



Volume 14, Issue 2
March – April 2016

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

Watch for the next issue of Ez-Minutes Tuesday, August 2nd, 2016

See us at: <http://www.pbm.va.gov/> or <https://vaww.cmopnational.va.gov/cmop/PBM/default.aspx>.

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The purpose of PBM-MAP-VPE Ez-Minutes Newsletter is to communicate with the field on items which will impact clinical practice in the VA. Please send and feedback and/or comments to Janet.Dailey@VA.gov.

The recent issue of Ez Minutes can be read from your smart phone! Put the below link in your browser; hit search... and the current issue from the PBM INTERnet site will be ready to read. <http://www.pbm.va.gov/PBM/ezminutes/current/currentEzMinutes.pdf>

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Posting of National PBM Documents March – April 2016 Formulary Decisions

ADDED to the VA National Formulary (VANF)	NOT ADDED to the National Formulary (VANF)	Removed from the National Formulary (VANF)
<ul style="list-style-type: none"> CORRECTION: 5/10/16: Diclofenac 1% Topical Gel only (Patch, Gel and Solution) Empagliflozin Genvoya®-Restricted to specialists Naloxone nasal spray 4mg Nivolumab (with CFU) Pembrolizumab Pramipexole (with CFU) Siltuximab (Restricted to oncology; CFU is pending) Torsemide tablets 	<ul style="list-style-type: none"> Antihemophilic factor (recombinant), PEGylated Aripiprazole lauroxil (ARISTADA) Brexipiprazole Budesonide Rectal Foam Bupivacaine Liposome Injectable Suspension Carbidopa Levodopa Enteral Suspension Diclofenac Injectable Diclofenac Topical 1.5% & 2% Solution Correction 5/10/16: Diclofenac Patch Five Grass Pollen Allergen Extract-Restricted to VA Allergy or locally designated expert Insulin Lispro 200 U/ml Ibrutinib Lacosamide oral tablets Rifaximin in IBS-D Timothy Grass Pollen Allergen Extract-Restricted to VA Allergy or locally designated experts Trifluridine-tipiracil (CFU pending) Olaparib Obinutuzumab (CFU pending) Patiromer Sumatriptan nasal powder Vorapaxar 	<ul style="list-style-type: none"> None during this time frame
Drug Monograph		
<ul style="list-style-type: none"> Aripiprazole Long-acting IM [Updated March 2016] Brexipiprazole Budesonide Rectal Foam Bupivacaine Liposome Injectable Suspension-[Evidence Update March 2016] Carbidopa Levodopa Enteral Suspension Certolizumab Pegol in Psoriatic Arthritis [Updated April 2016] Dabigatran Hip Venous Thromboembolism Prophylaxis [Updated March 2016] Diclofenac Injectable Diclofenac Topical (Patch, Gel, and Solution) Genvoya® Five Grass Pollen Allergen Extract Ibrutinib [Updated March 2016] Nivolumab Obinutuzumab Olaparib Patiromer Pembrolizumab Rifaximin in IBS-D Siltuximab Timothy Grass Pollen Allergen Extract Trifluridine-tipiracil Ustekinumab in Psoriatic Arthritis [Updated April 2016] Vorapaxar 		
Criteria for Use (CFU)		
<ul style="list-style-type: none"> Anticoagulants, Direct Oral (DOACs) CFU and Algorithm for Venous Thromboembolism (VTE) Treatment [Updated March 2016] Anticoagulants, Direct Oral (DOACs) CFU and Algorithm for Nonvalvular Atrial Fibrillation [Updated Mar 2016] Anticoagulants, Direct Oral (DOACs) CFU for Venous Thromboembolism (VTE) Prophylaxis in Ortho Surgery [Updated March 2016] Carbidopa Levodopa Enteral Suspension Empagliflozin Ibrutinib [Updated March 2016] Lacosamide oral tablets Nivolumab Patiromer Pembrolizumab 		
Archived Documents		
<ul style="list-style-type: none"> Anticoagulants, Direct Oral (DOACs) CFU for Venous Thromboembolism (VTE) Prophylaxis in Ortho Surgery Anticoagulants, Direct Oral (DOACs) CFU and Algorithm for Nonvalvular Atrial Fibrillation Anticoagulants, Direct Oral (DOACs) CFU and Algorithm for VTE Bupivacaine Liposome Injectable Suspension Evidence Update Sodium-Glucose Co-Transporter 2(SGLT2) Inhibitor CFU 		
Clinical Recommendations		
<ul style="list-style-type: none"> VA National Formulary Hormonal Contraceptive Agents [Updated April 2016] Naloxone Rescue Kit 		
Abbreviated Review		
<ul style="list-style-type: none"> Insulin Lispro 200 U/ml Naloxone Nasal Spray 		
<p>Field Reminder: Oral sodium phosphate is on VANF but restricted to GI</p>		
<p> How does STORM help Opioid Overdose Education and Naloxone Distribution (OEND)? Read Page 4!</p>		



VA Center for Medication Safety

**Posting of Center for Medication Safety (VAMedSAFE) Documents
March-April 2016**

- Metformin Revised Warnings 04/18/2016 [National PBM Bulletin](#)
- Thyrogen® (thyrotropin alfa for injection) Recall Due to Glass Particulates 04/01/2016 [National PBM Patient Level Recall Communication](#)
- Idelalisib Safety 03/29/2016 [National PBM Bulletin](#)

National Contract Awards for Calendar Year 2016

Click on [this link](#) to view the National Contract Awards CY 2016. [InTRANet only]

Pharmacy-Prosthetics-Logistics (PPL)* Workgroup

The table below depicts the various products reviewed during Febr.–March 2016 meetings. The X marks which service(s) is responsible for managing the respective products. Click [HERE](#) for recommendation and minutes made from earlier meetings.

**The PPL workgroup was created to help clarify the responsibility for management (e.g., ordering, storing, purchasing, and/or dispensing) of those products in which it is not clear which service should provide. The workgroup is not responsible for determining formulary status, clinical merit, or appropriate use of the products reviewed.*

Products	Pharmacy+	Prosthetics+	Logistics+
Barium containing product-contrast agents	X (be involved in handling them and does not mean is responsible for ordering or purchasing all barium products)		X (approved as devices and approval by P&T to stock in radiology for specific uses)
Disposable nasal stents	X (outpatients)		X (inpatients)
Disposable insulin administration ports	X (outpatients)		X (inpatients or long-term care residents)
Implanted nasal stents durable nasal stents (lasting > 30 days)		X	
Kits used in the AURIX centrifuge system for wound management			X (inpatients or clinic use)
Nitric oxide gas (INOMAX) Drug-Device Combination			X (inpatient or clinic use)
Vibralong acoustical percussor		X (outpatients)	X (inpatients)

+ Contingent upon approval from VISN or local Clinical Products Review Committee (CPRC). Implementation of these recommendations should be coordinated between services at local sites to ensure a smooth transition if recommendations 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.

DO YOU KNOW???

What are the differences between these 2 lists?

The [VA Non-Promotable List](#) is a list of drug or supply items that are not to be promoted or detailed by pharmaceutical sales representatives.

The product Exparel (liposomal bupivacaine) has been removed from the list. Please note that this product remains non-formulary, so any promotion must be approved by the local Chief of Pharmacy as per Formulary Management Handbook.

Questions to test your knowledge:

What drug is on the VA Non-Promotable List?

What are the criteria used to determine whether a product is added to the list?

Click [HERE](#) to learn more!

The [VA Drug Standardization List](#) is a list of pharmaceutical products for which substitution is not permitted under normal circumstances. The decisions to place products on this list are based on reviews of therapeutic equivalency and/or patient safety data.

Prograf was removed and replaced by generic tacrolimus (Golden State Medical Supply/Mylan). The contract is a mandatory source for generic tacrolimus, but there is no mandatory conversion of brand Prograf to generic tacrolimus. Whether or not to switch to the generic is left to the discretion of the provider/local medical center.

Which agents are on the VA Drug Standardization List?

Under what circumstance is substitution permitted?

Click [HERE](#) to learn more!

FDA Withdraws Approval of Niaspan ER and Fenofibric Acid DR in Combination with Statins

On April 18th 2016, the FDA announced retraction of prior approvals related to combinations of statins with niacin extended release (ER) and statins with fenofibric acid delayed release (DR).¹ The decision to remove these indications was prompted by evidence from three large published trials, which failed to show reductions in important cardiovascular events when either niacin ER or fenofibric acid DR was added to statin therapy in the populations studied.²⁻⁴ The FDA has concluded that existing evidence does not support that reducing triglycerides or raising of high-density lipoprotein cholesterol (HDL) with any drug, including fenofibric acid or niacin, improves cardiovascular risk in patients on statins and therefore, the benefit of either combination with statins no longer exceeds the potential risk. The VA Pharmacy Benefits Management (PBM), Medical Advisory Panel (MAP) and VISN Pharmacist Executives' (VPEs) position on statin-niacin and statin-fibrate combination therapies are consistent with the recent FDA ruling and with the 2014 VA/DoD Clinical Practice Guideline for the Management of Dyslipidemia for Cardiovascular Risk Reduction.

In August 2014, MAP-PBM-VPE, Office of National Program Director for Cardiology and VA MedSAFE released a bulletin detailing the results of two of the three trials which pertained to niacin. Based upon the evidence from those trials, provider considerations and recommendations for managing patients on statin-niacin combinations were provided (See below).⁶

PROVIDER CONSIDERATIONS/RECOMMENDATIONS

1. Review and discuss niacin use with patients who are currently receiving niacin or being considered for niacin at their next visit.
 - a. Niacin should not be routinely used or combined with statins. Evidence supports statin monotherapy as the having the best evidence for cardiovascular risk reduction.
 - b. If niacin was added solely for the purpose of increasing HDL-C in a patient receiving at least a moderate dose statin, PBM recommends discontinuing the niacin. A recent meta-analysis of lipid therapies (niacin, fibrates or cholesterol ester transfer protein [CETP] inhibitors) added to statins to increase HDL-C were not shown to improve cardiovascular outcomes.
 - c. Niacin may be recommended for initiation or continued as monotherapy in selected patients not able to tolerate statins, as clinically appropriate. However, providers should discuss the risks (as observed in HPS2-THRIVE) of niacin therapy (including the use of over the counter niacin products) with their patients if the decision is made to initiate or to continue niacin therapy.
2. Assess statin choice and dosage at the time of discontinuation of niacin. If appropriate, consider increasing the dose of the particular statin and/or changing to a higher potency statin at recommended dosing for the underlying condition/cardiac risk profile.
 - a. If the patient is not receiving at least a moderate dose statin, increase the dose of statin as tolerated to moderate (reduces baseline LDL-C 30 to <50%) or high dose (reduces baseline LDL-C >50%), as clinically indicated and discontinue niacin.
 - b. If the statin dose has been maximized but the desired percent reduction in baseline LDL-C has not been achieved (30 to >50%), consider switching to an alternate high potency statin (e.g., atorvastatin or rosuvastatin).
3. If, despite the potential risks and lack of outcomes evidence with statin combination therapy, a clinician and patient choose combination therapy for further reducing LDL-C, consider continuation of niacin or alternatively, replacement of niacin with ezetimibe or bile acid sequestrants (e.g., colestipol, cholestyramine). However, it is important to recognize, and for patients to be aware, that the addition of other lipid lowering drugs (e.g., niacin, fibrates, ezetimibe*, bile acid sequestrants) to statin based therapy for the purpose of lowering LDL-C levels has not been proven to reduce cardiovascular events and therefore, these combinations should not be routinely used.
4. In patients who are on statins and have severely elevated triglyceride levels (>500 mg/dL), despite life-style modification and management of secondary causes of hypertriglyceridemia, formulary fish oil should be used rather than niacin. If fish oils inadequately reduced triglycerides or if the patient cannot tolerate fish oils, the best option for combination therapy is unclear given the potential for interaction/harm and the lack of evidence for benefit in reducing cardiovascular events or for preventing pancreatitis when a statin is combined with either a fibrate or niacin for reducing triglyceride levels. Therefore, caution should be used when considering combining a statin with either a fibrate or niacin in these patients.

*Ezetimibe improved nonfatal events in a study of >18,000 patients with acute coronary syndrome when added to moderate dose statins over a period of 6 years.⁶ This trial was published in 2015, after the bulletin had been released.

The VA PBM, MAP and VPEs have not previously advocated for combining statins with fibrates, including fenofibrate or fenofibric acid. Therefore recommendations for avoiding routine combinations of statins with fibrates remain.⁷⁻⁹

The VA/DoD Clinical Practice Guideline for the Management of Dyslipidemia for Cardiovascular Risk Reduction was finalized in December 2014. The guideline recommends against routine combination therapy with statins and other lipid lowering therapies for reducing cardiovascular risk due to the lack of evidence.¹⁰⁻¹¹

In light of the available evidence and the recent FDA withdrawal of approved indications for combination therapy, VA providers are encouraged to individually reconsider the appropriateness of combination therapy with niacin or fibrates in patients on statin therapy.

Article submitted by: Cathy Kelley, PharmD, National PBM Clinical Pharmacy Program Manager- PBM Formulary Management. Reviewed by Bernie Good, MD, FACP, MAP Chair; John R. (Rick) Downs, MD, FACP, MAP Member, VA/DoD Evidence Based Work Group CPG Steering Committee Member; and Mark McConnell, M.D., General Internal Medicine, Iron Mountain, MI and member of VA/DoD Lipid CPG Workgroup.

Editor's Note: The references were omitted due to space constraint. To view the entire submission including the references, [please click here](#).

Safety of Testosterone Replacement Therapy

Remarks included in a recent issue of JAMA Medical Letter, published April 12, 2016 were consistent with the updated PBM-MAP-VPEs Criteria for Use (updated Feb. 2016) on the safety and assessment of testosterone replacement therapy. Based on clinical evidence, the safety of testosterone replacement therapy remains unclear. There is no convincing evidence available that testosterone replacement therapy increases the risk of prostate cancer. There is conflicting evidence with regard to an association with cardiovascular (CV) events. While some trials and meta-analyses suggest a higher incidence of CV events in men treated with testosterone, others found a protective effect and decreased incidence of CV events when normalizing serum testosterone levels.

For more information, please refer to: Safety of Testosterone Replacement Therapy. JAMA. 2016; 315(14):1512-1513. doi: 10.1001/jama.2016.3450 <http://jama.jamanetwork.com/article.aspx?articleid=2512781>

PBM-MAP-VPE Criteria of Use: Testosterone Replacement Therapy (TRT) in Adult Men

https://vaww.cmopnational.va.gov/cmop/PBM/_layouts/OSSSearchResults.aspx?k=testosterone&cs=This%20Site&u=https%3A%2F%2Fvaww.cmopnational.va.gov%2Fcmop%2FPBM

Stratification Tool for Opioid Risk Mitigation is Here

The [VA Stratification Tool for Opioid Risk Mitigation \(STORM\)](#) is a new clinical decision support tool available to VA staff that leverages VA administrative data and predictive modeling to help improve opioid safety. Key features of STORM include: **(1) identifying patients** who are at-risk for adverse events such as drug overdose or suicide, **(2) listing risk factors** that place patients at-risk (e.g., previous adverse events, mental health and medical diagnoses, MEDD, co-Rx benzodiazepines), **(3) displaying risk mitigation strategies, including non-pharmacological treatment options**, which have been employed and/or could be considered, and **(4) displaying patients' upcoming appointments and current treatment providers** to facilitate care coordination. STORM is updated nightly and provides risk scores and risk mitigation strategies for patients with an active outpatient opioid prescription. VA staff has access to summary-level data on STORM. Access to patient-level STORM data requires LSV SSN-level permission. Anecdotally, we have been told that STORM has helped clinicians identify patients who may be appropriate candidates for [Opioid Overdose Education and Naloxone Distribution \(OEND\)](#) and has also been used clinically in shared decision-making conversations with patients to highlight patient's risk and need for opioid safety interventions (e.g., tapering). For additional information on STORM included in the **Naloxone Rescue Kit RFU**, [click here](#). Please contact Elizabeth.Oliva@va.gov if you have any questions about STORM.

2016 PBM Webinar Schedule: Third Tuesday of the month @ 3 PM ET

- May 17th, 2016: Part 3 of 3 Part Series on Demystifying Statistics for the Clinician
- June 21st, 2016: Hypoglycemia Safety Initiative
- July 19th, 2016: OEND Initiative (Updates)

All PBM-MAP-VPE webinars are conducted using the same Adobe Connect meeting link and VANTs number. <http://va-eerc-ees.adobeconnect.com/pbm-monthly-webinars/>

VANTS: 1-800-767-1750 Access Code 49792#

All webinars are ACPE, ACPE-T, ACCME, ACCME-NP accredited. Pre-registration (i.e. before the program starts) in TMS is required if desiring CEUs. Below are the registration links for all PBM webinars listed above. Register for one or all webinars using the links below.

For ACPE, ACCME, and ACCME-NP: [RSS: Pharmacy Benefits Management Virtual Series for Pharmacists and Clinicians](#)

For ACPE-T only: [RSS: Pharmacy Benefits Management Virtual SERIES - RSSTECHS](#)