**Pharmacy Benefits Management - Medical Advisory Panel - VISN Pharmacist Executives**

**Ez - MINUTES**

Volume 15, Issue 2
February 2017 – April 2017

Watch for the next issue of Ez-Minutes Tuesday, August 1st, 2017


Click Here to Subscribe to the Ez Minutes

---

**Inside This Issue**

- **Posting of National PBM Documents**
  - February - April 2017
- **PEARLS for PACT PROVIDERS**
- **National Contract Awards for CY 2017**
- **Pharmacy-Prosthetics-Logistics and Acquisitions (PPL) Workgroup**
  - February - March 2017
- **Treada vs. Bendeka Formulations: What are the differences?**
- **Beta-Blockers in Heart Failure with Reduced Ejection Fraction (HFrEF). How’s the VA Doing?**
- **Important Miscellaneous Announcements**
- **PBM-MAP-VPE Monthly Webinars: May and June 2017**

Read the recent issue of Ez-Minutes from your smart phone! Put the below link in your browser; hit search and read the current issue from the PBM INTERnet [http://www.pbm.va.gov/PBM/ez_minutes/current/currentEzMinutes.pdf](http://www.pbm.va.gov/PBM/ez_minutes/current/currentEzMinutes.pdf).

---

**Posting of National PBM Documents February – April 2017 Formulary Decisions**

<table>
<thead>
<tr>
<th>ADDED to the VA National Formulary (VANF)</th>
<th>NOT ADDED to the National Formulary (VANF)</th>
<th>Removed from the National Formulary (VANF)</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Breast milk storage bags</td>
<td>- Brivaracetam</td>
<td>- Daclizumab</td>
</tr>
<tr>
<td>- Fingolimod</td>
<td>- Canakinumab Injection</td>
<td></td>
</tr>
<tr>
<td>- Halobetasol Cream</td>
<td>- Glycoprotein-Formoterol Inhaler</td>
<td></td>
</tr>
<tr>
<td>- Halobetasol Ointment</td>
<td>- Glycoprotein-Indacaterol Inhaler</td>
<td></td>
</tr>
<tr>
<td>- Micronized Progestrone (oral)</td>
<td>- Halobetasol Lotion, Topical</td>
<td></td>
</tr>
<tr>
<td>- Naltrexone-Bupropion</td>
<td>- Hyaluronic Acid (GELSYN-3)</td>
<td></td>
</tr>
<tr>
<td>- Pemexrexed injection</td>
<td>- Hyaluronic Acid (MONOVISC)</td>
<td></td>
</tr>
<tr>
<td>- Phentermine-Toriparamide</td>
<td>- Insulin Glargine (BASAGLAR)</td>
<td></td>
</tr>
<tr>
<td>- Terifunomide</td>
<td>- Maccitentan</td>
<td></td>
</tr>
<tr>
<td>- U500 Insulin Pens - * PA-F Note: U500 vials &amp; syringes remain nonformulary</td>
<td>- Obeticholic Acid Panobinostat</td>
<td></td>
</tr>
<tr>
<td>*PA-F-Prior authorization at facility level</td>
<td>- Pomalidimide</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Venetoclax</td>
<td></td>
</tr>
</tbody>
</table>

**Clinical Recommendations**

- Ocrelizumab (Ocrevus) Interim Considerations [INTRAnet only]
- Recommendations/Guidance for Disease Modifying Therapy
- Selection in Multiple Sclerosis 2017

**Drug Monograph**

- Brivaracetam
- Glycoprotein-Formoterol Inhaler
- Glycoprotein-Indacaterol Inhaler
- Hyaluronic Acid (GELSYN-3)
- Hyaluronic Acid (MONOVISC)
- Maccitentan
- Obeticholic Acid
- Panobinostat
- Pomalidimide
- Tenofovir Alafenamide

**Abbreviated Review**

- Insulin Glargine (BASAGLAR)
- Progestrone, Micronized
- Urea Powder, Oral [INTRAnet only]

---

**PACT PEARLS**

Editor’s Note: The purpose of PBM-MAP-VPE Ez-Minutes Newsletter is to communicate with the field on items which will impact clinical practice. This section is aimed at communicating helpful information that is of particular interest to any PACT Provider. Please send and feedback and/or comments to Janet.Dailey@va.gov.

- Infliximab-dyyb. (INFLECTRA), first biosimilar of infliximab (REMICADE). Infliximab-dyyb may be used in new starts in lieu of infliximab and, with prior provider authorization, interchanged for infliximab. The following CFU were revised to incorporate infliximab-dyyb: **Anti-TNF DMARDs for Rheumatoid Arthritis [Updated Apr 2017]**
  - Atezolizumab PA-F CFU [Updated March 2017]
  - Biologics in Psoriasis and Psoriatic Arthritis [Updated Apr 2017]
  - Endothelin Receptor Antagonist [Updated Feb. 2017]
  - Fidaxomycin [Updated Feb. 2017]
  - Fingolimod [Updated March 2017]
  - Patiromer [Updated Feb. 2017]
  - Sacubitril Valsartan [Updated Mar. 2017]
  - Tocilizumab
  - Tenofovir alafenamide
  - Terifunomide [Updated Mar. 2017]
  - Urea Powder, Oral [INTRAnet only]

- The fixed-dose LAMA/LABA combination inhaler, tiotropium/olodaterol Respimat is on the VANF. Other LAMA/LABA inhalers that are nonformulary include glycoprotein/indacaterol, glycoprotein/formoterol, and umeclidinium/vilanterol. There are no trials directly comparing the LAMA/LABA products. However, tiotropium has the most extensive clinical data including long-term outcomes and safety data. Additionally, the combination tiotropium/olodaterol Respimat has favorable pricing compared to the other agents. It is recommended that the nonformulary products be reserved for those unable to use the tiotropium/olodaterol

- It is recommended to use guideline-concordant Beta-Blockers in HF in Veterans with Reduced Ejection Fraction (HFrEF). See page 3.
Comparison of Bendamustine Formulations

Background: Bendamustine (Treanda) was FDA-approved in 2008. Bendamustine functions as an alkylating agent. The drug was originally available in 2 single-dose vial formulations: injectable solution (45 mg/0.5 ml, 180 mg/2ml) as well as lyophilized powder for reconstitution (25 mg, 100 mg). Current FDA-approved indications include: Chronic Lymphocytic Leukemia (CLL) and Indolent B-cell non-Hodgkin lymphoma (NHL) that has progressed during or within 6 months of treatment with rituximab or a rituximab-containing regimen.

In December 2015, the FDA approved bendamustine (Bendeka) as a 100 mg/4ml (25 mg/ml) multi-dose vial for the same indications. The Treanda injectable solution (45 mg/0.5 ml, 180 mg/2ml) was discontinued in March 2016, leaving only the lyophilized powder formulation.

Safety and tolerability of the Bendeka formulation was studied in an 8-week open-label, crossover trial of 81 ‘end-of-life’ cancer patients with various malignancies. Adverse reactions occurring within one hour post-infusion included nausea (8.2%) and fatigue (5.5%). Reactions occurring within 24 hours of infusion included nausea (10.9%) and fatigue (8.2%). Those leading to study withdrawal included: pyrexia (1.2%), nausea (1.2%), vomiting (1.2%), pneumonia (1.2%) and fatigue (1.2%).

Table 1. Differences Between Treanda and Bendeka Formulations

<table>
<thead>
<tr>
<th>Diluent options</th>
<th>Admixture stability</th>
<th>Infusion time</th>
<th>Contraindications</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.9% sodium chloride</td>
<td>24 hours refrigerated</td>
<td>30 min CLL; 60 min NHL</td>
<td>CLL: 100 mg/m² IV over 30 min. on days 1 and 2 of a 28-day cycle, up to 6 cycles</td>
</tr>
<tr>
<td>2.5% dextrose/0.45% sodium chloride</td>
<td>3 hours room temp/room light</td>
<td>10 min CLL and NHL</td>
<td>NHL: 120 mg/m² IV over 60 min. on days 1 and 2 of a 21-day cycle, up to 8 cycles</td>
</tr>
</tbody>
</table>

Summary: The Bendeka formulation of bendamustine provides many practical advantages to the lyophilized formulation of Treanda, namely the lack of need for reconstitution (solution vs. powder), smaller volume diluent (50 ml vs. 500 ml), sodium-free diluent option (D5W vs. NSS only), short infusion time (10 min. vs. 30- or 60- min.), multi-dose vial option (vs. single-dose vials) and potential cost-savings. Not all patients will be able to receive the Bendeka formulation due to allergies with polyethylene glycol 400, propylene glycol or monothioglycerol, which is a contraindication to use. Those without contraindication should receive the Bendeka formulation. Bendamustine is not on the VA National Formulary.
Beta-Blockers in Heart Failure with Reduced Ejection Fraction (HFrEF)

VA Utilization: Per a recent PBM and VA MedSAFE database evaluation of beta-blocker use in VA, it was noted that approximately 64% of patients with HFrEF (estimate per select diagnosis coding) being treated with a beta-blocker were prescribed guideline concordant beta-blockers.

Guideline Recommendations and Evidence for Beta-Blockers with Improved Mortality Data in Patients with HFrEF:
- A beta-blocker that has proven to reduce mortality is recommended for patients with current or prior symptoms of HFrEF, unless contraindicated, to reduce morbidity and mortality (Class I Recommendation; Level of Evidence A).
- Meta-analyses of beta-blocker trials show a reduction in mortality of approximately 30 to 35%. The beta-blockers that are recommended in HFrEF and that have demonstrated a reduction in morbidity and mortality include bisoprolol, carvedilol, and sustained release metoprolol succinate. It is unknown if other beta-blockers have a similar benefit, as not all beta-blockers studied have shown a clear reduction in mortality.

Table 1: COMPARISON OF EVIDENCE-BASED BETA-BLOCKERS FOR HFrEF

<table>
<thead>
<tr>
<th>Beta-Blocker</th>
<th>Bisoprolol</th>
<th>Carvedilol</th>
<th>Metoprolol XL</th>
</tr>
</thead>
<tbody>
<tr>
<td>VA National Formulary</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>FDA Indication</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Heart Failure</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Angina</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Post-AMI with LVEF ≤ 40%</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Hypertension</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Beta-cardioselective</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Alpha-blocker</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Once daily regimen</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
</tr>
</tbody>
</table>

Approximate Dose Equivalents of Beta-Blockers Used in HFrEF
- The beta-blockers atenolol and immediate-release metoprolol tartrate have been studied in patients with heart failure; however, data as to their long-term clinical outcome benefit and optimal dose have not been determined.
- According to an internal database evaluation, close to 3% of patients prescribed atenolol (~250 to 550 uniques per VISN), and nearly 8% of patients prescribed metoprolol tartrate (~1500 to 4000 uniques per VISN) had a diagnosis representative of HFrEF, and may be eligible for consideration of treatment with bisoprolol, carvedilol, or metoprolol succinate, as per clinical practice guideline recommendations for HFrEF.
- The following dose equivalences have been developed to assist practitioners who elect to convert their patients to a beta-blocker with established mortality benefit in HFrEF, and may be used for site level evaluation, education and intervention, as indicated.

Note: recommendations are not based on head-to-head comparison trials; dosage conversions are derived from the initial, mean, and target doses reported in long-term, outcome trials and from national guideline recommendations. The following may be modified based on clinical judgment and used if conversion deemed appropriate.

<table>
<thead>
<tr>
<th>Atenolol</th>
<th>Metoprolol IR*</th>
<th>Bisoprolol</th>
<th>Carvedilolβ</th>
<th>Metoprolol XLα</th>
</tr>
</thead>
<tbody>
<tr>
<td>25 mg once or divided twice daily</td>
<td>6.25 to 12.5 mg twice daily</td>
<td>1.25 mg once daily</td>
<td>3.125 mg twice daily</td>
<td>25 mg once daily (12.5 mg once daily if &gt; NYHA class II)</td>
</tr>
<tr>
<td>50 mg once or divided twice daily</td>
<td>12.5 to 25 mg twice daily</td>
<td>2.5 mg once daily</td>
<td>6.25 mg twice daily</td>
<td>50 mg (or 25 mg) once daily</td>
</tr>
<tr>
<td>75 mg once or divided twice daily</td>
<td>25 to 50 mg twice daily</td>
<td>5 mg once daily</td>
<td>12.5 mg twice daily</td>
<td>100 mg (or 50 mg) once daily</td>
</tr>
<tr>
<td>100 mg once or divided twice daily</td>
<td>50 to 100 mg twice daily</td>
<td>10 mg once daily</td>
<td>25 mg twice daily (may titrate to 50 mg twice daily if &gt; 85 kg)</td>
<td>200 mg (or 100 mg titrated to 200 mg) once daily</td>
</tr>
</tbody>
</table>

* Metoprolol IR=immediate release metoprolol tartrate; Metoprolol XL=sustained release metoprolol succinate
β Dosing recommendations for carvedilol; carvedilol CR (extended-release formulation dosed once daily) also available non-formulary

For additional discussion, information on recommended target doses, and references: refer to Beta-Blockers in Heart Failure, Clinical Recommendations (Rev Dec 2016)

Additional Resources:
- Urea powder, oral is not a FDA approved drug; the one pre-packaged product available for hyponatremia is being marketed as a medical food
- Amend VANF listing of difluprednate to include optometry as prescribers
- Enrollees in Moodle DM Certificate Program: Module 4 will close 5/15-5/30/17 for updating. Complete all work (quiz too) by 5/15/17 PM so your work won’t be lost.

MONTHLY PBM-MAP-VPE Webinars (3rd Tues of the month @ 3:10 ET)

VANTS: 1-800-767-1750 Access Code 49792# for all webinars below


All webinars are accredited for ACPE, ACPE-T, ACCME, and ACCME-NP unless specified.

5/16/17: Regulatory Issues in Pharmacy Practice (Register in TMS by 5/15/17)
- ACPE/ACCME accreditation: **PBM Monthly Series - Regulatory Issues**
- ACPE-T accreditation: **PBM Monthly Series - Regulatory Issues - Pharmacy Technicians**

REMINDER: ACPE accredited weekly BCPS/BCACP board certification webinars (Every Thurs at 12 noon ET) are in progress. Anyone can attend.

PLUS, ACPE accredited “Mental Health” webinars will begin June 14th @ 3:10 PM ET. Contact Janet.Dailey@va.gov for more details.