**Inside This Issue**

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

**ADDED to the VA National Formulary (VANF):**
- Breast milk storage bags
- Fingolimod
- Halobetasol Cream
- Halobetasol Ointment
- Micronized Progesterone (oral)
- Naltrexone-Bupropion
- Pemtrexed injection
- Phentermine-Tipramate
- Teriflunomide
- U500 Insulin Pens
- Urea Powder Oral
- Urodine triacetate
- U500 Insulin vials & syringes remain nonformulary

**NOT ADDED to the National Formulary (VANF):**
- Brivaracetam
- Canakinumab Injection
- Glycopyrrolate-Formoterol Inhaler
- Glycopyrrolate-Indacaterol Inhaler
- Halobetasol Lotion, Topical
- Hyaluronic Acid (GELSYN-3)
- Hyaluronic Acid (MONOVISC)
- Insulin Glargine (BASAGLAR)
- Maccetan
- Otezolol Acid Panobinostat
- Pomalidomide
- Venetoclax

**Removed from the National Formulary (VANF):**
- Daclizumab

**Criteria for Use (CFU):**
- Anti-TNF DMARDs for Rheumatoid Arthritis [Updated Apr 2017]
- Atezolizumab PA-F CFU [Updated March 2017]
- Biologics in Psoriasis and Psoriatic Arthritis [Rev Apr 2017]
- Endothelin Receptor Antagonist [Updated Feb. 2017]
- Fidaxomicin [Updated Feb. 2017]
- Fingolimod [Updated March 2017]
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- Sacubitril Valsartan [Updated March 2017]
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**Clinical Recommendations:**
- Ocrelizumab (Ocrevus) Interim Considerations [INTRANet only]
- Recommendations/Guidance for Disease Modifying Therapy Selection in Multiple Sclerosis 2017

**Drug Monograph:**
- Brivaracetam
- Glycopyrrolate-Formoterol Inhaler
- Glycopyrrolate-Indacaterol Inhaler
- Hyaluronic Acid (GELSYN-3)
- Hyaluronic Acid (MONOVISC)
- Maccetan
- Otezolol Acid Panobinostat
- Pomalidomide
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**Patient-Provider Letters:**
- Disopyramide SA (Drug Shortage) Patient Letter [INTRANet only]
- Disopyramide SA (Drug Shortage) Provider Letter [INTRANet only]

**Important Miscellaneous Announcements:**
- PBM-MAP-VPE Monthly Webinars: May and June 2017


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**Read the recent issue of Ez-Minutes from your smartphone:**
Put the below link in your browser, hit search and read the current issue from the PBM INTERnet

**Abbreviated Review:**
- Insulin Glargine (BASAGLAR)
- Progesterone, Micronized
- Urea Powder, Oral [INTRANet only]

**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.Daiely@va.gov

- Infliximab-dybb. (INFLLECTRA), first biosimilar of infliximab (REMICADE). Infliximab-dybb 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-dybb: Anti-TNF DMARDs for Rheumatoid Arthritis; Biologics in Psoriasis and Psoriatic Arthritis.

- The fixed-dose LAMA/LABA combination inhaler, tiotropium/olodaterol Respimat is on the VANF. Other LAMA/LABA inhalers that are nonformulary include glycopyrrolate/indacaterol, glycopyrrolate/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.
National Contract Awards for Calendar Year 2017
Click on this link to view the National Contract Awards CY 2017. [InTRAnet only]

National Pharmacy-Prosthetics-Logistics (NPPL)* Committee

The table below depicts the various products reviewed during January-March 2017. The X marks which service(s) is responsible for managing the respective products. Click HERE for recommendations made and minutes from earlier meetings.

<table>
<thead>
<tr>
<th>Products</th>
<th>Responsible Service</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cologuard collection kit</td>
<td>X (clinic use)</td>
</tr>
<tr>
<td>Hydrogel and Medi-Honey wound dressing</td>
<td>X (outpatients)</td>
</tr>
<tr>
<td>Skin protectant moisture barrier creams/ointments</td>
<td>X (outpatients)</td>
</tr>
<tr>
<td>Stronghold anti-disconnect device</td>
<td>X (outpatients)</td>
</tr>
<tr>
<td>Sunscreen</td>
<td>X (inpatients, CLC, outpatients)</td>
</tr>
<tr>
<td>Transtracheal catheter cleaning supplies</td>
<td>X (outpatients)</td>
</tr>
<tr>
<td>Post-cataract surgery patient care kits (eye clinic)</td>
<td>X (inpatient or clinic use)</td>
</tr>
</tbody>
</table>

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>Availability</th>
<th>Bendamustine (Treanda)</th>
<th>Bendamustine (Bendeka)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SDV or MDV</td>
<td>25 mg, 100 mg lyophilized powder for reconstitution</td>
<td>100 mg/4ml (25 mg/ml) solution for injection</td>
</tr>
<tr>
<td>Diluent options</td>
<td>0.9% sodium chloride 2.5% dextrose/0.45% sodium chloride</td>
<td>0.9% sodium chloride 2.5% dextrose/0.45% sodium chloride 5% dextrose</td>
</tr>
<tr>
<td>Admixture final volume</td>
<td>500 ml</td>
<td>50 ml</td>
</tr>
<tr>
<td>Infusion time</td>
<td>30 min CLL; 60 min NHL</td>
<td>10 min CLL and NHL</td>
</tr>
<tr>
<td>Contraindications</td>
<td>Patients with a history of hyper-sensitivity reaction to bendamustine</td>
<td>Patients with a history of hyper-sensitivity reaction to bendamustine, polyethylene glycol 400, propylene glycol or monothioglycerol</td>
</tr>
<tr>
<td>Dosing</td>
<td>CLL: 100 mg/m2 IV over 30 min. on days 1 and 2 of a 28-day cycle, up to 6 cycles NHL: 120 mg/m2 IV over 60 min. on days 1 and 2 of a 21-day cycle, up to 8 cycles</td>
<td>CLL: 100 mg/m2 IV over 10 min on days 1 and 2 of a 28-day cycle, up to 6 cycles NHL: 120 mg/m2 IV over 10 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- 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 (HF\(rEF\))

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 HF\(rEF\) (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 HF\(rEF\):**

- A beta-blocker that has proven to reduce mortality is recommended for patients with current or prior symptoms of HF\(rEF\), 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 HF\(rEF\) 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 HF\(rEF\)**

<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>
</tbody>
</table>

- **FDA Indication**
  - Heart Failure
  - Angina
  - Post-AMI with LVEF < 40%
  - Hypertension
  - Beta-cardioselective
  - Alpha-blocker
  - Once daily regimen

**Approximate Dose Equivalents of Beta-Blockers Used in HF\(rEF\):**

- 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 unique per VISN), and nearly 8% of patients prescribed metoprolol tartrate (~1500 to 4000 unique per VISN) had a diagnosis representative of HF\(rEF\), and may be eligible for consideration of treatment with bisoprolol, carvedilol, or metoprolol succinate, as per clinical practice guideline recommendations for HF\(rEF\).
- 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 HF\(rEF\); 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.

- **Atenolol**
  - 25 mg once or divided twice daily
  - 50 mg once or divided twice daily
  - 75 mg once or divided twice daily
  - 100 mg once or divided twice daily

- **Metoprolol IR**
  - 6.25 to 12.5 mg twice daily
  - 12.5 to 25 mg twice daily
  - 25 to 50 mg twice daily
  - 50 to 100 mg twice daily

- **Bisoprolol**
  - 1.25 mg once daily
  - 2.5 mg once daily
  - 5 mg once daily
  - 10 mg once daily

- **Carvedilol**
  - 25 mg once daily
  - 50 mg once daily
  - 100 mg once daily

- **Metoprolol XL**
  - 50 mg twice daily if > 85 kg
  - 100 mg (or 50 mg) once daily

**Table 1 Legend**

AM\(I\)=acute myocardial infarction
LVEF=left ventricular ejection fraction
XL=sustained release metoprolol succinate

* Restricted to patients with heart failure

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**Posting of Center for Medication Safety VA MedSAFE Documents: October 2016-February 2017**

Editor’s Note: This section was absent in last issue due to SharePoint upgrading. Posted documents prior to the interruption has been included in this issue.

**Safety Issue**

- **EpiPen and EpiPen Jr Auto-Injector: Recall-Failure**
  - Date of Release: 4/4/2017
  - Safety Information: National PBM Patient Level Recall Communication

- **Direct-Acting Antiviral Safety Issues**
  - Date of Release: 03/14/2017
  - Safety Information: National PBM Bulletin

- **ADDENDUM: Mirtazapine Tablets, USP 45mg – Ongoing Recall Due to Commingled Tablets**
  - Date of Release: 03/08/2017
  - Safety Information: National PBM Patient Level Recall Communication

- **Alprostadil for Injection (Edex®) – Recall Due to Potential Lack of Sterility Assurance**
  - Date of Release: 03/06/2017
  - Safety Information: National PBM Patient Level Recall Communication

- **Chlorhexidine Gluconate Safety**
  - Date of Release: 02/07/2017
  - Safety Information: National PBM Bulletin

- **Liquid Products Recall (PharmaTech) Due to Potential Risk of Product Contamination**
  - Date of Release: 10/12/2016
  - Safety Information: National PBM Patient Level Recall Communication

**Other Announcements**

- **VA Drug Standardization List - Mar. 2017** Updated with prenatal vitamins. Refer to Aug-Oct 2016 Ez Minutes for further details. Also included in Drug Standardization List.
- **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.**
- **Editor’s Note:** This section was absent in last issue due to SharePoint upgrading. Posted documents prior to the interruption has been included in this issue.

**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


**Article Submitted by:** Elaine Furmaga, PharmD, National PBM Clinical Pharmacy Program Manager-PBM Formulary Management

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