Platte Valley Medical Center
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# Pharmacy, Nutrition, & Therapeutics Newsletter

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***Dabigatran is a new oral anticoagulant. As such it is essential to educate patients on the signs and symptoms of bleeding.***

## Dabigatran (Pradaxa®) 101

Dabigatran is an oral anticoagulant that acts as a direct thrombin inhibitor. It is approved as an alternative to warfarin for the prevention of stroke/systemic embolism in patients with non-valvular atrial fibrillation. Dabigatran is not approved for other indications, such as prevention or treatment of deep vein thrombosis or pulmonary embolism. We may see more patients taking this new anticoagulant admitted to PVMC.

**Initial Dabigatran Dose**

| **Renal Function (CrCl ml/min)** | **➢ 30** | **15-30** | **< 15** |
|---|---|---|---|
| Recommended Starting Dose | 150 mg BID | 75 mg BID | DO NOT USE |

**Converting to Dabigatran**

| **Agent** | **Conversion Instructions** |
|---|---|
| Heparin | Start dabigatran at the time the heparin infusion is turned off. |
| Enoxaparin | Start dabigatran at the time the next dose of enoxaparin was to be administered (may overlap by up to 2 hours). If enoxaparin was adjusted for renal function, dabigatran may also require adjustment. |
| Warfarin | Discontinue warfarin and start dabigatran when the INR is < 2.0 |

**Converting Dabigatran to Warfarin (A. Fib patients only)**

| **Renal Function (CrCl ml/min)** | **Conversion Instructions** **Note : Dabigatran may contrib. to an elevated INR for up to 2 days after D/C.** |
|---|---|
| ➢ 50 | Start warfarin & overlap w/dabigatran for 3 days, D/C on day 4. |
| 31-50 | Start warfarin & overlap w/dabigatran for 2 days, D/C on day 3. |
| 15 – 30 | Start warfarin & overlap w/dabigatran for 1 day, D/C on day 2. |

**Converting Dabigatran to Parenteral Anticoagulants (Heparin, Enoxaparin)** NOTE: **Conversion to heparin has not been studied/based on the pharmacokinetics of the drug.**

| **Renal Function (CrCl ml/min)** | **Conversion Instructions** |
|---|---|
| ≥ 30 | Start parenteral anticoagulant 12 hours after last dabigatran dose. |
| < 30 | Start parenteral anticoagulant 24 hours after last dabigatran dose. |

**Adverse Effects :** Compared to warfarin, **more** patients discontinue dabigatran due to its adverse effects. The most common non-hemorrhagic adverse effects are GI-related and may include dyspepsia, nausea, upper abdominal pain, and diarrhea. Although overall bleeding rates between dabigatran and warfarin are similar in clinical trials, dabigatran is associated with a greater risk of GI bleeding compared to warfarin. It is important to educate patients on the signs and symptoms of bleeding.

**Management of Dabigatran-Related Bleeding Events :** There is no pharmacologic antidote for dabigatran, so management of hemorrhagic complications is primarily supportive. Dabigatran is mostly excreted in the urine (80%), so appropriate diuresis must be maintained in order to promote adequate drug clearance.

Other new oral anticoagulants that have or will be hitting the market include Rivaroxaban (Xarelto®) and Apixaban (Eliquis®).

# Pseudomonas aeruginosa: What's The Fuss?

Resistance to anti-pseudomonal antibiotics is becoming more and more prevalent in hospitals up and down the Front Range. It is essential that PVMC utilize antibiotics judiciously to minimize the emergence of antimicrobial resistant pathogens. Initial empiric antimicrobial therapy should take into consideration the risk factors for the causative organism as well as PVMC susceptibility patterns. Streamlining or de-escalation of empirical antimicrobial therapy on the basis of culture results and elimination of redundant combination therapy more effectively targets the causative pathogen, resulting in decreased antimicrobial exposure and cost savings to the organization. Let's review *Pseudomonas aeruginosa* (*P. aeruginosa*), its risk factors, and drugs utilized to treat it.

**What is it?:** *P. aeruginosa* is an aerobic, gram-negative bacillus. It inhabits moist environments. In hospitals it has been isolated from respirators, disinfectants, water faucets, and sinks. *P. aeruginosa* is highly pathogenic and is primarily a health care-associated bacterium; however, within the community setting immunocompromised patients are more susceptible. It is the second most commonly identified pathogen in intensive care units, and drug resistance to it is on the rise nationally. *P. aeruginosa* can cause a variety of severe infections, such as bacteremia, pneumonia, endocarditis, urinary tract, skin, bone and joint, ear, and eye.[1]

**What are the risk factors?:** Common risk factors for *P. aeruginosa* by type of infection are detailed in Table 1.

**Table 1 – *P. aeruginosa* Risk Factors[1]**

| Type of Infection | Risk Factors |
|---|---|
| Bacteremia | Neutropenia, hematologic malignancy, organ transplantation, vascular and urinary tract catheterization, antibiotic use |
| Pneumonia | Mechanical ventilation, neutropenia, chronic lung disease, antibiotic use |
| Endocarditis | Injection drug use, prosthetic heart valves |
| Urinary Tract | Indwelling urinary catheter, diabetes |
| Skin | Neutropenia, diabetes, injection drug use, post-operative |
| Bone and Joint | Injection drug use, puncture wounds, contiguous spread |
| Ear | Swimmer's ear, diabetes, elderly |
| Eye | Contact lens wear |

**What drugs treat *P. aeruginosa*?:** Early appropriate antibiotic therapy significantly improves mortality, while a delay in treatment increases mortality. The data is not definitive, but it is generally recommended to empirically treat with two anti-pseudomonal drugs from different classes in high risk patients with severe infections. Skin, soft tissue, and urinary tract infections (UTI) do not require combination therapy. Aminoglycosides are used in combination with other drugs for treatment, but are not recommended as monotherapy unless treating a UTI. Susceptibility testing should be used to guide final choices for known *P. aeruginosa* infections when deescalating drug therapy.[2]

Only certain antibiotics have reliable activity against *P. aeruginosa*. See Table 2.

***Please refer to the PVMC Antibiogram for susceptibility data of these antibiotics versus P. aeruginosa at PVMC.***

**Table 2 – Antipseudomonal Drugs on Formulary at PVMC[2,3,4]**

| Drug | Dosing |
|---|---|
| Piperacillin/Tazobactam | 3.375gm IV q4-6h, 4.5gm IV q6-8h |
| Ticarcillin/Clavulanate | 3.1gm IV q4h |
| Ceftazidime | 2gm IV q8h |
| Cefepime | 2gm IV q8-12h |
| Aztreonam | 2mg IV q6-8h |
| Doripenem | 500mg IV q8h |
| Meropenem | 1gm IV q8h |
| Levofloxacin | 750mg IV q24h |
| Gentamicin/Tobramycin | 2-3mg/kg IV load, then 1.7-2mg/kg IV q8h<br>or 5-7mg/kg IV q24h |
| Amikacin | 8-12mg/kg IV load, then 7-8mg/kg IV q8h-12h or 15-20mg/kg q24h |

References:

1) Daniels TL, Gregory DW. Pseudomonas, Stenotrophomonas, and Burkholderia. In: Schlossberg D, ed. Clinical Infectious Disease. New York, NY: Cambridge University Press; 2008:1031-37.
2) Kanj SS, Sexton DJ. Treatment of Pseudomonas aeruginosa infections. In: UpToDate, Calderwood SB, Baron EL (eds), Waltham, MA, 2011.
3) Gilbert DN, Moellering Jr. RC, Eliopoulos GM, eds. The Sanford Guide to Antimicrobial Therapy. 39th ed. Sperryville, VA: Antimicrobial Therapy, Inc.; 2009:37,96.
4) Bartlett JG, Auwaerter PG, Pham PA, eds. Johns Hopkins ABX Guide Diagnosis and Treatment of Infectiouis Deseases 2010. 2nd ed. Sudbury, MA: Jones & Bartlett Learning; 2010:314-15.

## Levalbuterol (Xopenex®) vs Albuterol : What is the Difference?

Levalbuterol & albuterol are both short-acting beta-2 agonist bronchodilating drugs. Current guidelines indicate that levalbuterol and albuterol are equally effective agents in patients with asmtha[1] and COPD[2], but levalbuterol is 42 times more expensive than albuterol ($5.54/dose vs. $0.13/dose, respectively). Levalbuterol does not decrease the incidence of tachycardia and does not relieve tremors associated with albuterol. **In 1999, the Food and Drug Administration (FDA) ordered the manufacturer of levalbuterol to stop promoting these unfounded benefits.[3]**

**Rumor: Because levalbuterol contains only the R-isomer, unlike albuterol which contains both the R and S-isomers, it causes fewer side effects than albuterol.**
**Truth:** It is the R-isomer that causes both the beneficial effects and side effects of levalbuterol and albuterol.[4] The S-isomer's pharmacologic effects are unknown. One 45 microgram inhalation of levalbuterol is equivalent with a 90 microgram inhalation of albuterol and has similar side effects.[5] Thus, 1.25 mg of levalbuterol inhalation solution is equal to 2.5mg of albuterol inhalation solution.

**Rumor: Levalbuterol causes less tachycardia than albuterol.**
**Truth:** Two cross-over design studies have shown similar increases in heart rate after administration of albuterol and levalbuterol.[6,7] Both studies demonstrated that the maximum increase in heart rate 30 minutes after inhalation was 4 and 6 beats per minute. Often tachycardia is caused by overuse of albuterol and combinations of albuterol with long-acting bronchodilators. Decreasing the dose of albuterol often decreases tachycardia.[6]

**Rumor: Levalbuterol causes fewer tremors than albuterol.**
**Truth:** A cross-over design study examined tremor changes at 30 minutes, 1 hour, and 2 hours after administration of albuterol, albuterol/ipratropium, levalbuterol, and placebo. There were no significant treatment and placebo differences at either of the points in time.[7]

**Rumor: Levalbuterol causes less airway secretion in intubated patients since airway secretion is caused by the S-isomer of albuterol.**
**Truth:** A cross-over design trial looked at airway secretion in long-term intubated patients, consecutively receiving albuterol, levalbuterol, saline, and placebo. There were no differences in the volumes of secretion between albuterol, levalbuterol, and saline.[8]

**Rumor: What's the deal since these products are clinically proven to be similar?**
**Truth:** Using albuterol as the preferred short-acting bronchodilator will help prevent mediation errors by decreasing inventory and preventing confusion. In addition, using albuterol can save PVMC money and aid in efforts to decrease costs.[9]
References Available by Request

## PVMC Current Medication Shortages

| | |
|---|---|
| Hydromorphone Inj. | Prochlorperazine Inj. |
| Fentanyl Inj. | Heparin Inj. |
| Magnesium Sulfate Inj. | Levofloxacin Inj. |
| Etomidate Inj. | Famotidine Inj. |
| Midazolam Inj. | Diazepam Inj. |
| Potassium Phosphate Inj. | Lorazepam Inj. |
| Sodium Acetate Inj. | Bleomycin Inj. |
| Bupivacaine with Epi Inj. | Etoposide Inj. |
| Lidocaine with Epi Inj. | Mannitol Inj. |
| Ropivacaine Inj. | Enalaprilat Inj. |
| Protamine Inj. | Morphine 4 mg Inj. |

## P&T Formulary Additions & Deletions for 2011

| **Additions** | **Indication** | **Notes** |
|---|---|---|
| Sevelamer (Renagel & Renvela) | Non calcium based phosphate binder for dialysis or other patients with high calcium that require a phosphate binder. | Both Carbonate and HCL formulations are available. |
| Hydrocodone/APAP 5-325mg & 7.5-325mg | Acute pain management | Added to replace formulations with 500 mg of Acetaminophen |
| Nephro-Vite | Vitamin B Complex/Renal Vitamin | |
| Fish Oil | Patient's admitted to the hospital are commonly taking Fish Oil capsules to assist in managing their cholesterol. | |
| Nebivolol (Bystolic) | Cardioselective Beta-blocker for Heart Failure patients | |
| Methylnaltrexone (Relistor) Inj. | Restricted to the Emergency Department for management of Opioid induced constipation not resolved by other means. | |
| Nicardipine Inj. | Neurologic Hypertensive Emergencies including Stroke | |
| Lacosamide (Vimpat) | Adjunct in Partial Seizures | |
| **Deletions** | **Reason** | **Notes** |
| Propoxyphene Containing Products | Cardiac Toxicity risk led to the FDA requesting manufacturers remove product from the market | Darvocet<br>Propoxyphene |
| Hydrocodone products containing 500 mg of Acetaminophen | FDA requested manufacturers remove these products from the market within 3 years due to Acetaminophen content and on-going issues with liver failure from overdose. PVMC P&T Committee deleted these products and moved to 325 mg APAP narcotic combination products. | Hydrocodone/APAP 5-500 mg<br>Hydrocodone/APAP 7.5-500 mg |
| Xigris | Xigris (Drotrecogin alfa) has been withdrawn from the market by Lilly pursuant to the PROWESS-SHOCK trial's results showing no survival benefit in severe sepsis and septic shock patients. | |

# Same Drug, Different Formulation

A number of medications on the market have been reformulated to last longer, allowing the patient to take fewer doses per day. Although this is more convenient for the patient, it creates look-alike/sound-alike medication names that can cause medication errors. These medications often have the same brand or generic name but with an added acronym for the release formulation. At a quick glance, the drug names can be easily confused. It is important to understand the difference between these medications. Immediate-release (IR) medications are the quickest and shortest acting; therefore, they need to be dosed more frequently. Often immediate release medications were the first to market and may not carry the IR designation as part of their drug name. Controlled, extended, or sustained-release ("CR", "ER", "XL", "XR", "SR") medications have been formulated to slowly release the drug, which is then absorbed into the body over time. For this reason, CR, ER, XL, XR, and SR formulations have a longer duration of action and require less frequent administration. Unfortunately, there is no standardization with each suffix regarding how many times it should be dosed per day.

It is very important to correctly select and identify which formulation the patient needs. If the patient does not receive the appropriate formulation, they are at risk for medication side effects and/or worsening of their condition. One example of this can be seen with Oxycodone and Oxycodone SR. If a patient is given Oxycodone (the immediate release formulation) every 12 hours (instead of (Oxycodone SR), then the patient's pain could be uncontrolled. However, if a patient is given Oxycodone SR every 4 hours (instead of Oxycodone), then the patient could overdose. One good way to help prevent look-alike/sound-alike medication errors is to be aware of which medications have more than one formulation and to be on the lookout for such errors. Some common examples are listed below, with the typical dosing regimen.

| **Examples of Commonly Confused Immediate & Sustained Release Medications** | |
|---|---|
| **Immediate Release Drug** | **Sustained Release Drug** |
| Oxycodone : **Dosing Interval** = Q4 – 6 Hrs | Oxycodone SR (OxyContin) :**Dosing Interval**= Q12H/BID |
| Metoprolol : **Dosing Interval** = BID | Metoprolol ER (Toprol XL) : **Dosing Interval** = Daily |
| Diltiazem : **Dosing Interval** = TID to QID | Diltiazem ER : **Dosing Interval** = Daily |
| Venlafaxine (Effexor) : **Dosing Interval** = BID to TID | Venlafaxine ER (Effexor-XR):**Dosing Interval** = Daily |
| Isosorbide Mononitrate : **Dosing Interval** = up to TID | Isosorbide Mononitrate ER:**Dosing Interval** = Daily |
| Bupropion : **Dosing Interval** = BID to TID | Bupropion SR : **Dosing Interval** = BID |