



Pharmacy Benefits Management- Medical Advisory Panel- VISN Pharmacist Executives E_z - MINUTES

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	<p>ADDED to the VA National Formulary (VANF)</p> <ul style="list-style-type: none"> • Breast milk storage bags • Fingolimod • Halobetasol Cream • Halobetasol Ointment • Micronized Progesterone (oral) • Naltrexone-Bupropion • Pemetrexed injection • Phentermine-Topiramate • Teriflunomide • Urea Powder Oral • Uridine triacetate • U500 Insulin Pens - * PA-F <p><i>Note: U500 vials & syringes remain nonformulary</i> *PA-F-Prior authorization at facility level</p>	<p>NOT ADDED to the National Formulary (VANF)</p> <ul style="list-style-type: none"> • Brivaracetam • Canakinumab Injection • Glycopyrrolate-Formoterol Inhaler • Glycopyrrolate-Indacaterol Inhaler • Halobetasol Lotion, Topical • Hyaluronic Acid (GELSYN-3) • Hyaluronic Acid (MONOVISC) • Insulin Glargine (BASAGLAR) • Macitentan • Obeticholic Acid Panobinostat • Pomalidomide • Venetoclax 	<p>Removed from the National Formulary (VANF)</p> <ul style="list-style-type: none"> • Daclizumab
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	<p>Patient-Provider Letters</p> <ul style="list-style-type: none"> • Disopyramide SA (Drug Shortage) Patient Letter [<i>INTRAnet only</i>] • Disopyramide SA (Drug Shortage) Provider Letter [<i>INTRAnet only</i>] 		<p>Abbreviated Review</p> <ul style="list-style-type: none"> • Insulin Glargine(BASAGLAR) • Progesterone, Micronized • Urea Powder, Oral [<i>INTRAnet only</i>]- See PG 3 for more info on urea powder

PACT PEARLS

Editor's Note: The purpose of PBM-MAP-VPE E_z-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](#); [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 (HF_rEF). 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 (NPPLI)* Committee

**The PPL committee is established to clarify the responsibilities for the management and provision of primarily non-drug products; with the intent to improve the consistency of care associated with the provision of those selected products across the VHA. The committee is not responsible for determining formulary status, clinical merit, or appropriate use of the products reviewed.*

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.

Cologuard collection kit			X (clinic use)
Hydrogel and Medi-Honey wound dressing	X (outpatients)		X (inpatients, clinic use)
Skin protectant moisture barrier creams/ointments	X (outpatients)		X (inpatients, clinic use)
Stronghold anti-disconnect device	X (outpatients)	X (home ventilator)	X (inpatients, clinic use or VA long term care)
Sunscreen	X (inpatients, CLC, outpatients)		
Transtracheal catheter cleaning supplies	X (outpatients)		X (inpatient or clinic use)
Post-cataract surgery patient care kits (eye clinic)			X

+ Contingent upon approval from VISN or local Clinical Products Review Committee (CPRC). Implementation of these determinations should be coordinated between services at local sites to ensure a smooth transition if determinations lead to a change in responsible service. If you have any questions related to this announcement, please contact the responsible local service (Pharmacy, Prosthetics, or Logistics) for more detailed information.

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

	Bendamustine (Treanda)	Bendamustine (Bendeka)
Availability	25 mg, 100 mg lyophilized powder for reconstitution	100 mg/4ml (25 mg/ml) solution for injection
SDV or MDV	SDV	MDV 6 dose withdrawals/vial for up to 28 days from first use
Diluent options	0.9% sodium chloride 2.5% dextrose/0.45% sodium chloride	0.9% sodium chloride 2.5% dextrose/0.45% sodium chloride 5% dextrose
Admixture final volume	500 ml	50 ml
Admixture stability	24 hours refrigerated 3 hours room temp/room light	NSS-containing solution: 24 hours refrigerated 6 hours room temp/room light D5W solution: 24 hours refrigerated 3 hours room temp/room light
Infusion time	30 min CLL; 60 min NHL	10 min CLL and NHL
Contraindications	Patients with a history of hyper-sensitivity reaction to bendamustine	Patients with a history of hyper-sensitivity reaction to bendamustine, polyethylene glycol 400, propylene glycol or monoethioglycerol
Dosing	CLL: 100 mg/m ² IV over 30 min. on days 1 and 2 of a 28-day cycle, up to 6 cycles NHL: 120 mg/m ² IV over 60 min. on days 1 and 2 of a 21-day cycle, up to 8 cycles	CLL: 100 mg/m ² IV over 10 min on days 1 and 2 of a 28-day cycle, up to 6 cycles NHL: 120 mg/m ² IV over 10 min. on days 1 and 2 of a 21-day cycle, up to 8 cycles

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 monoethioglycerol, 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/EF)

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/EF (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/EF:

- A beta-blocker that has proven to reduce mortality is recommended for patients with current or prior symptoms of HF/EF, 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/EF 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/EF

Beta-Blocker	Bisoprolol	Carvedilol	Metoprolol XL
VA National Formulary	√*	√	√*
FDA Indication			
Heart Failure		√	√
Angina			√
Post-AMI with LVEF ≤ 40%		√	
Hypertension	√	√	√
Beta ₁ cardioselective	√		√
Alpha-blocker		√	
Once daily regimen	√		√

Table 1 Legend
 AMI=acute myocardial infarction
 LVEF=left ventricular ejection fraction
 XL=sustained release metoprolol succinate
 * Restricted to patients with heart failure

Approximate Dose Equivalents of Beta-Blockers Used in HF/EF

- 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 HF/EF, and may be eligible for consideration of treatment with bisoprolol, carvedilol, or metoprolol succinate, as per clinical practice guideline recommendations for HF/EF.
- The following dose equivalents have been developed to assist practitioners who elect to convert their patients to a beta-blocker with established mortality benefit in HF/EF; 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	Metoprolol IR ^a	Bisoprolol	Carvedilol ^b	Metoprolol XL ^a
25 mg once or divided twice daily	6.25 to 12.5 mg twice daily	1.25 mg once daily	3.125 mg twice daily	25 mg once daily (12.5 mg once daily if > NYHA class II)
50 mg once or divided twice daily	12.5 to 25 mg twice daily	2.5 mg once daily	6.25 mg twice daily	50 mg (or 25 mg) once daily
75 mg once or divided twice daily	25 to 50 mg twice daily	5 mg once daily	12.5 mg twice daily	100 mg (or 50 mg) once daily
100 mg once or divided twice daily	50 to 100 mg twice daily	10 mg once daily	25 mg twice daily (may titrate to 50 mg twice daily if > 85 kg)	200 mg (or 100 mg titrated to 200 mg) once daily

^a Metoprolol IR=immediate release metoprolol tartrate; Metoprolol XL=sustained release metoprolol succinate

^b 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 \(Rev Dec 2016\)](#)

Article Submitted by: [Elaine Furmaga, PharmD, National PBM Clinical Pharmacy Program Manager-PBM Formulary Management](#)

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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	Date of Release	Safety Information
EpiPen and EpiPen Jr Auto-Injector: Recall-Failure	4/4/2017	National PBM Patient Level Recall Communication
Direct-Acting Antiviral Safety Issues	03/14/2017	National PBM Bulletin
ADDENDUM: Mirtazapine Tablets, USP 45mg – Ongoing Recall Due to Commingled Tablets	03/08/2017	National PBM Patient Level Recall Communication
Alprostadil for Injection (Edex®) – Recall Due to Potential Lack of Sterility Assurance	03/06/2017	National PBM Patient Level Recall Communication
Chlorhexidine Gluconate Safety	02/07/2017	National PBM Bulletin
Liquid Products Recall (PharmaTech) Due to Potential Risk of Product Contamination	10/12/2016	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 a detailed description of the 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.
- 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

Adobe Connect Meeting Link: <http://va-eerc-ees.adobeconnect.com/pbm-monthly-webinars/>

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: APCE 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.

6/20/17: Update on Hepatitis C –Direct TMS Links pending