20 mg/kg q12h</td>
<td>7.5mg/kg q12h</td>
</tr>
<tr>
<td>Lower respiratory tract</td>
<td>No dose guidelines in children</td>
<td>13mg/kg q8h</td>
<td>15mg/kg q12h</td>
</tr>
<tr>
<td>Maximum dose per day</td>
<td>1g/day</td>
<td>1.5g/day</td>
<td>1g/day</td>
</tr>
</tbody>
</table>

#### Cefuroxime
- Injection 750 mg vial
- Tablet 250 mg, 500 mg

**CEFUROXIME ORAL LIQUID Therapeutic Interchange**

<table>
<thead>
<tr>
<th>Drug Ordered</th>
<th>Drug Supplied</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cefuroxime oral liquid</td>
<td>Cefprozil oral liquid (see table above for dose equivalency)</td>
</tr>
</tbody>
</table>

#### Third Generation Cephalosporins

**Cefixime**
- Tablet 400 mg
- Suspension 100 mg/5 mL

**CEFIXIME RESERVED STATUS**
- Treatment of mild/moderate typhoid fever
- Penicillin-resistant gonococcosis in pregnancy
- STDs in emergency treatment
- IV to PO step-down therapy

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Example: Halton Healthcare - Hospital Formulary Anti-infective Agents (includes therapeutic interchanges and restriction criteria) (continued)

**Cefotaxime**
Injection 500 mg, 1 g vial,

**Cefotaxime Therapeutic Interchange**

<table>
<thead>
<tr>
<th>Drug Ordered</th>
<th>Drug Supplied</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cefotaxime IV any dose prescribed more frequent than q8h, ADULT only</td>
<td>Cefotaxime same dose IV q8h</td>
</tr>
</tbody>
</table>

**EXCEPTION:**
Meningitis or other CNS infection: no therapeutic interchange

Either cefotaxime or ceftriaxone may be used. However, cefotaxime should preferentially be used in the following situations:
- Treatment of pyelonephritis or UTI
- Severe liver/biliary disease
- Use in neonates (≤ 28 days): Intravenous ceftriaxone use in neonates linked to neonatal jaundice (intramuscular route is acceptable). Intravenous/intramuscular use of ceftriaxone contraindicated in neonates receiving calcium-containing intravenous products (ceftriaxone and calcium-containing products should not be given within 48 hours of each other)

**Ceftazidime**
Injection 1 g vial, 2 g vial

**CEFTAZIDIME RESERVED INDICATIONS**
- Suspected/confirmed *Pseudomonas* infection
- Empiric therapy in CF and febrile neutropenia
- Empiric therapy of peritonitis in patients on chronic ambulatory peritoneal dialysis (CAPD)
- Suspected post-neurosurgical meningitis or ventriculoperitoneal (VP) shunt infection

**Ceftriaxone**
Injection 250 mg, 1 g, 2 g vial

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Example: Halton Healthcare - Hospital Formulary Anti-infective Agents (includes therapeutic interchanges and restriction criteria) (continued)

8:12:07 Miscellaneous B-Lactams

8:12:07:08 Carbapenems

Ertapenem
  Inwanz®
  Injection 1 g vial

**ERTAPENEM RESERVED INDICATIONS**
- Indicated for the following: complicated SSTI, pneumonia, complicated UTI/pyelonephritis, intra-abdominal infections and infection with an extended spectrum beta-lactamase (ESBL) producing organism
- Indicated where outpatient intravenous therapy is being considered for the above indications
- Not indicated in febrile neutropenia, meningitis or other CNS infection, necrotizing pancreatitis suspected/confirmed *Pseudomonas* or *Acinetobacter* infection

Meropenem
  Merrem®
  Injection 500 mg vial

**MEROPENEM RESERVED INDICATIONS**
- Empirical therapy in febrile neutropenia
- Alternative to Ertapenem for infection with an extended spectrum beta-lactamase (ESBL) producing organism
- Treatment of gram negative meningitis/CNS infection, or treatment of meningitis/CNS infection in beta-lactam allergic patient (do not use if prior severe reaction such as anaphylaxis or angioedema to beta-lactam antibiotics)
- Piperacillin-Tazobactam is indicated and *Pseudomonas* is suspected/confirmed, but allergy to beta-lactam antibiotics (do not use if severe reaction such as anaphylaxis or angioedema to beta-lactam antibiotics)
- Usual dose is 500 mg IV q8h, or 2 g IV q8h for meningitis/CNS infection

8:12:12 Macrolides

Azithromycin dihydrate
  Zithromax®
  Tablet 250 mg
  Suspension 200 mg/5 mL
  Injection 500 mg vial

Clarithromycin
  Biaxin®
  Tablet 250 mg
  Suspension 125 mg/5 mL

Erythromycin
  Tablet as base 250 mg
  Liquid as estolate 250 mg/5 mL
  Injection 500mg, 1 g vial

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Example: Halton Healthcare - Hospital Formulary Anti-infective Agents (includes therapeutic interchanges and restriction criteria) (continued)

8:12:16 Penicillins

Amoxicillin Amoxicil®
Capsule 250 mg, 500mg
Suspension 250 mg/5 mL
125 mg/6 mL

Amoxicillin/clavulanate Clavulin®
Tablet 250, contains Amoxicillin 250 mg/Clavulanic Acid 125 mg
Tablet 600F, contains Amoxicillin 500 mg/Clavulanic Acid 125 mg
Tablet 875, contains Amoxicillin 875 mg/Clavulanic Acid 125 mg
Liquid 125F, each 5 mL contains Amoxicillin 125 mg/Clavulanic Acid 31.25 mg
Liquid 250F, each 5 mL contains Amoxicillin 250 mg/Clavulanic Acid 62.5 mg

Ampicillin Ampicin®
Injection 250 mg, 500 mg, 1 g vial, 2 vial

**AMPICILLIN THERAPEUTIC INTERCHANGE**

<table>
<thead>
<tr>
<th>Drug Ordered</th>
<th>Drug Supplied</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amoxicillin PO (any dose or frequency)</td>
<td>Amoxicillin 500mg PO q8h</td>
</tr>
<tr>
<td>ADULT only</td>
<td></td>
</tr>
</tbody>
</table>

Cloxacillin Crbenin®
Capsule 250 mg, 500 mg
Suspension 125 mg/5 mL
Injection 500 mg, 2 gm vial, 1 gm vial

Penicillin G sodium Crystapen®
Injection 1 million units, 5 million units, 10 million units vial

**PENICILLIN G THERAPEUTIC INTERCHANGE**

<table>
<thead>
<tr>
<th>Drug Ordered</th>
<th>Drug Supplied</th>
</tr>
</thead>
<tbody>
<tr>
<td>Penicillin G (potassium or if no salt specified)</td>
<td>Penicillin G sodium</td>
</tr>
<tr>
<td>(same dose/frequency)</td>
<td></td>
</tr>
</tbody>
</table>

Penicillin G Benzathine Biocillin LA®
Injection 1,200,000 IU prefilled syringe

**PENICILLIN G BENZATHINE RESERVED STATUS**

- Treatment of syphilis infection
- Infectious Disease Service consultation is recommended

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Example: Halton Healthcare - Hospital Formulary Anti-infective Agents (includes therapeutic interchanges and restriction criteria) (continued)

**Penicillin V potassium**
- V-cillin-K®
  - Tablet 600,000 units (300 mg)
  - Suspension 300 mg/5 mL

**PENICILLIN VK THERAPEUTIC INTERCHANGE**

<table>
<thead>
<tr>
<th>Drug Ordered</th>
<th>Drug Supplied</th>
</tr>
</thead>
<tbody>
<tr>
<td>Penicillin VK 250mg tablet</td>
<td>Penicillin VK (generic) 300mg tablet (same frequency)</td>
</tr>
<tr>
<td>Penicillin V oral</td>
<td>Pen VK oral</td>
</tr>
</tbody>
</table>

**Piperacillin**
- Injection 3 g, 4 g vial
- Pipacil®

**PIPERACILLIN RESERVED STATUS**
Indicated for isolated *Pseudomonas* infection where the isolate is known to be susceptible. Use Piperacillin-Tazobactam for polymicrobial infections.

**Piperacillin/tazobactam**
- Tazocin®
  - Injection 2.25 g, 3.375 g, 4.5 g vial

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8:12:18 QUINOLONES

**Ciprofloxacin**
- Cipro®
  - Tablet 250 mg, 500 mg
  - Injection 200 mg minibag, 400 mg minibag
  - 100 mg/mL suspension

*Note: oral bioavailability of ciprofloxacin is 80-90%*

**QUINOLONE THERAPEUTIC INTERCHANGE**

<table>
<thead>
<tr>
<th>Drug Ordered</th>
<th>Drug Supplied</th>
</tr>
</thead>
<tbody>
<tr>
<td>Norfloxacin 400 mg po</td>
<td>Ciprofloxacin 500 mg po (same frequency)</td>
</tr>
</tbody>
</table>

**Levofloxacin**
- Levaquin®
  - Tablet 500 mg, 750 mg
  - Injection 500mg, 750mg

*Note: oral bioavailability of levofloxacin is ~99%*

**LEVOFLOXACIN THERAPEUTIC INTERCHANGE**

<table>
<thead>
<tr>
<th>Drug Ordered</th>
<th>Drug Supplied</th>
</tr>
</thead>
<tbody>
<tr>
<td>Levofloxacin 500 mg PO/IV daily</td>
<td>Levofloxacin 750 mg PO/IV q24h</td>
</tr>
</tbody>
</table>

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### Example: Halton Healthcare - Hospital Formulary Anti-infective Agents
(includes therapeutic interchanges and restriction criteria) (continued)

<table>
<thead>
<tr>
<th>8:12:20 SULFONAMIDES</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cotrimoxazole</strong></td>
</tr>
<tr>
<td>(Sulfamethoxazole/Trimethoprim)</td>
</tr>
<tr>
<td>Injection 80 mg/16 mg per 1 mL</td>
</tr>
<tr>
<td>Tablet 400 mg/80 mg (single strength)</td>
</tr>
<tr>
<td>Suspension 400 mg/80 mg per 10 mL</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>8:12:24 Tetracyclines</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Doxycycline</strong></td>
</tr>
<tr>
<td>Capsule 100 mg</td>
</tr>
</tbody>
</table>

| **Tetracycline** |
| Capsule 250 mg |
| Suspension 125 mg/5 mL |

<table>
<thead>
<tr>
<th>8:12:24.12 Glycylcyclines</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Tigecycline</strong></td>
</tr>
<tr>
<td>Injection 50 mg/vial</td>
</tr>
</tbody>
</table>

**TIGECYCLINE RESERVED INDICATIONS**

- Notify or consult infectious disease service
- Severe *Clostridium difficile* infection unresponsive to conventional therapies
- Treatment of MRSA, VRE or highly resistant gram negative infections (e.g. ESBLs) for which conventional therapies are not appropriate

---

### Miscellaneous Antibacterials

<table>
<thead>
<tr>
<th>8:12:28</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bacitracin</strong></td>
</tr>
<tr>
<td>Injection 50 000 units</td>
</tr>
</tbody>
</table>

| **Clindamycin** |
| Capsule 150 mg, 300 mg |
| Injection 150 mg/mL, 9g/60ml vial and 600mg/50ml, 900mg/100ml in NS bags |
| Suspension 75 mg/5 mL |

| **Colisitmethate** |
| Injection 150mg vial |

**COLISITMETHATE RESERVED INDICATIONS**

- Highly resistant gram negative infections for which alternative therapies are not appropriate
- Infectious Disease Service consultation is recommended

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Example: Halton Healthcare - Hospital Formulary Anti-infective Agents (includes therapeutic interchanges and restriction criteria) (continued)

<table>
<thead>
<tr>
<th>Daptomycin</th>
<th>Cubicin®</th>
</tr>
</thead>
<tbody>
<tr>
<td>Injection 500 mg/vial</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>DAPTOMYCIN RESERVED STATUS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Notify or consult the infectious disease service</td>
</tr>
<tr>
<td>- Isolated MRSA infection for which other first line therapies are contraindicated or not tolerated</td>
</tr>
<tr>
<td>- Isolated MRSA infection in a patient non-responsive to vancomycin</td>
</tr>
<tr>
<td>- Consider as first line therapy of MRSA bacteremia with MIC to vancomycin ≥ 2mcg/mL and/or persistent bacteremia on vancomycin</td>
</tr>
<tr>
<td>- Not indicated in: pulmonary infections</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Fidaxomicin</th>
<th>Dificid®</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tablet 200mg</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>FIDAXOMICIN RESERVED STATUS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Notify or consult the infectious disease service</td>
</tr>
<tr>
<td>- Second or later recurrence (i.e. third or later episode) of Clostridium difficile infection – restricted to ID physicians</td>
</tr>
<tr>
<td>- Completion of therapy of CDI initiated prior to admission</td>
</tr>
<tr>
<td><strong>Note:</strong> New start orders for this agent are restricted to ID physicians. Therapeutic interchange to PO vancomycin applies to all other new start orders</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>FIDAXOMICIN THERAPEUTIC INTERCHANGE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Drug Ordered</strong></td>
</tr>
<tr>
<td>Fidaxomicin any dose or frequency</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Exceptions:</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>- The order is written in person or as a telephone order by an ID physician</td>
</tr>
<tr>
<td>- Completion of CDI initiated prior to admission</td>
</tr>
</tbody>
</table>

| **Note:** New start orders for this agent are restricted to ID physicians. Therapeutic interchange to PO Vancomycin applies to all other new start orders |

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Example: Halton Healthcare - Hospital Formulary Anti-infective Agents (includes therapeutic interchanges and restriction criteria) (continued)

**Linezolid**
Injection 600 mg/300 ml
Tablets 600 mg

**Zyvoxam**

**LINEZOLID RESERVED STATUS**
Notify or consult the infectious disease service
- MRSA infection in a patient intolerant to or failed vancomycin
- MRSA infection in a patient with no intravenous access
- MRSA bacteremia with MIC to vancomycin ≥ 2mcg/mL and/or persistent bacteremia on vancomycin
- VRE infection
- Treatment of multi-drug resistant TB or non-tuberculous mycobacterial infection

**Vancomycin**
Injection 500 mg, 1 g vial

**NOTE:** For all po orders, vancomycin injection will be administered orally, diluted in a beverage just prior to administration.

**USUAL DOSAGE OF VANCOMYCIN FOR Clostridium Difficile COLITIS:**
125-250 mg po q8h
*refer to Clostridium Difficile Diagnosis & Management Algorithm on HOPP

**VANCOMYCIN THERAPEUTIC INTERCHANGE**

**Drug Ordered**
Vancomycin IV any dose or frequency

**Drug Supplied**
Vancomycin 1g IV q12h

**ADULT only**

**Exceptions:**
- Meningitis or other CNS infection: use 1.5g IV q12h
- Dose adjustment in treatment of deep/severe staphylococcal infection with trough level <10 mcg/mL: titrate dose to achieve trough 10-20 mcg/mL

---

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Example: Halton Healthcare - Hospital Formulary Anti-infective Agents (includes therapeutic interchanges and restriction criteria) (continued)

### Antifungals

#### Azoles

**Fluconazole**
Tablet 50 mg, 100 mg  
Suspension 10 mg/mL  
Injection 200 mg/100 mL, 400 mg/200 mL in 0.9% NaCl

**FLUCONAZOLE RESERVED STATUS**
Unable to take oral medication and one of the following:
- Invasive candidiasis (endophthalmitis, hepatosplenic candidiasis, *Candida* isolated from sterile site)
- Empiric therapy in ICU patient at high risk of disseminated candidiasis and cultures of 3 non-sterile sites yield *Candida* species

**Voriconazole**
Injection 200 mg VIAL  
Tablets 50 mg, 200 mg

**VORICONAZOLE RESERVED STATUS**
- Patients who are unresponsive to or intolerant of conventional Amphotericin B  
- Suspected/confirmed infection with *Histoplasma, Blastomyces, Aspergillus, Fusarium, Scedosporium*  
- Step-down therapy for confirmed or suspected invasive mycosis

**Itraconazole**
Capsule 100 mg

**ITRACONAZOLE RESERVED STATUS**
- Treatment of fluconazole-resistant *Candida*

#### Echinocandins

**Caspofungin**
Injection 70 mg, 50 mg vial

**CASPOFUNGIN RESERVED STATUS**
- Patients who are unresponsive to or intolerant of conventional Amphotericin B  
- Suspected or confirmed fungal infection and impaired renal function  
- Suspected/confirmed fluconazole resistant *Candida* infection  
- Salvage aspergillosis therapy if failure with standard therapy

---

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Example: Halton Healthcare - Hospital Formulary Anti-infective Agents (includes therapeutic interchanges and restriction criteria) (continued)

8:14:28 Polynes

Amphotericin B
Injection 50 mg vial
Fungizone®

AMPHOTERICIN B RESERVED STATUS
- Suspected/confirmed disseminated/deep organ fungal infection
- Empiric therapy for patient with profound neutropenia and fever >5 days despite appropriate empiric antibacterial therapy
- Initiation therapy in suspected/confirmed endemic mycosis (Aspergillus, Histoplasma, Blastomyces etc.)

Liposomal Amphotericin B
Injection 50 mg vial
Ambisome®

LIPOSOMAL AMPHOTERICIN B RESERVED STATUS
Same indications as for non-lipid amphotericin (except not recommended for endophthalmitis), but:
- Intolerant to conventional Amphotericin B (infusion reactions, electrolyte disturbance)
- Nephrotoxicity: baseline serum creatinine >175 μmol/L or patient has developed acute renal failure while on Amphotericin B

Nystatin
Mycostatin®, Nilstat®
Suspension 100 000 units/mL
Ointment 100 000 U/g

NYSTATIN THERAPEUTIC INTERCHANGE

<table>
<thead>
<tr>
<th>Drug Ordered</th>
<th>Drug Supplied</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nystatin – any oral tablet or suspension dose/frequency, ADULT only</td>
<td>Nystatin 500 000 units (5mL) q8h</td>
</tr>
<tr>
<td>Nystatin topical (no dosage form specified)</td>
<td>Ointment will be supplied</td>
</tr>
</tbody>
</table>

8:16 ANTIMYCOBACTERIALS

8:16:04 Antituberculosis Agents

Ethambutol
Tablet 100 mg, 400 mg
Etib®, Myambutol®

Isoniazid
Tablet 100 mg, 300 mg
Vial 1000 mg (SAP)
Isotamine®

ISONIAD 1000 MG VIAL (SAP) RESERVED INDICATIONS
- Treatment of tuberculous meningitis where the patient is unable to tolerate medications via the enteral route
- Infectious Disease Service consultation is recommended

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Example: Halton Healthcare - Hospital Formulary Anti-infective Agents (includes therapeutic interchanges and restriction criteria) (continued)

<table>
<thead>
<tr>
<th>Pyrazinamide</th>
<th>Tebrazid®</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tablet 500 mg</td>
<td></td>
</tr>
</tbody>
</table>

Rifampin

<table>
<thead>
<tr>
<th>Capsule 150 mg, 300 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vial 600 mg (SAP medication)</td>
</tr>
</tbody>
</table>

**RIFAMPIN 600 MG VIAL (SAP) RESERVED INDICATIONS**

- Treatment of tuberculous meningitis where the patient is unable to tolerate medications via the enteral route
- Infectious Disease Service consultation is recommended

<table>
<thead>
<tr>
<th>8:16:92 Miscellaneous Antimycobacterials</th>
</tr>
</thead>
</table>

Dapsone

<table>
<thead>
<tr>
<th>Avlosulfon®</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tablet 100 mg</td>
</tr>
</tbody>
</table>

**8:18 ANTIVIRALS**

**8:18:04 Adamantanes**

Amantadine

<table>
<thead>
<tr>
<th>Symmetrel®</th>
</tr>
</thead>
<tbody>
<tr>
<td>Capsule 100 mg</td>
</tr>
<tr>
<td>Syrup 50 mg/5 mL</td>
</tr>
</tbody>
</table>

Zanamivir

| Relenza® |
| Diskhaler 5mg/disk |

**18:08 Antiretrovirals**

**Note:** Selected HIV medications are included in the Formulary primarily for the indications specified. However, these medications may be prescribed for the treatment of HIV on an as needed basis. For patients who are maintained on antiretroviral therapy in the community, use of the patient’s own medication supply is preferred, but in cases where it is not feasible for the patient to provide their own supply, HHS shall provide the medication. For newly initiated HIV therapy, HHS shall provide the medications as prescribed. (Permission of the Director of Pharmacy or delegate will be obtained when any HIV medication needs to be procured for an indication other than a listed reserved indication.)

Raltegravir

| Isentress® |
| Tablet 400 mg |

Halton Healthcare Hospital Formulary
Date of last revision: September 2015

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Example: Halton Healthcare - Hospital Formulary Anti-infective Agents (includes therapeutic interchanges and restriction criteria) (continued)

Tenofovir/Emtricitabine  
Tablet 300/200mg

Raltegravir and Tenofovir/Emtricitabine Reserved Status indication:
- Post-exposure prophylaxis of HIV infection where indicated

Note: Selected HIV medications are included in the Formulary primarily for the indications specified. However, these medications may be prescribed for the treatment of HIV on an as needed basis. For patients who are maintained on antiretroviral therapy in the community, use of the patient’s own medication supply is preferred, but in cases where it is not feasible for the patient to provide their own supply, HHS shall provide the medication. For newly initiated HIV therapy, HHS shall provide the medications as prescribed. (Permission of the Director of Pharmacy or delegate will be obtained when any HIV medication needs to be procured for an indication other than a listed reserved indication.)

Lamivudine  
Tablet 150 mg
Oral Liquid 10mg/ml (Reserved antiretroviral agent)

Nevirapine  
Tablet 200mg
Oral liquid 10mg/ml (Reserved antiretroviral agent- SAP)

Lamivudine And Nevirapine Reserved Status Indications:
- Intrapartum suspected or confirmed HIV infection with no antiretroviral management during pregnancy (tablets)
- Prophylaxis of HIV in infants born to HIV infected mothers where indicated (oral liquid)

Zidovudine  
Capsule 100 mg
Oral liquid 50mg/5ml
Injection 200mg/20ml

Zidovudine Reserved Status Indications:
- Intrapartum suspected or confirmed HIV infection with no antiretroviral management during pregnancy (injectable)
- Postpartum suspected or confirmed HIV infection with no antiretroviral management during pregnancy (tablets)
- Neonatal prevention of mother to child transmission of HIV (oral liquid or injectable)

Note: Selected HIV medications are included in the Formulary primarily for the indications specified. However, these medications may be prescribed for the treatment of HIV on an as needed basis. For patients who are maintained on antiretroviral therapy in the community, use of the patient’s own medication supply is preferred, but in cases where it is not feasible for the patient to provide their own supply, HHS shall provide the medication. For newly initiated HIV therapy, HHS shall provide the medications as prescribed. (Permission of the Director of Pharmacy or delegate will be obtained when any HIV medication needs to be procured for an indication other than a listed reserved indication.)

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**8:18:28 Neuraminidase Inhibitors**

**Oseltamivir**
- Capsule 30 mg, 75 mg
- Suspension 8 mg/mL

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**Table for Interchange for Standard Dose Oseltamivir to Renally Adjusted Dose**

**Important notes:**
- Applies to non-critically ill patients only – double dose oseltamivir may be prescribed in the critically ill, and Therapeutic Interchange must not be applied to these orders.
- Extended treatment duration (i.e. >5 days) may be requested by the prescriber for influenza treatment in severely ill children or in adults who are immunocompromized and/or critically ill. In such cases, do not interchange treatment to 5 days.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Substitution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oseltamivir for influenza treatment, any standard dose prescribed for patient with CrCl 31-60mL/min - ADULT ONLY</td>
<td>Oseltamivir 75mg PO once daily</td>
</tr>
<tr>
<td>Oseltamivir for influenza treatment, any standard dose prescribed for patient with CrCl 10-30mL/min - ADULT ONLY</td>
<td>Oseltamivir 30mg PO once daily</td>
</tr>
<tr>
<td>Oseltamivir for influenza treatment, any standard dose prescribed for patient with CrCl &lt;10mL/min on neither Hemodialysis nor CAPD – ADULT ONLY</td>
<td>Oseltamivir 75mg PO x 1 dose</td>
</tr>
<tr>
<td>Oseltamivir for influenza treatment, any standard dose prescribed for patient on regular Hemodialysis – ADULT ONLY</td>
<td>Oseltamivir 75mg PO stat, then 75mg PO post each hemodialysis session</td>
</tr>
<tr>
<td>Oseltamivir for influenza treatment, any standard dose prescribed for patient on CAPD – ADULT ONLY</td>
<td>Oseltamivir 30mg PO x 1 dose</td>
</tr>
</tbody>
</table>

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Example: Halton Healthcare - Hospital Formulary Anti-infective Agents (includes therapeutic interchanges and restriction criteria) (continued)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Substitution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oseltamivir for influenza prophylaxis, any standard dose prescribed for patient with CrCl 31-60mL/min – ADULT ONLY</td>
<td>Oseltamivir 75mg PO every 2 days</td>
</tr>
<tr>
<td>Oseltamivir for influenza prophylaxis, any standard dose prescribed for patient with CrCl 10-30mL/min – ADULT ONLY</td>
<td>Oseltamivir 30mg PO every 2 days</td>
</tr>
<tr>
<td>Oseltamivir for influenza prophylaxis, any standard dose prescribed for patient on regular Hemodialysis – ADULT ONLY</td>
<td>Oseltamivir 75mg PO stat, then 75mg PO post each hemodialysis session</td>
</tr>
<tr>
<td>Oseltamivir for influenza prophylaxis, any standard dose prescribed for patient on CAPD, or for patient with CrCl &lt;10mL/min on neither Hemodialysis nor CAPD – ADULT ONLY</td>
<td>Oseltamivir 30mg PO every seven days</td>
</tr>
</tbody>
</table>

8:18:32 Nucleosides and Nucleotides

**Acyclovir**

<table>
<thead>
<tr>
<th>Formulation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tablets 200 mg</td>
</tr>
<tr>
<td>Oral Suspension 40mg/ml</td>
</tr>
<tr>
<td>Injection 500 mg vial</td>
</tr>
</tbody>
</table>

**ACYCLOVIR IV RESERVED STATUS**

- Patient unable to take oral therapy
- Disseminated varicella (chicken pox) in normal host not responding to oral therapy or in an immunocompromised host
- Herpes Zoster (shingles):
  - immunocompromised host
  - severe disease: >1 dermatome, disseminated, trigeminal nerve
- Suspected/confirmed HSV encephalitis or disseminated disease
- Suspected neonatal disease

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Example: Halton Healthcare - Hospital Formulary Anti-infective Agents (includes therapeutic interchanges and restriction criteria) (continued)

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Supplier</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gancyclovir</td>
<td>Cytovene®</td>
</tr>
<tr>
<td>Valacyclovir</td>
<td>Valtrex®</td>
</tr>
</tbody>
</table>

### Gancyclovir Reserved Status
- Treatment of suspected/confirmed cytomegalovirus (CMV) deep organ disease: retinitis, esophagitis, colitis, etc.
- Suspected/confirmed disseminated CMV viremia or focal CMV infection
- Graft rejection post solid organ transplant

### Valacyclovir Therapeutic Interchange
<table>
<thead>
<tr>
<th>Drug Ordered</th>
<th>Drug Supplied</th>
</tr>
</thead>
<tbody>
<tr>
<td>Famciclovir (any dose or frequency), ADULT only</td>
<td>Valacyclovir 1g PO q6h</td>
</tr>
</tbody>
</table>

### 8:30 ANTIPROTOZOALS
8:30:08 Antimalarials

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Supplier</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydroxychloroquine</td>
<td>Plaquenil®</td>
</tr>
<tr>
<td>Quinine sulphate</td>
<td>Quinine®</td>
</tr>
<tr>
<td>Quinine Dihydrochloride</td>
<td></td>
</tr>
</tbody>
</table>

### Quinine Injectable Reserved Status
- Severe malaria in pregnant patient during first trimester
- Therapy of non-severe malaria where oral treatment is not possible
- Infectious Disease Service consultation is recommended

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Supplier</th>
</tr>
</thead>
<tbody>
<tr>
<td>Choloroquine phosphate</td>
<td></td>
</tr>
<tr>
<td>Atovaquone/Proguanil</td>
<td>Malarone®</td>
</tr>
<tr>
<td>Primaquine Phosphate</td>
<td>Primaquine®</td>
</tr>
</tbody>
</table>

### Primaquine Reserved Status
- Primaquine in combination with clindamycin is an option for the treatment of PCP in patient who are unable to

---

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Example: Halton Healthcare - Hospital Formulary Anti-infective Agents (includes therapeutic interchanges and restriction criteria) (continued)

<table>
<thead>
<tr>
<th>Tolerate co-trimoxazole</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primaquine is also indicated for terminal prophylaxis for prevention of relapses of malaria caused by <em>Plasmodium vivax or Plasmodium ovale</em></td>
</tr>
<tr>
<td>The possibility of G6PD deficiency should be excluded before treatment is initiated</td>
</tr>
<tr>
<td>Infectious Disease Service consultation is recommended</td>
</tr>
</tbody>
</table>

**Atovaquone**

Meprone

Oral Suspension 150mg/ml

**Artesunate**

Injectable 110mg vial

**ARTESANATE RESERVED STATUS**

- First line choice for severe malaria in adults and children (parasitemia greater than 5%, signs of end organ disease, etc.)
- **EXCEPTIONS:** Pregnant patient, first trimester only
- Therapy of non-severe malaria where the patient is unable to tolerate medication via the enteral route
- Infectious Disease consultation is recommended

### 8:30:92 Miscellaneous Antiprotozoals

**MetroNIDazole**

Flagyl®

- Tablet 250 mg
- Injection 500 mg mini-bag

**METRONIDAZOLE THERAPEUTIC INTERCHANGE**

<table>
<thead>
<tr>
<th>Drug Ordered</th>
<th>Drug Supplied</th>
</tr>
</thead>
<tbody>
<tr>
<td>MetroNIDazole 250 mg PO q6h</td>
<td>MetroNIDazole 500 mg q8h</td>
</tr>
</tbody>
</table>

**Exception**

Gastrointestinal intolerance

**MetroNIDazole IV (any dose or frequency)**

MetroNIDazole 500mg IV q12h

**ADULT only**

**Exceptions:**

- Use 500mg IV q8h for *C. difficile* infection, flare of Crohns/Ulcerative Colitis, *H. pylori*, CNS infection where
  - MetroNIDazole is indicated, or pediatric use
- Use 750mg IV q8h for parasitic infections

**USUAL DOSAGE OF METRONIDAZOLE FOR Clostridium Difficile COLITIS:**

250 mg po q6H or 500 mg po q8H

*refer to Clostridium Difficile Diagnosis & Management Algorithm on HOPP*

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**Pentamidine**
Injection 300 mg vial

**PENTAMIDINE RESERVED STATUS**
Suspected/confirmed *pneumocystis jiroveci* pneumonia (PCP) for which intravenous administration is required and patient is allergic to or intolerant of co-trimoxazole

**8:36 URINARY ANTI-INFECTIVES**

<table>
<thead>
<tr>
<th>Nitrofurantoin macrocrystals</th>
<th>Macrodantin®</th>
</tr>
</thead>
<tbody>
<tr>
<td>Capsule 50 mg</td>
<td></td>
</tr>
</tbody>
</table>

**NITROFURANTOIN THERAPEUTIC INTERCHANGE**

<table>
<thead>
<tr>
<th>Drug Ordered</th>
<th>Drug Supplied</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nitrofurantoin microcrystals (tablets)</td>
<td>Nitrofurantoin macrocrystals (Macrodantin®)</td>
</tr>
<tr>
<td>same dose and frequency</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Nitrofurantoin macrocrystals</th>
<th>Macrobid®</th>
</tr>
</thead>
<tbody>
<tr>
<td>Capsule 100 mg</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Trimethoprim</th>
<th>Proloprim®</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tablet 100 mg</td>
<td></td>
</tr>
</tbody>
</table>

---

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