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Issue # 66: May 15, 2019

## I. Additions to Hospital Formulary

**A NSHA Systemic Antimicrobial Formulary with Protected Antimicrobials Stoplight System** has been approved. The NSHA Formulary has been updated to reflect these recommendations including the addition of the following systemic antimicrobials (refer to Section VI):

**Amphotericin B liposomal\***, *AmBisome*<sup>®</sup>  
**Caspofungin\***, *Cancidas*<sup>®</sup>

**Cefepime**

**Cefoxitin**

**Cefprozil**

**Cidofovir**

**Imipenem/ cilastatin**, *Primaxin*<sup>®</sup>

**Minocycline**

\* refer to Appendix 1 for further details

### Neomycin

Neomycin (Mycifradin<sup>®</sup>), an oral aminoglycoside, was removed from the Canadian market several years ago; therefore, neomycin was not included on the Hospital Formulary.

Surgical site infections (SSIs) following surgical procedures are amongst the most common healthcare-associated infections and represent a tremendous burden both for patient recovery and the overall healthcare system cost. To decrease the rates of SSIs, the preoperative use of oral neomycin in combination with other antibiotics (e.g., metronidazole, erythromycin) and other treatment modalities (e.g., mechanical bowel preparation) has been encouraged in patients undergoing elective colorectal procedures. Since neomycin is not marketed in Canada, it is obtained from a compounding pharmacy.

There are an extensive number of published cohort studies, RCTs and systematic reviews that have evaluated numerous types and combinations of oral antibiotics for reducing SSIs. It is difficult to determine the best single preoperative antibiotic combination given the heterogeneity of antibiotic use in trials; however, evidence does favour the overall use of oral antibiotic prophylaxis, regardless of choice, assuming it has appropriate bacterial coverage and is administered appropriately based upon the current evidence and best practice guidelines.

### Approved Use:

For inpatients receiving elective colorectal surgery.

The following policies were approved by the Medical Advisory Committee (Oct18, Jan19, Feb19) on the recommendation of the Drugs and Therapeutics Committee (Sept18, Oct18, Nov18, Dec18).

## II. Removal from Hospital Formulary

**A NSHA Systemic Antimicrobial Formulary with Protected Antimicrobials Stoplight System** has been approved. The NSHA Formulary has been updated to reflect these recommendations including the removal of the following systemic antimicrobials (refer to Section VI):

**Amphotericin B lipid complex\*, *Abelcet*<sup>®</sup>**

**Chloramphenicol**

**Famciclovir**

**Itraconazole**

**Ketoconazole**

**Micafungin\***

**Moxifloxacin\***

**Piperacillin**

\* refer to Appendix 1 for further details

## III. Revised Guidelines

### **Oxaliplatin**

Oxaliplatin injection has been restricted on the NSHA Formulary for the indications of colorectal cancer and advanced/metastatic pancreatic cancer only. The cost of oxaliplatin has reduced dramatically and oxaliplatin is used in standard treatment protocols for gastric/gastroesophageal cancer, in the adjuvant treatment of pancreatic cancer and in HIPEC protocols for colorectal cancer carcinomatosis (for this indication there is substantial cost savings and equivalent efficacy over the alternate drug mitomycin C); therefore, the current formulary restrictions for oxaliplatin are removed

## IV. Expanded Guidelines

### **Pembrolizumab, *Keytruda*<sup>®</sup>**

Two new Guidelines have been approved for pembrolizumab.

A new Guideline for the role of pembrolizumab for locally advanced/ metastatic non-small cell lung cancer (NSCLC) first line treatment has been approved by the Drugs and Therapeutics Committee.

#### **Approved Restriction**

As a single agent treatment option for the treatment of locally advanced (Stage IIIB, not eligible for potentially curative concurrent chemoradiotherapy) or previously untreated metastatic non-small cell lung cancer (NSCLC) in patients whose tumours express PD-L1 Tumour Proportion Score (TPS)  $\geq 50\%$  as determined by a validated test and who do not harbor a sensitizing epidermal growth factor receptor (EGFR) mutation or anaplastic lymphoma kinase (ALK) translocation. Patients should have a good performance status. Treatment should continue until confirmed disease progression or unacceptable toxicity, or to a maximum of two years (35 cycles), whichever comes first.

A new Guideline for the role of pembrolizumab for advanced/ metastatic non-small cell lung cancer (NSCLC) second or subsequent line treatment has been approved by the Drugs and Therapeutics Committee.

#### **Approved Restriction**

As a single agent treatment option for the treatment of metastatic non-small cell lung cancer (NSCLC) in patients whose tumours express PD-L1 (Tumour Proportion Score (TPS)  $\geq 1\%$ ) as determined by a validated test and who have disease progression on or after cytotoxic chemotherapy and targeted therapy for mutations of either epidermal growth factor receptor (EGFR) or anaplastic lymphoma kinase (ALK) for those patients whose tumours express these genomic aberrations. Patients should have a good performance status. Treatment should continue until confirmed disease progression or unacceptable toxicity, or to a maximum of two years (35 cycles), whichever comes first.

### **RITUXimab subcut, *Rituxan*<sup>®</sup> SC**

#### **Approved Restriction**

The treatment of diffuse large B cell lymphoma (DLBCL).

## V. Therapeutic Interchange

The process to develop a NSHA Systemic Antimicrobial Formulary, includes approval of the following therapeutic interchanges that provide therapeutically equivalent alternative to non-formulary antimicrobials or address common dosing issues to expedite and simplify clarifications. Previous formulary systemic antimicrobial interchanges are removed from the formulary.

Antimicrobial order	Interchange*
Cefazolin* 1 g IV any frequency	Cefazolin 2 g IV same frequency
Cefazolin* __g IV q6h	Cefazolin 2g IV q8h
Cefazolin 500mg PO q6h	Cephalexin 500mg PO q6h
Cefoxitin 1g IV q6-8h	Cefazolin 2g IV q8h and metronidazole 500 mg IV q12h Exceptions: Pelvic inflammatory disease (PID), postpartum x 1 dose for 3 <sup>rd</sup> or 4 <sup>th</sup> degree tears, and surgical prophylaxis for gynecologic procedures.
Cefoxitin 2g IV q6-8h	Cefazolin 2 g IV q8h and metronidazole 500 mg IV q12h Exceptions: Pelvic inflammatory disease (PID), postpartum x 1 dose for 3 <sup>rd</sup> or 4 <sup>th</sup> degree tears, and surgical prophylaxis for gynecologic procedures.
Ceftriaxone (Rocephin®) 1 g IV q12h or 2 g IV q24h	Ceftriaxone 1 g IV q24h Exceptions: meningitis or CNS infections, necrotizing fasciitis, periorbital/orbital cellulitis, osteomyelitis, joint infections, typhoid, Lyme disease and endocarditis.
Ciprofloxacin 400 mg tablet	Ciprofloxacin 500 mg tablet
Ciprofloxacin 500 mg IV	Ciprofloxacin 400 mg IV
Ciprofloxacin extended release (Cipro® XL) PO	Ciprofloxacin regular release product, same dose PO
Clindamycin __ mg IV q 6h	Clindamycin __ mg IV q 8h (total daily dosage no more than 1800 mg), Exception: Gynecology patients being treated for PID, necrotizing fasciitis, and toxic shock syndrome may receive 900 mg IV q8h
Cloxacillin* IV any dose q4-6 hours	Cloxacillin 2g IV q4h
Erythromycin IV (all regimens)	Azithromycin 500 mg IV daily Exception: erythromycin IV used as motility agent

Antimicrobial order	Interchange*
Erythromycins, oral: Base (enteric/particle - coated tab) 250mg	Erythromycins, oral - Base (conventional release)
Erythromycins, oral: Estolate tablets 250mg	Erythromycins, oral: Stearate tablets 250mg
Erythromycins, oral: Ethylsuccinate tablets 400mg	Erythromycins, oral: Base Tablet 250mg
Meropenem 1g or 2g* IV q8h	Meropenem 500mg IV q6h *dose is not interchanged if treating CNS, cystic fibrosis, or endophthalmitis infections
Metronidazole __ mg IV q 6-8h	Metronidazole __ mg IV q12h (Exception: <i>Clostridium difficile</i> infection, subdural empyema or brain abscess)
Metronidazole 250 mg PO/IV q12h	Metronidazole 500 mg PO/IV q12h
Micafungin*	Caspofungin 70mg IV on day 1 , followed by 50mg IV q24h
Nitrofurantoin regular as follows: 50 mg PO bid 50 mg PO qid	Nitrofurantoin Macrocrystals (Macrobid®): 100 mg PO daily 100 mg PO bid Exceptions include: Tube and crushing administration, patients with gut absorption issues i.e. ileostomy, short gut syndrome
Nystatin oral suspension 100,000 units/mL, doses written for 1mL, any frequency/schedule	Nystatin oral suspension 500,000 units/mL (5mL) same frequency/schedule-if no frequency written will be dispensed as 5mL QID for 10 days Exception – Palliative Care
Penicillins - Penicillin G 500 000 IU (300 mg), oral - Penicillin G IV - Penicillin G potassium IV - Penicillin V potassium 250 mg (400 000 IU) - Penicillin V potassium 500 mg - Penicillin V 300 mg	Penicillins - Penicillin V potassium 300 mg, oral  - Penicillin G sodium IV - Penicillin G sodium IV  - Penicillin V potassium 300 mg (500 000 IU)  - Penicillin V potassium 600 mg  - Penicillin V potassium 300 mg

\* refer to Appendix 1 for further details

\*\* The dosing recommendations are for adults. For pediatrics, please refer to IWK Spectrum app. or other resource.

## VI. Other

**A NSHA Systemic Antimicrobial Formulary with Protected Antimicrobials Stoplight System** has been developed by the NSHA Antimicrobial Stewardship Program (ASP) with input from Infectious Disease experts and the Antimicrobial Subcommittee.

The NSHA Formulary has been updated to reflect these recommendations. Since this review did not include non-systemic antimicrobials, anti-parasitic, antiretroviral, or direct acting antiviral (hepatitis C) medications, the formulary status of these medications remain as previously approved.

Former formulary restrictions for systemic antimicrobials have been removed and replaced with the Stoplight Guiding System to preserve certain antimicrobials and/or provide alerts for adverse effects:

**NSHA Systemic Antimicrobial Formulary with Protected Antimicrobial Stoplight System**

**Green** - No restrictions.

**Yellow** - Protected antimicrobial. Defined criteria for use and/or important safety considerations.

**Red** - Protected antimicrobial. Requires ASP review within 72 hours.

Drug	Protection Status
Acyclovir	green
Amikacin	yellow
Amoxicillin	green
Amoxicillin/ Clavulanate	yellow
Amphotericin B deoxycholate	yellow
Amphotericin B liposomal (Ambisome)	yellow
Ampicillin	green
Azithromycin	yellow
Caspofungin	yellow
CeFAZolin	green
Cefepime	red
CeFIXime	yellow
CefoTAXime	yellow
Cefoxitin	yellow
Cefprozil	green
CeftAZIDime	yellow
Ceftolozane - Tazobactam	red
CefTRIAxone	yellow
CefUROXime Axetil	green
CefUROXime Sodium	green
CephALEXin	yellow
Cidofovir	yellow
Ciprofloxacin	yellow
Clarithromycin	yellow

Drug	Protection Status
Clindamycin	yellow
Cloxacillin	green
Colistin	yellow
Dapsone	yellow
Daptomycin	red
Doxycycline	green
Ertapenem	yellow
Ethambutol	green
Erythromycin	yellow
Fidaxomicin	red
Fluconazole	green
Fosfomycin	yellow
Ganciclovir	yellow
Gentamicin	yellow
Imipenem/Cilastatin	red
Isoniazid	green
Levofloxacin	yellow
Linezolid	red
Meropenem	yellow
Metronidazole	green
Minocycline	green
Neomycin	yellow
Nitrofurantoin	green
Nystatin	green
Oseltamivir	yellow
Penicillin G Benzathine	green
Penicillin G Sodium	green
Penicillin V Potassium	green
Pentamidine Isethionate	yellow
Piperacillin-Tazobactam	yellow
Pyrazinamide	green
Pyrimethamine	yellow
RifABUTin	green
RifAMPin	green
Tetracycline	green
Tigecycline	red
Tobramycin	yellow
Trimethoprim	yellow
Trimethoprim/ Sulfamethoxazole	yellow
ValACYclovir	green
ValGANCIclovir	yellow
Vancomycin	yellow
Voriconazole	yellow

As part of this process, Antimicrobial Stewardship Guidelines for Antimicrobial Use were approved to guide appropriate use and safety precautions for the yellow and red antimicrobials. These Guidelines can be accessed on the Antimicrobial Stewardship website:

<http://www.cdha.nshealth.ca/nsha-antimicrobial-stewardship/antimicrobial-formulary>.

## VII. Medication Policies

The following hospital policies have been approved by the Medical Advisory Committee on the recommendation of the Drugs and Therapeutics Committee. These policies will be added to the Medication Policy and Procedure Manual.

BEL-MM-001 Dalteparin for Anticoagulation in the Extracorporeal Circuit during Hemodialysis  
 MM-NC-010 Nova Scotia Antidote Program  
 MM-SR-045 Preprinted Orders (PPOs)

## VIII. Pre-Printed Orders

The following pre-printed orders have been approved by the Medical Advisory Committee on the recommendation of the Drugs and Therapeutics Committee.

PPO 0333 Intrathecal Chemotherapy Protocol  
 PPO 0493 Folfirinox – Advanced Pancreatic Adenocarcinoma  
 PPO 0560 Gynecology Post-Operative Orders  
 PPO 0603 Psychiatry Inpatient Admission – Acute Care and Short Stay  
 PPO 0611 High Risk APL – Induction – The Iland Protocol  
 PPO 0612 High Risk APL – Consolidation I – The Iland Protocol  
 PPO 0613 High Risk APL – Consolidation II – The Iland Protocol  
 PPO 0614 High Risk APL – Maintenance – The Iland Protocol  
 PPO 0627 MiniBeam Protocol  
 PPO 0628 PACLitaxel Weekly – Breast Regmen  
 PPO 0629 DOCEtaxel/OXALiplatin/Fluorouracil/Leucovorin – GI Regimen  
 PPO 0635 Lumbar Drain Management Post Cardiovascular Surgery  
 PPO 0637 Haploidentical Donor Transplant Orders  
 PPO 0638 Reduced Intensity Transplant Orders  
 PPO 0644 IVIG Dermatology Adult and Pediatric  
 PPO 0645 IVIG Hematology Pediatric  
 PPO 0646 IVIG Infectious Diseases Adult and Pediatric  
 PPO 0647 IVIG Rheumatology Adult and Pediatric  
 PPO 0648 IVIG Solid Organ Transplant Adult and Pediatric  
 PPO 0649 IVIG Immunology Adult and Pediatric  
 PPO 0650 IVIG Neurology Adult and Pediatric  
 PPO 0651 IVIG Hematology Adult  
 PPO 0652 SCIG Adult and Pediatric  
 PPO 0632 Nivolumab/ Ipilimumab – Advanced Melanoma

PPO 0633 Nivolumab/ Ipilimumab – Advanced Renal Cell Carcinoma  
 PPO 0343 Pre-op Gynecological High Dose Rate Brachytherapy  
 PPO 0504 PERTuzumab/TRASStuzumab (with Taxane) – Metastatic Breast Cancer  
 PPO 0639 Linker Induction 1A Acute Lymphoblastic Leukemia (age greater than 50 years)  
 PPO 0640 Linker Consolidation 1B 2B Acute Lymphoblastic Leukemia (age greater than 50 years)  
 PPO 0641 Linker Consolidation 1C 2C 3C Acute Lymphoblastic Leukemia (age greater than 50 years)  
 PPO 0642 Linker – Consolidation 2A Acute Lymphoblastic Leukemia (age greater than 50 years)  
 PPO 0643 Linker- Maintenance Acute Lymphoblastic Leukemia (age greater than 50 years)  
 PPO 0655 TRASStuzumab (every 21 days) – Adjuvant or Metastatic Breast  
 PPO 0044 Allogenic Bu (12.8) Cy (120) Transplant Orders  
 PPO 0080 Admission Orders – Hematology Inpatient Orders  
 PPO 0140 Subcutaneous Insulin Orders  
 PPO 0394 Management of Confirmed Pathogen Peritonitis Associated With Peritoneal Dialysis  
 PPO 0557 Obinutuzumab and Chlorambucil – Chronic Lymphocytic Leukemia (CLL) or Small Lymphocytic Lymphoma (SLL) – Cycle 1  
 PPO 0596 BENDAmustine/RITUXimab  
 PPO 0618 NIVOLumab Single Agent – 14 Day Cycle  
 PPO 0619 PEMBROlizumab Single Agent – 21 Day Cycle  
 PPO 0620 NIVOLumab Single Agent – 28 Day Cycle  
 PPO 0632 NIVOLumab/Ipilimumab – Advanced Melanoma  
 PPO 0633 NIVOLumab/Ipilimumab – Advanced Renal Cell Carcinoma  
 PPO 0659 Carfilzomib/CycloPHOSPHAMIDE/Dexamethasone Relapsed Multiple Myeloma  
 PPO 0660 Carfilzomib/Lenalidomide/Dexamethasone Relapsed Multiple Myeloma

## IX. IV Manual

### New Monographs:

Cabazitaxel  
 Famotidine  
 Nanoparticle Albumin Bound (NAB) PACLitaxel  
 Pemetrexed  
 PERTuzumab

Amphotericin B liposomal (Ambisome)  
 Caspofungin  
 Cefepime  
 Ceftolozane Tazobactam  
 Cefoxitin  
 Cidofovir

**Revised Monographs:**

Acetylcysteine  
Acyclovir  
Ceftazidime  
Cetuximab  
Danaparoid  
DilTIAZem  
DimenhyDRINATE  
DOBUTamine  
Epoetin Alfa  
Estrogens, conjugated  
Fluorescein  
Ibutilide  
InFLIXimab  
Irinotecan  
Linezolid  
Lymphocyte immune globulin, anti-thymocyte globulin (equine)  
Magnesium Sulfate  
Meperidine  
Methotrimeprazine  
Metoprolol  
Nitroglycerin 200 mcg/mL Infusion Table  
Oxaliplatin  
Protamine  
Remifentanil  
Rocuronium  
Salbutamol  
Tenecteplase

Adenosine  
Alteplase  
Ceftriaxone  
Dextrose 50%

**Removed Monographs:**

Bortezomib  
Bretylium  
Chloramphenicol  
PENTObarbital  
Quinupristin/ dalfopristin  
Sodium acetate

Aprotinin  
Amphotericin B lipid complex (Abelcet)  
Micafungin  
Piperacillin

The information contained in this newsletter may also be accessed online:

<http://cdhaintra/departmentservices/pharmacy/Formulary/index.cfm>

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Appendix 1  
NSHA Antimicrobial Stewardship Program

There is a <b>NEW</b> antimicrobial formulary for NSHA <i>Effective May 1, 2019</i>		
Change	Reason	Implications
Antimicrobials classified into <a href="#">stoplight system</a> : green, yellow, red	<ul style="list-style-type: none"> <li>Protect broad-spectrum antimicrobials</li> <li>Optimize safe antimicrobial use</li> </ul>	<ul style="list-style-type: none"> <li><b>Green:</b> No restrictions</li> <li><b>Yellow:</b> Clinical guideline available (<a href="#">see website</a>)</li> <li><b>Red:</b> Antimicrobial stewardship team review within 72 hours</li> </ul>
Levofloxacin replacing moxifloxacin	<ul style="list-style-type: none"> <li>Oral levofloxacin is less expensive</li> <li>Levofloxacin is narrower-spectrum</li> <li>Moxifloxacin has <b>poor</b> anaerobic activity so should not be used for gastrointestinal infections</li> </ul>	
Caspofungin replacing micafungin	<ul style="list-style-type: none"> <li>More evidence for pediatric patients</li> <li>Same spectrum of activity</li> </ul>	Dosing: <ul style="list-style-type: none"> <li>- 70mg IV on day 1, then 50mg IV q24h</li> <li>- New orders for micafungin will be changed to caspofungin</li> </ul>
Cefazolin Dosing	Ensure adequate dosing for serious Gram-positive infections like <i>S. aureus</i>	Orders for cefazolin 1g will be changed to 2g. (frequency adjusted for renal function)
Cloxacillin Dosing	Ensure adequate dosing for serious Gram-positive infections like <i>S. aureus</i>	Orders for any dose of cloxacillin IV will be changed to cloxacillin 2g IV q4h
Amphotericin formulations:	<ul style="list-style-type: none"> <li>- Amphotericin B liposomal (Ambisome®)               <ul style="list-style-type: none"> <li>o <b>formulation of choice in most situations</b></li> </ul> </li> <li>- Amphotericin B deoxycholate/conventional:               <ul style="list-style-type: none"> <li>o for compounded preparations (ex: irrigation solutions)</li> <li>o preparation of choice in neonates</li> </ul> </li> <li>- See <a href="#">guideline</a> for indications and safety considerations</li> </ul>	
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