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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Inside this Issue…

The following policies were approved by the Medical Advisory Committee (May 24, Jun 24, Jul 24) on the recommendation of the Drugs and Therapeutics Committee (Mar 24, Apr 24, May 24, Jun 24).

I. Additions to Hospital Formulary

Macitentan/ *Opsumit*®

Macitentan (Opsumit ®) is an endothelin receptor antagonist (ERA) indicated for long-term treatment of pulmonary arterial hypertension (PAH WHO Group 1) to reduce morbidity in patients of WHO Functional Class II or III whose PAH is either idiopathic or heritable, or associated with connective tissue disease or congenital heart disease. PAH is a disabling, progressive condition that is characterized by a sustained pulmonary arterial pressure of >20 mmHg. Despite available drug therapies, pulmonary hypertension carries a high risk of progression to right heart failure and death. A multidisciplinary approach is required for comprehensive management and the proper classification of underlying cause is essential to select appropriate drug therapy.

ERAs, either alone or in combination with phosphodiesterase type 5 (PDE5) inhibitors (e.g., sildenafil, tadalafil), are the mainstay of PAH treatment. ERAs act by blocking the binding of endothelin to ET_A and ET_B receptors on vascular smooth muscle. Since ET_B receptors are located primarily in the lung, blocking these receptors results in the inhibition of vasoconstriction, fibrosis, hypertrophy, and inflammation. Although there are no clinical trials directly comparing the available ERAs, there are proposed advantages to macitentan therapy. Compared to bosentan, which is dosed BID, macitentan provides convenient once daily administration. Other macitentan advantages over bosentan include fewer drug interactions (e.g., bosentan can reduce the efficacy of PDE5 inhibitors and hormonal contraception) and a reduced incidence of liver toxicity (macitentan requires less frequent monitoring). The landmark macitentan trial, SERAPHIN, demonstrated long term efficacy outcomes that have not been shown with other ERA options. The recent European Society of Cardiology Guideline recommendations reflect the advantages of macitentan.

Approved Restriction:
For the treatment of patients with Group 1 pulmonary arterial hypertension (PAH) with a World Health Organization (WHO) functional class of at least II.

Difelikefalin/ *Korsuva*®

Difelikefalin (Korsuva®) is a peripherally acting selective kappa-opioid receptor agonist indicated for the treatment of moderate to severe pruritis in chronic kidney disease-associated pruritis (CKD-aP) in adult patients on hemodialysis. Difelikefalin entered the Canadian market in February 2023 and is intended for use only at hemodialysis (HD) centers. The usual dose (0.5 mcg/kg) is based on target post-dialysis dry body weight and the IV bolus is administered into the venous line of the dialysis circuit at the end of each HD treatment or after rinse-back.

CKD-aP is experienced by approximately 60% of patients undergoing HD and is described as intense generalized itching experienced daily, or almost daily, despite the absence of primary dermatologic findings. CKD-aP can have a substantial impact on quality of life (e.g., contribute to poor sleep, poor social functioning, depression), increase infection risk, hospitalization, and death. Although the pathophysiology of CKD-aP is not fully understood, it is thought that accumulation of uremic toxins plus activation of non-histaminergic itch pathways can result in an imbalance of opioid receptors activity, peripheral neuropathy, and immune system dysregulation.

A stepwise approach to the management of CKD-aP includes hydrous emollients to moisturize the skin as well as other topical treatments such as menthol/camphor, capsaicin or tacrolimus; however, these topicals may be difficult to apply, require frequent application and may require pharmacy compounding. Oral gabapentin or pregabalin may modify neuronal pathways involved in itch sensation; however, use may be limited by side effects. UV-B phototherapy is another treatment option.

Difelikefalin is thought to reduce the sensation of itch by acting on kappa-opioid receptors and immune cells. Due to its small-peptide, hydrophilic structure, it is not able to cross the blood brain barrier and has no activity on central opioid receptors.

The CADTH Canadian Drug Expert Committee (CDEC) recommendation for difelikefalin was "do not reimburse"; therefore, it is not listed as a benefit on the NS Provincial Drug Plan Formulary (i.e., Pharmacare). The CDEC recommendation was based on two multi-centered randomized placebo-controlled clinical trials (KALM-1 and KALM-2) that evaluated the efficacy of difelikefalin in patients with moderate to severe CKD-aP [i.e., a weekly mean score of ≥ 4 points on the 24-hour Worst Itching Intensity Numerical Rating Scale (WI-NRS)] who were undergoing HD three times per week for at least 3 months. CDEC concluded that the evidence considered did not demonstrate a clinically meaningful therapeutic benefit of difelikefalin over placebo since the magnitude of the difference in pruritis observed was uncertain. The most frequently reported adverse effects in these trials included diarrhea, dizziness and vomiting.

Approved Restriction:

For the treatment of adult patients on hemodialysis with moderate to severe chronic kidney disease-associated pruritis (CKD-aP) with a Worst Itching Intensity Numerical Rating Scale (WI-NRS) score of 7 or higher.

- NS Health is the payor of last resort.

Additions to Hospital Formulary to facilitate OPOR Design/ CPOE Process - Appendix 1

To facilitate the One Person One Record (OPOR) design of the Oracle Health Computerized Provider Order Entry (CPOE) catalog, 63 non-formulary medications have been approved for addition to the NS Health Hospital Formulary (Appendix 1).

OPOR is a multi-year collaboration between NS Health, IWK Health and the Province of Nova Scotia designed to transform the way we use and share health information to enable a digitally supported, patient-centered healthcare transformation in NS. The Oracle Health Clinical Information System (CIS) CPOE catalog will only include Hospital Formulary medications. Although there is a non-formulary process, the automation of the order entry process with the CPOE catalogue provides numerous clinical and safety benefits for patients and the healthcare system including reduced medication errors and increased efficiency. Therefore, a review of non-formulary medications was completed to identify those that may be considered appropriate for inclusion in the NS Health Hospital Formulary and the CPOE catalog.

Ideally, a non-formulary designation would be evidence and/ or economic based with an identifiable Formulary alternative. The current NS Health Hospital Formulary process is request driven; therefore, some non-formulary drugs in common use have not been reviewed for Formulary inclusion (i.e., there has not been a Formulary request for drug review). These non-formulary medications may be appropriate for patient care.

To facilitate the OPOR design, timeline and CPOE build, Subject Matter Expert (SME) pharmacists worked with the OPOR pharmacy team and identified select non-formulary drugs for Formulary inclusion. Although these medications may not have been previously evaluated for Hospital Formulary inclusion, there is robust clinical experience with these medications that are considered standard of care. The Formulary status recommendations are based on: NS Pharmacare benefit status [may be based on CADTH Canadian Drug Expert Committee (CDEC) CDR recommendation]; hospital drug utilization data; cost (e.g., low generic drug cost); and the need for continuation of established therapy.

II. Expanded Restrictions

Idarucizumab/ *Praxbind*®

Idarucizumab is the only Health Canada approved reversal agent specific for the direct oral anticoagulant (DOAC) dabigatran. In 2016, idarucizumab was added to the NS Health Hospital Formulary with restriction criteria [i.e., rapid reversal of the anticoagulant effects of dabigatran in patients with (1) overt, uncontrolled, or life-threatening bleeding; OR, (2) who require surgery or other invasive procedures that cannot wait for at least 8 hours for the effect of dabigatran to wear off]. Idarucizumab is a humanized, mouse, monoclonal antibody fragment that binds to dabigatran and its metabolites causing reversal of the anticoagulant effects of dabigatran within a few minutes.

Patients with atrial fibrillation may be prescribed dabigatran for the prevention of an ischemic stroke; however, despite preventative therapy, the yearly incidence of acute ischemic stroke in dabigatran treated patients is 0.92% (standard dose) and 1.34% (reduced dose). The administration of a thrombolytic such as alteplase or tenectaplase may be contraindicated in these patients due to the increased risk of intracranial hemorrhage; therefore, idarucizumab reversal of dabigatran has been described for safer thrombolytic therapy. The restriction criteria for idarucizumab has been expanded to include dabigatran treated patients in the setting of acute ischemic stroke.

Approved Restriction:
For the reversal of dabigatran to enable intravenous thrombolysis in dabigatran-treated acute ischemic stroke patients.

III. Removal of Restrictions

Levetiracetam IV/ *pdp- levetiracetam*

The IV formulation of the antiepileptic levetiracetam was approved by Health Canada in Oct. 2019 and added to the NS Health Hospital Formulary in May 2020 as a restricted medication (i.e., status epilepticus in critically ill patients with no enteral access; NPO patients established on oral levetiracetam; neurology consultation). Oral levetiracetam is Formulary without restrictions (added in 2014) and there are no IWK Formulary restrictions for levetiracetam including the IV formulation. Also, the cost of levetiracetam IV has decreased since the 2020 review.

Literature and treatment guidelines support the use of levetiracetam IV for indications outside of the current Formulary restrictions (i.e., status epilepticus; seizure prophylaxis following traumatic brain injury; seizure management in critically ill patients). Levetiracetam has predictable pharmacokinetics and fewer drug interactions compared to alternatives and is also considered a safer option for use in patients who may become pregnant, are pregnant or are breastfeeding. When enteral medications are an option, levetiracetam IV can be switched to an enteral dosage form at the same dose and interval.

The restrictions for levetiracetam IV have been removed from the NS Health Hospital Formulary.

IV. Therapeutic Interchange

The OPOR Oracle Health Clinical Information System (CIS) includes functionality to automate and appropriately document therapeutic interchanges (TIs). To optimize this functionality and facilitate the OPOR design, Subject Matter Expert (SME) pharmacists worked with the OPOR pharmacy team to identify nine TIs that have been approved for inclusion in the NS Health Hospital Formulary:

Oral Proton Pump Inhibitors

Ordered as	Interchanged to
Low dose PPIs: Dexlansoprazole 30 mg po daily or BID Esomeprazole 20 mg po daily or BID Lansoprazole 15 mg cap po daily or BID Omeprazole 10 mg po daily or BID Pantoprazole sodium 20 mg po daily or BID Rabeprazole 10 mg po daily or BID	Pantoprazole sodium 20 mg at the same frequency OR Lansoprazole FasTab* 15 mg at the same frequency *for enteral tubes, dysphagia, and medication crushing (disperse FasTabs)
Standard dose PPIs: Dexlansoprazole 60 mg po daily or BID Esomeprazole 40 mg po daily or BID Lansoprazole 30 mg cap po daily or BID Omeprazole 20 mg po daily or BID Pantoprazole magnesium 40 mg po daily or BID Pantoprazole sodium 40 mg po daily or BID Rabeprazole 20 mg po daily or BID	Pantoprazole sodium 40 mg at the same frequency OR Lansoprazole FasTab* 30 mg at the same frequency *for enteral tubes, dysphagia, and medication crushing (disperse FasTabs)

Lubricating Eye Products

Ordered as	Interchanged to
Any lubricating eyedrop/ artificial tears product	Lubricating eye drop contract brand
Any preservative free lubricating eyedrop/artificial tears product	Lubricating eye drop preservative free contract brand
Any lubricating eye gel product	Lubricating eye gel contract brand
Any lubricating eye ointment	Lubricating eye ointment contract brand
Formulary removals: all products except current contract brands	

Nasal Corticosteroids

Ordered as	Interchanged to
Beclomethasone 50 mcg/ spray Budesonide 64 mcg, 100 mcg/ spray Ciclesonide 50 mcg/ spray Fluticasone furoate 27.5 mcg/ spray Fluticasone propionate 50 mcg/ spray Triamcinolone 55mcg/ spray Any dose and frequency	Mometasone 50 mcg/ spray 2 sprays each nostril once daily* 1 spray each nostril once daily if age under 12* *order will remain prn if ordered as prn
Formulary removals: Budesonide 64 mcg, 100 mcg Beclomethasone 50 mcg	

Topical Corticosteroids

Potency	Class	Ordered as	Interchanged to*
Ultra-High	I	Betamethasone dipropionate glycol (augmented) 0.05% cream, ointment, lotion Clobetasol 17-propionate 0.05% cream, lotion Halobetasol propionate 0.05% ointment, 0.01% lotion Any frequency	Clobetasol 17-propionate 0.05% Cream, ointment, scalp lotion At the same frequency
High	II III	Amcinonide 0.1% cream, lotion, ointment Betamethasone dipropionate 0.025% cream, 0.05% cream, ointment Desoximetasone 0.25% cream, ointment Fluocinonide 0.05% cream, ointment Halobetasol propionate 0.05% cream Any frequency	Betamethasone dipropionate 0.05% cream, ointment At the same frequency
Moderate	IV V	Beclomethasone dipropionate 0.025% cream Betamethasone dipropionate 0.05% lotion, scalp lotion Betamethasone valerate 0.05% cream, ointment, scalp lotion Clobetasone 17 butyrate 0.05% cream Desoximetasone 0.05% cream Fluocinolone acetonide 0.025% ointment Hydrocortisone 17-valerate 0.2% cream, ointment Mometasone furoate 0.1% cream, ointment, scalp lotion Prednicarbate 0.1% cream, ointment Triamcinolone acetonide 0.1% cream, ointment and 0.5% cream Any frequency	Betamethasone valerate 0.1% cream, ointment, scalp lotion At the same frequency
Low	VI VII	Desonide 0.05% cream, lotion, ointment Hydrocortisone 0.5% cream, lotion, ointment; 2.5% cream, ointment Any frequency	Hydrocortisone 1% cream, ointment At the same frequency
*Creams interchanged to creams; ointments interchanged to ointments; scalp lotion interchanged to scalp lotion; shampoo interchanged to scalp lotion; interchange does not apply to gel products			

Statins

Ordered as	Interchanged to
Lovastatin any dose	Rosuvastatin 5 mg po daily
Fluvastatin any dose	Rosuvastatin 5 mg po daily

Angiotensin Receptor Blockers (ARBs)

Ordered as	Interchanged to
Azilsartan 20 mg, 40 mg, 80 mg po daily	Candesartan 8 mg, 16 mg, 32 mg po daily
Olmesartan 20 mg, 40 mg po daily	Candesartan 8mg, 16 mg po daily

Angiotensin Converting Enzyme (ACE) Inhibitors

Ordered as	Interchanged to
Benazepril 5mg, 10 mg, 20 mg, 40 mg po daily	Perindopril 1mg, 2 mg, 4 mg, 8 mg po daily
Cilazapril 1mg, 2.5 mg, 5 mg, 10 mg po daily	Perindopril 1 mg, 2 mg, 4 mg, 8 mg po daily
Fosinopril 5 mg, 10 mg, 20 mg, 40 mg po daily	Perindopril 1 mg, 2mg, 4 mg, 8 mg po daily
Quinapril 5 mg, 10 mg, 20 mg, 40 mg po daily, 20 mg po bid	Perindopril 1 mg, 2 mg, 4 mg, 8 mg po daily, 8 mg po daily
Perindopril arginine/ amLODIPine 3.5 mg/ 2.5 mg po daily Perindopril arginine/ amLODIPine 7 mg/ 5 mg po daily Perindopril arginine/ amLODIPine 14 mg/ 10 mg po daily	Perindopril 3 mg po daily + amLODIPine 2.5 mg po daily Perindopril 6 mg po daily + amLODIPine 5 mg po daily Perindopril 12 mg po daily + amLODIPine 10 mg po daily

Calcium Channel Blockers

Ordered as	Interchange to
Felodipine 2.5 mg, 5 mg, 10 mg po daily	amLODIPine 2.5 mg, 5 mg, 10 mg po daily

Dalteparin Prefilled Syringe Dose Banding

Ordered as:	Interchanged to:
Dalteparin Treatment Dose Range (units)	**Dalteparin Dose (units) (Syringes dispensed)**
6,400 to 8,600*	7,500 (1 x 7,500)
8,601 to 11,200	10,000 (1 x 10,000)
11,201 to 13,600	12,500 (1 x 12,500)
13,601 to 15,600	15,000 (1 x 15,000)
15,601 to 17,000	16,500 (1 x 16,500)
17,001 to 19,000	18,000 (1 x 18,000)
19,001 to 21,200	20,000 (2 x 10,000)
21,201 to 23,600	22,500 (1 x 10,000 + 1 x 12,500)
23,601 to 26,200	25,000 (2 x 12,500)
26,201 to 27,600	27,500 (1 x 12,500 + 1 x 15,000)
27,601 to 30,600	30,000 (2 x 15,000)
30,601 to 33,600	33,000 (2 x 16,500)
33,601 to 36,600	36,000 (2 x 18,000)
36,601 to 38,000*	38,000 (1 x 18,000 + 2 x 10,000)
*Contact prescriber for treatment doses Less than 6,400 units OR Greater than 38,000 units	

Removal from Hospital Formulary (Therapeutic Interchange)

Resulting from the approval of the therapeutic interchanges, the following medications are removed from the NS Health Hospital Formulary:
Omeprazole
Pantoprazole magnesium
Rabeprazole
Hydrocortisone valerate 0.2% cr, oint
Budesonide nasal
Beclomethasone nasal
All lubricating eye products except current contract brands

V. New Guidelines

Tebentafusp/ *Kimmtrak*®

A new guideline has been approved for the role of tebentafusp in unresectable or metastatic uveal melanoma.

Approved Restriction:
For the first line treatment of adult patients with human leukocyte antigen (HLA)A*02:01-positive unresectable or metastatic uveal melanoma (mUM).

Plerixafor/ *Mozobil*®

A new guideline has been approved for the role of plerixafor for hematopoietic stem cell mobilization.

Approved Restriction:
For hematopoietic stem cell mobilization in patients or donors identified at being at high risk of having an unsuccessful stem cell harvest attempt with either filgrastim plus chemotherapy or filgrastim alone.

Busulfan IV

A new guideline has been approved for the role of busulfan IV in conditioning regimens for hematopoietic stem cell transplants.

Approved Restriction:
As a therapeutic alternative to the oral version of busulfan in common conditioning regimens for allogeneic hematopoietic stem cell transplants (SCT).

Tremelimumab/ *Imjudo*® *& durvalumab*

A new guideline has been approved for the role of tremelimumab and durvalumab in unresectable or metastatic hepatocellular carcinoma.

Approved Restriction:
Tremelimumab in combination with durvalumab for the first-line treatment of adult patients with unresectable or metastatic hepatocellular carcinoma (HCC) who require systemic therapy.

VI. Revised Guidelines

niLOtinib/ *Tasigna*®

A new guideline has been approved for the role of niLOtinib in adult patients with Philadelphia chromosome positive chronic myeloid leukemia (Ph+ CML).

Approved Restriction:
First Line
For the first-line treatment of adult patients with Philadelphia chromosome positive chronic myeloid leukemia (Ph+ CML) in chronic phase.
Second Line +
For the treatment of chronic phase and accelerated phase Philadelphia chromosome positive (Ph+) chronic myeloid leukemia (CML) in adult patients who:

- Are resistant to iMAtinib;
- Have progressed to accelerated phase while on iMAtinib;
- Are intolerant to previous oral tyrosine kinase inhibitors (TKIs) (i.e. iMAtinib or daSATinib or both). Sequential use of niLOtinib and daSATinib is not permitted except in cases of intolerance (i.e. grade 3 or 4 toxicity).

daSATinib/ *Sprycel*®

A new guideline has been approved for the role of daSATinib in Philadelphia chromosome-positive chronic myeloid leukemia (Ph+ CML) and Ph+ acute lymphoblastic leukemia (Ph+ ALL).

Approved Restriction:
CML:
For the treatment of adult patients with Philadelphia chromosome-positive chronic myeloid leukemia (Ph+ CML) in chronic, accelerated, or blast phase.
ALL:
For the treatment of patients with Philadelphia chromosome-positive acute lymphoblastic leukemia (Ph+ ALL).

VII. Expanded Guidelines

Durvalumab/ *Imflinzi*®

Two new Guidelines have been approved for durvalumab.

A new guideline has been approved for the role of durvalumab and tremelimumab in unresectable or metastatic hepatocellular carcinoma.

Approved Restriction:
Durvalumab in combination with tremelimumab for the first-line treatment of adult patients with unresectable or metastatic hepatocellular carcinoma (HCC) who require systemic therapy.

A new guideline has been approved for the role of durvalumab in locally advanced or metastatic biliary tract cancer.

Approved Restriction:
For the first-line treatment of patients with locally advanced or metastatic biliary tract cancer (BTC) in combination with gemcitabine plus platinum-based chemotherapy.

VIII. Removal of Guidelines

iMAtinib/ *Gleevec*®

The oral medication iMAtinib has been listed in the NS Health Hospital Formulary with restriction guidelines. iMAtinib is now a multi-source generic medication that has been approved and listed as an open benefit with the NS Provincial Drug Plan Formulary (i.e., NS Pharmacare); therefore, the restriction guidelines for iMAtinib have been removed from the Hospital Formulary to align with the NS Pharmacare Formulary.

IX. Medication Policies

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

PH-HP-015 Immunization

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Appendix I – Additions to Hospital Formulary (to Facilitate OPOR Design/ CPOE Process)

Acamprosate Calcium EC Tab 333 mg
Alfuzosin 10 mg SR tab
Betamethasone Dipropionate-Calcipotriol Gel 0.5mg/0.05mg
Betamethasone Dipropionate-Calcipotriol Oint 0.5mg/0.05mg
Bimatoprost opht 0.01% (Lumigan)
Brimonidine/Timolol opht 0.2%/0.5% (Combigan)
Brinzolamide/Brimonidine opht 1%/0.2% (Simbrinza)
Brinzolamide/Timolol opht 1%/0.5% (Azarga)
Brinzolamide 1% opht
Budesonide CR 3 mg cap
Bumetanide 5 mg tab
Cannabis Sativa Extract spray 25mg/mL
Clioquinol 1% and 0.02% flumetasone otic
Chlorthalidone 50 mg tab
Ciprofloxacin/dexamethasone 0.3%/0.1% otic
Cyclosporine 0.05% opht emulsion
Cyproterone 50mg tab
Desloratadine 5mg tab
Diclofenac 10% in PLO Gel (G&B)
Diphenoxolate 2.5 mg with atropine tab
Dorzolamide/Timolol 0.2%/0.5% (Cosopt)
Entacapone Tab 200 mg
Entecavir Tab 0.5 mg
Estradiol 1 mg
Fusidic acid opht 1%
Galantamine 8 mg cap, 16 mg cap, 24 mg cap
Ganciclovir Eye Gel 0.15%
Gatifloxacin opth 0.3%
Hydrocortisone 1% in Clotrimazole 1% Cream (50g) (G&B)
Insulin glargine 300 units/mL (Toujeo)
Insulin lispro (Admelog)
Latanoprost/Timolol opht 0.005%/0.5%
Latanoprostene opht 0.024% (Vylutza)
Letrozole 2.5mg
Linaclotide 145mg
Menthol 0.25% Camphor 0.25% In Glaxal Cream (G&B)
Mirtazapine 15 mg OD tab
Naloxegol 25 mg tab
Olopatadine opht 0.2%
Oxcarbazepine 150 mg tab, 300 mg tab, 60mg/mL suspension
Perampanel 2 mg tab, 4 mg tab
Pinaverium 50,100mg
Polyethylene Glycol-Propylene Glycol Gel
Prucalopride 1,2 mg
Rivastigmine 1.5 mg cap, 3 mg cap, 4.5 mg cap
Rivastigmine patch 4.6 mg, 9.5 mg, 13.3 mg
Rizatriptan RPD 5, 10 mg (IWK)
Salicylic Acid-Betamethasone Dipro.Oint 3%/0.05%
Salicylic Acid-Betamethasone Dipro.Lotion 2%/0.05%
Sildenafil 25 mg
Silodosin 4 mg cap
Sitagliptin 50 mg, 100 mg tab
Sumatriptan Nasal 20mg/dose (IWK)
Tacrolimus PA (Envarsus) 0.75 mg, 1 mg, 4 mg
Tadalafil Tab 20 mg
Tadalafil 5mg (BPH)
Testosterone oral 40mg
Testosterone topical 1%
Thyroid desiccated 30mg
Timolol XE opht 0.25%, 0.5%
Tizanidine 4mg
Travoprost opht 0.004%
Travoprost/Timolol opht 0.004%/0.5%