D&T Decisions

… from the Drugs and Therapeutics Committee

The information in this newsletter may also be accessed online.
To request a change to the NS Health Hospital Formulary, select & complete the online "Formulary Request Form":
NSH Pharmacy Formulary (nshealth.ca)

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Medication Policies

The following policies were approved by the Medical Advisory Committee (Jul 23, Oct 23) on the recommendation of the Drugs and Therapeutics Committee (Jun 23, Sep 23).

I. Additions to Hospital Formulary

Estrone vaginal cream/ *Estragyn*®

Estrone vaginal cream (Estragyn®) has been added to the NS Health Hospital Formulary based on the IWK Health Formulary status.

Amphetamine mixed salts/ *Adderall XR*®
Dextroamphetamine/ *Dexedrine*®
Lisdexamfetamine/ *Vyvanse*®

Amphetamine mixed salts, dextroamphetamine and lisdexamfetamine have been added to the NS Health Hospital Formulary based on the IWK Health Formulary status.

Fosphenytoin/ *Cerebyx*® PEDIATRIC APPROVAL

The NS Health D&T Committee considered a pediatric specific formulary request for fosphenytoin (WZ request). Fosphenytoin is non-formulary at IWK Health.

Fosphenytoin is a water-soluble prodrug formulation of phenytoin that is indicated for short-term parenteral administration when other means of phenytoin administration are unavailable, inappropriate or deemed less advantageous. The safety and effectiveness of fosphenytoin in this use has not been systematically evaluated for more than 5 days. Fosphenytoin can be used for the control of generalized convulsive status epilepticus (CSE) and prevention and treatment of seizures occurring during neurosurgery.

Fosphenytoin itself has no known antiepileptic activity; however, following IV administration, 1.5 mg of fosphenytoin rapidly and completely converts to 1 mg of phenytoin sodium. To prevent dosing confusion, the dose of fosphenytoin is expressed as "phenytoin equivalents" or "PE" (i.e., 100 mg PE of fosphenytoin and 100 mg of phenytoin yield the same molar amounts of phenytoin sodium).

Although non-formulary at the IWK, there was a request to add fosphenytoin to the NS Health Hospital Formulary for the treatment of status epilepticus refractory to benzodiazepines **in children**. Both the 2022 TREKK (Translating Emergency Knowledge for Kids) and 2021 Canadian Paediatric Society Guidelines include fosphenytoin/ phenytoin as options for the second-line emergency management of pediatric CSE. TREKK was launched to improve emergency care for Canadian children as it was recognized that most Canadian acutely ill and injured children who require Emergency Department care are not receiving care from a specialized pediatric hospital. TREKK facilitates research, education and collaborates to develop tools and resources for these non-specialized settings.

Since fosphenytoin is water soluble, it may be given IM (if no IV access); however, therapeutic phenytoin concentrations may not be reached as quickly as with IV administration. Fosphenytoin can be given at a faster rate than phenytoin, has less admixture compatibility issues and has a lower risk of injection site problems (unlike phenytoin, fosphenytoin is not considered a vesicant). However, fosphenytoin and phenytoin have the same drug interactions and toxicity (e.g., cardiac arrhythmias, bradycardia, hypotension). When administered as second-line status

epilepticus therapies, fosphenytoin and phenytoin should not be administered to the same patient (i.e., if one has already been administered, the other should not be used).

Approved Restriction:

Children less than 18 years for the emergency treatment of status epilepticus refractory to benzodiazepines.

Fosfomycin injection/ *Ivozfo™*

Treating infections caused by multidrug resistant (MDR) bacteria is challenging as antimicrobial options are limited and alternative treatment options may be required due to antimicrobial shortages.

Intravenous fosfomycin is an epoxide antimicrobial with a unique mechanism of action and a broad spectrum of activity against a wide range of gram-positive and gram-negative bacteria. Fosfomycin kills bacteria by irreversibly inactivating the MurA enzyme which is responsible for the first step of peptidoglycan synthesis in the bacterial cell wall; therefore, fosfomycin impacts cell wall synthesis earlier in the process than other cell wall agents making it less likely to promote cross resistance to other antimicrobial classes.

When used alone, IV fosfomycin has no or limited activity against some organisms (e.g., *Acinetobacter* sp., *Pseudomonas* sp., *Stenotrophomonas* sp. and *Bacteroides* sp.) and there is concern that monotherapy may lead to resistance. Therefore, parenteral fosfomycin is recommended to be used in combination with other agents (e.g., beta lactams, colistin, aminoglycosides). Although the exact synergistic mechanism is unknown, studies demonstrate improved cure rates for many MDR pathogens including *Pseudomonas* and *Acinetobacter*. Due to its niche indication and development prior to rigorous regulatory standards, high quality randomized controlled trials are not available comparing the addition of fosfomycin to standard therapy versus standard therapy alone; therefore, most of the evidence is observational.

The World Health Organization added IV fosfomycin to the list of essential medicines classified in the "Reserve" group. This group includes antibiotics that should be treated as "last resort" options or tailored to highly specific patients and settings, and when other alternatives would be inadequate or have already failed. Targeted monitoring and utilization reporting of these medicines should be prioritized.

Approved Restriction:

Addition to the systemic antimicrobial formulary as a red category agent (i.e., requiring Antimicrobial Stewardship review within 72 hours). Guidelines for use are available on the NS Health Antimicrobial Stewardship website and app.

Inhaler Devices

In 2019, NS Health aligned the Hospital Formulary listing of inhaled medications and associated inhaler devices with that of the NS Provincial Drug Plan Formulary (i.e., Pharmacare). Patients with chronic obstructive lung diseases (i.e., COPD, asthma) are frequently hospitalized and this provides an opportunity to start patients on appropriate maintenance inhaled therapies and/ or continue the treatments that they are already using at home. Since inhaled medications each have a unique inhaler device, hospitalization is an opportunity to assess and teach patients proper inhaler technique. (D&T Decisions #67 Aug. 1, 2019).

With this approval, realignment of the NS Health Hospital Formulary is required when changes are made to the NS Pharmacare Formulary and an update was approved in 2022 (D&T Decisions #73 May 18, 2022).

Since 2022, two new inhalers have been added to the NS Pharmacare Formulary (one as an exception status benefit and the other as an open benefit); therefore, these inhalers have been approved for the NS Health Hospital Formulary. Also, the Hospital Formulary restrictions for Zenhale® required revision to align with the NS Provincial Drug Plan Formulary.

Formoterol + glycopyrronium + budesonide/ *Breztri™ Aerosphere®*

Long-acting beta2 agonist (LABA) plus long-acting muscarinic antagonist (LAMA) plus inhaled corticosteroid (ICS)

Approved Restriction:

For the treatment of chronic obstructive pulmonary disease (COPD), as defined by spirometry, in patients who experience inadequate control while being treated with a long-acting beta-2 agonist/long-acting muscarinic antagonist (LABA/LAMA).

Fluticasone/ *Aermony RespiClick™*

The inhaled corticosteroid (ICS) fluticasone Aeromony RespiClick™ (fluticasone powder for oral inhalation) has been added to the NS Health Hospital Formulary.

Formoterol + mometasone / *Zenhale®*

Long-acting beta2 agonist (LABA) plus inhaled corticosteroid (ICS)

Revised Restriction:

For the treatment of moderate to severe asthma in patients who:

- are compliant with inhaled corticosteroids at optimal doses;

AND

- require additional symptom control, (e.g., cough, awakening at night, missing activities such as school, work or social activities because of asthma symptoms);

AND

- require increasing amounts of short-acting beta2-agonists, indicative of poor control.

II. Therapeutic Interchange – Removal

Ceftriaxone

The standard dosing recommendation of the NS Health Antimicrobial Formulary ceftriaxone therapeutic interchange (i.e., ceftriaxone 1 g IV q24h) may not be adequate for all patients. Although the therapeutic interchange identifies indications that are exceptions to the ceftriaxone standard dose, there are other factors to be considered (e.g., pharmacokinetic parameters) that may necessitate higher doses in certain patient populations to reduce the risk of treatment failure and to improve outcomes.

Since ceftriaxone dosing requires clinical judgement and higher than standard doses (daily dose of 2 g versus 1 g) should be

considered in certain patient populations (e.g., obesity, critically ill), the following ceftriaxone therapeutic interchange is **removed** from the NS Health Hospital Antimicrobial Formulary:

DELETED Therapeutic Interchange	
Antimicrobial order	Dispensed as
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.

III. New Guidelines

Sacituzumab govitecan/ *Trodelvy*®

A new guideline has been approved for the role of sacituzumab govitecan for the treatment of adult patients with unresectable locally advanced or metastatic triple negative breast cancer (TNBC)

Approved Restriction:

For the treatment of adult patients with unresectable locally advanced or metastatic triple negative breast cancer (TNBC) who have received at least two prior therapies, at least one of which was for metastatic disease.

Treatment should continue until disease progression or unacceptable toxicity.

IV. Revised Guidelines

Bortezomib

Revised guidelines have been approved for the role of bortezomib in adult patients with Multiple Myeloma, Mantle Cell Lymphoma and Waldenstrom Macroglobulinemia.

Revised Restrictions:

Multiple Myeloma:

As part of a combination regimen or as a single agent for the treatment of Multiple Myeloma in both first-line and relapsed treatment settings.

Mantle Cell Lymphoma:

As a single agent for the treatment of relapsed or refractory Mantle Cell Lymphoma.

Waldenstrom Macroglobulinemia:

As a single agent or as part of a combination regimen for the treatment of Waldenstrom Macroglobulinemia.

V. Expanded Guidelines

Pembrolizumab/ *Keytruda*®

Three new guidelines have been approved for pembrolizumab.

A new guideline has been approved for the role of pembrolizumab for the treatment of adult patients with unresectable or metastatic triple negative breast cancer (TNBC).

Approved Restriction:

For the treatment of adult patients with locally recurrent unresectable or metastatic triple negative breast cancer (TNBC) that expresses PD-L1 (combined positive score [CPS] ≥10 as determined by a validated test) in combination with chemotherapy.

Treatment should continue until disease progression, unacceptable toxicity, or a maximum of 24 months of therapy, whichever occurs first.

A new guideline has been approved for the role of pembrolizumab for the adjuvant treatment of adult patients with renal cell carcinoma.

Approved Restriction:

For the adjuvant treatment of adult patients with renal cell carcinoma at intermediate-high or high risk of recurrence following nephrectomy or following nephrectomy and resection of metastatic lesions.

Treatment should continue until disease progression, unacceptable toxicity, or maximum of 1 year of therapy, whichever occurs first.

A new guideline has been approved for the role of pembrolizumab for the treatment of adult patients with high-risk early-stage triple-negative breast cancer (TNBC).

Approved Restriction:

For the treatment of adult patients with high-risk early-stage triple-negative breast cancer (TNBC) in combination with chemotherapy as neoadjuvant treatment, followed by pembrolizumab as adjuvant treatment after surgery.

Treatment should continue until disease progression, recurrence, unacceptable toxicity, or maximum of 1 year of therapy, whichever occurs first.

Nivolumab/ *Opdivo*®

Two new guidelines have been approved for nivolumab.

A new guideline has been approved for the role of nivolumab for the treatment of advanced or metastatic gastric, gastroesophageal junction (GEJ), or esophageal adenocarcinoma.

Approved Restriction:

In combination with platinum and fluoropyrimidine-based chemotherapy for the first-line treatment of patients with HER-2 negative advanced or metastatic gastric, gastroesophageal junction, or esophageal adenocarcinoma.

Treatment should continue until confirmed disease progression or unacceptable toxicity to a maximum of 2 years, whichever occurs first.

A new guideline has been approved for the role of nivolumab for the adjuvant treatment of completely resected esophageal or gastroesophageal junction (GEJ) cancer.

Approved Restriction:

For the adjuvant treatment of completely resected esophageal or gastroesophageal junction (GEJ) cancer in patients who have residual pathological disease following prior neoadjuvant chemoradiotherapy.

Treatment with nivolumab should be initiated within 4 to 16 weeks of complete resection and continued for a maximum treatment duration of 1 year, or until confirmed disease progression or unacceptable toxicity whichever occurs first.

VI. Medication Policies

The following hospital policies have been approved by the Medical Advisory Committee on the recommendation of the Drugs and Therapeutics Committee.

CAN-GA-035	Parenteral Systemic Therapy for Cancer Levels of Care (Effective Jan. 9, 2024)
MM-MA-025	Patient's Own Medication (POM)
MM-MA-005	Medication Independent Double Check
MM-MS-030	Take Home Naloxone Program Training and Distribution

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