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 (Nov12, Dec12, Jan13) on the recommendation of the District Drugs and Therapeutics Committee (Oct12, Nov12, Dec12).

I. Additions to Formulary

Rilpivirine, *Edurant*®

Rilpivirine, is a non-nucleoside reverse-transcriptase inhibitor that has a Health Canada indication for the treatment of HIV-1 infection when used in combination with other antiretroviral agents in treatment-naive adult patients.

In two double-blind randomized controlled trials, rilpivirine was compared to efavirenz in treatment-naive patients with HIV-1 infection. Both treatment arms were also treated with two additional antiretroviral agents. Rilpivirine was found to be non-inferior to efavirenz, based on the percentage of patients achieving undetectable viral loads (< 50 copies/mL) at 48 weeks. Rilpivirine is less costly than current antiretroviral therapy and offers another treatment option for chronic HIV infection.

Rilpivirine/Tenofovir/Emtricitabine, *Complera*®

Rilpivirine/tenofovir/emtricitabine has a Health Canada indication for use alone as a complete regimen for the treatment of HIV-1 infection in antiretroviral treatment-naive adults. It is a fixed-dose combination of two nucleoside/nucleotide reverse transcriptase inhibitors (emtricitabine and tenofovir) plus a non-nucleoside reverse transcriptase inhibitor (rilpivirine).

One double blind non-inferiority RCT of treatment naïve patients with HIV-1 infection compared rilpivirine to efavirenz. All patients received emtricitabine plus tenofovir. At 48 weeks, the percentage of patients achieving undetectable viral load was approximately equal for rilpivirine and efavirenz. Rilpivirine/tenofovir/emtricitabine is less costly than current antiretroviral therapy and offers another treatment option for chronic HIV infection.

II. Revised Restrictions

Rivaroxaban, *Xarelto*®

Rivaroxaban is on the Capital Health Formulary restricted to use in the prevention of venous thromboembolism (VTE) in total hip (THR) and total knee replacement (TKR) surgery. Treatment has been limited to 14 days. This duration of therapy was added to the criteria as it complied with both the Provincial Formulary as well as the Common Expert Drug Advisory Committee (CEDAC) recommendations.

The cost of rivaroxaban has been reduced significantly. Currently, rivaroxaban is less expensive for VTE prophylaxis as compared to low molecular weight heparins and dabigatran. As a result, the Provincial Formulary changed their criteria for use in VTE prophylaxis in THR to up to 35 days which is supported by clinical trial evidence. The DD&T Committee has recommended that the current Capital Health restrictions be revised for use in VTE prophylaxis for THR surgery for 35 days. The duration of therapy for VTE prophylaxis in TKR surgery will remain the same.

Revised Restriction: For the prophylaxis of venous thromboembolism following total knee replacement and total hip replacement.

- The dose is limited to 10 mg per day for up to 14 days for total knee replacement.
- The dose is limited to 10 mg per day for up to 35 days for total hip replacement.

III. Addition of Restrictions

Meperidine IV, *Demerol IV*®
Prompted by medication error reports as well as the need to standardize and limit the availability of narcotic products to improve patient safety, the Institute for Safe Medication Practices Canada has raised concerns regarding the place of meperidine in hospitals.

Meperidine can cause potentially severe reactions. It is metabolized to an active metabolite normeperidine that has neurotoxic potential, especially in patients with renal dysfunction. Meperidine is reported to have a duration of action between 2-3 hours; however, dosing more frequently predisposes patients to toxicity. Meperidine is poorly tolerated in the elderly and is the opioid most often associated with delirium. There appears to be no specific benefit to meperidine compared to other opioids at equianalgesic doses when compared in clinical trials. Additionally, meperidine's euphoria and mood altering effects make it a poor choice in patients with drug seeking behavior.

After consulting with various clinical services, it was determined that for most clinical situations there are reasonable treatment alternatives to parenteral meperidine. As a result, restricted criteria will be added to IV meperidine:

Restriction:Treatment of drug induced or blood product rigors.

IV. Removal from Formulary

Delavirdene, *Rescriptor*®
The non-nucleoside reverse transcriptase inhibitor delavirdene is no longer used at CDHA and has been removed from the Formulary. The Department of Health and Wellness has also delisted delavirdine from the High Cost Drug Program list.

V. New Guidelines

Pazopanib, *Votrient*®
Approved Use: Advanced or Metastatic Cell Renal Carcinoma

As an alternate single agent for first line treatment of patients with documented evidence of histologically confirmed advanced or metastatic clear cell renal cell carcinoma who have an ECOG performance status of 0 or 1 and are unable to tolerate sunitinib.

Denosumab, *Xgeva*®
Approved Use: Metastatic Castrate Resistant Prostate Cancer

As a single agent for prevention of skeletal related events for metastatic castrate resistant prostate cancer patients with one or more documented bone metastases who have an ECOG performance status of 0 to 2.

Busulfan IV, *Busulfex*®
Approved Use: Myeloablative Regimens for Hematopoietic Stem Cell Transplantation

IV busulfan is a therapeutic option to oral busulfan in common conditioning regimens for allogenic hematopoietic stem cell transplantation.

VI. Revised Guidelines

Sunitinib, *Sutent*®
Approved Use: Advanced or Metastatic Renal Cell Carcinoma

As a single agent first line treatment in patients with documented evidence of histologically confirmed advanced or metastatic clear cell renal cell carcinoma with an ECOG performance status of 0 or 1. In any patient, the following conditions must be met.

- Sunitinib may not be used after another tyrosine kinase inhibitor (i.e. sorafenib or pazopanib) as sequential therapy.
- In the event of significant toxicity, a switch to another tyrosine kinase inhibitor (i.e. sorafenib and pazopanib) may be allowed.

Everolimus, *Afinitor*®
Approved Use: Advanced or Metastatic Renal Cell Carcinoma

As a single agent for metastatic renal cell carcinoma patients with documented clear cell histology who have a Karnofsky performance status of 70% or higher after progression or intolerance of the VEGF multi-targeted tyrosine kinase inhibitors (i.e. sunitinib, pazopanib and/or sorafenib).

Capecitabine, *Xeloda*®
Approved Use: Advanced or Metastatic Breast Cancer

As a single agent or in combination with HER2 directed therapy as one line of therapy in patients with advanced or metastatic breast cancer who have an ECOG performance status of 0 to 2. In any one patient, a capecitabine-based regimen may only be used as one line of therapy for the treatment of metastatic breast cancer.

Approved Use: Colon and Rectal Cancer

Neoadjuvant and Adjuvant Colon and Rectal Cancer

- Neoadjuvant treatment of stage II or stage III rectal cancer as a single agent prior to radiotherapy and/or concurrent with radiotherapy.
- Adjuvant treatment of stage II or stage III rectal cancer as a single agent and/or concurrent with radiotherapy
- Adjuvant treatment of stage III colon cancer as a single agent
- Adjuvant treatment of stage III colon or rectal cancer as part of the XELOX (CAPOX) regimen as an alternative to infusional 5-FU in the FOLFOX regimen

Metastatic Colorectal Cancer

- First line single agent as an alternative to combination chemotherapy
- Alternative to the infusional 5-FU in the FOLFOX regimen as part of the XELOX (CAPOX) regimen

VII. Expanded Guidelines

Imatinib, *Gleevec*®
Approved Use: Primary Gastrointestinal Stromal Tumors

As a single agent for adult patients with a histological diagnosis of localized primary gastrointestinal stromal tumors, which are KIT positive, and have a high risk of recurrence after surgery. The duration of adjuvant therapy with imatinib (400 mg/day) for 36 months is currently recommended.

Bortezomib, *Velcade*®
Approved Use: Multiple Myeloma

In combination with melphalan and prednisone for the treatment of patients with previously untreated multiple myeloma who are not candidates for stem cell transplantation.
OR
In combination (± cyclophosphamide and dexamethasone) or as a single agent in previously untreated multiple myeloma patients who are eligible for stem cell transplantation.
AND/OR
In combination (± cyclophosphamide and dexamethasone) or as a single agent in refractory or relapsed multiple myeloma patients (second line and beyond).

VIII. Medication Policies

The following policies have been approved by the 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 15-010	Immunization by Family Practice Nurses
MM xx-xxx	Parenteral Lidocaine for Neuropathic Pain
MM xx-xxx	Samples Policy
CC 25-023	Parenteral Nutrition (PN)
MM xx-xxx	Nebulized Epoprostenol (Flolan®/Prostacyclin/Prostaglandin I2)
MM 50-015	Diversion and Trading or Abuse of Prescribed Medication
MM 20-036	Over the Counter Medications, Vitamins and Dietary Supplements in Offender Health Services
MM 35-xxx	Methadone Administration – Offender Health Services

IX. Pre-Printed Orders

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

PPO 0397	Pneumococcal, Influenza and Tetanus-Diptheria-Pertussis (Tdap) Vaccine
PPO 0192	Orthopaedic Surgery Post-op Orders
PPO 0426	Orthodpaedic Surgery Pain Management

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

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