Tolvaptan/conivaptan Formulary Review

A review of tolvaptan and conivaptan was presented to the P&T Committee for addition to the adult formulary. Tolvaptan and conivaptan are selective vasopressin V2 receptor antagonists. Tolvaptan and conivaptan were approved for addition to the adult formulary with the following restrictions:

A. Patients with euvoletic or hypervolemic hyponatremia (SIADH, heart failure and cirrhosis) who have failed fluid restriction
   a. Fluid restriction is defined as 1.2 liters every 24 hours x 2 days
B. Serum sodium < 125mEq/L and plasma osmolality < 285 mOsm/kg
C. Must NOT have hypovolemic hypotonic hyponatremia or signs of dehydration.
D. Must have serum sodium monitored every 6 hours for the first 24 hours then daily
E. Patient is not receiving potent CYP3A4 inhibitors
F. Patient is not anuric
G. Failure of diuretics if concomitant heart failure exacerbation (>\= 120 mg intravenous furosemide or equivalent daily x48 hours)
H. Automatic 4 day stop for tolvaptan
I. An MD documentation form and a Cerner order set that includes required monitoring will be developed to promote appropriate and safe use of these medications. Note: Neither tolvaptan nor conivaptan will be added to the formulary until this is completed, which is expected to be sometime in March 2013

Clinical Pearls
Dosing/Administration: The starting dose of tolvaptan is 15 mg once daily. Tolvaptan maintenance dose can be increased at intervals of at least 24 hours to 30 – 60 mg PO once daily. Maximum dose is 60 mg daily. Tolvaptan should be initiated and re-initiated in patients only in a hospital where serum sodium can be monitored closely.
Conivaptan dosing is 20 mg IV over 30 minutes then 20 mg IV over 24 hours (max duration of 96 hours). Conivaptan is available as a premix infusion in D5W. For Y-Site administration, conivaptan is incompatible with Lactated Ringers.

Drug interactions: Tolvaptan and conivaptan are contraindicated in patients receiving strong CYP3A4 inhibitors such as ketoconazole, clarithromycin, itraconazole, nelfinavir, ritonavir, indinavir.

Adverse effects: Most common include thirst, dry mouth, polyuria

Note: The FDA recently issued a drug warning with tolvaptan on the potential risk of liver injury with the medication. At this time, FDA recommends that health care providers should perform liver tests in patients reporting symptoms of liver injury. If liver injury is suspected, the prescriber should discontinue tolvaptan.
Rivaroxaban – New indication and a review of dosing guidelines

Rivaroxaban is a Factor Xa inhibitor that was recently approved by the FDA for the treatment of DVT/PE based on the outcomes of the EINSTEIN trials. These studies indicate that rivaroxaban is non-inferior to warfarin in the acute treatment period and superior to placebo for ongoing treatment. Rivaroxaban does not require any routine laboratory monitoring. It has not been compared head to head with dabigatran, an oral direct thrombin inhibitor, but has an advantage of once-daily dosing compared to twice daily with dabigatran. A review of rivaroxaban dosing guidelines is presented at right.

DVT prophylaxis following orthopedic surgery:
10 mg PO daily with or without food
Contraindicated in patients with CrCl < 30 mL/min

Nonvalvular Atrial fibrillation:
20 mg PO daily with the evening meal for CrCl > 50 mL/min
15 mg PO daily with the evening meal for CrCl 15-50 mL/min
Contraindicated in patients with CrCl < 15 mL/min

Treatment of DVT/PE:
Initial treatment: 15 mg PO BID with food for the first 21 days
Following initial treatment period: 20 mg PO daily with food
Contraindicated in patients with CrCl < 30 mL/min

Brief Updates

I. Patient Controlled Analgesia Pharmacy Service Update:
The results of the PCA Pharmacy Service Pilot Project at University Hospital were presented. P&T Committee approved implementation of the pharmacy managed consult service as an option across the adult system. The pharmacy department is currently developing comprehensive processes and guidelines to implement the service across the system.

II. FDA Communication regarding citalopram and risk of QTc prolongation:
In March 2012, the FDA issued a safety communication regarding the risk of clinically significant QTc prolongation with citalopram doses of 60 mg and higher. For patients age 60 and older, the maximum recommended dose is 20 mg. For patients less than 60 years old, the maximum recommended dose is 40 mg. An automatic dose adjustment by pharmacists was approved for doses higher than the maximum recommended doses.

III. The following items were reviewed and approved: Morrison New Patient Menu Cycle, Anticoagulation Management Policy, Label Prepared by Pharmacy Policy

IV. Order Sets/Power Plans approved: Minimally Invasive GYN Surgery pre and post op plans, PULM Mechanically Ventilated orders, CC Transfuse Blood/Blood products Plan, Factor IX Complex (Bebulin VH) for Warfarin Induced ICH Plan, HEM Sickle Cell Admit Plan

V. Fidaxomicin Medication Use Evaluation (MUE): Based on the results of the MUE and clinical information, the following changes to the restrictions for fidaxomicin will be implemented: The use of concomitant broad spectrum antibiotics as an independent risk factor qualifying a patient for fidaxomicin was recommended for addition to prescribing criteria. Also, removal of ≥2 SIRS criteria from the list of qualifying risk factors was recommended

VI. Critical Drug Shortage Updates:
IV loop diuretics: IV bumetanide and IV furosemide are on critical national shortage. Oral therapy should be used whenever possible. If IV therapy is clinically necessary, a 48-hour auto-stop will be placed on order. An equivalent PO dose of same medication will be ordered to start at time of IV discontinuation.
IV potassium/sodium phosphate: Due to the critical national shortage, an automatic interchange to oral phosphate supplementation by the pharmacist is approved if patient is able to take PO, phosphate ≥ 1 mg/dL, and no documented adverse reaction (i.e. – diarrhea) to oral phosphates.

Upcoming P&T Agenda Items:
Formulary reviews: Adalimumab, Annual Formulary Review
Next P&T Meeting: February 7, 2013