



Pharmacy Benefits Management- Medical Advisory Panel E_z-Minutes

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PBM-MAP DISTANCE
LEARNING
BROADCAST TOPICS
FOR 2005 include:
Challenges and
Treatment Options for
Schizophrenia, Bipolar
Disorder, and the
Metabolic Syndrome for
Veterans and a program
on BPH and much much
more. Click on
<http://www.vapbm.org/PBM/dislearning.htm> for
details of future programs
as more information
becomes available.

Good-Bye 2004 – Hello 2005

HAPPY NEW YEAR!

Recent National PBM Reviews Postings on Web Site

Criteria for Use

<http://www.vapbm.org/PBM/criteria.htm>

**Combination Alpha-Blocker and Finasteride
Therapy for BPH, Recommendations for VA
Primary Care Providers**

Criteria for Nonformulary Use

<http://www.vapbm.org/PBM/criteria.htm>

Teriparatide (Forteo[®])

Ramipril (Altace[®])-reissued 11/04

Cinaclet (Sensipar[®])—will post ~ 1/10/05

Alfuzosin/Tamsulosin- see Criteria for NF of

**Clinically Uroselective α_1 -Adrenergic
Blockers in VA Pts with Benign Prostatic
Hyperplasia**

Treatment Guidelines

<http://www.vapbm.org/PBM/treatment.htm>

Drug Class Reviews

<http://www.vapbm.org/PBM/reviews.htm>

Drug Monographs

Drug Monographs

<http://www.vapbm.org/PBM/drugmonograph.htm>

Cetuximab (Erbix[®])

Cinaclet (Sensipar[™])

Osletamivir (Tamiflu[®])

Sertaconazole (Ertaczo[®])

Teriparatide (Forteo[®])

Tiotropium (Spiriva[®])

Frequently Asked Questions -NEW!

<http://www.vapbm.org/PBM/faq.htm>

Therapeutic Interchange Guidance

(Formerly Patient and/or Provider Information

Letters) <http://www.vapbm.org/PBM/tiq.htm>

New Molecular Entities Review

- Cetuximab (Erbix[®])-
Not added to VANF or
VISNs Formularies
- Fosamprenavir
Calcium (Lexiva[®]) -
Added to VANF and
VISNs Formularies

Formulary Reviews

- High dose Vitamin
Supplementation for
Macular Degeneration -
Not added to national
formulary; VISNs may
add to or remove from
local formulary at their
discretion.
- Rivastigime-
(Exelon[®])- Not
added to VANF but
VISNs may add at
their discretion.

PBM Projects in Progress:

Short acting nifedipine Rx
Data- Follow-up

Criteria for Use:

Clopidogrel/ASA in CABG/PVD

Drug Class Review:

Antiobesity Agents
Insomnia Agents
Impotence Agents
Ophthalmic antihistamine/
mast cell agents

COX-2 CONCERNS

Please note: Recently following the release of the July-September 04 issue of the PBM-MAP Ez-Minutes, the manufacturer of valdecoxib (Bextra[®]) announced that an increased risk for MI and stroke was observed in patients receiving an injectable form of valdecoxib (parecoxib) after cardiac bypass surgery. An updated version of the newsletter addressing this breaking news with valdecoxib was soon posted on the PBM web site. Please click on <http://www.vapbm.org/ezminutes/Ez-MinutesVol2Iss3July-Sept041.pdf> to view the revised newsletter.

But the news regarding COX-2 didn't stop there did it?

On December 17th, 2004, the National Cancer Institute (NCI) and Pfizer, Inc. discontinued a long-term clinical trial evaluating celecoxib versus placebo in the prevention of adenomas in a trial called The Adenoma Prevention with Celecoxib (APC) Study. In APC, a statistically significant increased risk for major fatal and nonfatal cardiovascular events was observed in both celecoxib groups compared to placebo.

On December 20th, 2004, the National Institute of Health (NIH) announced that the administration of naproxen (220mg twice daily) and celecoxib (200mg twice daily) in the Alzheimer's Disease Anti-Inflammatory Prevention Trial (ADAPT) would be suspended due to increased cardiovascular safety risks observed with celecoxib in the APC study. The ADAPT trial was designed to evaluate the potential benefit of naproxen and celecoxib in reducing the risk for Alzheimer's Disease in asymptomatic patients 70 years or older who were considered to be at higher risk for developing the disease due to family history. The number of CV events or a statistical analysis of these events has not been provided for the individual groups (naproxen, celecoxib, and placebo). Our own internal VA-MAP evaluation

of the available data from ADAPT do not support a statistically significant difference between naproxen and celecoxib or placebo.

On December 23rd 2004, In light of the preliminary reports from ADAPT, a Question and Answer document along with a sample draft of a patient letter regarding the 2 remaining COX-2s (celecoxib/ valdecoxib) was sent to the VISN Formulary Leaders. By the second week of January, 2005 (following approval from VISN Formulary Leaders and Medical Advisory Panel) additional COX-2 guidance document for clinicians will be posted on the PBM InTRAnet web-site. Please click on <http://www.vapbm.org/PBM/menu.asp> to locate the document and for additional information on the COX-2 drug class.

Submitted by Catherine L. Kelley, PharmD

Tobacco Use Cessation Guidelines

Check out the updated guidelines at http://www.oqp.med.va.gov/cpg/TUC3/TUC_Base.htm

APOMORPHINE DISTRIBUTION DOCUMENT

As a follow-up from July-Sept04 Ez-Minutes Newsletter, the Apomorphine (Apokyn[®]) Distribution document has been finalized and is posted on the following PBM InTRAnet sites:

[http://vaww.pbm.med.va.gov/procurement/Apokyn_VA%20\(6\).pdf](http://vaww.pbm.med.va.gov/procurement/Apokyn_VA%20(6).pdf)

and

<http://vaww.pbm.med.va.gov/procurement/ApokynFlow.pdf>

Look-alike, NOT-alike Kaopectate Confusion

Have you checked the ingredients label of Kaopectate recently? For those of you who thought it still contained a combination of kaolin and pectin, it may come as a shock that Kaopectate has undergone two reformulations since the original kaolin-pectin combination that gave the product its name (Table 1).

Table 1: Reformulation History of Kaopectate

Year(s)	Reformulation	Reason
Late 1980s to Early 1990s	Kaolin and pectin changed to attapulgite	FDA considered attapulgite a Category I agent (safe and effective). Kaolin and pectin were considered Category III (insufficient data to permit classification).
2003	Attapulgite changed to bismuth subsalicylate	FDA advisory committee recommended that the FDA reverse the above classification, making attapulgite Category III and kaolin and pectin Category I. In the April 17, 2003 final rule, only bismuth subsalicylate and kaolin were listed as safe and effective as OTC antidiarrheal agents.

As a result of the Food and Drug Administration's (FDA's) ongoing review of over-the-counter (OTC) drug products, the first change in ingredients, made in the late 1980s to early 1990s, substituted the combination of kaolin (a clay consisting of hydrated aluminum silicate) and pectin with attapulgite (another clay agent consisting of hydrated magnesium aluminum silicate). The second change occurred in 2003, when attapulgite was replaced with bismuth subsalicylate, the current active ingredient. A look-alike, not-alike confusion may occur because there have been three different formulations that have used the Kaopectate brand name.

But the confusion may not end with Kaopectate. Since the FDA's final rule in 2003, all OTC antidiarrheal products that contained ineffective ingredients had to be reformulated within 1 to 2 years to contain bismuth subsalicylate or kaolin—the only OTC antidiarrheal agents generally regarded as safe and effective. Like Kaopectate, other products may retain their brand names despite a formulation change, so it may sound like they contain kaolin-pectin (e.g., Kao-tin) but they actually consist of bismuth subsalicylate.

Bismuth subsalicylate may not be appropriate in some individuals. Salicylates may be associated with a number of adverse events, including Reye's syndrome (in children), salicylate allergy, and salicylate overdose.

Bismuth subsalicylate use may result in stool darkening (which may be potentially misdiagnosed as gastrointestinal bleeding) and colorectal stool impaction in debilitated patients and infants. Bismuth is radiopaque and may interfere with radiologic examinations of the gastrointestinal tract. Bismuth

subsalicylate may also be involved in a number of potentially significant drug-drug interactions (Table 2).

Table 2: Bismuth subsalicylate drug interactions

ACE Inhibitors	Salicylates may ↓ hypotensive and vasodilator effects of angiotension converting enzyme inhibitors
Beta-blockers	Salicylates may ↓ hypotensive effects of beta-blockers; may also ↓ beneficial effects of beta-blockers on left ventricular ejection fraction in heart failure
Corticosteroids	Corticosteroids may ↓ concentrations and effects of salicylates
Insulin	Salicylates may ↑ insulin concentrations and glucose-lowering effects
Methotrexate	Salicylates may ↑ methotrexate concentrations and toxic effects
Sulfinpyrazone	Salicylates may ↓ sulfinpyrazone concentrations and uricosuric effects
Tetracycline	Tetracycline absorption may ↓ because of adsorption to Mg-Al silicate (Veegum) suspending agent present in some products. Interaction does not seem to be clinically significant in eradication of intraluminal <i>Helicobacter pylori</i> infections.
Valproic acid	Salicylates may ↑ free (active) valproic acid concentrations

Source: Drug Interaction Facts online¹. Table shows drug interactions with a significance rating of 1 (potentially severe or life-threatening) or 2 (may cause deterioration in patient's condition).

At this time, no manufacturers are producing kaolin products, so bismuth subsalicylate and loperamide are the OTC antidiarrheal options available. Alternative antidiarrheal agents include the prescription-only formulary agents, loperamide and paregoric (C-III). There may be additional changes ahead as more OTC antidiarrheals are reformulated and the FDA continues their review of OTC products. In the meantime, be sure to check the labeled ingredients of OTC antidiarrheals, instruct patients to discard any products containing the old, ineffective ingredients, and be aware of potential adverse events and drug interactions when a patient is switched to bismuth subsalicylate.

Reference:

1. eFacts. Drug Interaction Facts online. Available at: <http://www.efactsweb.com/Index.asp>. Wolters Kluwer Health, Inc. Accessed 16 December 2004.

Submitted by Francine Goodman, PharmD, BCPS

VAMedSAFE

High-Dose Vitamin E (≥ 400 International Units per day) in Cardiovascular Disease

Several large, long-term clinical trials evaluating the role of vitamin E in the prevention of certain chronic diseases are available. The premise for these trials was based upon the knowledge that vitamin E possesses antioxidant properties and its use may result in a reduced risk for certain chronic diseases including cancer, Alzheimer's disease as well as cardiovascular (CV) disease.

The use of Vitamin E supplementation in CV disease resulted in no statistically significant effect on CV outcomes including all-cause mortality, CV mortality, fatal or nonfatal myocardial infarction or blood lipids in three published meta-analyses.¹⁻³ These meta-analyses investigated the use of vitamin E as monotherapy or in combination with other vitamins in the prevention of CV disease.

Recently, investigators observed in another published meta-analysis an increase in all-cause mortality in those users of high-dose vitamin E (≥ 400 IU/day) versus placebo.⁴ The analysis was performed with the intent of determining whether there was a dose-response relationship between vitamin E supplementation and all-cause mortality since previously

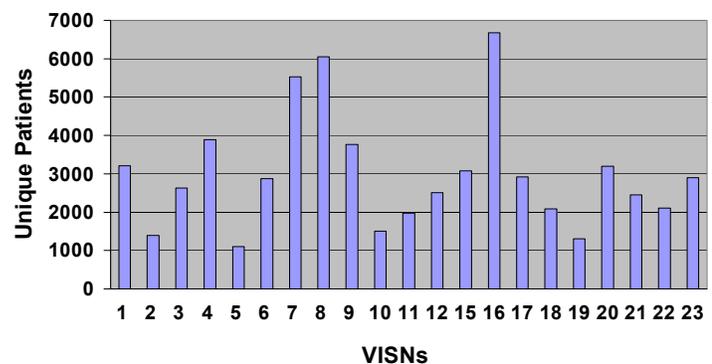
published meta-analyses had not explored varied doses of vitamin E. Based upon their findings, the authors concluded that high-dose vitamin E should be avoided *for the treatment of CV disease*. Graph 1 reflects the number of unique patients within the Department of Veterans Affairs per VISN receiving ≥ 400 IU/day of Vitamin E. Indications for the usage of Vitamin E is not depicted in the graph. Please refer to the posted VA MEDSAFE Bulletin for additional information regarding the usage of Vitamin E in other disease states. Click on

<http://www.vapbm.org/PBM/vamedsafe.htm>.

CONCLUSION & RECOMMENDATIONS:

1. An abundance of data suggests that vitamin E supplementation has no apparent benefit in preventing or reducing cardiovascular events and some data suggests an increased risk in all-cause mortality. Therefore, VA PBM-MAP recommends that high dose vitamin E NOT be used for the purpose of CV disease prevention.
2. It is recommended that VA clinicians consider the evidence for benefit and risks in those patients using high-dose vitamin E for other chronic disease indications on a patient-to patient basis.

Graph 1: Unique Patients per VISN Receiving Vitamin E ≥ 400 mg IU/day in FY2004



References:

1. Shekelle PG, Morton SC, Jungvig LK, et al. Effect of Supplemental Vitamin E for the Prevention and Treatment of Cardiovascular Disease. *J Gen Intern Med* 2004; 19:380-389.
2. Vivekananthan DP, Penn MS, Sapp SK, et al. Use of Antioxidant Vitamins for the Prevention of Cardiovascular Disease: Meta-Analysis of Randomized Trials. *Lancet* 2003; 361:2017-2023.
3. Eidelman RS, Hollar D, Hebert PR, et al. Randomized Trials of Vitamin E in the Treatment and Prevention of Cardiovascular Disease. *Arch Intern Med* 2004; 164:1552-1556.
4. Miller ER, Pastor-Barriuso R, Dalal D, et al. Meta-Analysis: High Dose Vitamin E Supplementation May Increase All-Cause Mortality. *Ann Intern Med* 2004;142:1-11 (published online, ahead of print)

Submitted by Catherine L. Kelley, PharmD

HEY VA! DID YOU HEAR?

On November 18th, 2004 a HEY VA! HAVE YOU HEARD? message was delivered to you via VISTA. The following is the message in its entirety in case you didn't hear (or see) it. The information remains applicable.

How can you stay current with VHA National Drug Formulary changes? Criteria for Use or VHA treatment guidelines? How about medication safety issues and other drug related topics? Join the 5,000 VA care providers who subscribe to the Pharmacy Benefits Management and Medical Advisory Panel (PBM-MAP) "Ez-Minutes" newsletter. This quarterly online newsletter is designed to help connect the PBM-MAP to VA field-based providers. The best part is....the information can literally be read in minutes. It's easy, or rather E_z! To access previous issues of the newsletter, click on this link: <http://vaww.pbm.med.va.gov/pbm/ezminutes.htm>. To subscribe, email subscribe@verdict.uthscsa.edu with "subscribe to Ez-Minutes" in the subject line.

On that note...if you ever want to submit an article to the next PBM-MAP E_z -Minutes, please e-mail: Editor: Janet Dailey, PharmD at vhapbh.Dailey.JH OR Co-Editor: Pete Glassman, MBBS, MSc at peter.glassman@med.va.gov. Feedback and suggestions/comments are always welcomed!

COMMENT FROM THE FIELD

A comment was received from the field regarding the use of JCAHO prohibited abbreviations in the Criteria for Use documents. The comment is derived from some difficulty enforcing clinicians in the field to avoid using these abbreviations in an attempt to meet JCAHO goals and to limit drug and dosing errors when they were being used in national documents. It was requested that the PBM reconsider use of these abbreviations in order to be consistent within our system.

PBM COMMENT: Good point! Consensus was achieved that all PBM-MAP documents from this time forward will avoid using the unapproved drug dosing abbreviations (e.g. qd, bid) in sections of any documents listing dosage and administration information including in tables depicting this information. Tables listing clinical trial information and not specifically intended to educate clinicians/readers regarding proper dose may utilize these abbreviations within the table if properly footnoted.

CONTRACT REVIEW

The insulin contract was awarded to Novo Nordisk. The new contract includes the Novolin vials (R, N, 70/30) as well as the Novolin® Innolet® device (N, 70/30). Additionally, the contract includes NovoLog® and NovoLog® Mix 70/30 available in vials and FlexPens®. Guidance for conversion from Humalog® (insulin lispro) to NovoLog® (insulin aspart) is being developed. Once the guidance is approved by the MAP and VFLs, it will be sent to the field. Be on the look-out for it!

Miscellaneous Information: Products no longer manufactured and therefore removed from VANF include: Cefixime po (Suprax®); Lidocaine 10% oral aerosol

CORRECTION: An error was noted in the EZ-MinutesVol2Issue2 Apr-Jun 04 in the VHA National AUE Summary Report: Quinolones Causing Dysglycemias article on page 2. We sincerely regret and apologize for the decimal-typo oversight. The incidence of hypoglycemia was stated to be 2.6/1000 patients for Azithromycin instead of 0.26/1000. Click on <http://www.vapbm.org/ezminutes/Ez-MinutesVol2Iss2Apr-June04.pdf> to view the corrected graph.