



# Pharmacy Benefits Management- Medical Advisory Panel Ez-Minutes

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## Ez-Minutes Wants You! Attention: Physicians

**Did you know that as of March 07, there were 11, 306 subscribers to the PBM-MAP Ez-Minutes? Of that total, approximately 16% were physicians.**

*Physicians: The quarterly on-line Ez-minutes newsletter is for you. It is the our way of communicating with you changes to the VHA National Drug Formulary and to provide information on and links to treatment guidelines, criteria for use and other prescribing and safety information that will aid in your practice at the VA. The best part is....the information can literally be read in minutes. It's that easy, or rather Ez!*

**Come on now...what are you waiting for? Subscribe today. It's EASY!  
See Pg 4. HOW TO SUBSCRIBE TO Ez-MINUTES**

### Recent Postings of National PBM Documents

#### Criteria for Use/Nonformulary Use

- <http://vaww.pbm.va.gov/pbm/criteria.htm>
- <http://www.pbm.va.gov/CriteriaForUse.aspx>

- Leflunomide and Biologic DMARDs in the Treatment of Moderate to severe RA
- Lubiprostone (Amitiza®)
- Monoamine Oxidase Inhibitors (MAOI) for the Treatment of Major Depressive Disorder: Oral and Transdermal Routes of Administration
- Pregabalin (Lyrica®)
- Quadrivalent Human Papillomavirus (Types 6/11/16/18) recombinant Vaccine (Gardasil®)
- Recombinant Activated Human Coagulation Factor Seven (Novoseven®)
- Recombinant Erythropoietin for Hepatitis C Treatment-Related Anemia

#### Treatment Guidelines

- <http://vaww.pbm.va.gov/pbm/treatment.htm>
  - <http://www.pbm.va.gov/TreatmentGuidelines.aspx>
- Recommendations for Atypical Antipsychotic use in schizophrenia and Schizoaffective Disorders

#### Therapeutic Interchange Guidance

- <http://vaww.pbm.va.gov/pbm/tig.htm>
- <http://www.pbm.va.gov/TherapeuticInterchangeGuidance.aspx>
- Prescribing and Dispensing Information for Vardenafil (Levitra®)
- Recommendations for the Use of Beta-Adrenergic Blockers in VA patients with CHF with Left Ventricular Systolic Dysfunction-Update

#### Directives, Policies and Information Letters

- <http://vaww.pbm.va.gov/pbm/directive.htm>
- Compassionate Use of Nutriceuticals in VHA
- Coordinated Care Policy for Traveling Veterans

### Drug Monographs

- <http://vaww.pbm.va.gov/pbm/drugmonograph.htm>
- <http://www.pbm.va.gov/DrugMonograph.aspx>

- Adefovir Dipivoxil (Hepsera®) Addendum
- Mycophenolate Sodium (Myfortic®)
- Recombinant Activated Human Coagulation Factor VII (Novoseven®)
- Panitumumab (Vectibix™)
- Pregabalin (Lyrica®)
- Quadrivalent HPV Vaccine (Gardasil®)
- Rasagiline (Azilect®)
- Selegiline Transdermal System (EMSAM)
- Telbivudine (Tyzeka™)

### Formulary Decisions

#### New Molecular Entities (NME)

- Dasatinib (Sprycel®)- Not added to the VA National Formulary (VANF)
- Rasagiline (Azilect®)-Not added to the VANF

### Other Formulary Decisions

- Carvedilol CR-Not added to the VANF
- Levalbuterol-Removed from the VANF
- Sitagliptin/Metformin (Janumet™)-Not added to the VANF
- Polyethylene Glycol 3350 (PEG 3350)-Added to the VANF
- Nitrofurantoin monohydrate/macrocryalline (Macrobid®)-Added to the VANF
- Telbivudine (Tyzeka™)-Not added to the VANF
- Adefovir dipivoxil (Hepsera®) Added to the VANF; restricted to GI and ID

## Use of Thiazolidinediones in NYHA Class I and II Heart Failure

Clinical trials have shown that edema and heart failure are adverse events associated with use of thiazolidinediones (TZDs). In the pivotal clinical trials, it should be noted that patients with NYHA Class III/IV heart failure were excluded and that the incidence of patients with Class I-II that were enrolled was not precisely known. Since then, trials specifically looking at use of TZDs in patients with NYHA Class I-II heart failure have been conducted.

Rosiglitazone and placebo were compared in a 52-week randomized, double-blind trial in patients (n= 224) with Class I or II heart failure and left ventricular ejection fraction  $\leq$  45%. Additional entry requirements included use of an angiotensin converting enzyme inhibitor or angiotensin receptor blocker. There was an increased rate of worsening heart failure (6.4 vs. 3.5%), new or worsening edema (25.5 vs. 8.8%), new or worsening dyspnea (26.4 vs. 16.7%), higher rate of cardiovascular-related hospitalization (19 vs. 13%), increase in heart failure medication (32.7% vs. 17.5%), MI (4.5% vs. 1.8%), and cardiovascular deaths (4.5 vs. 3.5%). There was no significant change in ejection fraction (primary outcome).

In a 24-week study, pioglitazone and glyburide were compared in patients with NYHA II or III heart failure and ejection fraction < 40% (n=518). The primary endpoint was the composite of first occurrence of death due to cardiovascular causes,  $\geq$  24 hour hospitalization for worsening heart failure, or emergency room visit for heart failure. The composite event rate was 13.4% in the pioglitazone group and 8.2% in the glyburide group. This was primarily driven by hospitalization for heart failure (9.9% vs. 4.7%). Emergency room visit for heart failure (1.5% vs. 1.2%) and cardiovascular mortality (1.9% vs. 2.3%) were similar between the groups. As would be expected, lower limb edema and increased weight occurred in a greater frequency with pioglitazone. The study was terminated early because of a trend between the groups for the primary endpoint favoring glyburide (p=0.09). Explanations for these outcomes include concomitant use of insulin allowed and that the maximum dose of pioglitazone was used early in therapy.

The labeling for rosiglitazone has been revised to include a warning that patients with NYHA Class I and II heart failure are at increased risk of cardiovascular events. Both rosiglitazone and pioglitazone will have a new Boxed Warning to heighten awareness of the risk of CHF.

Submitted by Debbie Khachikian, PharmD-VACO Pharmacy Benefits Management-Hines, IL.

**VA Negative Formulary Abolishment:** The VA Negative Formulary has been abolished. There is now one list termed the VA Do Not Substitute List.

**Link to the VA Do Not Substitute List:** The Do Not Substitute List is a list of pharmaceutical products for which substitution is not permitted. See more details at: <http://vawww.pbm.va.gov/natform/Do%20Not%20Substitute%20List%205-07.doc> or <http://www.pbm.va.gov/natform/Do%20Not%20Substitute%20List%205-07.doc>

## Availability of IV Quinidine for Treatment of Severe Malaria

**Background:** Severe malaria is considered a medical emergency, which requires urgent and aggressive treatment. Delay in therapy can potentially lead to an increase in mortality and morbidity. The CDC treatment recommendations for severe malaria are IV quinidine gluconate plus doxycycline, tetracycline, or clindamycin.

Because of the non-formulary status of IV quinidine, it may not be readily stocked in VA pharmacies or distribution centers.

**Action:** Determine a mechanism to obtain IV quinidine urgently for VA patients diagnosed with severe malaria.

**Plan:** Through communications with McKesson, the following has been agreed upon:

- All VA Distribution Centers will be stocked with a minimum of 10 vials of IV quinidine gluconate (800mg/10mL salt; 500mg base).
- Upon request, McKesson will immediately ship IV quinidine to a VA facility for arrival within a 4 hour window.

### Contact information:

- During regular business hours, VA facilities should call the "VA Service First Phone Number" (800-364-6198) and arrange for the shipment of IV quinidine gluconate.
- During non-business hours (e.g., after hours, holidays, weekends), VA facilities should call the "Distribution Center Emergency Phone Number" to arrange for shipment of IV quinidine gluconate.

Another option is that a facility can stock a small of supply of IV quinidine gluconate in their pharmacy.

Submitted by Melinda Neuhauser, PharmD-VACO Pharmacy Benefits Management-Hines, IL.

**Methodone-Related Deaths:** Analyses from several national databases (CDC, National Center for Health Statistics, DEA, Poison Control Centers) suggest that methadone-related poisoning deaths are outpacing all poisoning deaths (see Figure 1). Although data are incomplete, the findings suggest that the increasing rates of methadone-related deaths may be occurring among patients treated with methadone for pain. The PBMSHG is in the process of evaluating VA data and is working collaboratively with the National Pain Management Strategy Coordinating Committee and Substance Use Disorder experts to determine the best strategy for addressing this issue. *STAY TUNED FOR FUTURE UPDATES.* All clinicians are encouraged to review the National PBM Bulletin on methadone, issued in November 2006:

<http://vaww.pbm.va.gov/alerts/National%20PBM%20Bulletin%20-%20Methadone.pdf>

Submitted by Francine Goodman, PharmD, BCPS  
VACO Pharmacy Benefits Management-Hines, IL.

**Don't forget** that the VA National Formulary is available in a PDA format. A small program called "List" is required to view it. The formulary can be sorted by drug or by class. Both the program and the formulary can be downloaded from the PBM Internet and Intranet Websites, either from the "PDA National Formulary" link on the "National Formulary" page or directly at:

<http://vaww.pbm.va.gov/pdanatform/pdanatform.htm> or

<http://www.pbm.va.gov/NationalFormulary-PDANationalFormulary.aspx>

**Did you know?** The New VA National Formulary (VANF) is now posted on the PBM website. Facilities should review the formulary and make any changes necessary to accommodate the new formulary drugs.

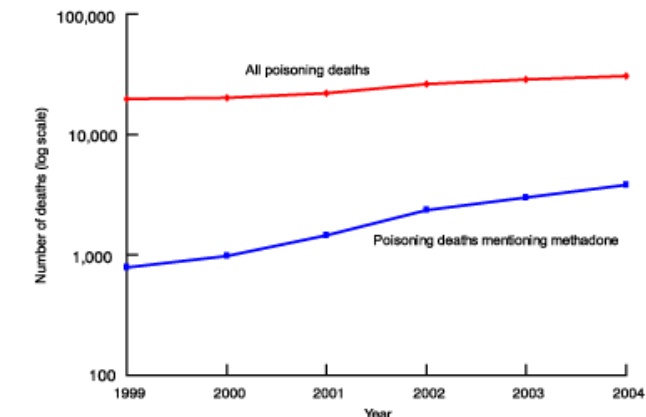
Please remember that the VISN Formularies will remain in effect until the handbook, with the new formulary policy in it is signed.

### NATIONAL DUE "CLEARING HOUSE"

If you have suggestions for future DUE to be conducted at a national level or would like to share results of local DUE, please send them to [Burk.Muriel@va.gov](mailto:Burk.Muriel@va.gov). This communication of results will assist the national PBM to keep abreast of what is going on at the local level, and if something warrants taking a closer look, the Outcomes Research Department could potentially examine the issue at a national level. Thanks in advance!

Muriel Burk, Pharm.D.  
VACO PBM SHG  
Outcomes Research  
Hines VA

**Figure 1. Poisoning and methadone-related poisoning deaths: 1999-2004**



SOURCE: National Center for Health Statistics, data from the National Vital Statistics System.

**Did you know?** Metformin is no longer contraindicated in patients with congestive heart failure requiring pharmacologic management? However, the black box warning remains.

Patients with congestive heart failure requiring pharmacologic management, in particular those with unstable or acute congestive heart failure who are at risk of hypoperfusion and hypoxemia, are at increased risk of lactic acidosis.

### VA National Formulary Contraceptive Agents

Don't forget to view the available contraceptive agents debut in last issue of Ez-minutes. The link below provides a current listing of the VA National Formulary hormonal contraceptive agents. As a reminder, to allow for substitution of the least expensive equivalent product, all contraceptives are listed on the National Formulary as the generic components. The table includes FSS/BIG 4 pricing as of 03/07 listed per cycle which is defined as 28 days. The table is too large to insert in the newsletter but can be easily viewed by clicking this link: (VA InTRAnet only) <http://vaww.pbm.va.gov/clinicians/VA%20National%20Formulary%20Contraceptive%20Agents.pdf>

### ATTENTION: VA Psychiatric/Behavioral Health Pharmacists

Twenty-one VA pharmacists met for a roundtable discussion during the annual CPNP (College of Psychiatric and Neurology Pharmacists) Meeting in April 2007. A variety of topics were discussed included scopes of practice, processing nonformulary medications, clinical responsibilities including medication education groups, mental health intakes as well as sites of practice (i.e. community based outpatient clinics, inpatient units and outpatient clinics). A new email list serve (titled VHA psychiatric pharmacists) has been formed to share common issues. If you are interested in joining this email discussion list, please send an e-mail to

[Michelle.Twitty@va.gov](mailto:Michelle.Twitty@va.gov).

**Generic Pred Forte:** Some questions have been raised regarding the formulation of 1% Econopred Plus®, a branded generic, which is being used as a therapeutic interchange for Pred Forte®. The generic formulation has an AB rating and is considered to be bioequivalent to Pred Forte®. There have been anecdotal reports of caking, precipitation and “streaming” from the bottle tip instead of drops. These concerns were discussed in 1998 and 2001 letters to the editor.<sup>1,2</sup> In 1999 the milling process for the Econopred® product was improved to allow a more homogenous particles size distribution which removed the potential “caking” of the product. Additionally, in 2003, the dispensing plug was changed from a round tip to a flat design which provides a consistent drop size and delivery. A literature review revealed a study conducted by Gayton<sup>3</sup> in 2005 who investigated both products (Econpred® and Pred Forte®) in a 4 week, randomized, parallel group, single center, active control design. Primary outcomes were anterior chamber flare scores, keratitis and cells. The Econpred® product produced significantly lower anterior chamber flare scores (p<0.05) and the other outcomes were equivalent between products. The product recalls cited in Fiscella’s letter to the editor were actually voluntary recalls of two lots by Alcon/Falcon due to loose clumping of the active ingredient which occurred after freezing during shipment.

Patient education is a critical component of dispensing ophthalmic medications. Patients should be able to demonstrate proper technique for both installation and “shaking” of the bottle prior to use. Additionally, they should be able to recognize hardening of the product and when to contact their physician or pharmacists with concerns concerning use of the product.

1. Fiscella RG, Gaynes BI, Jensen M. Equivalence of generic and brand-name ophthalmic products. *Am J Health Syst Pharm.* 2001 Apr 1;58(7):616-7.

2. Fiscella RG, Jensen M, Van Dyck G. Generic prednisolone suspension substitution. *Arch Ophthalmol.* 1998 May;116(5):703.

3. Gayton JL. A clinical comparison of two different prednisolone acetate formulations in patients undergoing cataract surgery. *Curr Med Res Opin.* 2005 Aug;21(8):1291-5.

Submitted by Kathy Tortorice, PharmD, BCPS-VACO Pharmacy Benefits Management-Hines, IL.

### HOW TO SUBSCRIBE TO PBM-MAP Ez-MINUTES: FOR **NEW** SUBSCRIPTIONS ONLY

Click [stxcollage@va.gov](mailto:stxcollage@va.gov) to send an email to subscribe. If this feature is disabled on your computer, send an email to [stxcollage@va.gov](mailto:stxcollage@va.gov) with “PBM subscribe” in the subject line. We hope to make Ez-Minutes available via PDA format in the near future. Any questions, comments, please e-mail: Janet H. Dailey, PharmD. at [Janet.Dailey@va.gov](mailto:Janet.Dailey@va.gov) OR Co-Editor: Peter A. Glassman, at [Peter.Glassman@va.gov](mailto:Peter.Glassman@va.gov). To access previous issues of the newsletter, click on this link: <http://vaww.pbm.va.gov/pbm/ezminutes.htm> or <http://www.pbm.va.gov/PBM-MAPEzMinutes.aspx>.

**PBM Advisory on Non VA Meds:** Click this link to read tips for improving your facility’s data and compliance with performance monitors that use PBM’s Non-VA Medications Data: <http://www.pbm.va.gov/ezminutes/AdvisoryOnNonVAMeds.pdf>

**2007 1<sup>st</sup> Annual VA Clinical Pharmacy Programming Conference:** “Managing VA Clinical Pharmacy Programs into the Future” Sept. 25th —Sept. 28th. Check the PBM website in the near future for more details.

### New VA National Formulary Disclaimer

The following disclaimer will be included on the National Formulary lists on the PBM Website(s).

The VANF is dosage form specific. If a specific dosage form is not listed, the specific product in question should be considered non-formulary (although other dosage forms of that molecular entity may be included as formulary). Dosage forms such as TAB and CAP, ORAL are considered immediate release. Sustained release products are listed individually. Formulary products may also be available in many dosage forms and strengths. In the case of products with multiple dosage forms and strengths, not all forms and strengths need to be stocked. Facilities should make those dosages available that are necessary to meet their patient needs.

### Future PBM-MAP Broadcast Programs

Coming soon to your viewing screen/desktop nearest you  
*“When HIV Treatment Fails-Optimizing Therapy”* and  
*“New Treatment for Hepatitis B Virus”*

Check the PBM websites for additional information. Please note that these programs can be viewed as an ON Demand Video to the Desktop via Content Distribution Network (if available at your site) two weeks after the initial broadcast. Click on this link in the near future for viewing information via CDN.  
<http://vaww.vakncdn.lrn.va.gov/>

### Management and Treatment of Hepatitis C Viral Infection Recommendations from the Dept of VA Hepatitis C Resource Center Program and the National Hepatitis C Program Office

<http://vaww.hepatitis.va.gov/vahep?page=prtop04-gd-2006-00>

Click below for the definitive article from *Am J Gastroenterol* 2006; 101: 2360-2378 (PDF version) and information for free 3.0 CEUs Available for VA Nurses, Physicians, & pharmacists (VA Intranet only) through 10/07.

<http://vaww.hepatitis.va.gov/pdf/va01-pr/prtop-04/prtop04-gd-2006.pdf>

### “Risk Reduction for Thrombotic Events”

Check with your Employee Education System representative for the availability of this webcast program featuring the following VA faculty:

Robert Jesse, MD, PhD, FACC, FAHA from Richmond, Virginia VAMC and  
 Greg C. Larsen, MD from Portland VAMC  
 CE-Accredited now through November 2007

More information is available on PBM websites. Be sure to bookmark these websites:

[vaww.pbm.va.gov](http://vaww.pbm.va.gov) or  
[www.pbm.va.gov](http://www.pbm.va.gov)