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Antimicrobial Stewardship Strategy: Formulary restriction

Restricted dispensing of targeted antimicrobials on the hospital's formulary, according to approved criteria. The use of restricted antimicrobials may be limited to certain indications, prescribers, services, patient populations or a combination of these.

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This is a PHO CORE strategy

Priority Level: **A**

Difficulty Level: **2**

Program Stage:

- ✓ Early
- Intermediate
- Advanced

Antimicrobial Stewardship Outcomes:

- Drug utilization outcomes
- Reduction of *Clostridium difficile* infection
- Reduction in antimicrobial-resistant organisms

For more information on these criteria and how they were developed, please see the Antimicrobial Stewardship Strategy Criteria Reference Guide

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.

Rationale

Hospital formularies include a variety of anti-infective agents that are ideally selected based on the needs of the facility and best-in-class choices (see *Formulary review/streamlining*). A number of these agents require restrictions or specific guidance for use because of one or more of the following:

- Potential to promote resistance.
- Potential for/documented overuse or misuse (e.g., use of broad-spectrum agents where narrower-spectrum agents are more appropriate).
- Need to reserve for treatment of multi-drug-resistant organisms.
- Broad spectrum.
- High cost.
- Risk for serious adverse effects.

Examples of antimicrobials whose use is frequently restricted include the carbapenems, piperacillin/tazobactam, vancomycin, linezolid, daptomycin, echinocandin antifungal agents etc.

Antimicrobial restrictions can help control use, decrease costs and limit antimicrobial resistance.

Implementation

Dispensing of targeted antimicrobials may be restricted or limited based on one or more of the following:

- Approved criteria.
- Certain indications.
- Specific prescribers (e.g., by infectious diseases specialists).
- Specific services or wards (e.g., critical care units).
- Specific patient populations (e.g., patients with immunosuppression or cystic fibrosis).

Restrictions are typically developed by the hospital or region's antimicrobial stewardship program or antimicrobial subcommittee and require approval by the institution/region's pharmacy and therapeutics committee or similar group and should be periodically reviewed and updated.

Antimicrobial restrictions are more effective when they are enforced, but the ability or degree of enforcement may vary depending on hospital resources. Prescribing restrictions may be enforced either **prospectively** (requiring preauthorization prior to dispensation—see *Formulary restriction with preauthorization*) or **retrospectively** (audit of restricted antimicrobials after dispensation). Some institutions' policies allow 24 to 72 hours of unrestricted use to prevent delays in patient care. In smaller institutions, pharmacists may contact the prescriber from the dispensary to discuss whether the indication conforms to restrictions, or they may review the patient's chart and contact the prescriber or leave a notice if prescribing criteria are not met.

If computerized physician order entry is available, restriction criteria can be incorporated into the drug-ordering process, along with recommendations for alternative therapy.

Education of staff about restriction policies and criteria is necessary. It is most effective if several approaches are used (e.g., posters, emails, presentations, academic detailing, etc).

Advantages

- Sends a message that some antimicrobials require greater caution or infectious diseases expertise when prescribing.
- Provides guidelines for the appropriate use of restricted antimicrobials.
- Provides cost savings for the institution if high-cost antimicrobials are restricted.
- Enforced restriction can lead to immediate and significant reductions in antimicrobial use, particularly if used with preauthorization. Can lead to decreased resistance rates in the restricted antibiotics in the short term, and introducing new restrictions to limit use of specific antibiotics can help control nosocomial outbreaks.
- Potential opportunity to provide prescriber education and/or recommendations for use of alternative agents or specialist consultation (if applicable).

Disadvantages

- Requires enforcement to be effective; prescribers may circumvent restrictions if there is no enforcement.

- Can lead to “squeezing the balloon,” with an increase in the use of and resistance to antimicrobial agents that are not restricted.
- Prescribers may see prescribing restrictions as a loss of autonomy.
- Delays in initiation of treatment may be a concern with preauthorization types of enforcement; this can be avoided by allowing a first dose or 24 to 72 hours of therapy before restriction is enforced.

Requirements

- Process and/or personnel to restrict dispensing, educate staff about restriction policies and perform audits to determine if restrictions are followed.

Associated Metrics

- Percentage of restricted antimicrobials prescribed according to guidelines.
- Audit susceptibility patterns of antibiotics to assess impact of restrictions and monitor for the “squeezing the balloon” phenomenon (advanced).

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.

- Dellit TH, Owens RC, McGowan JE Jr, Gerding DN, Weinstein RA, Burke JP, et al; Infectious Diseases Society of America; Society for Healthcare Epidemiology of America. Infectious Diseases Society of America and the Society for HealthcareEpidemiology of America guidelines for developing an institutional program to enhance antimicrobial stewardship. Clin Infect Dis. 2007;44(2):159–77. Available from: http://cid.oxfordjournals.org/content/44/2/159.long

- Buising K. Formularies and antimicrobial approval systems. In: Duguid M, Cruickshank M, editors. Antimicrobial stewardship in Australian hospitals 2011. Sydney, Australia: Australian Commission on Safety and Quality in Health Care; 2010. Chapter 2. Available from: http://www.safetyandquality.gov.au/wp-content/uploads/2011/01/Antimicrobial-stewardship-in-Australian-Hospitals-2011.pdf

  Discusses the importance of maintaining an antimicrobial formulary and ways to enforce restrictions.

- Drew RH, White R, MacDougall C, Hermsen ED, Owens RC Jr; Society of Infectious Diseases Pharmacists. Insights from the Society of Infectious Diseases Pharmacists on antimicrobial stewardship guidelines from the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America. Pharmacotherapy. 2009;29(5):593–607.

- Po JL, Nguyen BQ, Carling PC. The impact of an infectious diseases specialist-directed computerized physician order entry antimicrobial stewardship program targeting linezolid use. Infect Control Hosp Epidemiol. 2012;33(4):434–5.

  Institutional restrictions for the use of linezolid were incorporated into a computerized physician order entry–antimicrobial stewardship template.

  S*ignificant decreases in linezolid use were seen in the 16-month follow-up after implementation.*

- Rahal JJ, Urban C, Horn D, Freeman K, Segal-Maurer S, Maurer J, et al. Class restriction of cephalosporin use to control total cephalosporin resistance in nosocomial *Klebsiella*. JAMA. 1998;280(14):1233–7. Available from: http://jama.jamanetwork.com/article.aspx?articleid=188047

  Extensive restrictions on the use of cephalosporins were implemented hospital-wide.

  Significant decrease in the incidence of ceftazidime-resistant Klebsiella *infections and colonization was achieved one year later, but an increase in the incidence of imipenem-resistant* Pseudomonas aeruginosa *was observed.*

- Lewis GJ, Fang X, Gooch M, Cook PP. Decreased resistance of *Pseudomonas aeruginosa* with restriction of ciprofloxacin in a large teaching hospital's intensive care and intermediate care units. Infect Control Hosp Epidemiol. 2012;33(4):368–73.

  Restriction of ciprofloxacin led to increases in carbapenem use, but was associated with a significant decreasing trend in the percentage and rate of resistance of Pseudomonas aeruginosa *to ciprofloxacin and carbapenems.*

  No significant increase in resistance of nosocomial Enterbacteraciae to carbapenems.

Samples/Examples

- Example 1: Winchester District Memorial Hospital - Restricted Antibiotic Criteria Stickers
- Example 2: Halton Healthcare - List of Reserved Anti-infectives
- Example 3: North York General Hospital - Restricted Antimicrobial Guidelines
- Example 4: London Health Sciences Centre - Restricted (Tier 3) Antimicrobials

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 with preauthorization
- Formulary review/streamlining
- General antimicrobial order forms

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For further information

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Example 1: Winchester District Memorial Hospital - Restricted Antibiotic Criteria Stickers

Restricted Antibiotic Criteria Stickers

<table>
<tr>
<td>Ceftazidime Restricted Criteria:
<u>Patient has Mild-Moderate penicillin allergy</u>
Plus any of the following conditions:
1. Proven or highly suspected pseudomonal infection
2. Febrile neutropenia
3. Meningitis or brain abscess post neurosurgery</td>
<td>Ciprofloxacin IV Restricted Criteria:
<u>Patient is not a candidate for Cipro PO</u>
Plus:
Proven and/or serious gram-negative infection due to an organism resistant to other antibiotics or other antibiotics are contraindicated.</td>
</tr>
<tr>
<td>Meropenem Restricted Criteria:
1. Infection involving an organism documented or likely resistant to all other antibiotics
2. Due to ID consult</td>
<td>Piperacillin-Tazobactam Restricted Criteria:
1. Sepsis
2. Empiric therapy of febrile neutropenia ± aminoglycosides.
3. Suspected or proven severe nosocomial pneumonia
4. Suspected or proven polymicrobial and/or nosocomial infection when combination therapy with other antibiotics is not desirable
5. Necrotizing fasciitis</td>
</tr>
<tr>
<td>Vancomycin IV Restricted Criteria:
1. Serious allergy to beta-lactam antibiotics plus infection due to gram positive organism(s)
2. Serious infections with suspected MRSA
3. Add on for febrile neutropenia patients
4. Orally for C. difficile colitis (unresponsive to metronidazole)
5. Osteomyelitis or cellulitis in IV drug users
6. Meningitis</td>
<td></td>
</tr>
</table>

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Example 2: Halton Healthcare - List of Reserved Anti-infectives

ANTI-INFECTIVE RESERVED ANTI-INFECTIVES

Drug	Reserved Status
Acyclovir injectable	• Patient unable to tolerate medication via the enteral route • 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
Amikacin injectable	• Highly resistant gram negative infections for which alternative therapies are not appropriate • Note: Drug level monitoring for amikacin is performed at an off site laboratory ** Use of an aminoglycoside beyond 7 days will be subject to Antimicrobial Stewardship Review **
Amphotericin B injectable (Fungizone®)	• Suspected/confirmed disseminated/deep organ fungal infection • Empirical therapy for patient with profound neutropenia and fever >5 days despite appropriate empirical antibacterial therapy • Initiation therapy in suspected/confirmed endemic mycosis (*Aspergillus, Histoplasma, Blastomyces* etc.)
Amphotericin B Liposomal injectable (AmBisome®)	**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
Artesunate injectable (Revised. Available only via Canadian Malaria Network)	• 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 Service consultation is recommended

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Example 2: Halton Healthcare - List of Reserved Anti-infectives (continued)

Drug	Reserved Status
Caspofungin injectable (Cancidas®)	• Patients who are unresponsive to or intolerant of conventional Amphotericin B • Suspected or confirmed fungal infection and impaired renal function • First line therapy for suspected or confirmed candidemia in severely ill • Suspected/confirmed fluconazole resistant Candida infection • Salvage aspergillosis therapy if failure with standard therapy
Cefixime tablets (Suprax®)	• Treatment of mild/moderate typhoid fever • Penicillin-resistant gonococcus in pregnancy • STDs in emergency treatment • IV to PO step-down therapy
Cefotaxime injectable (Claforan®)	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 eachother)
Ceftazidime injectable (Fortaz®)	• Suspected/confirmed *Pseudomonas* infection • Empirical therapy in cystic fibrosis (CF) and febrile neutropenia • Empirical therapy of peritonitis in patients on chronic ambulatory peritoneal dialysis (CAPD) • Suspected post-neurosurgical meningitis or ventriculoperitoneal (VP) shunt infection
Chloramphenicol injectable (Non-Formulary)	• Treatment of meningitis in the setting of severe beta-lactam allergy • Infectious Disease Service consultation is recommended
Clarithromycin tablets (Biaxin®)	• Eradication of *Helicobacter pylori* • Treatment of non-tuberculous mycobacterial infection • See Therapeutic Interchange Policy
Colistimethate injectable (Colistin®)	• Highly resistant gram negative infections for which alternative therapies are not appropriate • Infectious Disease Service consultation is recommended

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Example 2: Halton Healthcare - List of Reserved Anti-infectives (continued)

Drug	Reserved Status
Daptomycin injectable (Cubicin®)	• Isolated MRSA infection for which other first line therapies are contraindicated or not tolerated • Isolated MRSA infection in a patient non-responsive to vancomycin • Consider as first line therapy of MRSA bacteremia with MIC to vancomycin ≥ 2mcg/mL • Consider for therapy of MRSA bacteremia where bacteremia persists on vancomycin • **Not** indicated in pulmonary infections • Infectious Disease Service consultation is recommended
Ertapenem injectable (Invanz®)	• 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
Erythromycin tablets (base), liquid (estolate) and injectable	• Gastrointestinal prokinetic when all other reasonable therapeutic attempts have failed (base tablets) • Pertussis in children (liquid or injectable forms)
Fidaxomicin tablets (Dificid™) (Not routinely stocked in Pharmacy)	• Second or later recurrence (i.e. third or later episode) of *Clostridium difficile* Infection – **restricted to ID physicians** • Completion of therapy of CDI initiated prior to admission **Note:** New start orders for this agent are **restricted** to ID physicians. Therapeutic interchange to PO vancomycin applies to all other new start orders **** RESTRICTED ANTI-INFECTIVE AGENT ****

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Example 2: Halton Healthcare - List of Reserved Anti-infectives (continued)

Drug	Reserved Status
Fluconazole injectable (Diflucan®)	**Unable to take oral medication <u>and</u> one of the following:** • Invasive candidiasis (endophthalmitis, hepatosplenic candidiasis, *Candida* isolated from sterile site) • Empirical therapy in ICU patient at high risk of disseminated candidiasis **and** cultures of 3 non-sterile sites yield *Candida* species • Alternative to nystatin for mucocutaneous candidiasis, because of lack of efficacy, severe adverse events or drug interactions • Candiduria in patients with symptoms of pyelonephritis • Induction therapy for respiratory, cutaneous or meningeal cryptococcal infection, treatment of coccidiomycosis
Ganciclovir injectable and oral	• 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
Gentamicin injectable	** Use of an aminoglycoside beyond 7 days will be subject to Antimicrobial Stewardship review ** • Refer to Therapeutic Interchange Policy
Isoniazid injectable (available only via SAP)	• Treatment of tuberculous meningitis where the patient is unable to tolerate medications via the enteral route • Infectious Disease Service consultation is recommended
Itraconazole capsules (Sporanox®)	• Treatment of fluconazole-resistant *Candida* • Treatment of invasive *Aspergillus*, allergic bronchopulmonary aspergillosis • Therapy of suspected/confirmed endemic mycosis (*Aspergillus, Histoplasma, Blastomyces, Coccidiodes,* etc.)
Ivermectin tablets (Non-Formulary – available only via SAP)	• Treatment of crusted (Norwegian) scabies

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Example 2: Halton Healthcare - List of Reserved Anti-infectives (continued)

Drug	Reserved Status
Lamivudine tablets and oral liquid 10mg/mL (3TC®)	• Intrapartum and postpartum 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) 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 anti-retroviral 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.)
Linezolid intravenous and tablets (Zyvoxam®)	• 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 • Infectious Disease Service consultation is recommended
Meropenem injectable (Merrem®)	• 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 500mg IV q8h, or 2g IV q8hr for meningitis/CNS infection
Mupirocin cream or ointment (Topical) (Bactroban®)	• Decolonization of MRSA, applied to anterior nares BID for 7 days • No longer routinely employed • Notify/consult Infectious Diseases of any "no-substitution" use (Adult or Pediatric). See Therapeutic Interchange Policy.

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Example 2: Halton Healthcare - List of Reserved Anti-infectives (continued)

Drug	Reserved Status
Nevirapine tablets and oral liquid 10mg/mL Note: oral liquid available only via SAP. (Viramune)	• 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) 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 anti-retroviral 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.)
Penicillin G Benzathine injectable (Bicillin LA®) (Available via Public Health)	• Treatment of syphilis infection • Infectious Disease Service consultation is recommended
Pentamidine injectable	• Suspected/confirmed *pneumocystis jiroveci* pneumonia (PCP) for which intravenous administration is required **and** patient is allergic to or intolerant of co-trimoxazole • Infectious Disease Service consultation is recommended
Piperacillin injectable	• Indicated for isolated *Pseudomonas* infection where the isolate is known to be susceptible. Use Piperacillin-Tazobactam for polymicrobial infections.
Primaquine tablets	• Primaquine in combination with clindamycin is an option for the treatment of PCP in patient who are unable to tolerate co-trimoxazole • Primaquine is also indicated for terminal prophylaxis for prevention of relapses of malaria caused by *Plasmodium vivax* or *Plasmodium ovale* • The possibility of G6PD deficiency should be excluded before treatment is initiated • Infectious Disease Service consultation is recommended
Quinine injectable (Available only via Canadian Malaria Network)	• 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

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Example 2: Halton Healthcare - List of Reserved Anti-infectives (continued)

Drug	Reserved Status
Raltegravir tablets	• 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 anti-retroviral 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.)
Rifampin injectable (available only via SAP)	• Treatment of tuberculous meningitis where the patient is unable to tolerate medications via the enteral route • Infectious Disease Service consultation is recommended
Ribavirin injectable, inhalation, capsules (with peginterferon) (Non-Formulary, IV form available only via SAP)	• Intravenous ribavirin may be used experimentally for the treatment of serious viral infections under expert supervision. • Non-Formulary • Infectious Disease Service consultation is recommended • Note: Inhaled ribavirin cannot be administered at HHS, as ribavirin is potentially teratogenic and poses an exposure risk to healthcare workers • Note: Oral ribavirin (with peginterferon) is used for management of chronic hepatitis C infection. This medication is Non-Formulary
Tenofovir/ Emtricitabine tablets	• 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 anti-retroviral 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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Example 2: Halton Healthcare - List of Reserved Anti-infectives (continued)

Drug	Reserved Status
Tigecycline injectable (Tygacil®)	• Severe *Clostridium difficile* infection unresponsive to conventional therapies • Treatment of MRSA, VRE or highly resistant gram negative infections (e.g. extended-spectrum beta-lactamase producing organisms (ESBLs), carbapenem-resistant Enterobacteriaceae (CREs)) for which conventional therapies are not appropriate • Infectious Disease Service consultation is recommended
Tobramycin injectable	IV route: • Aminoglycoside therapy is indicated but there is documented resistance to gentamicin • Note: Drug level monitoring for tobramycin is performed at an off site laboratory Inhaled route: • Treatment of lower respiratory tract infections in cystic fibrosis or bronchiectasis patients where an aminoglycoside is indicated, but there are concerns/contraindications to parenteral aminoglycoside therapy ** Use of an aminoglycoside beyond 7 days will be subject to Antimicrobial Stewardship review **
Valganciclovir tablets (Non-Formulary)	• Oral step-down from ganciclovir for suspected/proven cytomegalovirus (CMV) disease • Treatment of mild-moderate CMV deep organ disease • Pre-emptive therapy in allogeneic stem cell transplant recipients • Prophylaxis of high risk solid organ transplant/bone marrow transplant patients • Non-Formulary
Voriconazole injectable and tablets	• 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
Zanamavir diskhaler (Relenza®)	• Prophylaxis or treatment of influenza where the patient is unable to tolerate medication via the enteral route • Prophylaxis or treatment of influenza where oral agents cannot be used due to resistance

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Example 2: Halton Healthcare - List of Reserved Anti-infectives (continued)

Drug	Reserved Status
Zidovudine injectable, capsules and oral liquid	• 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 anti-retroviral 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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Example 3: North York General Hospital - Restricted Antimicrobial Guidelines

Restricted Antimicrobials

North York General Antimicrobial Guidelines

Drug	Service	Indication
Caspofungin	ID	Proven or suspected non-*albicans* candidemia or invasive candidiasis or salvage therapy for aspergillosis
Ceftazidime	ID	Proven or suspected pseudomonas infection Reassess after 48 hours and tailor to C&S results
Colistin	ID	For the treatment of multi-drug resistant gram-negative infections (e.g. carbapenem-resistant enterobacteriaceae)
Daptomycin	ID	1. Alternate therapy for patients with MRSA bacteremia with or without right sided endocarditis who are intolerant to (e.g. renal failure) or failing standard therapy (e.g. vancomycin) 2. Alternate therapy for patients with complicated skin and skin structure infections (cSSSIs) due to MRSA who are intolerant to (e.g. renal failure) or failing standard therapy (e.g. vancomycin) 3. Invasive infections (proven or suspected) caused by vancomycin resistant Enterococcus faecium (VRE) such as bacteremias, intra-abdominal infections, and deep cSSSIs
Ertapenem **Meropenem**	ID ICU (x 72h)	Empiric therapy: 1. For the empiric therapy of severe sepsis of unknown origin (may be used in combination with other agents) 2. For the empiric treatment of severe intra-abdominal sepsis 3. For the empiric treatment of severe hospital-acquired pneumonia (HAP) or ventilator-associated pneumonia (VAP) *For each of the above indications (#1-3), the carbapenem should be de-escalated after 3 days in the absence of fulfilling the criteria for targeted therapy* 4. Prophylaxis of severe necrotizing acute pancreatitis x 14 days. If infection proven, tailor antibiotics to infection. Targeted therapy: 1. For the treatment of **proven** infection with an ESBL or AmpC producing organism or other multi-drug resistant (MDR) organisms for which there are no other effective treatment options and documented carbapenem susceptibility 2. For the treatment of infectious syndromes that require gram-negative coverage in a patient known to be colonized with an ESBL, AmpC or MDR organism and in which no other causative pathogen has been identified

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Example 3: North York General Hospital - Restricted Antimicrobial Guidelines (continued)

Drug	Service	Indication
Fidaxomicin	ID	1. Recurrent mild to moderate *C difficile* infection in patients who have failed a tapering course of oral vancomycin in the last 6 months, with no previous trial of fidaxomicin 2. Documented immune-mediated allergy to oral vancomycin
Linezolid	ID	For the treatment of refractory MRSA, VRE, and other resistant gram-positive pathogens
Tigecycline	ID	For the treatment of multi-drug resistant gram-negative infections (e.g. carbapenem-resistant enterobacteriaceae) Usually used in combination with other agents
Voriconazole	ID	1. For the treatment of proven or suspected invasive aspergillosis 2. For the treatment of proven or suspected infections due to *Fusarium* spp. or *Scedosporium apiospermum* (*Pseudallescheria boydii*) when other antifungal therapy has failed

Reviewed by:
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Approved by:
P&T Committee, MAC March 2015

North York General Antimicrobial Guidelines: Restricted Antimicrobials 2

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Example 4: London Health Sciences Centre - Restricted (Tier 3) Antimicrobials

Tier 3 Antimicrobials at LHSC

A	H	P
Amphotericin B, Liposomal Amikacin Artesunate Asparaginase (Erwinia) Aztreonam (SAP)	HIV Medications	Palivizumab (Synagis) Perfluten Posaconazole
B	**I**	**QR**
C Caspofungin Cefixime Cefotaxime Colistimethate (colistin)	**K**	**S** Sulfamethoxazole/Trimethoprim IV
D Dapsone Daptomycin	**L** Linezolid	**T** Tobramycin Powder
E Ertapenem	**M** Meropenem	**V** Voriconazole
F	**O** Oseltamivir	**Z** Zanamivir

Amikacin	• This drug can only be prescribed under the direction of an Infectious Diseases consultant.
Amphotericin B, Liposomal	• NICU prescribers (for use in NICU patients) **OR** • Mandatory Infectious Disease Service Consult **AND at least one of** the following criteria (click here for detailed prescribing restrictions): ◦ renal dysfunction ◦ infusion-related reactions ◦ hypokalemia ◦ other clinical scenarios
Artesunate	• Restricted to use for patients with severe/complicated malaria, under the direction of an Infectious Diseases consultant.
Aztreonam (SAP)	• This drug can only be prescribed under the direction of an Infectious Diseases consultant.

Disclaimer: *Every effort has been made to ensure that the following information provided is accurate, up-to-date, and complete, but no guarantee is made to that effect. The drug information contained herein may be time sensitive and additional information may have become available since the time of writing. This document is a reference resource designed as a supplement to, and not a substitute for, the expertise, skill, knowledge, and judgement of the healthcare practitioners. The information contained herein is not intended to cover all possible uses, directions, precautions, warnings, drug interactions, allergic reactions, or adverse effects. This information is for use within the London Health Sciences Centre only.*

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Example 4: London Health Sciences Centre - Restricted (Tier 3) Antimicrobials (continued)

Drug	Restriction
Caspofungin	For adult and pediatric patients, prescribing is restricted to: • An Infectious Diseases consult; **OR** • Use by Hematology/Oncology Service
Cefixime	• Use by Emergency Services for adult and children with N. gonorrhea disease as a single dose.
Cefotaxime	• For use in infants less than 10 weeks old.
Colistimethate INH	• These medications will be restricted to cystic fibrosis patients. • Respiratory physicians for use in Cystic Fibrosis patients.
Colistimethate IV	For adult and pediatric patients, prescribing is restricted to: • An Infectious Diseases consult; **OR** • Respiratory physicians for use in Cystic Fibrosis patients
Dapsone	• **Adults:** as second line agent for Pneumocystis Carinii Pneumonia (PCP) treatment or prophylaxis in patients who have an intolerance to sulfamethoxazole/trimethoprim • **Pediatrics:** PCP treatment or prophylaxis in patients who have failed sulfamethoxazole/trimethoprim as a third line agent after inhaled pentamidine
Daptomycin	• This drug can only be prescribed under the direction of an Infectious Diseases consultant.
Ertapenem	• For 1st dose only for CCAC patients pending discharge

HIV Medications	• NEW starts of HIV medications to be restricted to:
	  • ID specialists **OR**
	  • Post-exposure prophylaxis **OR**
	  • For vertical transmission prophylaxis
	• Continuation of home medications

Linezolid	• This drug can only be prescribed under the direction of an Infectious Diseases consultant.
Meropenem	• Approval by Infectious Diseases consultant, OR • Cystic fibrosis patients (adult or pediatric), OR • Pediatrics patients for 72 hours – must be approved by Pediatric Infectious Diseases consultant to extend therapy beyond 72 hours.
Oseltamivir	• Prescribed in consultation with Infectious Control/Public Health for pre-exposure and post-exposure prophylaxis • Prescribed for patients patient presenting with acute Influenza Like Illness (ILI) requiring hospital admission and **treatment** • For initiating **treatment** in patients at high risk of complications

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Example 4: London Health Sciences Centre - Restricted (Tier 3) Antimicrobials (continued)

Palivizumab (Synagis)	• Restricted to use in patients as outlined in the Ontario RSV Prophylaxis Request Form • Enrollment Form & Assessment Tool
Posaconazole	• This drug can only be prescribed under the direction of an Infectious Diseases consultant.
Sulfamethoxazole/ Trimethoprim IV	• Restricted to Infectious Disease prescribers ONLY
Tobramycin Powder	• Restricted to intra-operative use by Orthopedic Surgery in antibiotic-loaded bone cement for patients undergoing revision surgery for infected joints.
Voriconazole	For adult and pediatric patients, prescribing is restricted to: • An Infectious Diseases consult; **OR** • Use by Hematology/Oncology Service
Zanamivir	• For use in the event of an outbreak under the guidance of Middlesex-London Health Unit (MLHU)

Updated: Sep 2015

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