Vancouver Coastal Health
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PHARMACY AND THERAPEUTICS NEWSLETTER

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In This Issue...

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Changes to Formulary

In order to align with the provincial BCHA Formulary, the following medications have been stocked or deleted at Vancouver Acute.

Additions

1. Lacosamide 50 mg, 100 mg, 200 mg tablets, 10 mg/mL injection (Vimpat®)

- Antiepileptic drug
- Restricted to adjunctive therapy for refractory partial-onset epilepsy, status epilepticus where other suitable anti-epileptic agents have been ineffective, or for patients on this medication prior to admission. The IV formulation is restricted to patients unable to take lacosamide PO.

Deletions

1. Clotrimazole 100 mg troche

- Alternative: Nystatin suspension

2. Pilocarpine 4% gel (Pilopine HS®)

- Discontinued by manufacturer

Updated Policies

1. METHADONE CONCENTRATION CHANGE

Methadone oral solution 10 mg/mL strength is now the standard formulation in the community. To align with the community and decrease the risk of medication errors, on March 6, 2014, the methadone concentration stocked at VA was changed from 1 mg/mL to 10 mg/mL strength. To prevent dosing errors:

- Methadone doses should be written and communicated in terms of **mg** rather than in mL.
- Pharmacy will clarify all methadone doses prescribed in mL.
- Be aware that methadone concentration on a patient's PharmaNet profile or Medication Reconciliation (Med Rec) form may differ from the methadone concentration that is currently available. There may be multiple methadone entries with different concentrations on the PharmaNet profile or Med Rec form.

2. ENDOCARDITIS PROPHYLAXIS NOT INDICATED FOR GI/GU PROCEDURES

Administration of antibiotics solely to prevent infective endocarditis (IE) is no longer recommended for patients undergoing genitourinary (GU) or gastrointestinal (GI) tract procedures, including diagnostic

esophagogastro-duodenoscopy or colonoscopy.[1] There is no data to either support a link between GI or GU tract procedures and development of IE, nor demonstrate that the administration of antimicrobial prophylaxis prevents IE in association with these procedures.[1] Only in high risk patients with active GI/GU infection undergoing GI/GU procedures, coverage for *Enterococcus* should be provided (ie. amoxicillin/ampicillin, or vancomycin in pencillin-allergic patients)

Reference

[1] Wilson W et al. Prevention of Infective Endocarditis. Circulation 2007;115:1736-54.

New Drugs/Drug Products

FERUMOXYTOL (FERAHEME®)

Rince Wong, B.Sc.(Pharm); Karen Shalansky, Pharm.D.

Ferumoxytol is a new IV iron formulation approved by the BCHA P&T Committee for use in patients with chronic kidney disease (CKD), or in non-CKD iron deficient patients who cannot tolerate other IV iron preparations. The advantage of ferumoxytol is that it may be administered at a faster infusion rate than currently available iron formulations.

Pharmacology

Ferumoxytol is a superparamagnetic iron oxide nanoparticle with a carbohydrate shell. The carbohydrate shell lowers the amount of bioactive iron released into the bloodstream before it reaches the reticuloendothelial system (RES), which may decrease the incidence of hypersensitivity reactions compared to other IV iron formulations. Once the iron enters the RES, it is stored as part of the ferritin complex or incorporated into immature red blood cells within 24 hours, thereby increasing iron stores and bound iron.[1] Ferumoxytol is not dialyzable due to its high molecular weight.

Adverse events

The major adverse effects reported with ferumoxytol are hypotension, peripheral edema, injection site reaction (erythema, swelling), nausea, vomiting, diarrhea, constipation, and dizziness. Rarely, anaphylaxis or anaphylactoid reactions, and arthralgias (joint, back pain) can occur. The superparamagnetic iron core of ferumoxytol can interfere with the interpretation of magnetic resonance imaging (MRI) and the manufacturer recommends delaying MRI studies for a minimum of 3 months after the last dose of ferumoxytol. Table 1 lists the duration of effect of ferumoxytol on specific MRI locations.[3] Note that ferumoxytol does not interfere with other radiological tests such as X-ray, CT, ultrasound or nuclear medicine imaging.

Dosage and Monitoring

Ferumoxytol is available as a 510 mg IV injection given in 1-2 doses spaced 2-7 days apart for repletion of iron stores. Each 510 mg dose of ferumoxytol can be administered over 17 seconds, although VA recommendations are to administer over 60 seconds. Patients should be monitored for 30 minutes after each dose for hypersensitivity reactions and hypotension. Iron studies (ferritin and transferrin saturation (TSAT)) should be taken 4 weeks after repletion to assess for efficacy, then routine iron studies should be done every 3 months to identify patients who require further repletion. Ferumoxytol has not been studied for maintenance dosing; oral iron should be continued as maintenance therapy.

Table 1. Anticipated Effects on MRI Following Ferumoxytol Therapy[3]

Location of MRI	Affected by Ferumoxytol	Onset of Effect	Duration of Effect
CNS	No effect in healthy tissue	Not applicable	Not applicable
Liver and spleen	Yes	Immediately after dose	Greater than 30 days
Vasculature	Yes	Immediately after dose	1-2 days, possibly longer
Kidney	Yes	Immediately after dose	Unknown, likely similar to vasculature effects
Lymph nodes	Yes	1-3 days after dose	Greater than 30 days
Bone marrow	Unknown	Unknown	Unknown
Bone, muscle, fat	No effect in healthy tissue	Not applicable	Not applicable

Comparative data

There are currently no published trials comparing ferumoxytol to other IV iron formulations on the market; only two studies have compared ferumoxytol to oral iron.[4,5] Ferumoxytol was compared to oral ferrous fumarate in prospective, open label, phase III clinical trials in both hemodialysis[4] (HD, n=230) and CKD[5] patients (n=304). After 35 days, increases from baseline hemoglobin, ferritin, and TSAT levels were significantly greater in the ferumoxytol IV group (510-1020 mg) compared to those receiving oral ferrous fumarate (200 mg elemental iron daily) or other oral iron formulations.[4,5] The number of patients requiring further iron repletion treatment was also lower in the ferumoxytol group.[4] Serious adverse events in the HD group included hypotension (n=2, ferumoxytol arm), cellulitis (n=2, ferrous fumarate arm), and COPD exacerbation (n=2, ferrous fumarate arm).[4] In the CKD group, adverse events occurred in 10.6% of ferumoxytol patients (dizziness, nausea, diarrhea) and 24% in the oral iron group (nausea, vomiting, diarrhea, constipation, abdominal pain).[5]

Place in therapy

Ferumoxytol is currently restricted to ambulatory CKD patients registered with the B.C. Provincial Renal Agency (BCPRA) ie. pre-dialysis, peritoneal dialysis or home HD patients who are intolerant to or inadequately treated with oral iron. Ferumoxytol is also approved for use in patients on intermittent HD or in non-CKD patients who experience adverse events with other available IV iron preparations. Ferumoxytol has the advantage of requiring fewer doses for iron repletion due to the larger dose of iron that can be given with each administration. This, along with its fast administration rate, translates to shorter and fewer visits to a facility for iron repletion. The cost of ferumoxytol is comparable to that of iron sucrose, which is also commonly used for iron repletion in the outpatient setting (Table 2).

References

1. McCormack PL. Ferumoxytol. Drugs 2012;72:2013-22.
2. Schwenk MH. Ferumoxytol: A new intravenous iron preparation for the treatment of iron deficiency anemia in patients with chronic kidney disease. Pharmacotherapy 2010;30:70-9.
3. Anon. Feraheme injection: Effects on Magnetic Resonance Images. AMAG Pharmaceuticals, Inc. January 2011.
4. Provenzano R *et al*. Ferumoxytol as an intravenous iron replacement therapy in hemodialysis patients. Clin J Am Soc Nephrol 2009;4:386-93.
5. Spinowitz BS et al. Ferumoxytol for treating iron deficiency anemia in CKD. J Am Soc Nephrol 2008;19:1599-1605.
6. Moist LM et al. CSN Commentary on the 2012 KDIGO clinical practice guidelines for anemia. AJKD 2013;62:860-73.
7. Shalansky K *et al*. Iron indices after administration of sodium ferric gluconate complex in hemodialysis patients. AJKD 2011;58:684-5.

Table 2. Comparison of IV Iron Products

Drug	Iron Dextran (Dexiron®)	Iron Sucrose (Venofer®)	Sodium Ferric Gluconate (Ferrlecit®)	Ferumoxytol (Feraheme®)
Test Dose	Yes	No	No	No
Maximum Infusion Rate (at VA)	100 mg/h	100 mg/h	125 mg/h	510 mg over 60 seconds[a]
Maximum Allowable Single Dose (at VA)	1000 mg	300 mg	125 mg	510 mg
Repletion Dose	1000 mg IV over 6-8 hrs (or in increments of 100-500 mg administered 2-7 days apart)	900-1000 mg given in increments of 100-300 mg administered 2-7 days apart	1000 mg given in increments of 125 mg x 8 doses administered 2-3 days apart	1020 mg given in 2 doses of 510 mg administered 2-7 days apart
Timing for Retesting Iron Studies[1,6]	14 days after last dose	48 hours after last dose	7 days after last dose[7]	4 weeks after last dose

[a]recommended to be given over 60 seconds at VA, however, 510 mg can be administered over 17 seconds per product monograph

PARENTERAL ANTIBIOTIC ALLERGY CROSS-SENSITIVITY CHART (ASPIRES, 2014)

The Parenteral Antibiotic Allergy Cross-Sensitivity chart has been updated. Current literature suggests that the cross-reactivity between penicillins and cephalosporins is < 1% (~ 0.1% of patients without skin-test-confirmed penicillin allergy, 0.1% for those with mild reactions to penicillin, and 2% for patients who are penicillin skin test-positive). The 1st generation cephalosporins have the highest cross-reactivity. For carbapenems (e.g. meropenem), cross-reactivity with penicillins is estimated to be ~1%. The main changes to the chart are as follows:

- **For <u>non-anaphylactic</u> beta-lactam allergies, a 2nd or 3rd generation cephalosporin or carbapenem may be considered with montoring;**
- **For <u>anaphylactic</u> reactions to beta-lactams, a carbapenem may be considered with close monitoring since its cross-sensitivity is relatively low.**

If you would like a copy of this revised chart, please contact Karen Shalansky at 604-875-4839.

	Amikacin	Ampicillin	Azithromycin	Cefazolin	Cefotaxime	Cefoxitin	Ceftazidime	Ceftriaxone	Cefuroxime	Ciprofloxacin	Clindamycin	Cloxacillin	Cotrimoxazole\	Daptomycin	Ertapenem	Erythromycin	Gentamicin	Imipenem	Levofloxacin	Meropenem	Metronidazole	Moxifloxacin	Penicillin	Piperacillin	Streptomycin	Ticarcillin	Tigecycline	Tobramycin	Vancomycin
Amikacin																	X								X			X	
Ampicillin				X	*	*	*	*	*			X			**			**		**			X	X		X			
Azithromycin																X													
Cefazolin		X			X	X	X	X	X			X			**			**		**			X	X		X			
Cefotaxime		*		X		X	X	X	X			*			**			**		**			*	*		*			
Cefoxitin		*		X	X		X	X	X			*			**			**		**			*	*		*			
Ceftazidime		*		X	X	X		X	X			*			**			**		**			*	*		*			
Ceftriaxone		*		X	X	X	X		X			*			**			**		**			*	*		*			
Cefuroxime		*		X	X	X	X	X				*			**			**		**			*	*		*			
Ciprofloxacin																			X			X							
Clindamycin																													
Cloxacillin		X		X	*	*	*	*	*						**			**		**			X	X		X			
Cotrimoxazole																													
Daptomycin																													
Ertapenem		**		**	**	**	**	**	**			**						X		X			**	**		**			
Erythromycin			X																										
Gentamicin	X																								X			X	
Imipenem		**		**	**	**	**	**	**			**			X				X				**	**		**			
Levofloxacin										X										X		X							
Meropenem		**		**	**	**	**	**	**			**			X			X					**	**		**			
Metronidazole																													
Moxifloxacin										X									X										
Penicillin		X		X	*	*	*	*	*			X			**			**		**				X		X			
Piperacillin		X		X	*	*	*	*	*			X			**			**		**			X			X			
Streptomycin	X																X											X	
Ticarcillin		X		X	*	*	*	*	*			X			**			**		**			X	X					
Tigecycline																													
Tobramycin	X																X								X				
Vancomycin																													

* = May consider using if non-anaphylactic reaction to the penicillin or cephalosporin; monitor closely

** = There is little potential for cross-reactivity between penicillin/cephalosporins and carbapenems; however, monitor closely if previous anaphylactic reaction to penicillins or cephalosporins

X = Potential for cross-sensitivity

Blank = Not cross-sensitive