Antimicrobial Stewardship Strategy:
Formulary automatic substitution/therapeutic interchange policies

The process whereby an order for a specific drug or dosing regimen is automatically changed or substituted according to preapproved procedures and conditions, without needing to consult the prescriber.

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This is a PHO CORE strategy

Priority Level: **A**

Difficulty Level: **1**

Program Stage:

- ✓ Early
- Intermediate
- Advanced

Antimicrobial Stewardship Outcomes:

- Prescribing outcomes

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

Updated June 2016

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

Formulary automatic substitution/therapeutic interchange policies are useful methods of streamlining certain aspects of antimicrobial use in an institution. Not limited to antimicrobials, these programs allow pharmacists to automatically change an order for a specific drug or dosing regimen without needing to consult the prescriber, according to preapproved procedures and conditions.

A common application of this strategy involves substituting a nonformulary antimicrobial with a formulary alternative considered to be therapeutically similar, but that may have different pharmacokinetics, adverse effects, costs etc. (e.g., substituting cefotaxime with ceftriaxone). Other applications may include limiting the use of agents known to drive resistance or discouraging the use of less ideal agents (e.g., automatic substitution of cefoxitin to the combination of cefazolin and metronidazole).

Automatic substitution/therapeutic interchange polices may be implemented to:

- Operationalize the use of a closed formulary.
- Control costs.

- Standardize the dose of an agent based on best practices, pharmacokinetics, risk of adverse effects and/or costs (e.g., switch meropenem 1 g IV q8h to meropenem 500 mg IV q6h; cefazolin q6h to q8h; oral vancomycin 500 mg q6h to 125 mg q6h for *Clostridium difficile* infection).
- Optimize dosage forms (e.g., switch clarithromycin 250 mg regular release tablet twice daily to clarithromycin 500 mg extended-release tablet daily).
- Restrict or direct prescribing of an agent: introduction of a new agent to the formulary to replace an existing one or removal of an existing agent from the formulary.
- Deal with backorders, drug shortages and discontinuations (e.g., tobramycin automatic substitution/interchange for gentamicin during backorder).

Implementation

Formulary automatic substitution/therapeutic interchange policies and procedures should be developed by individuals with sufficient expertise and approved by the institution's senior medical administration (e.g., pharmacy and therapeutics committee).

Prescribing staff must be informed of and educated about the automatic substitutions/interchanges prior to introduction.

A mechanism must be in place to override the interchange when clinically appropriate (e.g., via consultation with a pharmacist or another physician).

Therapeutic interchanges must be reviewed periodically to ensure they are up to date and reflect both formulary changes/additions and changes in practice.

The policy and procedure should indicate that automatic substitutions must be consistently performed and well documented in the patient's chart when applied, with patient monitoring for any untoward effects.[1]

Advantages

- Relatively easy to implement.
- Can achieve cost savings with minimal intervention.
- Potential for improved pathogen susceptibility.
- More timely order processing, as the pharmacist does not need to contact the prescriber for a change to be made.
- Useful to efficiently manage drug shortages of formulary agents.
- Adaptable to all institutions, including smaller hospitals.

Disadvantages

- May not influence future prescribing, as no feedback is provided to prescribers at the time of ordering.
- In rare circumstances, substitution could be clinically inappropriate, leading to potential risk of inadequate treatment[2] and liability concerns.

Requirements

- Health professionals with sufficient expertise (indications, exceptions) to create, review and update automatic substitution/therapeutic interchange policies.
- Pharmacy involvement to identify orders and make the substitution (computerized physician order entry may facilitate this process).

Associated Metrics

- Compliance with automatic substitution policies; most common reasons (nonformulary drugs/specific prescribers) for nonadherence.
- Cost savings resulting from automatic substitution/interchange policies.

References

1. Canadian Society of Hospital Pharmacists. Guidelines for drug use control [Internet]. Ottawa, ON: Canadian Society of Hospital Pharmacists; 2008 [cited 2015 Sep 24]. Available from: http://www.cshp.ca/productsServices/officialPublications/type_e.asp

   Thorough guidelines on aspects of medication dispensing and management; includes a statement on therapeutic interchange (section 4.1.8.6).

   Freely available to Canadian Society of Hospital Pharmacists members.

2. Haas DW, Bonczar T. Effect of replacing cefotaxime with ceftizoxime in a hospital where penicillin-resistant pneumococcal disease is prevalent. J Antimicrob Chemother. 1996;38:293–9. Available from: http://jac.oxfordjournals.org/content/38/2/293.full.pdf+html

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.

- Schachtner JM, Guharoy R, Medicis JJ, Newman N, Speizer R. Prevalence and cost savings of therapeutic interchange among U.S. hospitals. Am J Health Syst Pharm. 2002;59(6):529–33.
- Gray T, Bertch K, Galt K, Gonyeau M, Karpiuk E, Oyen L et al. ACCP position statement: guidelines for therapeutic interchange 2004. Pharmacotherapy 2005;25(11):1666–80. Available from: https://www.accp.com/docs/positions/guidelines/pharm2511_accp-therapintchg.pdf

Samples/Examples (updated June 2016)

- Example 1: Sunnybrook Health Sciences Centre - Automatic Substitution Policies
- Example 2: Halton Healthcare - Anti-Infective Therapeutic Interchange Policies
- Example 3: Alberta Health Services Antimicrobial Stewardship Backgrounder - Meropenem Dosage Therapeutic Interchange
- Example 4: The Scarborough Hospital - Change in Carbapenem Formulary Listing Memo 2014

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 restriction
- Formulary review/streamlining

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For further information

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Example 1: Sunnybrook Health Sciences Centre - Automatic Substitution Policies

Sunnybrook
HEALTH SCIENCES CENTRE
when it matters MOST

AUTOMATIC SUBSTITUTION POLICIES

DOCTOR'S ORDER	AUTOMATIC CONVERSION
Aminoglycoside Antibiotics	• ***Once-daily*** therapy (gentamicin or tobramycin 7 mg/kg, or amikacin 15 mg/kg) – the prescribed dose will be automatically rounded OFF to the nearest 50 mg. • ***Traditional*** therapy (gentamicin or tobramycin 2 mg/kg Q8H) – the prescribed dose will be automatically rounded UP to the nearest 20 mg.
Ampicillin Oral	Orders for oral ampicillin Q8H, Q6H, or QID will be automatically converted to amoxicillin PO Q8H.
Cefazolin	Orders for doses in excess of 3 g per day will be converted to the maximum of 1 g Q8H. ***Exceptions:*** Infectious Diseases consultation. A 2 g preop dose is used in surgery. Intrapartum prevention of perinatal group B streptococcal disease in penicillin allergic patients (low risk for anaphylaxis) requires a loading dose of cefazolin 2 g IV, followed by 1 g IV Q8H until delivery.
Ceftazidime	Orders for ceftazidime specifying a dose of less than 2 g be automatically converted to a dose of 2 g at the dosing interval specified in the original order. ***Exception***: dosing must be individualized in renal insufficiency.
Ceftriaxone	Orders for doses in excess of 1 g per day will be converted to the maximum of 1 g Q24H. ***Exceptions:*** Infectious Diseases consultation. Higher dosages are recommended for endocarditis, meningitis and osteomyelitis (see page 40).
Ciprofloxacin IV	Orders for 200 mg IV Q12H in renal insufficiency will be converted to 400 mg IV Q24H.
Clindamycin IV	Orders for IV doses in excess of 1800 mg per day will be automatically converted to the standard maximum allowable dosage of 600 mg IV Q8H. ***Exceptions:*** Infectious Diseases consultation. 900 mg IV Q8H is recommended for: cerebral toxoplasmosis; pelvic inflammatory disease; postpartum endometritis; intrapartum prevention of perinatal group B streptococcal disease in patients who cannot take penicillin.
Ear Drops, combination (antibiotic + steroid)	Orders for combination ear drops containing antibiotics + a corticosteroid (e.g., Cortisporin®, Cipro-HC®, Garasone®) will be substituted with Ciprodex® ear drops at the appropriate dosage.
Erythromycin oral liquid	Orders for erythromycin oral liquid 250 mg or 500 mg will be converted to erythromycin ethylsuccinate 400 mg or 800 mg, respectively.
Fluoroquinolone Eye Drops	Orders for fluoroquinolone eye drops other than moxifloxacin (e.g., ciprofloxacin, gatifloxacin, and ofloxacin eye drops) will be substituted with moxifloxacin (Vigamox®) at the appropriate dosage.

Sunnybrook Antimicrobial Handbook 2013
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Example 1: Sunnybrook Health Sciences Centre - Automatic Substitution Policies (continued)

Sunnybrook
HEALTH SCIENCES CENTRE
when it matters MOST

AUTOMATIC SUBSTITUTION POLICIES

DOCTOR'S ORDER	AUTOMATIC CONVERSION
Meropenem	Orders for > 2 g/day will be converted to 500 mg IV Q6H. ***Exceptions:*** Infectious Diseases consultation. Meningitis may require 2 g IV Q8H.
Metronidazole	Orders for > 1 g IV per day will be automatically converted to 500 mg IV Q12H. ***Exceptions:*** Brain abscess may require a higher dose; NPO patients with *C. difficile* colitis may be prescribed 500 mg IV Q8H.
Mupirocin	Orders for mupirocin (Bactroban®) ***ointment*** will be dispensed as the ***cream*** formulation.
Nitrofurantoin	Orders for MacroBID® will be automatically converted to nitrofurantoin as indicated in the table. **Doctor's Order** / **Automatic Conversion** MacroBID 100 mg BID → Nitrofurantoin 50 mg QID MacroBID 100 mg Daily or QHS → Nitrofurantoin 100 mg Daily or QHS
Norfloxacin	Orders for norfloxacin 400 mg po BID will be converted to ciprofloxacin 500 mg po BID.
Nystatin Oral Suspension	Orders for individual doses < 500,000 Units will be automatically converted to 500,000 Units. ***Exception:*** Neonatal Intensive Care Unit.
Oseltamivir	Orders for **treatment** of influenza will automatically expire after a total of 5 days or therapy.
Piperacillin-Tazobactam	Orders in patients with renal insufficiency for a reduced dose of 2.25 g IV Q6H or Q8H will be automatically converted to 3.375 g IV Q8H or Q12H, respectively.
Vaginal Antifungal Products	***Non-pregnant patients:*** • Orders for any antifungal vaginal inserts will be converted to Canesten® 3 Insert Combipak (clotrimazole 200 mg vaginal tablet QHS and topical cream BID for 3 days). • Orders for any antifungal vaginal cream will be converted to clotrimazole 2% vaginal cream (Canesten® 3 Cream) given QHS for 3 days. • ***Exception:*** Gynecology may prescribe nystatin vaginal products for resistant candida infection. ***Pregnant patients:*** • Orders for vaginal antifungal will be converted to miconazole 2% vaginal cream (Monistat® 7 Cream) given QHS for 7 days.
Vancomycin IV	Orders for "irregular" doses of vancomycin will be automatically converted to the nearest standard dose (multiple of 250 mg). Example: order for vancomycin 1.2 g Q12H would be converted to 1.25 g Q12H.

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Example 2: Halton Healthcare - Anti-Infective Therapeutic Interchange Policies

ANTI-INFECTIVE THERAPEUTIC INTERCHANGE POLICIES

Drug	Substitution
*Ampicillin PO (any dose or frequency) ADULT only	Amoxicillin 500mg PO q8h
*Ampicillin PO (stat dose)	Amoxicillin PO (mg for mg)
*Bacitracin Ointment	Polysporin® Ointment
*Bactroban	See Mupirocin
*Cefaclor oral suspension	Cefprozil oral suspension (see table for dose equivalency)
*Cefaclor 250mg or 500mg capsules (any dose or frequency), ADULT only	Cefuroxime 500mg PO tablets q12h
*Cefazolin IV any dose prescribed more frequent than q8h, ADULT only	Cefazolin same dose IV q8h
*Cefotaxime IV any dose prescribed more frequent than q8h, ADULT only	Cefotaxime same dose IV q8h **Exception:** • Meningitis or other CNS infection: no automatic substitution
*Ceftazidime IV any dose prescribed more frequent than q8h, ADULT only	Ceftazidime same dose IV q8h **Exception**: CF patient: no automatic substitution
*Cefuroxime oral liquid	Cefprozil oral liquid (see table for dose equivalency)
*Cephalexin 250-500mg tablets any frequency	Cefadroxil 500mg po q12h **Exception:** no substitution for Cephalexin suspension
*Cephalexin 750mg–1 g tablets any frequency	Cefadroxil 1 g po q12h **Exception:** no substitution for Cephalexin suspension

Halton Healthcare Hospital Formulary | Date of last revision: September 2015

Example 2: Halton Healthcare - Anti-Infective Therapeutic Interchange Policies (continued)

Drug	Substitution
*Clindamycin 300-600mg IV any frequency, ADULT only	Clindamycin 600mg IV q8hr
*Cortisporin® eye drops/ointment	Sofracort® eye drops
*Famciclovir (any dose or frequency), ADULT only	Valacyclovir 1g PO q8h
*Fidaxomicin any dose or frequency	Vancomycin 125mg PO q6hr **Exception:** • The order is written in person or as a telephone order by an ID Physician • The order is for completion of therapy initiated prior to admission.
*Gentamicin injection	Tobramycin injection (same dose and frequency)
*Framycetin 1% Dressing (Sofratulle®)	Chlorhexidine 0.5% dressing
*Lactobacillus (Bacid®) (any dose or frequency)	*Saccharomyces boulardii* (Florastor®) 250 mg po q12h x 4 weeks
*Levofloxacin 500 mg PO/IV daily	Levofloxacin 750 mg PO/IV q24h
*Metronidazole 250 mg PO q6h	Metronidazole 500 mg q8h **Exception**: • Gastrointestinal intolerance
*Metronidazole IV (any dose or frequency), ADULT only	Metronidazole 500mg IV q12h **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
*Miconazole 2% cream (Micatin® or Monistat®)	Clotrimazole 1% cream
Miconazole vaginal cream/suppositories	See vaginal preparations

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Example 2: Halton Healthcare - Anti-Infective Therapeutic Interchange Policies (continued)

Drug	Substitution
*Mupirocin (Bactroban®) ointment or cream (including pediatrics)	Polysporin® ointment or cream **Exceptions**: (use mupirocin **cream** for decolonization) • MRSA decolonization of the nares • Staphylococcal decolonization in preparation for transfer to Trillium Hospital for CABG
*Neosporin® Eye drops/ointment	Polysporin eye drops/ointment
*Nitrofurantoin microcrystals (tablets)	Nitrofurantoin macrocrystals (Macrodantin®) same dose and frequency
*Norfloxacin 400mg PO	Ciprofloxacin 500mg PO (same frequency)
*Nystatin – any oral tablet or suspension dose/frequency, ADULT only	Nystatin 500 000 units (5mL) q6h
*Nystatin topical (no dosage form specified)	Ointment will be supplied
*Penicillin G oral	Penicillin VK oral
*Penicillin G or Penicillin G Potassium (K) Injection	Penicillin G Sodium at same dose and frequency **Exception:** • Patient cannot tolerate sodium load (high sodium level or CHF – may use sodium salt for first 24-48hr until potassium salt available)
*Penicillin VK 250mg tablet	Penicillin VK (generic) 300mg tablet (same frequency)
*Penicillin V oral	Pen VK oral
Polysporin® topical (no dosage form specified)	Ointment will be supplied
Sodium Sulfacetamide eye drops	10% Sodium Sulfacetamide eye drops
*Vaginal antifungal inserts	Clotrimazole 200mg vaginal tabs qhs x 3 days **Exception:** • Vaginal infections due to *Candida sp.* resistant to azole antifungal agents (e.g. clotrimazole): use Nystatin vaginal cream 1 applicatorful PV q24h x 14 days

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Example 2: Halton Healthcare - Anti-Infective Therapeutic Interchange Policies (continued)

Drug	Substitution
*Vaginal antifungal cream	Clotrimazole 2% Vaginal Cream qhs x 3 days **Exception:** • Vaginal infections due to *Candida sp.* resistant to azole antifungal agents (e.g. clotrimazole): use Nystatin vaginal cream 1 applicatorful PV q24h x 14 days
*Vancomycin IV any dose or frequency, ADULT only	Vancomycin 1g IV q12h **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

* Drug items listed with an asterisk * must have an order written on the chart (e.g. change "___" to "___" as per Hospital Therapeutic Interchange Policy.

Note: All antibiotic dosing is subject to renal clearance adjustment
All Interchanges apply in adult and pediatric patients unless otherwise specified

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

Indication	If Cefuroxime (Ceftin) Oral Suspension Ordered	If Cefaclor (Ceclor) Oral Suspension Ordered	Give Cefprozil (Cefzil) Oral Suspension
Skin/soft tissue	15mg/kg q12h	10mg/kg q12h	20mg/kg q24h
Otitis	15mg/kg q12h	20mg/kg q12h	15mg/kg q12h
Upper respiratory tract (pharyngitis/tonsilitis)	10mg/kg q12h	20 mg/kg q12h	7.5mg/kg q12h
Lower respiratory tract	No dose guidelines in children	13mg/kg q8h	15mg/kg q12h
Maximum dose per day	1g/day	1.5g/day	1g/day

Example 2: Halton Healthcare - Anti-Infective Therapeutic Interchange Policies (continued)

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.

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

Halton Healthcare Hospital Formulary | Date of last revision: September 2015

Example 2: Halton Healthcare - Anti-Infective Therapeutic Interchange Policies (continued)

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

Halton Healthcare Hospital Formulary | Date of last revision: September 2015

Example 3: Alberta Health Services Antimicrobial Stewardship Backgrounder - Meropenem Dosage Therapeutic Interchange

Alberta Health Services Pharmacy Services

Issue 1 – January 2014

Antimicrobial Stewardship Backgrounder

Meropenem Dosage Therapeutic Interchange

Meropenem is a broad spectrum carbapenem antibacterial which should be reserved for polymicrobial and/or serious infections where there is an increased risk of resistant organisms.

When meropenem is indicated, the majority of infections can be treated with a dosage of 500 mg IV every 6 hours. This dosage provides similar clinical outcomes as 1 g IV every 8 hours, and reduces unnecessary drug exposure while maintaining activity against relevant pathogens.
To facilitate this, the following therapeutic interchange is approved in Alberta Health Services:

Original Order	Therapeutic Interchange	Complexity Level†
Meropenem 1-2 g IV q6-8h in adults	Meropenem 500 mg IV q6h‡ EXCEPT in cystic fibrosis, central nervous system infections, or ophthalmologic infections. For these infections, contact prescriber to suggest dose of 2g IV q8h.	2

† Level 2: Mid Complexity - Additional patient specific information required/additional pharmacist assessment required.

‡ Dosage adjustment for renal dysfunction in adult patients	
Creatinine Clearance (CrCl) (mL/min)	**Recommended Dose & Interval using 500 mg q6h as standard dose**
26-50	500 mg q8h
10-25	500 mg q12h
Less than 10	500 mg q24h
For patients on intermittent hemodialysis	500 mg q24h – administered after dialysis
Continuous veno-venous hemodialysis (CVVHD)	Dose as CrCl greater than 50 mL/min = 500mg IV q6h
Peritoneal dialysis	500 mg q24h

EFFICACY

PHARMACODYNAMICS

- Meropenem exhibits time-dependent bactericidal activity, whereby its efficacy is best predicted by the percentage of time (T) that free drug concentrations exceed the minimum inhibitory concentration (MIC) for a bacterial pathogen (%fT>MIC). Maximal bactericidal activity occurs when fT>MIC ≥ 40% of the dosing interval.[1,2]
    - **Key point**: Meropenem 500 mg q6h has similar or greater T>MIC than 1 g q8h.[3,4]

Reference	%fT>MIC	
	500 mg q6h	**1 g q8h**
Kuti et.al.[3]	43.9%	45.8%
Ariano et.al.[4]	75%	68%

CLINICAL EVIDENCE

- Studies demonstrate that meropenem 500 mg q6h has equivalent clinical outcomes (e.g. time to defervescence, clinical and microbiological success, treatment duration, length of stay, mortality) as 1 g q8h.[5,6,7]

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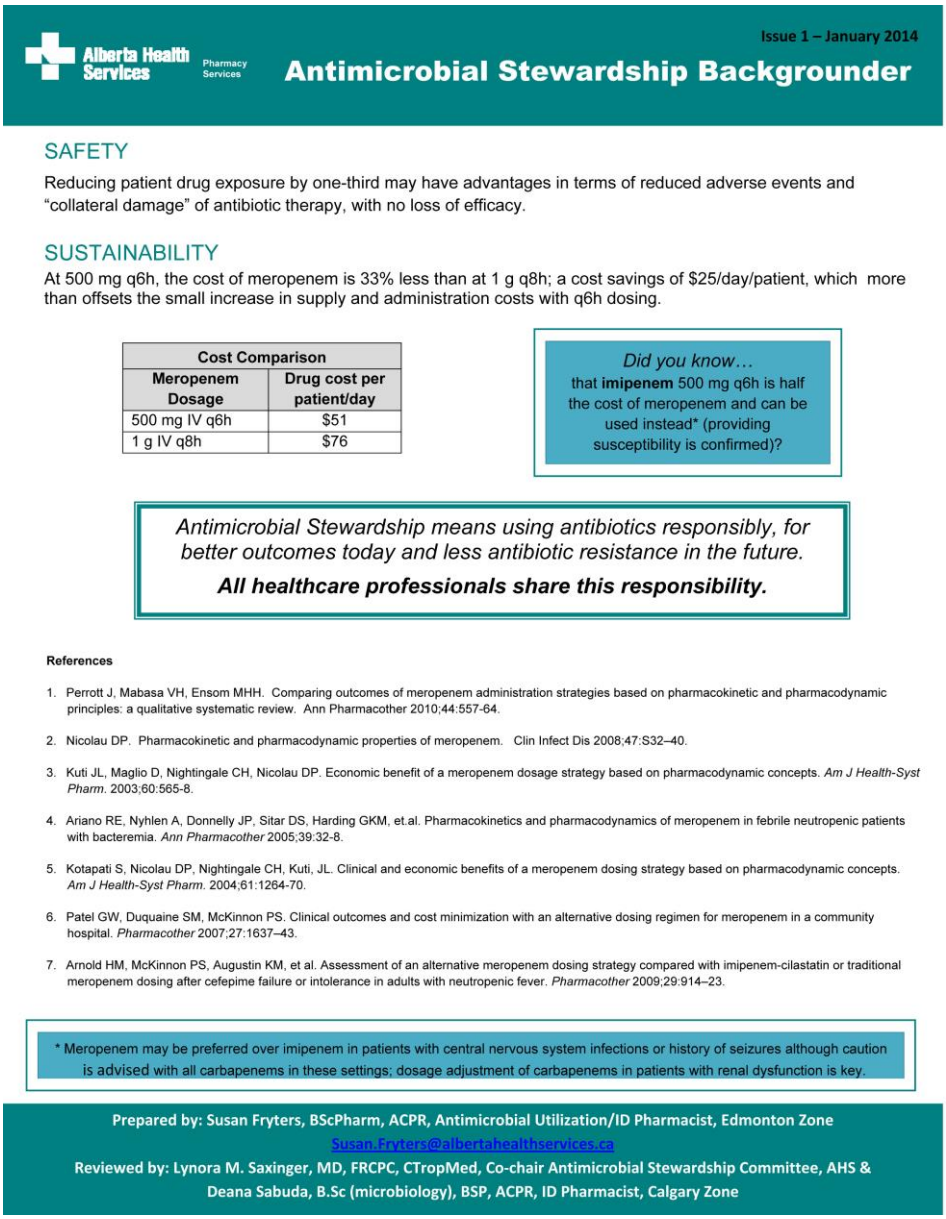
Available online from:
http://www.albertahealthservices.ca/assets/Infofor/hp/if-hp-antimicrobial-stewardship-backgrounder-2014-01.pdf

Example 3: Alberta Health Services Antimicrobial Stewardship Backgrounder - Meropenem Dosage Therapeutic Interchange (continued)



Alberta Health Services Pharmacy Services

Issue 1 – January 2014

Antimicrobial Stewardship Backgrounder

SAFETY

Reducing patient drug exposure by one-third may have advantages in terms of reduced adverse events and "collateral damage" of antibiotic therapy, with no loss of efficacy.

SUSTAINABILITY

At 500 mg q6h, the cost of meropenem is 33% less than at 1 g q8h; a cost savings of $25/day/patient, which more than offsets the small increase in supply and administration costs with q6h dosing.

Cost Comparison	
Meropenem Dosage	**Drug cost per patient/day**
500 mg IV q6h	$51
1 g IV q8h	$76

Did you know…
that **imipenem** 500 mg q6h is half the cost of meropenem and can be used instead* (providing susceptibility is confirmed)?

Antimicrobial Stewardship means using antibiotics responsibly, for better outcomes today and less antibiotic resistance in the future.

All healthcare professionals share this responsibility.

References

1. Perrott J, Mabasa VH, Ensom MHH. Comparing outcomes of meropenem administration strategies based on pharmacokinetic and pharmacodynamic principles: a qualitative systematic review. Ann Pharmacother 2010;44:557-64.
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6. Patel GW, Duquaine SM, McKinnon PS. Clinical outcomes and cost minimization with an alternative dosing regimen for meropenem in a community hospital. *Pharmacother* 2007;27:1637–43.
7. Arnold HM, McKinnon PS, Augustin KM, et al. Assessment of an alternative meropenem dosing strategy compared with imipenem-cilastatin or traditional meropenem dosing after cefepime failure or intolerance in adults with neutropenic fever. *Pharmacother* 2009;29:914–23.

* Meropenem may be preferred over imipenem in patients with central nervous system infections or history of seizures although caution is advised with all carbapenems in these settings; dosage adjustment of carbapenems in patients with renal dysfunction is key.

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Available online from:

http://www.albertahealthservices.ca/assets/Infofor/hp/if-hp-antimicrobial-stewardship-backgrounder-2014-01.pdf

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Example 4: The Scarborough Hospital - Change in Carbapenem Formulary Listing Memo (2014)

MEMO

To: All Physicians
From: The Antimicrobial Stewardship Program (ASP)
Date: Nov 17, 2014
Re: **Change in Carbapenem Listing on the TSH Formulary**

Please note Imipenem/Cilastatin has been delisted from the TSH Formulary.
The carbapenems currently on the TSH Formulary are Meropenem and Ertapenem.
Orders written for imipenem will be automatically substituted to meropenem and dosed according to the patient's creatinine clearance (non-meningitis dosing) by pharmacy. The automatic substitution policy was approved by DTC and MAC.

Key differences between meropenem and ertapenem:

1) Meropenem is the ONLY carbapenem indicated for the treatment of bacterial meningitis
2) Unlike meropenem, ertapenem is NOT active against *Pseudomonas aeruginosa* or *Acinetobacter spp.*
3) Once daily dosing for Ertapenem
    - *For example, for the treatment of infections caused by ESBL organisms, ertapenem offers the advantage of once daily dosing and narrower spectrum of therapy compared to meropenem (minimizes the risk of pseudomonas developing resistance to meropenem).*

Ertapenem	
Creatinine clearance	**Dosing**
Equal or greater than 30 mL/min	1 g IV Q24H
Less than 30 mL/min	500 mg IV Q24H
CAPD	
Hemodialysis (3x/wk)	500 mg IV Q24H (on dialysis days, give the dose after HD)
CVVHD	500-1000 mg IV Q24H

Example 4: The Scarborough Hospital - Change in Carbapenem Formulary Listing Memo (2014) (continued)

Meropenem		
Creatinine clearance	**Non-meningitis Dosing**	**Meningitis Dosing**
Equal or greater than 30 mL/min	500 mg IV Q6H*	2 g IV Q8H
10-29 mL/min	500 mg IV Q8H	Loading dose of 2 g, then 1 g IV Q8H
Less than 10 mL/min	500 mg IV Q12H	Loading dose of 2 g, then 500 mg IV Q8H
Hemodialysis (3x/wk)	500 mg IV Q24H (on dialysis day, schedule dose after HD)	Loading dose of 1 g, then 1 g IV Q8H (on dialysis day, schedule dose after HD)
CVVHD	500 mg IV Q8H	Loading dose of 2 g, then 500 mg IV Q6H
CAPD	500 mg IV Q12H	Loading dose of 1 g, then 500 mg IV Q8H

*For the non-meningitis dosing regimen of meropenem 500 mg Q6H, studies have found similar clinical success rates, duration of therapy, and mortality rates compared to the 1 g Q8H regimen. Meropenem is time dependent killing and the 500 mg Q6H dosing regimen has the advantage of greater percentage of time above MIC for bacterial kill, decreased total drug exposure (lower risk of CDAD) and lower total daily cost. This dosing regimen has been approved by DTC and MAC.

Our goal is to create and maintain consistency in hospital practices along with promoting safe and effective antibiotic therapy. Thank you for your cooperation as we work towards improving patient care and outcomes. If you have any questions, please feel free to contact the Antimicrobial Stewardship Program.