UMMC Pharmacy Newsletter

January – February 2013

2012 Formulary and Medication Policy Updates

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The pharmacy and therapeutics (P&T) committee at UMMC meets monthly to vote on requests for addition of medications to the formulary, as well as to review medication usage and safety policies, evaluations, and recommendations. A formulary is a list of medications pre-approved for use within an organization based on analysis of efficacy, safety, and cost. The committee can vote to approve or deny a formulary addition request, or can approve the request with certain stipulations for use. If a request is approved with limitations, a medication use evaluation will be conducted after a defined period of time to ensure compliance. If a request is denied, an attending physician may complete a non-formulary drug authorization form to access the medication for patients on an individual basis.

A search tool to check for formulary status of a medication at UMMC can be accessed at: http://paws0.umsmed.edu/Pharmacy/search.action

2012 Updates

Formulary interchanges
Renvela® (sevelamer carbonate) will be substituted for Renagel® (sevelamer hydrochloride) by automatic therapeutic interchange. Doses will be converted on a milligram per milligram basis and rounded up to the nearest 800mg increment (August, 2012).

Medication Related Policies

Warfarin/Coumadin® and Vitamin K Intake (January, 2012)
If a “Coumadin diet” is ordered by a prescriber, the patient will receive a vitamin K restricted diet. If no such diet is ordered, Food and Nutrition Services will be prompted by the daily Pharmacy Food/Drug Interaction Report to recognize patients on Coumadin and will encourage consistency of vitamin K intake.

Amiodarone has been added to the high risk medications list due to a recently reported case of pulmonary fibrosis and a recently reported case of 3rd degree heart block (May, 2012).
Intravenous Immune Globulin (IVIG) Dosing in Adults (June, 2012)

- Adjusted body weight will be used for dose calculations of IVIG in adult patients for the following reasons:
  - Morbidly obese patients have been excluded from most studies of IVIG
  - IVIG is known to have low distribution to adipose tissue
  - Case reports have been published of thrombotic events in relation to IVIG
- Epic will make the adjustment, so there should be no need for the prescriber to calculate this.

Adult Institutional Pharmacokinetics (PK) Protocol (June, 2012)

A protocol has been approved for pharmacy to manage vancomycin and aminoglycoside use in adults. The scope includes full medication dosing privileges, ordering of serum drug concentration levels, and ordering of relevant labs for any PK consult indicating “consult pharmacy” or “pharmacy to dose”.

Policy for IV Infusions of Potassium Chloride, Potassium Acetate, and Potassium Phosphate (November, 2012):

- General nursing floors:
  - New maximum order is 120mEq of potassium
  - Doses exceeding 40mEq will be dispensed in separate 40mEq/400ml increments
  - Maximum concentration remains 10mEq/100ml with a maximum rate of 10mEq/hour
- Critical care areas (including BMT):
  - Maximum concentration remains 20mEq/50ml with a maximum rate of 20mEq/hour by central vein (40mEq/hour in emergent situations)
  - Maximum concentration remains 40mEq/250ml with a maximum rate of 10mEq/hour by peripheral vein
- Total parenteral nutrition (TPN):
  - New concentration limits of 130mEq/L by central vein and 60mEq/L by peripheral vein
  - In most cases the maximum rate remains 10mEq/hour
    - When necessary, the absolute maximum rate is 20mEq/hour
    - Rates greater than 10mEq/hour require telemetry and a central line

Subcommittee Adjustments to the Formulary (April, 2012)

Additions: Azacitidine (Vidaza®), bortezomib (Velcade®), arsenic trioxide (Trisenox®)
Deletions: Nesiritide, aspirin with codeine, colchicine inj, corticotropin inj, etidronate, moricizine, oxycodone/aspirin (Percodan®), sulfinpyrazone, thiabendazole.
**New Medication Additions**
The following medications were added to the UMMC formulary in 2012: Nulojix® (belatacept), Xarelto® (rivaroxaban), Macrobid® (nitrofurantoin macrocrystal/monohydrate), Ablavar® (gadofosveset), Cleviprex® (clevidipine), Xifaxan® (rifaximin)

**Nulojix® (belatacept) (January, 2012)**

**Indications:** Renal transplant

**Contraindications:** Patients who are EBV seronegative or with unknown status due to increased risk of post-transplant lymphoproliferative disorder (PTLD)

**MOA:** Selective T-cell costimulation blocker which inhibits T lymphocyte proliferation and cytokine production

**Place in therapy:** Prophylaxis of organ rejection in adult kidney transplantation

**Adverse effects:**
- **Common:** Hypertension, UTI, diarrhea, constipation, nausea, vomiting, hyperkalemia, hypokalemia, graft dysfunction, peripheral edema, pyrexia, anemia, leukopenia, cough
- **Serious:** Progressive multifocal leukoencephalopathy (REMS program), polyoma virus nephropathy

**Box warnings:** PTLD (REMS program), malignancies, serious infections (including tuberculosis and polyoma virus), not recommended in liver transplant

**Availability:** 250mg vial (powder for reconstitution)

**Dosing:** Use actual body weight at time of transplant (adjust if body weight changes >10%) and round dose to the nearest 12.5mg increment
- **Day 1 & day 5:** 10mg/kg
- **End of weeks 2, 4, 8, & 12:** 10mg/kg
- **End of week 16 & every 4 weeks after transplant:** 5mg/kg

**Other:**
- Avoid use of live vaccines.
- May store at room temperature for up to 4 hours or in refrigerator for up to 24 hours after reconstitution.
**Xarelto® (rivaroxaban)** (January, 2012)

**Indications/Dosing:**

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| Venous thromboembolism prophylaxis for adults undergoing knee or hip replacement surgery | • 10mg by mouth daily for 35 days (hip)  
• 10mg by mouth daily for 12 days (knee)  
• Avoid if CrCl < 30ml/min |
| Stroke prophylaxis for adults with non-valvular atrial fibrillation       | • 20mg by mouth daily with evening meal (CrCl > 50ml/min)  
• 15mg by mouth daily with evening meal (CrCl 15-50 ml/min)  
• Avoid if CrCl < 15 ml/min |
| Treatment and secondary prevention of deep vein thrombosis (DVT) or pulmonary embolism (PE) (November, 2012) | • 15mg by mouth twice daily with food x 21 days, then 20mg by mouth daily with food for duration of treatment |

**Contraindications:** Active pathological bleeding

**Pharmacology:**

- MOA: Orally bioavailable, direct, reversible factor Xa inhibitor which prolongs prothrombin time (PT) and activated partial thromboplastin time (aPTT)
- Avoid combination with CYP3A4 inhibitors or inducers and avoid if moderate to severe hepatic dysfunction (Child-Pugh B or C)
- Half-life: 5 – 9 hours
- Adjust in renal dysfunction (see above)

**Adverse effects:**

Bleeding, pregnancy related hemorrhage

**Box warnings:**

- Risk of spinal/epidural hematoma with spinal anesthesia or puncture while on anticoagulation
- Increased risk of stroke after discontinuing in nonvalvular atrial fibrillation; if pathological bleeding is not the reason for discontinuation, transitioning to another anticoagulant is recommended (REMS program added November, 2012)

**Availability:** 10mg, 15mg, & 20mg tablets

**Other:**

- Rivaroxaban 15mg & 20mg should be taken with evening meal for optimal efficacy (REMS program)
- No direct antidote exists
- More GI bleeds observed than with warfarin
- Stop 24 hours prior to surgical procedures
- No routine monitoring parameters are recommended. Prothrombin time (PT) and antifactor Xa activity will be affected by rivaroxaban and therefore may be used to detect presence of medication, but no guidelines exist to suggest use in adjusting therapy.

**Macrobid® (nitrofurantoin macrocrystal/monohydrate) (February, 2012)**

**Indication:** Treatment of urinary tract infection (UTI)

**Contraindications:**
Renal impairment (CrCl < 60 ml/min); infants < 1 month old or pregnancy at term

**MOA:** Inhibits bacterial acetyl coenzyme A

**Place in therapy:** Slow release mechanism allows treatment twice daily compared to four times daily with Macrodantin®. The Macrodantin® product might still be preferable for long term prophylaxis use.

**Adverse effects:**
Hemolytic anemia (G6PD deficiency or neonates), peripheral neuropathy, hepatotoxicity, pulmonary toxicity, *Clostridium difficile*-associated diarrhea

**Availability:** 100mg capsule

**Dosing:** 100mg by mouth twice daily

**Other:** Not for treatment of pyelonephritis

**Ablavar® (gadofosveset) (May, 2012)**

**Indication:** Magnetic resonance angiography (MRA) contrast agent for evaluation of known or suspected peripheral vascular disease

**Contraindications:** Allergic reaction to any gadolinium-based contrast agent

**MOA:** Specifically designed to image vasculature by reversibly binding to serum albumin

**Place in therapy:** Only agent approved for MRA
Adverse effects: Low incidence of transient, mild to moderate adverse events, such as pruritus, headache, nausea, vasodilatation, and paresthesia

Boxed warning: Risk of nephrogenic systemic fibrosis (NSF) with any gadolinium-based contrast agent if renal function <30ml/min, or if any renal compromise in the setting of hepato-renal syndrome or perioperative liver transplant. All patients should be screened for renal insufficiency prior to initiation.

Other warnings:
- Risk of worsening of renal function in patients with baseline renal insufficiency
- Emergency resuscitative equipment should be available as serious anaphylactic reactions are possible
- Small increase in QTc interval is possible, but generally not clinically significant

Availability: 244mg/ml (0.25mmol/ml) in 10ml and 20ml single use vials

Dosing: 0.12ml/kg by manual or power injection

Cleviprex® (clevidipine) (May, 2012)

Indication: Reduction of blood pressure when oral therapy cannot be used or is undesirable

Contraindications:
- Hypersensitivity to soy or egg products
- Defective lipid metabolism
- Aortic stenosis

MOA: Ultra-short acting dihydropyridine calcium channel blocker with selective arterial vasodilation

Place in therapy: Intravenous, titratable control of hypertension, studied for up to 72 hours of use

Adverse effects: Acute renal failure, atrial fibrillation, nausea/vomiting, and headache

Warnings:
- Use aseptic technique and discard unused vial after 12 hours due to contamination risk
- Monitor for hypotension and reflex tachycardia and decrease dose as needed; monitor for rebound hypertension for 8 hours after therapy discontinuation
- Avoid immediate discontinuation of beta-blocker during initiation
- Not studied in pheochromocytoma
- Formulation of 2Kcal/ml lipid should be accounted for in sensitive patients
- Negative inotrope with potential for heart failure exacerbation

**Availability:** 0.5mg/ml in 50ml and 100ml single use vials as 20% lipid emulsion

**Dosing:**
- Initiate at 1-2mg/hour
- Dose may be doubled at ~90 seconds; continue titrating up, but reduce titration to every 5-10 minutes and at smaller intervals as blood pressure approaches goal
- Maintenance dose is generally ~4-6mg/hour; maximum dose is 21mg/hour due to lipid load
- No adjustments required for hepatic or renal dysfunction

**Xifaxan® (rifaximin) (June, 2012)**
**FDA-approved indication:** Prevention of overt hepatic encephalopathy (HE) recurrence in adults

**Unapproved indication:** Irritable bowel syndrome

**UMMC-approved indication:** Use by gastrointestinal and transplant surgery providers only

**Contraindications:** Hypersensitivity reactions to any rifamycin antibiotic, including but not limited to exfoliative dermatitis, angioneurotic edema, and anaphylaxis

**Pharmacology:**
- **MOA:** Analog of rifamycin which inhibits bacterial RNA synthesis and may decrease ammonia production of gastrointestinal flora in patients with HE
- Minimal systemic absorption from the gut
- Possibility of CYP-3A4 induction (class effect)

**Place in therapy:**
- Fewer gastrointestinal adverse effects (flatulence, bloating) and easier dosing than lactulose
- May be used as monotherapy or in combination with lactulose

**Adverse effects:**
- Peripheral edema, dizziness, anemia
Several other adverse effects reported, but may be related to underlying disease as incidences are similar to population treated with placebo

**Warnings:**
- Risk of *Clostridium difficile*-associated diarrhea
- Development of drug-resistant bacteria may occur
- Caution in severe hepatic impairment (Child-Pugh C) due to increased risk of systemic exposure

**Availability:** 550mg tablet

**Dosing:** 550mg by mouth twice daily with or without food for hepatic encephalitis

**References**
1. Department of Pharmacy [Internet]. Therapeutic Interchange of Select Medications. Jackson, MS: University of Mississippi Medical Center [updated 2012 October]. Available from: [http://pharmacy.umc.edu/intranet/polproc/documents/C-017.pdf](http://pharmacy.umc.edu/intranet/polproc/documents/C-017.pdf)
7. Cleviprex® [package insert]. Fresenius Kabi Austria GmbH, Graz, Austria; December 2011.