Pharmacy Benefits Management-Medical Advisory Panel

E_z-Minutes

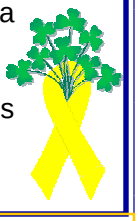
Volume 5, Issue 1
Jan– March 2007

Inside this Issue:

E_Z is Back! After a short hiatus, the EZ-Minutes is back in circulation. The previous issue was distributed in October, 2006. Many changes have occurred since then including the implementation of the VHA One National Formulary across all VISNs. What a major undertaking and accomplishment that has been. Through the process, the mission of the PBM remained the same and that was to improve the health status of veterans by encouraging the appropriate use of medications in a comprehensive medical care setting. As the process continues to be refined in the delivering of beneficial, safe, and consistent care in a cost-effective manner, we believe feedback from the field is extremely important. We are excited to announce that an electronic mechanism to assist in receiving direct feedback and comments on what you read in this national newsletter is currently under development. This newsletter has a circulation of 9500 subscribers so we know there are many great suggestions/comments in the field that needs to be captured. In the meantime, please notify your VISN Formulary Leaders on formulary issues/clinical topics that you believe need to be addressed on a national level.

In closing, it seems only appropriate to extend an Irish blessing to you as well as to the troops serving here and abroad. May the return of our troops be swift. Happy St. Patrick's Day!

Sláinte (Cheers), Janet O'Dailey, Co-editor of PBM-MAP E_Z-Minutes



WHAT IS Ez-MINUTES?-See Pg 2. HOW TO SUBSCRIBE TO Ez-MINUTES?-See Pg. 4

Recent Postings of National PBM Documents (11/06-3/07)

Criteria for Use/Nonformulary Use

http://vaww.pbm.va.gov/pbm/criteria.htm
http://vaww.pbm.va.gov/CriteriaForUse.aspx

- Clopidogrel (Plavix®)
- Darunavir (Prezista®)
- Ezetimibe (Zetia®)
- Flouroquinolone
- Topical Imiquimod
- Inhaled Insulin (Exubera®)
- Moxifloxacin Ophthalmic Solution
- Oxymorphone Oral Tablets
- Propoxyphene
- Thickening Agents for Outpatients
- Sitagliptin (Januvia™)
- Vardenafil Non-Responders
- Ziconotide for Intrathecal Infusion
- Zoster Vaccine Draft Guidance

Drug Monographs

http://vaww.pbm.va.gov/pbm/drugmonograph.htm
http://vaww.pbm.va.gov/DrugMonograph.aspx

- Conivaptin HCL Injection (Vaprisol®)

Drug Monographs Con't

- Darunavir (Prezista®)
- Entecavir (Baraclude®)
- Nelarabine (Arranon®)
- Posaconazole (Noxafil®)
- Ranibizumab (Lucentis®)
- Sitagliptin (Januvia™)
- Sunitinib (Sutent®)
- Ziconotide for Intrathecal Infusion (Prialt®)
- Zoster Vaccine Live (Zostavaz®)

Formulary Decisions:

New Molecular Entities (NME)

- Darunavir (Prezista®)-Added to VA National Formulary restricted to ID specialist in compliance with national Criteria for Use
- Posaconazole (Noxafil®)- Not added to VA National Formulary; restricted to ID and transplant specialists
- Nelarabine (Arranon®) Not added to VA National Formulary; restricted to hemonc in patients with T-cell ALL and T-cell lymphoma

Therapeutic Interchange Guidance

- Quinine for Leg Cramps Patient Letter

http://vaww.pbm.va.gov/tig/Quinine%20for%20Leg%20Cramps%20Patient%20Letter.pdf

VA National Formulary Contraceptive Agents:

Questions often arise regarding what contraceptive agents are available for women veterans. 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

QUININE NOT FOR LEG CRAMPS ANYMORE: Be sure to read the National PBM bulletin on recommendations that quinine should NOT be used for the prevention or treatment of nocturnal leg cramps because of the risk for serious adverse effects. http://vaww.pbm.va.gov/alerts/Quinine%20for%20Leg%20Cramps.pdf
http://www.pbm.va.gov/alerts/Quinine%20for%20Leg%20Cramps.pdf
A patient letter is available at: http://vaww.pbm.va.gov/tig/Quinine%20for%20Leg%20Cramps%20Patient%20Letter.pdf
http://www.pbm.va.gov/tig/Quinine%20for%20Leg%20Cramps%20Patient%20Letter.pdf
More information is available on the FDA web sites. http://www.fda.gov/bbs/topics/NEWS/2006/NEW01521.html
http://www.fda.gov/cder/drug/unapproved_drugs/quinineQA.pdf
At this time, there are no medication alternatives available. The following are some suggestions that may be helpful to tell your patients:

- Loosen up the covers/blankets over the feet at night. This helps your calf muscles to stay relaxed.
- Try stretching your calf muscles several times a day:
- Stand about two to three feet in front of a wall. Put your hands on the wall. Gently lean forward without taking your heels off the ground. Hold for 10-30 seconds.
- If a leg cramp does occur while lying in bed, stretch the muscle. To do that, try to straighten your legs and flex your feet towards your knees. Or, it may be helpful to sit up, hold your toes and pull them towards your knees while keeping your legs straight. You can bend your knees if needed. Or, you can try massaging the muscle during the cramp to help it relax.

Combination of Ezetimibe Plus Fibrates?

Read the detailed report at: (VA InTRAnet only)
http://vaww.pbm.va.gov/vamedsafe/Summary%20Evaluation%20of%20the%20Combination%20of%20Ezetimibe%20Plus%20Fibrates%20in%20VHA.pdf
Upon FDA approval of ezetimibe, the manufacturer recommended against combining ezetimibe with fibrates until human studies had been completed because fibrates can increase cholesterol excretion into the bile and in an animal study, ezetimibe was observed to have a similar effect thereby increasing the potential for cholelithiasis with the combination. Since that time, two trials (12-week and 48-week extension study) examining the combination of ezetimibe and fenofibrate in humans have been published. In June of 2006, the FDA approved the combination of ezetimibe with fenofibrate. The trials showed that insufficient evidence was available to conclude whether or not the combination will result in an increased risk of cholelithiasis or cholecystectomy.

The PBM Outcomes Research Group attempted to examine the rate of cholecystectomies and related procedures in veteran patients receiving ezetimibe plus fibrates in the VA. The data examined those patients receiving statins, statins plus ezetimibe, ezetimibe, fenofibrate, gemfibrozil or the combination of ezetimibe plus either fenofibrate or gemfibrozil from 9-03 through 6-06.

The rate of cholecystectomies/cholelithiasis or related procedures (ERCP) were as follows: **ezetimibe 1.89/1000 pt-yr, gemfibrozil 0.79/1000 pt-yr, fenofibrate 1.76/1000 pt-yr, statins 0.51/1000 pt-yr, ezetimibe + statins 0.65/1000 pt-yr, ezetimibe + gemfibrozil 1.78/1000 pt-yr**. There were no cases with ezetimibe plus fenofibrate due to the limited exposure of this combination. Many confounders were not accounted for in the analysis including age, weight, cholesterol levels, diet, and other medications. As a result, based upon these data, firm conclusions regarding a greater risk with the combination or not is not known. Because of the numerous confounding factors with the development of this disease, it is recommended that a study be done and that a database analysis conducted at a later date would unlikely provide conclusive results.
Updated ezetimibe criteria: http://vaww.pbm.va.gov/criteria/Ezetimibe.pdf or http://www.pbm.va.gov/criteria/Ezetimibe.pdf.
Refer to page 3 for more discussion regarding lipid topics.

What is the PBM-MAP Ez-Minutes?

The Ez-Minutes is a quarterly online newsletter that connects the PBM-MAP to VA field-based providers and colleagues. Our goal is to communicate 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. The best part is….the information can literally be read in minutes. It's easy, or rather Ez! To access previous issues of the newsletter, click on this link: **http://vaww.pbm.med.va.gov/pbm/ezminutes.htm.**

Interested in joining the already 9500+ subscribers to Ez Minutes Newsletter? See page 4 for more details.

Cardiac Events with imatinib (Gleevec®)

A precaution to the drug labeling has been added about severe congestive heart failure and left ventricular dysfunction with imatinib. Patients with cardiac disease or risk factors for cardiac failure should be monitored carefully, and any patient with signs or symptoms consistent with cardiac failure should be evaluated and treated.
Additional Information: FDA MedWatch Safety Alert - Gleevec® (imatinib mesylate) – October 19, 2006.
http://www.fda.gov/medwatch/safety/2006/safety06.htm#Gleevec

ATTENTION All Providers: Recommendations on LDL-C Lowering Goals

The Department of Veterans Affairs and Department of Defense (VA/DoD) Clinical Practice Guideline for the Management of Dyslipidemia has been updated. Highlights from the Clinical Practice Guidelines includes the following:

- Unless contraindicated, patients who are admitted with an AMI should be discharged and maintained on a moderate dose statin with a target LDL-C goal at least <100 mg/dL.
- Continue with a target LDL-C goal of <100 mg/dL for high risk patients and await more conclusive data with regard to more aggressive LDL-C lowering.
- A lower LDL-C goal as a therapeutic option may be considered in VERY HIGH RISK patients with recent documented ACS (AMI or true unstable angina), or those with established CV disease PLUS multiple major risk factors (e.g., smoking, HTN, diabetes) that are poorly controlled and/or multiple risk factors of the metabolic syndrome (high TG > 200 mg/dL plus non-HDL-C > 130 mg/dL with low HDL-C < 40 mg/dL).
- Clinicians are reminded to consider the potential harms of high dose statin therapy and educate all patients on statins to recognize and report symptoms of myopathy. Reinforce adherence with the patient and review signs of statin nonadherence prior to altering lipid-lowering treatments.

Read the complete guidelines posted at http://www.oqp.med.va.gov/cpg/DL/LIP_CPG/GOL.htm
Read the background information and a summary review of the evidence provided by PBM-MAP, Office of Patient Care Services, Office of Quality and Performance, Chief Consultant for Cardiology and Chief Consultant for Diabetes at http://vaww.pbm.va.gov/clinicians/LDL-C%20Lowering%20Goals%20in%20VHA.pdf

LDL-C lowering goals in VHA: Click here to read a document in which national leaders provided responses to field comments regarding the recommendations for LDL-C lowering goals in veteran patients. Much appreciation is extended to those that provided comments and feedback. (VA InTRAnet only)
http://vaww.pbm.va.gov/clinicians/LDL-C%20Lowering%20Goals%20in%20VHA%20Letter%20-%20Response%20to%20Comments.pdf

*VA**Med**SAFE:* Safety Concerns of Erythropoiesis Stimulating Agents (ESAs)

Read the detailed report at: http://vaww.pbm.va.gov/vamedsafe/Safety%20Concerns%20of%20Erythropoiesis%20Stimulating%20Agents%20(ESAs).pdf
Or http://www.pbm.va.gov/vamedsafe/Safety%20Concerns%20of%20Erythropoiesis%20Stimulating%20Agents%20(ESAs).pdf

Recent alerts have reported trials showing increased risk of serious events and mortality, and/or lack of benefit of ESAs in certain patient populations. This has prompted the FDA to strengthen safety information for ESAs to include a boxed warning and product labeling changes. The following summarizes the new boxed warning:

- Use the lowest dose of ESA to gradually increase Hgb to the lowest level needed to avoid RBC transfusion.
- ESAs increased the risk for death and for serious CV events when administered to target a Hgb > 12 g/dL.
- In patients not on prophylactic anticoagulation and receiving ESAs pre-operatively for reduction of allogeneic RBC transfusions (unapproved indication), a higher incidence of DVTs was documented.
- In cancer patients, the use of ESAs:
  - shortened the time to tumor progression in patients with advanced head and neck cancer receiving radiation therapy when dosed to target a Hgb >12 g/dL.
  - shortened overall survival and increased deaths attributed to disease progression at 4 months in patients with metastatic breast cancer receiving chemotherapy when dosed to target a Hgb >12 g/dL.
  - increased the risk of death when dosed to target a Hgb of 12 g/dL in patients with active malignant disease receiving neither chemotherapy nor radiation therapy (unapproved indication).

VA MedSAFE Recommendation: Avoid dosing ESAs to target Hgb levels above 12 g/dL.

For Cancer patients not on chemotherapy: Treatment with ESA is not recommended. Findings show no benefit and possibly increased serious harm.

For Chronic Renal Failure, oncology, zidovudine-treated HIV and HCV treatment-related anemia:
Measure Hgb at least once every 2 weeks after initiating treatment, and then every 4-6 weeks after Hgb has stabilized. More frequent monitoring has been recommended during initiation; however, the effect of dosage adjustments may not be appreciated in a timeframe shorter than 2 weeks.

- if Hgb increases > 1 g/dL in any 2-week period, or exceeds 12 g/dL, decrease dose of ESA.
- if the Hgb exceeds 13 g/dL, hold ESA and resume at lower dose.

For patients with a history of cardiovascular disease or hypertension: check blood pressure at initiation and each visit to ensure adequate blood pressure control.

NOTE: Medicare will no longer cover ESA treatment for anemia of cancer. Coverage will continue to cover ESA treatment of anemia due to chemotherapy. For more details, click on this link:
http://view.exacttarget.com/?ffcb10-fe68157077630179751 0-fdea10777666007b7c11757d-ff311d707460

Management and Treatment of Hepatitis C Viral Infection; Recommendations from the Department of Veterans Affairs 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 Gastroenteriol 2006; 101: 2360-2378 (PDF version) and information for free 3.0 CEUs Available for VA Nurses, Physicians, and pharmacists (VA Intranet only)

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

September 2006: National Pharmacy Conference

View the multiple presentations from the conference at this link

http://vhacmnapp3.vha.med.va.gov/PBM/PBM%20Presentations/National%20Pharmacy%20Conference%20-%20September%2011-15,%202006%20-%20Dallas,%20TX.pdf

TWO PENS-DIFFERENT USES: A new insulin pen by the name of HumaPen® Memoir™ (Eli Lilly and Company) was recently released. Don't be confused with the product Humira® Pen (Abbott) which is a pen used to inject HUMIRA® (adalimumab) for the treatment of Crohn's Disease. Both pens are not available on VHA National Formulary. Although pictures of the pens are not available for this newsletter, click on the respective links from the manufacturer to view a picture of each pen.

http://www.abbott.com/global/url/content/en_US/60.15:15/feature/Feature_0011.htm

http://www.humalog.com/patient/humapen_memoir.jsp

Azacitidine (Vidaza®) subcutaneous AND intravenous

Acacitidine for injection is now FDA approved for intravenous (IV) administration, in addition to subcutaneous administration, in the treatment of myelodysplastic syndrome. The same vial can be used for either subcutaneous or IV administration and the dose per body surface area is the same. For IV administration, the dose is added to 50 to 100 mL infusion bag of 0.9% sodium chloride or Lactated Ringer's solution and administered over 10-40 minutes.

Long-term Proton Pump Inhibitor Therapy and Risk of Hip Fracture

Yang et al. JAMA 2006; 296:2947-53

An interesting observational cohort study was recently released about PPI and hip fractures. If you are interested in reading more, here is the link to the abstract:

http://jama.ama-assn.org/content/vol296/issue24/index.dtl

"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

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.

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://www.pbm.va.gov/pdanatform/pdanatform.htm.

FOR *NEW* SUBSCRIPTIONS ONLY TO THE PBM-MAP Ez-MINUTES

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What's NEW on the PBM web page?

A list of VA pharmacy Residency Programs and current residents including desired practice areas and sites is now available. Be sure to check it out.

http://vaww.pbm.va.gov/pbm/Cummulative%20Resident%20Roster%202-16-2004.pdf

More information available on PBM websites. Be sure to bookmark these websites: vaww.pbm.va.gov or www.pbm.va.gov