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 (Jun13) on the recommendation of the District Drugs and Therapeutics Committee (May13, Jun13).

I. Additions to Formulary

Lanthanum, *Fosrenol*®
Sevelamer, *Renagel*®

Lanthanum and sevelamer are phosphate binding agents indicated for the management of hyperphosphatemia in patients with dialysis dependent end stage renal disease. Secondary hyperparathyroidism, associated hyperphosphatemia and vitamin D deficiency/ resistance are frequently encountered problems in the management of patients with chronic kidney disease. Current clinical strategies to control serum phosphorus levels include: restriction of dietary phosphorus, removal of phosphorus with regular dialysis and inhibiting intestinal absorption of phosphorus with the use of phosphate binders. Phosphate binders fall into one of three categories: heavy metal compounds, calcium-based compounds and nonabsorbable polymers.

Lanthanum carbonate is a heavy metal phosphate binder that is very poorly absorbed from the digestive tract and does not cross the blood-brain barrier. When compared to placebo, control of serum phosphate was achieved in more lanthanum treated patients. In active comparator trials, there were no statistically significant differences in outcome. In the trials comparing lanthanum to calcium based phosphate binders, there were statistically fewer episodes of documented hypercalcemia in lanthanum treated patients. The most common adverse effects during treatment with lanthanum are gastrointestinal symptoms including nausea, vomiting, abdominal cramping and diarrhea.

Sevelamer hydrochloride is a synthetic ion-exchange polymer. A pooled analysis of eight studies reporting on serum phosphate and calcium levels found overall control of phosphate was better with calcium based phosphate binders by approximately 0.1mmol/L; however, the overall serum calcium was lower with sevelamer therapy. The most common adverse effects during treatment with sevelamer hydrochloride are gastrointestinal side effects (dyspepsia, vomiting, peritonitis).

The District Drugs and Therapeutics Committee approved the addition of lanthanum and sevelamer to Formulary with restrictions as per the exception status criteria in the Nova Scotia Pharmacare Formulary:

Approved Restriction:
For the treatment of hyperphosphatemia (>1.8 mmol/L) and calciphylaxis (calcific arteriolopathy) or hypercalcemia after failure on a calcium-based binder.

Asenapine, *Saphris*®

Asenapine is an antipsychotic that functions as an antagonist at dopamine D2, serotonin 5-HT2A, and numerous other dopaminergic, serotonergic, adrenergic and histaminic receptors. It has a lack of affinity for muscarinic receptors. Available as 5mg and 10 mg sublingual tablets, asenapine is administered twice daily.

A review of eight double blind, randomized, controlled trials (RCTs) of asenapine treatment for patients with schizophrenia showed variable results; therefore, the District Drugs and Therapeutics Committee did not approve asenapine for Formulary treatment of schizophrenia.

In a review of three double blind RCTs in patients with current manic or mixed episodes of bipolar I disorder, asenapine was statistically significantly superior to placebo for proportion of remitters and responders. There was no significant difference between asenapine and placebo on most quality of life measures. There was a high frequency of withdrawals in all trials. The frequency of withdrawals due to adverse events was higher for asenapine versus olanzapine. Asenapine and olanzapine had numerically greater increases in body weight versus placebo in all trials.

The District Drugs and Therapeutics Committee approved the addition of asenapine to Formulary with restrictions as per the exception status criteria in the Nova Scotia Pharmacare Formulary:

Approved Restriction:
For the acute treatment of manic or mixed episodes associated with bipolar I disorder as either:

- monotherapy, after a trial of lithium or divalproex sodium has failed, and trials of less expensive atypical antipsychotic agents have failed due to intolerance or lack of response
- co-therapy with lithium or divalproex sodium, after trials of less expensive atypical antipsychotic agents have failed due to intolerance or lack of response

II. Expanded Restrictions

Rituximab, *Rituxan*®

Rituximab is a chimeric mouse/ human antibody that binds specifically to the transmembrane antigen CD20 receptor on B lymphocytes. B lymphocytes regulate immune responses by several mechanisms including producing antibodies and cytokines, presenting autoantigens to naïve T-cells and regulating the activation, differentiation and anergy of T-cells. Rituximab's anti-CD20 mode of action results in selective depletion of lymphocytes and an indirect reduction in the relative counts of activated T-cells. At Capital Health, rituximab has specific restrictions that apply to patients with low grade Non-Hodgkin's lymphoma, newly diagnosed diffuse large B-cell lymphoma, chronic lymphocytic leukemia, rheumatoid arthritis and systemic lupus erythramatosus.

Granulomatosis with polyangitis (GPA, also known as Wegener's granulomatosis) and microscopic polyangitis (MPA) are systemic small vessel vasculitides with predilection for the respiratory tract and kidneys. Managing patients with GPA and MPA is challenging due to the refractory and relapsing nature of the disease and the toxicities associated with the first line therapies (i.e., cyclophosphamide and corticosteroids). Two controlled trials (RITUXVAS and RAVE) indicate that rituximab has similar efficacy and safety to cyclophosphamide in patients with GPA and MPA.

The District Drugs and Therapeutics Committee approved the expansion of the Formulary restrictions for rituximab to include GPA and MPA as per the exception status criteria in the Nova Scotia Pharmacare Formulary:

Approved Restriction:
For the induction of remission in patients with severely active granulomatosis with polyangitis (GPA) or microscopic polyangitis (MPA) who have severe intolerance or other contraindication to cyclophosphamide, or who have failed an adequate trial of Cyclophosphamide.

III. Revised Guidelines

Doxorubicin, pegylated liposomal, *Caelyx*®

Approved Use:
In combination with carboplatin for the retreatment of platinum sensitive recurrent ovarian carcinoma patients who relapse six months or longer after receiving previous platinum based therapy (e.g. paclitaxel/carboplatin) as a therapeutic option where combination therapy is preferred.

This criteria is in addition to the previously approved indication as a single second line (and subsequent) agent in patients who have documented evidence of advanced or recurrent ovarian carcinoma with an ECOG performance status of 0-2, failed first line platinum based therapy (e.g. paclitaxel/carboplatin) and require a therapeutic intervention with chemotherapy.

For any one patient, a pegylated liposomal doxorubicin regimen (either alone or in combination) may only be used as one line of therapy for the treatment of advanced or recurrent ovarian carcinoma.

Nilotinib, *Tasigna*®

Approved Use:
First Line: As a single first line agent for the treatment of adults with chronic phase CML.

Second Line: As a single second line agent for the treatment of adults with chronic or accelerated phase CML with resistance or intolerance to prior therapy.

These second line criteria include:

1. Patients with CML in chronic phase who are intolerant to oral tyrosine kinase inhibitors (TKIs) (i.e. imatinib or dasatinib or both).
2. Patients with CML in chronic phase who are resistant to imatinib.
3. Patients with CML that have progressed to accelerated phase while on imatinib therapy.

- In any one patient, only two of the TKIs will be funded within these criteria during their lifetime.
- If a patient develops grade 3 or 4 toxicity to one of the TKIs used within 3 months of initiating therapy, access to a third agent will be funded.
- Sequential use of nilotinib and dasatinib is not permitted except in the circumstance described above (i.e. grade 3 or 4 toxicity).

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 05-025	Administrative Authorization for High-cost Non-formulary, Special Access and Restricted Drugs
MM 20-004	Insulin Dose Adjustment
MM 50-010	High Alert Medication
MM 50-xxx	Independent Double Check

V. 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 0192	Orthopaedic Surgery Post Op Orders
PPO 0111	Magrath Protocol Burkitt's Lymphoma – Regimen A (Codox-M) Plus Rituximab
PPO 0112	Magrath Protocol Burkitt's Lymphoma – Regimen B (IVAC) Plus Rituximab – High Risk Patients Only
PPO 0186	Multimodal Pain Management – Pre-op Arthroplasty
PPO 0189	Multimodal Pain Management – Post-op Arthroplasty
PPO 0424	Hemochromatosis Phlebotomy Standing Orders
PPO 0426	Pain Management – Orthopedic Surgery
PPO 0429	Cetuximab- Metastatic Colorectal Regimen
PPO 0430	Gemcitabine/ Cisplatin – Advanced Biliary Tract Regimen
PPO 0435	Post-op Open Heart Surgery
PPO 0452	Family Medicine Admission Order
PPO 0431	Euro-Lupus CycloPhosphamide Protocol for Lupus Nephritis

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

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Editor: Deborah MacIntyre, B.Sc. (Pharm.)
Drug Information

Tel: (902) 473-4248
Email: debbie.macintyre@cdha.nshealth.ca