Vancouver CoastalHealth
Promoting wellness. Ensuring care.

PHARMACY AND THERAPEUTICS NEWSLETTER

A publication of the CSU Pharmaceutical Sciences
Vancouver General Hospital, UBC Hospital, GF Strong

November 2015 ` *Volume 22 Number 3*

In This Issue...

This and previous editions of the VA Pharmacy and Therapeutics Newsletters are located on the Web at **www.vhpharmsci.com**

Changes to Formulary

The following medication changes have been implemented at VA in accordance with the BC Health Authorities (BCHA) Formulary.

Deletions

1. Prochlorperazine injection (Stemetil®)

- Discontinued by manufacturer
- Alternatives for PONV: ondansetron, metoclopramide, dimenhydrinate

2. Diazoxide capsules (Proglycem®)

- Alternatives for hypertensive urgencies: captopril, clonidine, labetalol, prazosin

3. Iodoquinol (diiodohydroxyquinoline) capsules (Diodoquin®)

- Discontinued by manufacturer

Updated Policies

1. AMIODARONE IV CONCENTRATIONS

For standardization across Lower Mainland sites, the amiodarone concentration for central line administration has been revised to 900 mg/250 mL (3.6 mg/mL). The standard peripheral line concentration remains the same at 450 mg/250 mL (1.8 mg/mL). The on-line PDTM has been updated.

2. INHALER CORTICOSTEROID THERAPEUTIC INTERCHANGE REVISION

Mometasone has been added to the inhaled corticosteroid interchange (Table 1).

Table 1. Inhaled Corticosteroid Therapeutic Interchange*

Inhaler Ordered	Inhaler Dispensed
Beclomethasone dipropionate (QVAR®) 100 mcg	Fluticasone 125 mcg (same number of puffs and frequency)
Ciclesonide (Alvesco®) 200 mcg once daily	Fluticasone 125 mcg BID
Cicelsonide (Alvesco®) 400 mcg once daily	Fluticasone 250 mcg BID
Cicelsonide (Alvesco®) 400 mcg BID	Fluticasone 500 mcg BID
Mometasone (Nasonex®) 200 mcg BID ****OR**** Mometasone (Nasonex®) 400 mcg daily	Fluticasone 250 mg BID
Mometasone (Nasonex®) 400 mcg BID	Fluticasone 500 mcg BID

***Exclusion:** Patients on Highly Active Anti-retroviral Therapy (HAART)

EDITORIAL STAFF:
Karen Shalansky, Pharm.D., FCSHP
Tim Lau, Pharm.D., FCSHP
Jane Day, B.Sc.(Pharm.), ACPR
Nilu Partovi, Pharm.D., FCSHP
Any comments, questions, or concerns with the content of the newsletter should be directed to the editors. Write to CSU Pharmaceutical Sciences Vancouver General Hospital, 855 W12th Ave, Vancouver BC V5Z 1M9, send a FAX to 604-875-5267 or email karen.shalansky@vch.ca
Find us on the Web at **www.vhpharmsci.com**

PHENYTOIN CLINICAL PEARLS

Ricky Turgeon, Pharm.D., Harjinder Parwana, Pharm.D.

A. Can phenytoin capsules be opened?

- There is no clinical need to open phenytoin capsules in patients with swallowing difficulties, as oral suspension is readily available. For patients on puree diets, the suspension can be mixed with apple sauce.

B. Why should oral phenytoin doses greater than 400 mg/day be split?

- Phenytoin undergoes saturable absorption due to low solubility in the GI tract, leading to slower absorption and an increase in time to maximum concentration (t_{max}) as the dose increases; this may lead to erratic absorption due to variations in GI motility.[1] For example:
  - ⇒ Phenytoin 400 mg: t_{max} 8.4 hrs
  - ⇒ Phenytoin 800 mg: t_{max} 13.2 hrs
  - ⇒ Phenytoin 1600 mg: t_{max} 31.5 hrs
- Oral/NG doses above 400 mg should be split to allow for more consistent absorption. IV maintenance therapy follows this same rule to facilitate conversion to PO therapy.

[1] Clin Pharmacol Ther 1980;28:479-485.

C. Do PO/NG suspension and IV formulations of phenytoin require BID or TID dosing?

- Phenytoin oral absorption is erratic; the fraction absorbed is dependent on dose and formulation.
- Phenytoin elimination is concentration-dependent due to saturable kinetics.
- The half-life of phenytoin is relatively long ($t_{1/2}$ ~22 hrs); once-daily dosing should achieve similar trough concentrations to TID dosing.
- Propylene glycol in the phenytoin IV solution may cause hypotension at higher concentrations or in susceptible patients (e.g. spinal cord injury patients); if hypotension is exhibited, the infusion rate can be prolonged or the dose may be split.
- In summary, maintenance doses of 400 mg/day or less should generally be given once daily.
  Exceptions (reasons to split the dose):
  - ⇒ Patients with breakthrough seizures at end of dosing interval while on once-daily dosing
  - ⇒ Patients on larger doses getting peak concentration-related adverse drug effects (e.g. sedation).

D. Should we always give a phenytoin load?

- An IV load should always be used when there is an immediate need to achieve a therapeutic phenytoin level.
- An IV load is preferred over a PO load as oral absorption is unpredictable and it could take up to 24 hours after the completion of a PO load to reach a therapeutic concentration.

E. How do we taper phenytoin off?

Tapering of phenytoin is dependent on the specific situation. In most cases, antiepileptics with long half-lives (similar to phenytoin) will self taper when stopped. See examples below:

- For severe cutaneous reactions (e.g. rash, Steven-Johnson's): discontinue immediately; no taper.
- For head injury prophylaxis: stop after 7 days of treatment; no taper required.
- When changing to a new anti-epileptic drug for monotherapy: cross-taper based on half-life of the new anti-epileptic agent being added.
- If seizure-free for an extended period (2 years or more): taper down by 100 mg every 1 to 2 weeks and continue as long as seizure-free.
  - ⇒ Note: There is no standardized tapering regimen
  - ⇒ If recent seizure, then taper more slowly
  - ⇒ There is no need to wean in increments smaller than 100 mg/day.

F. Are random phenytoin levels useful?

- When a patient is actively seizing, random phenytoin levels are most useful to determine the patient-specific therapeutic level (i.e. to determine if level is subtherapeutic or if patient requires a higher level within the therapeutic range).
  - ⇒ Note: When at steady-state, random levels should reflect a trough level but this cannot always be assumed without clearly knowing the patient's dosing compliance.
- When a patient is not actively seizing, a random phenytoin level does not offer any benefit. For routine monitoring and dose adjustments, trough levels are required.

G. In patients with a phenytoin-induced rash, what are the anti-epileptic alternatives?

Table 2. Phenytoin-induced Rash: Antiepileptic Medication Alternatives

AVOID	SAFE TO ADMINISTER
• Carbamazepine, Eslicarbazepine, Oxcarbazepine • Lamotrigine • Phenobarbital, Primidone • Phenytoin	• Clobazam • Gabapentin, Pregabalin • Lacosamide • Levetiracetam • Topiramate • Valproic acid