# D&T Decisions

*... from the Drugs and Therapeutics Committee*

nova scotia health authority


## Central Zone


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The following policies were approved by the Medical Advisory Committee (Nov15, Jan16) on the recommendation of the Drugs and Therapeutics Committee (Oct15, Dec15).

# I. Additions to Formulary

### Ocriplasmin, *Jetrea*®

Ocriplasmin is a recombinant truncated form of human plasmin that is administered by intravitreal injection for the treatment of symptomatic vitreomacular adhesion (VMA).

The vitreous body is adhered to the retina by proteoglycans including laminin, collagen and fibrinectin. During the natural aging process, vitreous gel undergoes liquefication and the vitreous body shrinks in size resulting in weakening vitreoretinal adhesions and detachment of the posterior vitreous from the retina. VMA occurs when the posterior vitreous remains partially attached to the macula. This causes focal traction that can pull on the macula and result in distorted vision, decreased visual acuity, central vision loss, macular edema and the formation of macular holes. Ocriplasmin has proteolytic activity against the proteoglycan components of the vitreous, thus dissolving the VMA and releasing the associated tractional force on the macula.

Ocriplasmin is administered on an outpatient basis and is not dispensed from the Central Zone Pharmacy. The cost of the medication will be coordinated with patients and third party insurance providers by a patient assistance program. Although there is no direct cost of the medication to the NSHA Central Zone, ocriplasmin was reviewed and added to Formulary because it is administered in a Central Zone clinic.

**Approved Restriction**:
For the treatment of symptomatic vitreomacular adhesion (VMA) if the following clinical criteria and conditions are met:
- diagnosis of VMA should be confirmed through optical coherence tomography
- patient does not have any of the following: large diameter macular holes (> 400 micrometre), high myopia (> 8 dioptre spherical correction or axial length > 28 millimetre), aphakia, history of retinal detachment, lens zonule instability, recent ocular surgery or intraocular injection (including laser therapy), proliferative diabetic retinopathy, ischemic retinopathies, retinal vein occlusions, exudative age-related macular degeneration, or vitreous hemorrhage

Conditions:
- Ocriplasmin should be administered by a retinal specialist or by a qualified ophthalmologist experienced in intravitreal injections
- Treatment with ocriplasmin should be limited to a single injection per eye (i.e., retreatments are not covered)

# II. Expanded Restrictions

### Duloxetine, *Cymbalta*®

Duloxetine is indicated for major depressive disorder, generalized anxiety disorder, neuropathic pain associated with diabetic peripheral neuropathy, chronic low back pain, and the management of pain associated with fibromyalgia and osteoarthritis of the knee. Duloxetine is currently listed on the Central Zone Formulary for patients with treatment resistant depression. At the time of this decision, it was requested that duloxetine also be reviewed for its pain indications.

Duloxetine acts as a serotonin (5HT) and norepinephrine (NE) reuptake inhibitor (SNRI). It is proposed that by inhibiting the uptake of these neurotransmitters, duloxetine enhances descending inhibitory pain pathways. Despite the multiple pain indications, the Canadian Drug Expert Committee (CDEC) of the Common Drug Review (CDR) recommended that duloxetine only be listed for neuropathic pain in diabetic patients; therefore, this is also the only indication approved as a NS Pharmacare benefit.

Studies have shown that duloxetine is superior to placebo for the reduction of neuropathic pain associated with diabetic

neuropathy and the Canadian Pain Society Guidelines recommend duloxetine as a first line agent for this indication.

**Approved Restriction**:
For the treatment of neuropathic pain in diabetic patients who are unresponsive to two adequate courses of less costly alternative agents such as tricyclic antidepressant agent or an anticonvulsant agent. The dose of duloxetine should be limited to a maximum of 60 mg daily.

### Meropenem, *Merrem*®

Meropenem and imipenem are carbapenem antibiotics with similar spectrum of activity. Meropenem may be more effective against gram negatives (one fold lower MIC activity) and imipenem may be more effective against gram positives (one fold lower MIC activity); however, the clinical significance of this is unclear.

In 2011, imipenem became the Formulary carbapenem of choice with the approval of a therapeutic interchange of meropenem orders to imipenem. This switch to imipenem was associated with cost savings. In 2013, the non-formulary status of meropenem was reevaluated because of superior CNS penetration. Meropenem was added to the Formulary, restricted to Infectious Diseases for CNS infections.

Meropenem is now less costly than imipenem; therefore, meropenem has been approved as the Formulary carbapenem of choice. Imipenem orders will be therapeutically interchanged to meropenem.

**Approved Restriction**:
The treatment of documented resistant infections or where resistance to piperacillin-tazobactam or third-generation cephalosporins is likely, resistant infections in cystic fibrosis patients, central nervous system infections, endophthalmitis infections, or on the recommendation of the Division of Infectious Diseases.

## III. Removal of Restrictions

### Zoledronic acid, *Zometa*®

Zoledronic acid is a potent bisphosphonate eliminated by renal excretion. Renal impairment (current or pre-existing), concomitant use of nephrotoxic drugs and dehydration may increase the potential for deterioration of renal function. Assessment of renal function and serum albumin-corrected calcium are recommended.

There are two zoledronic acid products available in Canada: the Zometa concentrate (4 mg/ 5 mL solution) and Aclasta (5 mg/ 100 mL ready to use bottle). These products have different indications and have separate Formulary restrictions.

The restrictions for zoledronic acid concentrate (Zometa) ensure that pamidronate is the Formulary drug of choice for metastatic bone disease. The availability of generics has resulted in a reduction in the cost of zoledronic acid and the concentrate solution is now a less expensive option than pamidronate; therefore, the restrictions for zoledronic acid concentrate (Zometa, generics) have been removed from the Formulary.

Zoledronic acid 5 mg/ 100 mL ready to use bottle (Aclasta, generics) will remain restricted as a single agent for the treatment of Paget's disease of the bone.

## IV. Therapeutic Interchange

### Imipenem/ meropenem

The following therapeutic interchanges have been approved for imipenem (therapeutic interchange to meropenem) and meropenem (therapeutic dosage interchange).

| Preparation: | Dispensed As: |
|---|---|
| Imipenem/ cilastatin<br>- 250 mg IV q12h<br><br>- 500 mg IV q12h<br><br>- 500 mg IV q8h<br><br>- 250 mg IV q6h<br>- 500 mg IV q6h<br>- 1 g IV q8h<br><br>- 2 g IV q8h* | Meropenem<br>- 500 mg IV q24h<br><br>- 500 mg IV q12h<br><br>- 500 mg IV q8h<br><br>- 500 mg IV q6h<br>- 500 mg IV q6h<br>- 500 mg IV q6h<br><br>- 1 g IV q6h<br>OR<br>- 2g IV q8h*<br><br>*dose is 2 g IV q8h for treating CNS, cystic fibrosis, or endophthalmitis infections |

| Preparation: | Dispensed As: |
|---|---|
| Meropenem<br>- 1 g IV q8h<br>- 2 g IV q8h* | Meropenem<br>- 500 mg IV q6h<br>- 1 g IV q6h |
| *dose is not interchanged if treating CNS, cystic fibrosis, or endophthalmitis infections | |

## V. Removal from Formulary

### Lorazepam sublingual, *Ativan*®

Lorazepam is an intermediate-acting benzodiazepine commonly used for anxiety, sedation, seizures, and treatment of alcohol withdrawal. Lorazepam is available as both oral and sublingual tablets. The oral tablet is less expensive than the sublingual tablet and limited data indicate that the lorazepam oral tablet can be administered under the tongue. A Canadian pharmacokinetic study comparing the sublingual administration of both the oral and sublingual tablet formulations found similar peak plasma concentrations and time to peak concentrations. The oral tablet given sublingually took longer to dissolve (1.1 minutes versus 0.3 minute), had significantly lower systemic availability and a significantly lower AUC compared to the sublingual tablet.

The benefits of removing lorazepam sublingual tablets from the Formulary include Formulary streamlining with other Zones, alignment with the NS Pharmacare Formulary and minor cost savings. Lorazepam oral tablets will be dispensed for administration by both the oral and sublingual route.

### Imipenem, *Primaxin*®

The removal of imipenem from the Formulary has been approved. The therapeutic interchange of meropenem to imipenem will also be removed from the Formulary.

# VI. New Guidelines

### Eribulin, *Halaven*®

**Approved Use**:
As a single agent for the treatment of metastatic or incurable locally advanced breast cancer for patients who have received previous treatment with a taxane and an anthracycline (in either the adjuvant or metastatic setting), and at least two prior chemotherapy regimens for metastatic or locally advanced disease with evidence of disease progression and an ECOG performance status (PS) ≤ 2.

### Obinutuzumab, *Gazyva*®

**Approved Use**:
In combination with chlorambucil for patients with previously untreated chronic lymphocytic leukemia (CLL) or small lymphocytic leukemia (SLL) who have adequate renal function for whom fludarabine based treatment is considered inappropriate.

# VII. Medication Policies

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

| | |
|---|---|
| MM 50-015 | Diversion, Trading or Abuse of Prescribed Medication |
| MM 35-011 | Methadone Administration – Offender Health Services |

# VIII. IV Manual

**New Monographs:**
Ferumoxytol
Temsirolimus

**Revised Monographs:**
Acyclovir
Amikacin
Calcium chloride
Ciprofloxacin
DOPamine
epHEDrine
Epoprostenol (Caripul)
Fluconazole
Gentamicin
Insulin
Methylene blue
Metronidazole
Piperacillin
Ranitidine

**Removed Monographs:**
Black Widow Spider antivenin – Special Access Program (IWK Regional Poison Centre website contains necessary information)
Droperidol – removed from Canadian market
Indigo carmine - removed from Canadian market
Appendix "Guidelines for the Management of Extravasation of Cancer Chemotherapy Agents" – updated information now contained in Administration of Cancer Chemotherapy Policy (MM 40-005)

# IX. Pre-Printed Orders

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

| | |
|---|---|
| PPO 0012 | Patient Controlled Analgesia – DGH Site |
| PPO 0291 | Intensive Care Unit Admission |
| PPO 0358 | Dexmedetomidine for ICU Sedation |
| PPO 0391 | Negative Pressure Wound Therapy |
| PPO 0427 | Systemic Therapy Regimen Change Form |
| PPO 0519 | Pre-op Kidney and Kidney/Pancreas Transplant |
| PPO 0520 | Post-op Kidney and Kidney/Pancreas Transplant |
| PPO 0523 | Central Diabetes Insipidus – Post-Operative Management |
| PPO 0534 | Azacitidine for Intermediate-2 or High Risk Myelodysplastic Syndrome or Acute Myelogenous Leukemia |
| PPO 0535 | Panitumumab – Metastatic Colorectal Cancer |

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

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