

November/December 2002

Editor:
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The Apothecary Bulletin

PHARMACY SERVICE & THERAPEUTICS COMMITTEES
US ARMY MEDDAC, FORT CARSON, COLORADO

FORMULARY CHANGES

The Pikes Peak Region Formulary Committee and the Evans Pharmacy & Therapeutics (P&T) Committee **added** the following medications to the Formulary at their November meetings:

- + estradiol hemihydrate 25mcg vaginal tablet (*Vagifem*)
- + formoterol fumarate inhalation (*Foradil*) — **restricted to Allergy**
- + malathion 0.5% lotion (*Ovide*) — **for permethrin failures**
- + miconazole 200mg vaginal suppositories 3 pack (generic *Monistat 3*) — **replaces clotrimazole vaginal cream**
- + oxcarbazepine 150mg, 300mg, 600mg tablets and 300mg/5ml liquid (*Trileptal*)
- + pantoprazole 40mg tablets (*Protonix*) — **use per GERD guidelines**
- + topiramate 25mg, 100mg, 200mg tablets; 15mg and 25mg sprinkle capsules (*Topamax*)

The following medications were **deleted** from the Formulary due to lack of use, product no longer being manufactured, or other reason as noted:

- actifed syrup
- clotrimazole vaginal cream — **replaced by miconazole vaginal suppositories**
- guaifenesin 600mg sustained release tablets (*Humibid LA*) — **deleted due to price increase from 2¢ to 37¢ (only one company approved to manufacture product)**
- naproxen 125mg/5ml suspension
- neosporin ophthalmic ointment
- pramipexole 1.5mg tablets (*Mirapex*)
- procainamide 500mg tablets (*Procan SR*)
- thioridazine 10mg and 25mg tablets (*Mellaril*)
- theophylline 125mg capsules (*SloBid*)
- vidarabine 3% ophthalmic

As part of the ongoing drug class review process, the Pikes Peak Region Formulary Committee (with representatives from the Air Force Academy, Peterson AFB, and Evans) will conduct reviews as follows:

January 2003 = central nervous system agents

March 2003 = dermatologic/ophthalmologic agents

Pharmaceuticals submitted for Formulary consideration will be reviewed based on the above schedule. If a medication is a new entity, it may be considered earlier if submitted via a New Drug Request. Providers desiring to have input into the drug class reviews are encouraged to contact one of the Pikes Peak Committee members: **LTC Edward Torkilson (Pharmacy), MAJ Robert Gray (Family Practice), and Dr. Garold Paul (Internal Medicine).**

The next Formulary Committee Meetings will be held on Friday, 10 January 2003 (Pikes Peak at the Air Force Academy) and Tuesday, 14 January 2003 (Evans' P&T). New Drug Requests must be received by the Chief, Pharmacy Service, no later than **27 December** to be considered at the next meetings.

Are Your Prescription Pads Secure???

Make sure all your prescription pads are secured —
that means **locked up or carried at all times.**

No prescription pads are to be left unsecured anywhere at anytime!!

Q & A

What is Evans' definition of an adverse drug reaction (ADR) and what options are available for reporting ADRs?

see page 4

In this issue....

- Formulary Committee News
- FDA Approvals
- Safety Information
- ADR Report
- Herb (Ginger)
- MUR Report

COST OF NEW FORMULARY MEDICATIONS — MTF pricing

Protonix (pantoprazole), proton pump inhibitor: \$0.88 per 40mg tablet

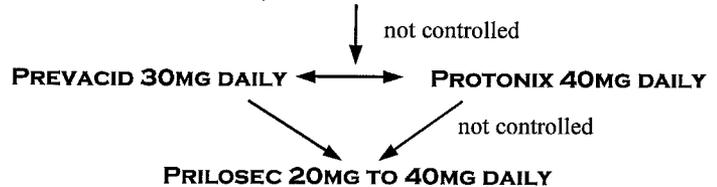
- comparison: *Aciphex* 20mg \$0.22/tab; *Prevacid* 30mg \$0.98/cap; *Prilosec* \$2.06/20mg cap, \$3.09/40mg cap
- GERD guideline:

In a nutshell:

1st line agent: start with *Aciphex* up to 40mg
2nd line agent: if not controlled, choose either *Prevacid* or *Protonix*; if not controlled, try other 2nd line agent or change to **3rd line agent** *Prilosec*

*** Patients will only be able to get refills for *Prilosec* at this facility. This product is nonformulary and not available at other MTFs.

ACIPHEX 20MG DAILY, INCREASE TO 40MG DAILY IF NEEDED



Foradil (formoterol fumarate), long-acting selective beta-2 agonist: \$35.81 per month

- comparison: *Serevent* \$42.20 per MDI, \$44.76 per diskus

Ovide (malathion), organophosphate pesticide: \$17.66 per 59ml bottle

Vagifem (estradiol hemihydrate), estrogen vaginal tablet for treatment of atrophic vaginitis: \$25.94 for starter pack of 18 tablets, \$11.53 for maintenance pack of 8 tablets

- comparison: *Premarin* vaginal cream \$21.13 per tube

Miconazole vaginal suppositories 3 pack, vaginal antifungal: \$8.56

Topamax (topiramate), anticonvulsant: \$0.76/25mg tab, \$1.77/100mg tab, \$2.08/200mg tab, \$0.71/15mg sprinkle cap, \$0.86/25mg sprinkle cap

Trileptal (oxcarbazepine), anticonvulsant: \$0.55/150mg tab, \$1.01/300mg tab, \$1.86/600mg tab, \$53.80 per 250ml bottle (300mg/5ml)

RECENT FDA APPROVALS

Aciphex (rabeprazole) ... for a 7-day treatment for *H. pylori* with amoxicillin and clarithromycin

Pravachol (pravastatin) ... for the treatment of pediatric patients ages 8 years and older with heterozygous familial hypercholesterolemia

Lipitor (atorvastatin) ... for the treatment of familial hypercholesterolemia in children 10 to 17 years of age

Zyrtec (cetirizine) ... for the treatment of year-round allergic rhinitis and chronic idiopathic urticaria in infants 6 months of age and older

EntreMed's derivative of thalidomide, ENMD 0995 ... received orphan drug status for the treatment of patients with multiple myeloma

Demegen, Inc.'s patented P113D peptide ... granted orphan drug status for the treatment of cystic fibrosis infections

Levaquin (levofloxacin) ... for the treatment of nosocomial pneumonia at a dose of 750mg daily

Testim (a patented testosterone replacement therapy gel) ... for treatment of men with low testosterone levels

Abilify (aripiprazole) ... for the treatment of schizophrenia

Philips Electronics' automatic external defibrillator (AED) ... designed for use at home to treat sudden cardiac arrest

Avandamet (rosiglitazone and metformin) ... for the treatment of type 2 diabetes

NEW SAFETY INFORMATION

Risperdal (risperidone):

- ◆ reported events of strokes and stroke-like events in clinical studies in elderly patients with dementia taking *Risperdal*

Cafergot (ergotamine tartrate and caffeine):

- ◆ reported events of serious and/or life-threatening peripheral ischemia associated with coadministration of *Cafergot* with potent CYP 3A4 inhibitors including protease inhibitors and macrolide antibiotics (CYP 3A4 inhibition increases serum levels of *Cafergot*)
- ◆ concomitant use of these agents is contraindicated

Accutane (isotretinoin):

- ◆ addition of "aggressive and/or violent behavior" to the WARNINGS and ADVERSE EVENTS section
- ◆ statement added to the PRECAUTIONS section for cautious use when prescribing *Accutane* to patients with a genetic predisposition for age-related osteoporosis, a history of childhood osteoporosis conditions, osteomalacia, or other disorders of bone metabolism

Bextra (valdecoxib):

- ◆ reported events of hypersensitivity reactions (anaphylactic reactions and angioedema) and skin reactions (including cases of Stevens-Johnson syndrome, toxic epidermal necrolysis, exfoliative dermatitis, and erythema multiforme) in patients treated with *Bextra* with and without a history of allergic-type reactions to sulfonamides
- ◆ use of *Bextra* is contraindicated in patients who have allergic-type reactions to sulfonamides

Serzone (nefazodone):

- ◆ reported events of life-threatening liver failure leading to transplant and/or death in patients treated with *Serzone*

ADVERSE DRUG REACTION REPORT



There were 62 adverse drug reactions (ADRs) documented for September (n=32) and October (n=30), of which 38 (61%) were reported **spontaneously** [30 from pharmacy (outpatient/inpatient/clinical); 4 from Family Practice; and 1 each from EENT, Internal Medicine, MBU, and Medical Exams]. The most prevalent adverse events reported involved the anti-infective agents (n=19; 31%) and the analgesic agents (n=12; 19%). The anti-infective agents continue to be the top medication class involved in reported adverse events with dermatologic manifestations of the adverse events the top system involved.

Three events (5%) were deemed preventable —

- (1) **contraindicated:** a 25yo female with amoxicillin noted on her appointment note allergy list was prescribed *Augmentin* and presented to the Emergency Department with SOB after taking 1 dose
- (2) **dose-related:** a 35yo female presented to Emergency Department c/o feeling weak, shaky, nauseated, SOB with hypotension (BP 124/73, 108/49) after a change in her antihypertensive therapy
- (3) **patient error/contraindication:** a 22yo male with known allergy to naproxen presented to the Emergency Department with c/o facial swelling, SOB, itchy throat after taking *Motrin* (no RX for ibuprofen in CHCS)

No events were deemed *moderate* on the severity scale (mild, moderate, severe, fatal).

One event was reported from an inpatient area: a 3 day old female who developed a rash on her trunk, face, and limbs after receiving ampicillin IV.

Thanks to all who continue to report adverse drug events.



HERB OF THE (every other) MONTH

Ginger, *zingiber officinale*, a perennial plant, grows in warm climates of India, Jamaica, Africa, and China. Used for hundreds of years, the roots and rhizomes of ginger have been used as a seasoning and as a herbal medicine. More than 5,000 years ago, the ancient Chinese and Indians looked upon ginger as the "universal medicine". The ancient Greeks ate ginger wrapped inside bread after meals to help digestion, and the early English made a soothing ginger beer to aid the stomach.

Claims for ginger include, but are not limited to, its use as an antiemetic, GI protectant, anti-inflammatory agent, a cardiovascular stimulant, an antitumor agent, an antioxidant, and also as therapy for microbial and parasitic infestations. The root of ginger contains both volatile and nonvolatile compounds. The nonvolatile constituents (including gingerols and gingerol-like compounds) are thought to be responsible for its flavor and aromatic properties as well as any pharmacologic activity. Human studies have shown ginger to inhibit platelet aggregation induced by ADP and epinephrine. In rodent models, ginger extracts have documented anti-inflammatory effects. Methanolic extracts of ginger have shown positive inotropic effects in a guinea pig model. The GI protective effect shown in animal models is postulated to be promoted by increased mucosal resistance and potentiation of the defensive mechanism against chemicals or alterations in prostaglandins, providing more protective effects.

The antiemetic effects of ginger, thought due to local effects on the GI tract rather than on the CNS, have been studied in humans for morning, motion, or sea sickness. Mowrey and Clayson in 1982 designed a study to mimic seasickness by using a revolving, motor-driven chair and gave 36 blindfolded, seasick-prone patients dimenhydrinate 100mg, ginger root 940mg, or chickweed herb prior to a "spin" in the chair. Patients given chickweed or dimenhydrinate were able to remain in the chair an average of 1.5 and 3.5 minutes respectively whereas those given ginger root tolerated an average of 5.5 minutes in the chair. Some question the authors study design. Two trials evaluated the incidence of postoperative nausea and vomiting in patients receiving powdered ginger root, metoclopramide, or placebo. The first randomized, double-blind study (Bone et al, 1990) evaluated 60 women undergoing major gynecologic surgery. The incidence and intensity of nausea favored both active treatment groups over placebo, but there was not a statistically significant difference that favored one active treatment over the other. The second study (Phillips et al, 1993) evaluated 120 patients undergoing gynecologic surgery receiving the same treatments as the previous study (different route for metoclopramide). Both treatment groups showed better results than placebo, and the need for postoperative antiemetics was lower in the group receiving ginger. In another study (Fisher-Rasmussen et al, 1991), ginger was given for 4 days to pregnant women with hyperemesis gravidarum with a significant percentage of women preferring ginger versus placebo treatment.

The German Commission E has indicated ginger for use in dyspepsia and the prevention of motion sickness. The dose of ginger varies depending on the condition treated. As an antiemetic, studies have used 500mg to 1,000mg of powdered ginger orally or 1,000mg of fresh ginger root orally. There are no reports of severe toxicity in humans from ingestion of ginger root, but large overdoses carry the risk for CNS depression and cardiac arrhythmias. Although ginger can provide relief for women suffering from morning sickness, it is contraindicated in pregnant patients because the effects are unknown. Patients on anticoagulants may have an enhanced risk of bleeding.

Resources: *Complementary & Alternative Medicines* (1999), *The Review of Natural Products* (1995), Various Websites

Q & A

Evans' definition of an ADR ... an adverse drug reaction (ADR) is **any unwanted or unintended effect of a drug** following prescribed doses that (1) requires some sort of management including, but not limited to, discontinuation of the causative medication or treatment with another drug; (2) adversely impacts the outcome or progress of the patient's clinical condition; or (3) results in death, hospitalization, prolongation of hospital stay, transfer to a more intense level of care, or significant discomfort/distress to the patient.

To report an ADR ...

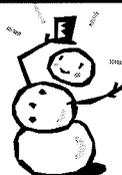
- ✦ Complete the **Adverse Drug Reaction Reporting Form** and return to the pharmacy. For forms, call the pharmacy at 526-7334.
- ✦ Use **CHCS e-mail and send to mail group G.ADR**. Please indicate the patient's name and SSN, date of occurrence, suspected drug, signs/symptoms of the event, and any changes/additions to therapy made.
- ✦ Use **Website ADR Reporting** located on the Evans Pharmacy Webpage. From the Evans Hospital homepage, choose "Medical Clinics", then "Pharmacy", then search for "ADR" and follow the instructions.
- ✦ **Phone-in the ADR to 52 I-ITCH (524-4824)**. Please include the patient's name and SSN, date of occurrence, suspected drug, signs/symptoms of the event, and any changes/additions to therapy made. Make sure you include your name and extension in case more information or follow-up is needed.
- ✦ **Phone-in the ADR to the Inpatient Pharmacy** at 524-4400 from 0600 to 2300 and leave a voice mail message with the information listed above. Make sure you include your name and extension in case more information or follow-up is needed.



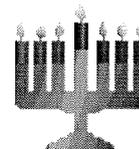
Seasons Greetings!!



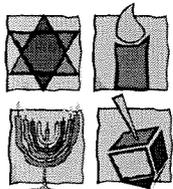
Happy Thanksgiving



Happy Kwanzaa



Happy Hanukkah



Merry Christmas



Happy New Year



Drug Interaction Corner

Selected Digoxin Drug Interactions

Drugs that may increase digitalis serum levels

Amiodarone
Benzodiazepines (alprazolam, diazepam)
Bepidil
Cyclosporine
Diphenoxylate
Indomethacin
Itraconazole
Macrolides (clarithromycin, erythromycin)
Propafenone
Propantheline
Quinidine
Quinine
Spironolactone
Tetracyclines
Verapamil

Drugs that may decrease digitalis serum levels

Aminoglycosides, oral
Antacids (aluminum and magnesium containing)
Certain antineoplastics
Charcoal, activated
Cholestyramine
Colestipol
Kaolin/pectin
Metoclopramide
Neomycin
Penicillamine
Rifampin
St. John's Wort
Sulfasalazine

MUR COMMITTEE REPORT, RHONDA EUSTICE, PHARMD

Medication Use Evaluation — URINARY TRACT INFECTIONS, November 2002

Purpose:

To evaluate antibiotics, duration of therapy, and *Levaquin* doses used for patients seen for UTIs. N = 67 patients

<u>Service:</u>	<u>Nov02</u>	<u>Mar02</u>
Family Practice	34%	29%
Internal Medicine	10%	29%
PACC	1%	15%
ER	31%	22%
OB		6%
Urology		10%
Pediatrics	9%	3%

<u>Diagnosis—Nov 2002:</u>	<u>#</u>	<u>%</u>
Uncomplicated UTI	57	85%
Complicated*	10	15%

* includes DM patients, recurrent UTIs, pregnant patients

<u>Medications prescribed:</u>	<u>Nov02</u>	<u>Mar02</u>
SMZ/TMP*	37%	41%
Nitrofurantoin	18%	16%
<i>Levaquin</i> **	32%	20%
<i>Keflex</i>	3%	
Amoxicillin	1%	5%
None	6%	2%

* drug of choice

** 2 patients failed SMZ/TMP

Conclusion:

- 37% of UTIs were treated with SMZ/TMP, the drug of choice.
- The recommended duration of therapy for uncomplicated UTI is 3 days. The percentage of patients receiving 3 days of treatment has increased from 9% to 29%.
- The dosing of *Levaquin* for UTI is 250mg qd. The prescriptions for *Levaquin* 500mg for the treatment of UTI have decreased from 63% to 15%.



Medication Use Evaluation — COPD, November 2002

Purpose:

To evaluate the usage of beta-2 agonists for patients with COPD

Sample/Population:

Random sampling of patients receiving *Combivent* or *Atrivent* for COPD diagnosis between 5/01 and 6/02; N=56 patients

Enrollment/Service:

Internal Medicine Clinic = 48 (86%); Family Practice Clinic = 5 (9%); Not Prime to EACH = 3 (5%)

Results:

Pneumovax given = 26 (46%)

Smoking history

Current Smokers = 10 (18%)

Former Smokers = 7 (13%)

Not smokers* = 31 (55%)

*not currently smoking/no mention of smoking history

Hospitalizations = 4 (7%)

ER visits for COPD = 6 (11%)

Deaths due to COPD = 3 (5%)

Pulmonary Rehab ordered = 3 (5%)

Combivent Review:

**Dosing of *Combivent* & Albuterol should not exceed 12 puffs/day. One inhaler should last 25 days.

<u>Source</u>	<u>avg # units/rx</u>	<u>min</u>	<u>max</u>	<u>mean</u>
Civilian Providers = 710	2.5	1	9	2
Evans Providers = 1451	1.8	1	6	2

ER/PACC appt review (5/01 – 6/02):

Hospitalizations = 56 patients/66 hospitalization

ER/PACC appointments = 106 patients/141 visits

Conclusions:

- Per the beta-2 agonist (*Combivent*) review, several COPD patients appear to be overusing their inhalers. A follow-up report of patients receiving >2 inhalers per 30 days will be compiled. This data will be disseminated to the patients' providers.
- 35 patients have had more than one visit to the ER or PACC for COPD exacerbation.
- A multidisciplinary team with representatives from pharmacy, nursing, respiratory therapy, physical therapy, and nutrition is being recruited to aid EACH in educating COPD patients. Dr. Elaine Gonsior has agreed to be the physician champion for this effort.

MUR COMMITTEE REPORT, CONTINUED

Medication Use Evaluation – *LANTUS*

completed by Jo Vickers, PharmD

Lantus, a new once daily dosed basal insulin, was recently added to the Basic Core Formulary (BCF). This review was done prior to BCF addition to evaluate potential benefit from using *Lantus*. *Lantus* has a different stability with storage than other insulins – **once the vial is opened it is stable for only 30 days, regardless of storage temperature**. Other insulin stability is 1 month at room temperature but longer if stored in the refrigerator after opening. The cost of *Lantus* is approximately **5 times** that of NPH (\$25.07 vs. \$4.43).

Patient Population – 100% receiving glargine (*Lantus*)

Type 1 DM	11 patients	38%
Type 2 DM	18 patients	62%

Other DM medications:

Lispro insulin (n=21; 72%)
Regular insulin (n=4; 14%)
<i>Avandia</i> (n=5; 17%)
Metformin (n=5; 17%)
Glipizide (n=2; 7%)

A1c Evaluation

	# pts	%
improved	10	34
worsened	8	28
no change	5	17
unable to assess	6	21

Rationalization for use

	# pts	%
hypoglycemia	13	45
improve compliance	4	14
improve efficacy	1	3
cannot assess	6	21
Endocrine initiated	5	17

Discussion

- Twenty-six of the 29 patients are (or were previously) enrolled in the DMC. Six of the DMC patients are disenrolled: 1 moved, 2 Med. Board, 2 patient preference, 1 multiple missed appointments. Endocrinology initiated glargine in 5 patients: 2 seen at U of CO, 2 at Barbara Davis, 1 unidentified. Two patients were already on glargine prior to being seen at Evans.
- Ten patients are receiving ≥ 50 units glargine daily. Seven of these patients are also receiving insulin sensitizers (metformin and/or rosiglitazone). Three patients with apparent insulin resistance have clinical contraindications to use of insulin sensitizers.
- Of the 13 patients receiving glargine for hypoglycemia, 9 were documented to have fewer HGM readings < 70 . Four patients with poor compliance in taking insulin had no improvement in DM based on A1c's. Of these 4 patients, 2 are type 1 DM young females who use insulin deficiency to control weight and 1 young male with type 1 DM (also with bipolar diagnosis) who goes for long intervals without taking insulin. It was suspected that NPH wasn't lasting long enough to control AM readings in 1 patient, but the A1c was not improved with glargine use.
- One patient came to Evans on BID dosing of glargine and was converted to once daily dosing.

Recommended Guidelines for Use

1. Endocrinology consult / prescription
2. Hypoglycemia – suspected association with NPH peak effect
3. Poor compliance with BID dosing of NPH or insufficient duration of effect with NPH
4. DMC active enrollment

A little bit of history ...

- 5000 B.C. ... The Sumarians use opium, suggested by the fact that they have an ideogram for it which has been translated as *HUL*, meaning "joy" or "rejoicing".
- 2500 B.C. ... Earliest historical evidence of eating poppy seeds among the Lake Dwellers in Switzerland.
- 1525 ... Paracelsus (1490—1541) introduces laudanum, or tincture of opium, into the practice of medicine.
- 1680 ... Thomas Sydenham (1625—1680): "Among the remedies which it has pleased the Almighty God to give to man to relieve his sufferings, none is so universal and efficacious as opium".
- 1911 ... A New Jersey pharmacy reports that it fills an average of 40 prescriptions per day, prices ranging from 25 to 85 cents, with an average prescription cost of 40 cents.
- 1933 ... Average pharmacy fills 10 prescriptions per day during the depths of the Great Depression.
- 1960 ... Kefauver hearing are held to investigate the "high costs of prescriptions" (\$3 a month)
- 2002 ... Evans average cost per prescription is \$30.