D&T Decisions
...from the District Drugs and Therapeutics Committee
Capital Health
Nova Scotia

Capital Health

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The following policies were approved by the District Medical Advisory Committee (Feb14, Apr14, May14, Jun14) on the recommendation of the District Drugs and Therapeutics Committee (Dec13, Feb14, Apr14, May 14).

I. Additions to Formulary

Boceprevir, *Victrelis™*

Boceprevir increases sustained virologic response at 24 weeks post treatment (SVR24) in genotype 1 chronic hepatitis C by an additional 25%. In three studies comparing placebo with boceprevir [used in combination with peginterferon alpha/ ribavirin (PegIFNα/RBV)] a higher percentage of patients on boceprevir reached a SVR. The benefit of boceprevir was seen in patients who had not received previous treatment, and in patients on PegIFNα/RBV treatment who had not improved enough or had worsened on treatment.

Approved Restriction:
For the treatment of chronic hepatitis C genotype 1 infection in combination with peginterferon alpha/ ribavirin (PegIFNα/RBV), if the following criteria are met:

- detectable levels of hepatitis C virus (HCV) RNA prior to treatment
- fibrosis stage of F2, F3, or F4 as determined by a biopsy/ fibroscan where available

OR

- recommendation of a hepatologist or a prescriber with a specialty in hepatitis
- one course of treatment only (up to 44 weeks duration)

Telaprevir, *Incivek ®*

Telaprevir increases sustained virologic response at 24 weeks post treatment (SVR24) in genotype 1 chronic hepatitis C by an additional 25%. In five double-blind, randomized controlled trials of either treatment-naïve (three trials) or treatment-experienced (two trials) patients treated with peginterferon alpha/ ribavirin (PegIFNα/RBV), a statistically significantly higher percentage of telaprevir treated patients achieved a SVR compared with placebo.

Approved Restriction:
For the treatment of chronic hepatitis C genotype 1 infection in combination with peginterferon alpha/ ribavirin (PegIFNα/RBV), if the following criteria are met:

- detectable levels of hepatitis C virus (HCV) RNA prior to treatment
- fibrosis stage of F2, F3, or F4 as determined by a biopsy/ fibroscan where available

OR

- recommendation of a hepatologist or a prescriber with a specialty in hepatitis
- one course treatment only (12 weeks duration)

Levetiracetam, *Keppra®*

Levetiracetam is a pyrrolidine antiepileptic agent used in the treatment of a variety of seizure types including: generalized tonic-clonic, absence, myoclonic, atonic, simple and complex partial (focal) seizures. Levetiracetam is Health Canada approved as adjunctive therapy in the management of patients with epilepsy who are not satisfactorily controlled by conventional therapy. Although approved as adjunctive therapy, there is some evidence for its use as monotherapy.

Compared to other new antiepileptic agents, levetiracetam has a favorable adverse reaction profile and several favorable pharmacokinetic properties. Since there are no known clinically significant drug interactions, levetiracetam is an option for patients who are on multiple medications. Levetiracetam exerts minimal to no change on hematologic indices, blood chemistry, or liver function tests; therefore, no routine laboratory monitoring is required.

Tamsulosin, *Flomax*

Tamsulosin is an alpha$_1$ adrenergic receptor (AR) antagonist approved by Health Canada for the treatment of lower urinary tract symptoms (LUTS) associated with benign prostatic hyperplasia (BPH). The use of alpha$_1$ AR antagonists relaxes smooth muscle and decreases urethral pressure relieving many of the symptoms of BPH. Alpha$_1$ AR antagonists are also associated with a reduction in blood pressure due to vascular blockade. Three distinct subtypes of the alpha$_1$ AR have been identified: alpha$_{1a}$, alpha$_{1b}$, and alpha$_{1d}$. It has been proposed that alpha$_{1a}$ has a prime role in prostatic contraction and alpha$_{1b}$ is predominantly present in vessel walls. Tamsulosin is claimed to be more selective for the alpha$_{1a}$ subtype; therefore, it is postulated that its selectivity will reduce the incidence of unwanted adverse effects, in particular, reductions in blood pressure (orthostatic hypotension). However, there are no comparative studies of alpha$_1$ AR antagonists that have clearly established that tamsulosin is associated with a lower incidence of cardiovascular effects.

Prostate brachytherapy has recently been implemented at Capital Health and tamsulosin may be utilized as part of this therapy to prevent urinary retention. Tamsulosin has also been used throughout Capital Health to continue patients' established therapy and it is a regular benefit with NS Pharmacare.

Apixaban, *Eliquis*®

Apixaban is an oral direct factor Xa inhibitor. The approved indications for apixaban include the prevention of stroke in patients with atrial fibrillation. Unlike warfarin, it does not require routine monitoring of blood work to ensure therapeutic efficacy.

The AVERROES trial was designed to test the superiority of apixaban versus ASA for stroke prevention in patients who could not tolerate a vitamin k antagonist. This study was terminated early due to the significantly reduced stroke or systemic embolism event rate in patients taking apixaban. The rate of major bleeding was not significantly different between treatment groups.

A large non-inferiority trial (ARISTOTLE) compared apixaban to warfarin in patients with atrial fibrillation and at least one additional risk factor for stroke. Compared to warfarin, apixaban had a significant absolute risk reduction in the primary endpoint of stroke or systemic embolism.

Although there are no direct comparative trials of the novel oral anticoagulants, the current evidence compares each of them to warfarin. Apixaban had a significantly reduced rate of major bleeding compared to warfarin while dabigatran and rivaroxaban had rates similar to that of warfarin. Apixaban was the only novel oral anticoagulant to have a statistically significant reduction in mortality rate when compared to warfarin.

Approved Restriction:
At risk patients with non-valvular atrial fibrillation (AF) who require apixaban for the prevention of stroke and systemic embolism AND in whom:

- Anticoagulation is inadequate following at least a 2-month trial on warfarin;

OR

- Anticoagulation with warfarin is contraindicated or not possible due to inability to regularly monitor via International Normalized Ratio (INR) testing (i.e., no access to INR testing services at a laboratory, clinic, pharmacy, and at home).

II. Revised Restrictions

Paliperidone Palmitate, *Invega Sustenna*®

Paliperidone palmitate is an ester prodrug of the active metabolite of risperidone. At Capital Health, there has been a restriction on the loading dose of prolonged release paliperidone palmitate injectable suspension: "Due to loading dose cost, a switch to paliperidone palmitate should be done directly from another long acting antipsychotic." However, paliperidone has the advantage of monthly maintenance doses that are associated with a reduced treatment cost compared to the every two week regimen for long acting injectable risperidone. Therefore, the paliperidone palmitate loading dose restriction has been removed.

Approved Restriction:
- for patients having problems with compliance on an oral antipsychotic

OR

- for patients who are currently receiving a conventional depot antipsychotic and are experiencing significant side effects (EPS or TD) or lack of efficacy

Argatroban

Argatroban is restricted to patients with heparin induced thrombocytopenia (HIT) who have severe renal impairment or who require hemodialysis. These renal restrictions ensure that danaparoid (the less expensive agent for the treatment of HIT) remains the drug of choice. However, there have been ongoing issues with the availability of danaparoid; therefore, the argatroban restrictions have been revised to allow its use when danaparoid is unavailable:

Approved Restriction:
Maintenance of anticoagulation in patients with presumed or documented heparin induced thrombocytopenia (HIT) who also have severe renal impairment or require hemodialysis. If danaparoid is unavailable, argatroban may be used in patients with HIT who have normal renal function.

III. Removal from Formulary

Tirofiban, *Aggrastat*®

Tirofiban has been removed from the formulary as it is no longer utilized. Integrilin is the glycoprotein inhibitor of choice in the cardiac catheterization laboratory.

IV. Medication Policies

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

MM 05-027	Funding of Drugs and Their Administration in Outpatient Settings
MM 40-010	Intraperitoneal Cancer Chemotherapy Administration

V. IV Manual

New Monographs:
Epoprostenol (Caripul)
Fosaprepitant
Ketamine 1 mg/mL Infusion Table

Revised Monographs:
Alprostadil
Anti-thymocyte globulin (rabbit)
Calcitriol
DOPamine
Hydroxocobalamin
Isoproterenol
Levothyroxine
Methylprednisolone SODIUM SUCCINATE
Milrinone
NORepinephrine
NORepinephrine 16, 32 and 64 mcg/mL Infusion Tables
Papaverine
Propofol
Propranolol
Pyridoxine
Tobramycin
Voriconazole
Zoledronic acid

Removed Monographs:
DOPamine 3200 mcg/mL Infusion Table
Epoprostenol (Flolan brand) – replaced on the Capital Health Formulary by Caripul brand
Mannitol 25% Infusion Table – not stable in PVC bag
Mechlorethamine - removed from the market
Pentastarch – removed from the market
Protirelin - removed from the market
Tirofiban – removed from the Capital Health Formulary

VI. Pre-Printed Orders

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

PPO 0124	Post-Splenectomy Vaccinations
PPO 0397	Tetanus – Diphtheria – Pertussis (Tdap) Vaccination
PPO 0440	Alcohol Withdrawal
PPO 0463	Subcutaneous Opioid Analgesia
PPO 0464	Bendamustine – Rituximab Indolent Non-Hodgkins Lymphoma
PPO 0465	Bendamustine Chronic Lymphocytic Leukemia
PPO 0466	Bowel Routine for Spinal Cord Injury Patients
PPO 0471	Request for Fibrinogen Concentrate
PPO 0472	Cardiac Day Unit – Pacemaker Device Implant
PPO 0473	Cardiac Catheterization Lab and Cardiac Day Unit Post Pacemaker Device Implant
PPO 0474	Rituximab Protocol for Vasculitis
PPO 0254	Therapeutic Abortion
PPO 0285	Continuous Local Anesthetic Infusions (CLAI) Paravertebral or Transversus Abcomininis Plane (TAP) Block
PPO 0468	PACLItaxel IV and Intraperitoneal (IP) with CISplatin IP
PPO 0469	PACLitaxel IV and Intraperitoneal (IP) with CARBOplatin IP
PPO 0475	Prostate High Dose Rate Brachytherapy Pre-operative
PPO 0476	Prostate High Dose Rate Brachytherapy Post-operative
PPO 0478	Cladribine Protocol Hairy Cell Leukemia
PPO 0479	GDP (Gemcitabine, Dexamethasone, Cisplatin) with or without Rituximab Protocol
PPO 0480	Pegylated Liposomal DOXOrubicin/CARBOplatin
PPO 0046	Routine Admission/Transfer to CCU/IMCU/General Cardiology
PPO 0252	Nicotine Replacement Therapy
PPO 0292	Subarachnoid Hemorrhage (SAH) and Post-SAH Cerebral Vasospasm Treatment in Intensive Care Unit
PPO 0399	Erythropoietin
PPO 0481	Colposcopy Clinic Orders
PPO 0483	Orders for the Actively Dying Resident LTC Facility
PPO 0484	Admission Orders – Long Term Care Facility
PPO 0485	Warfarin Maintenance Orders – Long Term Care Facility
PPO 0486	Coronary Care Unit – Additional Routine Orders
PPO 0487	Heart Rhythm Lab – Post Device Implant – Impatient
PPO 0491	Iron Therapy

The information contained in this newsletter may also be accessed online:
http://cdhaintra/departmentservices/pharmacy/Formulary/index.cfm

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