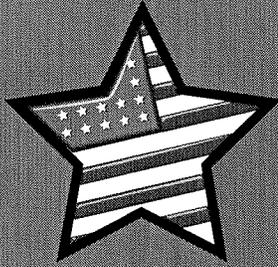


March/April 2003

Editor:  
Jean Eilertson, PharmD



# The Apothecary Bulletin

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

## FORMULARY CHANGES

The Pharmacy & Therapeutics (P&T) Committee met on 11 March 2003 and **added** the following medication to the Formulary (the March meeting of the Pikes Peak Formulary Committee was canceled due to conflict in schedules):

+ granisetron (*Kytril*) 1mg/ml for injection — **restricted to Anesthesia**

No medications were **deleted** from the Formulary.

The next Formulary Committee Meetings will be held on Thursday, 1 May 2003 (Pikes Peak at the Air Force Academy) and Tuesday, 13 May 2003 (Evans' P&T). New Drug Requests must be received by the Chief, Pharmacy Service, no later than **21 April 2003** to be considered at the next meetings.

## PREVACID ADDED TO BCF

The DoD P&T Executive Council has added *Prevacid* (lansoprazole) to the Basic Core Formulary (BCF). The BCF now includes two proton pump inhibitors (PPIs): *Aciphex* (rabeprazole) and *Prevacid*. Due to new pricing as listed below, ***Prevacid* may now be used as a first-line PPI for the treatment of GERD as an alternative to *Aciphex*. *Prilosec* (omeprazole) remains a second-line PPI for those failing treatment with either *Aciphex* or *Prevacid*.**

Pricing for the PPIs:

- current *Aciphex* price = \$0.35 per tablet
  - the price will increase to \$0.65 per tablet beginning 1 April 2003
- current *Prevacid* price = \$0.55 per capsule (due to a temporary price reduction that is effective 1 March to 31 March 2003)
  - the price will increase to \$0.65 per capsule beginning 1 April 2003
- current *Prilosec* price = \$2.08 per 20mg capsule; \$3.14 per 40mg capsule

### Life Expectancy Increases

The latest numbers from the U.S. Centers for Disease Control and Prevention show life expectancy increased 0.2 years, reaching a record of 77.2 years in 2001, up from 77 in 2000. Life expectancy increased for men and women as well as for blacks and whites.

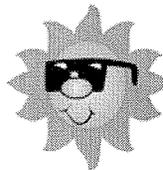
- ☞ for men, life expectancy rose from 74.3 years in 2000 to 74.4 years in 2001
- ☞ for women, life expectancy rose from 79.7 years in 2000 to 79.8 years in 2001
- ☞ white women have the highest life expectancy of 80.2 years, followed by black women (75.5 years), white men (75 years), and black men (68.6 years)

The largest decline among leading causes of death was for influenza/pneumonia (deaths fell more than 7%).

- ☞ deaths from heart disease declined nearly 4%
- ☞ deaths from cancer declined 2%
- ☞ deaths from stroke declined nearly 5%
- ☞ deaths from kidney disease, hypertension, and Alzheimer's disease increased

### Q & A

With spring here and summer just around the corner, which medications can cause photosensitivity and what recommendations can be made to patients to minimize the risk of this adverse event?



see page 5

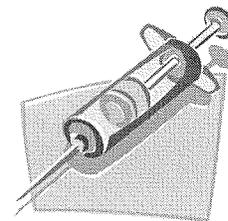
### In this issue....

- Formulary Committee News
- Syringes/Needles Available
- In the Literature
- ADR Report
- Herb (Guarana)
- National Guidelines
- Recent FDA Approvals
- New Contraindication

## AVAILABLE SYRINGES/NEEDLES FROM PHARMACY

The pharmacy now stocks a limited formulary of needles and syringes for patient self-injection of medications. A prescription, either written or entered into CHCS, is required for dispensing of these supplies. Patients should be evaluated to determine the appropriate needle size. Available products include:

- ▶ Insulin syringes (for SQ injection), issued in boxes of 100 syringes
  - ❖ 1cc, U-100 syringe with 28 gauge 1/2 inch needle, for 100 units or less
  - ❖ 1/2 cc, U-100 syringe with 28 gauge 1/2 inch needle, for 50 units or less
  - ❖ 3/10cc, U-100 syringe with 30 gauge 5/16 inch needle, for 30 units or less
- ▶ Syringes, issued as individual syringe
  - ❖ 1cc syringe (Tuberculin type) with 25 gauge 5/8 inch needle
  - ❖ 1cc syringe
  - ❖ 3cc syringe
- ▶ Needles, issued as individual needle
  - ❖ for IM injection: 20 gauge 1&1/2 inch (for thick injections, i.e. Delestrogen, Depo-Estradiol, Depo-Testosterone)
    - 21 gauge 1&1/2 inch
    - 22 gauge 1 inch
  - ❖ for SQ injection: 25 gauge 5/8 inch
    - 26 gauge 1/2 inch



For additional information, call the Inpatient Pharmacy at 524-4400.

## IN THE LITERATURE...



*New England Journal of Medicine: The PREVENT trial.* The National Heart, Lung, and Blood Institute (NHLBI) of the National Institutes of Health stopped the multi-center Prevention of Recurrent Venous Thromboembolism (PREVENT) trial, a long-term, low-intensity warfarin (target INR 1.5 to 2.0) study for the prevention of recurrent venous thromboembolism in patients who have had previous idiopathic venous thrombosis, due to a high degree of benefit to patients without significant adverse effects. The trial found a 64% reduction in episodes of DVT and PE in study participants taking low-intensity warfarin compared to those taking a placebo. Also, there was no evidence of significant risks such as major hemorrhage or other potential side effects of warfarin. At the time of study termination, patients had been followed for up to 4.3 years (mean of 2.1 years). All study participants had experienced a previous episode of idiopathic venous thromboembolism and were treated for a median of 6.5 months with full-intensity anticoagulation. Of the 253 patients assigned to placebo, 37 had a recurrent episode of DVT or PE compared to 14 of the 255 patients assigned to low-intensity warfarin. Risk reductions were similar for all subgroups, including those with and those without inherited thrombophilia. Major bleeding complications occurred in 2 patients in the placebo group compared to 5 in the low-intensity warfarin group. There were 8 deaths in the placebo group compared to 4 in the low-intensity warfarin group. The study will be published in the April 10th issue of the *NEJM*.

*Archives of Internal Medicine: New Hypertension Management Guidelines for African Americans.* The International Society on Hypertension in Blacks (ISHIB) has issued new management guidelines for hypertension in African Americans due to worse outcomes in this ethnic group. The ISHIB recommends a target blood pressure 10 mmHg lower than the previous standard of 140/90 mmHg and that pharmacologic interventions should be administered "early and persistently". According to the consensus statement, achievement of blood pressure less than 130/80 will often require two or even three drugs. The authors recommend initiating treatment with two drugs of different classes if the systolic blood pressure is at least 15 mmHg higher than the target or if diastolic blood pressure is 10 mmHg higher or more.

*American Journal of Epidemiology: SIDS risk.* Researchers at Kaiser Permanente in Northern and Southern California, supported by the National Institute of Child Health and Human Development and the National Institute on Deafness and Other Communications Disorders, interviewed 197 women whose infants had died of SIDS and 312 mothers of living infants. Each SIDS infant was compared to a living infant of the same race and age and born in the same country. Questions were answered about infant sleeping positions. The researchers found that infants last placed on their sides for sleep were twice more likely to die of SIDS than infants last placed on their backs. In addition, the risk of SIDS was significantly increased if infants turned from their sides to their stomachs during sleep. The researchers felt that a large part of the risk may be due to instability of the side sleeping position and the tendency for infants sleeping in this position to turn onto their stomachs. The researchers also found that if an infant who was usually placed to sleep in the low-risk position (on the back) was then placed to sleep in a high-risk position (the stomach or side), his or her SIDS risk was seven to eight times greater than that of an infant who was always placed to sleep on his or her back.

*Annals of Internal Medicine: MVI Reduces Infections in Type 2 Diabetes.* Researchers from the University of North Carolina School of Medicine studied 130 community-dwelling adults stratified by age and presence of type 2 diabetes. After one year, infectious illness was reported in 73% of those receiving placebo and in 43% of those receiving daily multivitamin and mineral supplement (MVI). Infection-related absenteeism affected 57% of the placebo group and 21% of the MVI group. Subjects with type 2 diabetes (n=51) accounted for this finding. Among diabetics, infectious illness occurred in 93% of those receiving placebo and in 17% of those receiving MVI. An accompanying editorial noted that study limitations included small sample size and limited statistical power.

## ADVERSE DRUG REACTION REPORT



There were 100 adverse drug reactions (ADRs) reported for January (n=17; 3 involving anthrax and/or smallpox vaccine) and February (n=83; 61 involving anthrax and/or smallpox vaccine), of which 25 (25%) were reported **spontaneously** (6 from outpatient pharmacy; 4 from TMC #10; 3 from the SRP site; 2 each from Family Practice, Internal Medicine, OB/GYN, and Special Forces TMC; and 1 each from Dermatology, PACC, Pediatrics, and TMC #9. The most prevalent adverse events reported involved the vaccines; if the anthrax/smallpox vaccines are not included, then the anti-infective agents (n=12), the analgesic agents (n=4), and the cardiovascular agents (n=4) were the most prevalent reported adverse events (consistent with past months).

One event (1%) was deemed preventable —

- 1) An 18 year old female presented to the Emergency Department with scleral irritation due to excessive use of gentamicin ophthalmic drops. She was prescribed the antibiotic drops for pink eye to use for 5 days, but when she was unable to obtain a follow-up appointment, she continued to use the drops (presented to the ER after 16 days of use); on exam, she had mild sclera swelling.

Five events (5%) were deemed *moderate* in severity —

- 1) An 86 year old male was admitted to the hospital with flushing and shivering episodes thought possibly due to medication effect/interaction with low magnesium contributing. Medication changes were made (*Xanax* changed to *Klonopin*, *Celexa* *Ritalin*/HCTZ discontinued), and the patient improved and was discharged.
- 2) A 25 year old female experienced nausea and vomiting along with left chest pain with left arm numbness 5 minutes after administration of phenergan. ECG was normal.
- 3) A 23 year old male was hospitalized for cellulitis and erythema to the entire upper extremity after administration of anthrax vaccine.
- 4) A 38 year old male was hospitalized at a civilian hospital with altered mental status and fever and was diagnosed with encephalopathy after administration of smallpox vaccine. On follow-up, the patient was improving.
- 5) A 32 year old male was hospitalized at a civilian hospital with malaise, fatigue, chills, fever, and possible cellulitis after administration of anthrax and smallpox vaccine. On follow-up, the patient stated he felt “100%”.

The anthrax and smallpox vaccine adverse events were reported to the FDA through the VAERS system. The adverse event involving phenergan listed above was reported to the FDA.

**Thanks to all who continue to report adverse drug events.**

### To Report an ADR...

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 it 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 phone number 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 phone number in case more information or follow-up is needed.





Guarana is a dried paste made from the crushed seeds of *Paullinia cupana*, a woody vine or shrub native to Brazil and the Amazon Basin. The indigenous people of the Amazon rainforest used crushed guarana seed as a beverage and for medicinal purposes. Guarana was said to treat diarrhea, decrease fatigue, reduce hunger, and help arthritis. It also has a history of use in treating hangovers from alcohol abuse and headaches related to menstruation. The plant was introduced to France during the 19th century by a physician who was returning from Brazil. It has since been used in the treatment of migraine and nervous headaches, neuralgia, paralysis, urinary tract irritation, and chronic diarrhea. In 1826, the major alkaloid was isolated and named guaranine, which was later shown to be nearly identical to caffeine. Theophylline and theobromine were also

isolated. Today, the plant is known and used worldwide – it is the main ingredient in the “national beverage” of Brazil, “Guarana Soda”. Guarana is included in the ingredients of several aphrodisiacs, weight loss supplements, energy drinks, vitamin supplements, candies, and chewing gum.

The effects of guarana are attributed to its high caffeine content – roasted guarana seeds may contain up to 6% caffeine – and include CNS stimulation, diuresis, hyperglycemia, cardiac stimulation, coronary and peripheral vasodilation, cerebrovascular vasoconstriction, skeletal muscle stimulation, increased gastric acid secretion, and bronchial smooth muscle relaxation. The plant also contains tannins (may be cause of antidiarrheal and astringent properties) and saponins, including trace amounts of timbonine, similar to the timbo fish poisons used by Amazonian Indians.

The dosage of guarana is highly variable and depends on the product and the batch, with single doses often containing 200 to 800 mg guarana. Daily intake of guarana should not exceed 3 grams of guarana powder or its equivalent. A cup of guarana, prepared by adding 1 to 2 grams of crushed seed or resin to 250 ml of water and boiling for 10 minutes, can be consumed three times a day. Each cup may provide up to 50 mg of guaranine.

Normal consumption of guarana may cause insomnia and diuresis with excessive consumption causing agitation, anxiety, diarrhea, headache, irritability, nausea, PVCs, seizures, tachycardia, tremors, and vomiting. Withdrawal symptoms after regular daily consumption include anxiety, headache, and irritability. Guarana should be avoided in pregnant and breastfeeding women and in patients with arrhythmias. Avoid or use with caution in patients with cardiovascular disease, gastric ulcers, chronic headaches, diabetes, and those currently taking theophylline. Drug-drug interactions include all CNS stimulants, oral contraceptives, MAOIs, antidiabetic agents, CNS depressants, and theophylline. Drug-herbal interactions include ephedra, ma huang, and black or green tea.

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

## NATIONAL GUIDELINES

The National Comprehensive Cancer Network (NCCN) is an alliance of the world’s leading cancer centers. At its 8th annual conference, the group presented changes to its colorectal cancer and breast cancer guidelines. These guidelines, along with various other oncology guidelines by the NCCN, can be found at:

<http://www.nccn.org/index.html>



The American Heart Association will publish pediatric guidelines for the prevention of heart disease in the March 25th issue of *Circulation*. Health promotion goals for children include assessment of diet, tobacco use, and physical activity level at every physician visit. Education of parents about heart-healthy habits in children, including restricting high-fat food after age 2, limiting salt and sugar intake, and reducing sedentary time by limiting television viewing to no more than two hours daily are recommended. To identify children and adolescents at high risk for cardiovascular disease, physicians should monitor height, weight, body mass index, and blood pressure; update family medical history regularly; and test cholesterol levels in high-risk children.

*“In matters of style, swim with the current.  
In matters of principle, stand like a rock.”*  
— Thomas Jefferson

From *Health Affairs*:

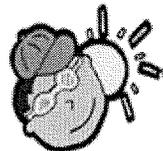
- ❖ Heart disease cost the nation \$58 billion in 1997, making it the most expensive health problem to treat that year. Cancer ranked second, with a price tag of \$46 billion, followed by trauma at \$44 billion and mental disorders at \$30 billion.
- ❖ Prescription drugs accounted for a relatively tiny proportion of total costs for treating each of the top 3 conditions. In the case of heart disease, medications accounted for just 9% of the cost of treatment. Hypertension was the only condition studied for which drugs, at 48.5% of total expenditures, came close to accounting for half of the cost of treatment. It also was the condition with the highest out-of-pocket costs.
- ❖ Private insurance and Medicare were the primary sources of payment for most of the top five conditions.

## Q & A

Photosensitivity is a general term that describes either the common *phototoxic response* or the uncommon *photoallergic reaction*. The differences between these 2 types of photosensitivity reactions are based on the mechanism of action, the onset of rash, and the clinical presentation. Phototoxic reactions are nonimmunologic and resemble a sunburn. In comparison, photoallergic reactions are immunologic and require previous exposure to the photosensitizing agent. The initial eruption caused by a phototoxic reaction appears within 30 minutes up to hours after exposure to light energy (i.e., sunlight, filtered light, or artificial light). In comparison, photoallergic reactions appear 1 to 14 days after exposure to light energy. Patients who experience a phototoxic reaction may present with erythema, pain, and edema (usually limited to exposed areas). Patients who experience photoallergic reactions may present with papulovesicular eruptions, pruritus, and eczematous dermatitis (may extend beyond exposed areas). Treatment consists of burn care and avoidance of the offending agent for phototoxic reactions. Antihistamines and steroids may be required for photoallergic reactions. **Source:** *Micromedex*

The following is a **PARTIAL** list of medications or classes of medications that may cause photosensitivity (drug classes in upper case):

- Antiacne agents**— benzoyl peroxide, isotretinoin, tretinoin
- Anticonvulsants**— carbamazepine, gabapentin, phenytoin, valproic acid
- Antidepressants**— SSRIs, trazodone, TRICYCLICS
- Antihistamines**— brompheniramine, chlorpheniramine, cyproheptadine, diphenhydramine, loratadine
- Antimicrobials**— azithromycin, erythromycin, griseofulvin, QUINOLONES, SULFONAMIDES, TETRACYCLINES, trimethoprim
- Antineoplastics**— fluorouracil, flutamide, methotrexate, vinblastine
- Antiparasitics**— chloroquine, mefloquine, thiabendazole, quinine
- Antipsychotics**— haloperidol, PHENOTHIAZINES, olanzapine, risperidone, thiothixene
- Cardiovasculars**— ACE INHIBITORS, amiodarone, diltiazem, disopyramide, HMG-CoA-REDUCTASE INHIBITORS, losartan, methyl dopa, minoxidil, nifedipine, quinidine
- Diuretics**— acetazolamide, amiloride, furosemide, metolazone, THIAZIDES, triamterene
- Gastrointestinal agents**— mesalamine, olsalazine, sulfasalazine
- Herbal/Organic agents**— Dong Quai, Gotu Kola, St. John's Wort
- Other classes**— BARBITURATES, ESTROGENS, SALICYLATES, SULFONYLUREAS, NSAIDs, ORAL CONTRACEPTIVES
- Miscellaneous**— amantadine, coal tar, gold salts, interferon beta-1b, isoniazide, pseudoephedrine, selegiline, vitamin A



The photoreaction depends on the patient, the amount of drug, and the length of time exposed to sunlight. Persons at risk should wear protective clothing (broad-rimmed hats, long sleeves, and pants), use a good sunscreen (minimum SPF of 15, reapply every 2 hours and more frequently after swimming, sweating, or toweling), and avoid prolonged exposure to sunlight (particularly between 10 a.m. and 3 p.m.).

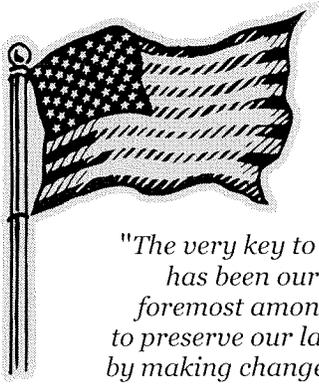
## WEBSITES OF INTEREST

- <http://www.evans.amedd.army.mil> — Evans' page
- <http://www.evans.amedd.army.mil/Pharmnew/default.htm> — Pharmacy website; access to the Formulary
- <http://www.pec.ha.osd.mil> — DoD Pharmacoeconomic Center, Ft Sam Houston
- <http://www.qmo.amedd.army.mil/pguide.htm> — DoD/VHA Practice Guidelines



### Poison Prevention Websites (Poison Prevention Week 16 to 22 March)

- <http://www.rmpdc.org/> — Rocky Mountain Poison and Drug Center
- <http://www.poisonprevention.org/index.html> — Poison Prevention Week Council
- <http://www.aapcc.org/> — American Association of Poison Control Centers
- [http://wellness.ucdavis.edu/safety\\_info/index.html](http://wellness.ucdavis.edu/safety_info/index.html) — UC Davis Health System Wellness Center; download their *California Poison Control System Answer Book*
- <http://www.cdc.gov/ncepc/> — CDC's National Center for Injury Prevention and Control
- <http://checc.sph.unc.edu/rooms/library/lead/> — The Environmental Resource Program at UNC-Chapel Hill's Childhood Lead Poisoning Prevention Site with links to other websites on this subject
- <http://www.aspca.org/site/PageServer> — Animal Poison Control Center
- <http://www.epa.gov/grtlakes/seahome/housewaste/src/dispose.htm> — guide to household waste disposal



"The very key to our success  
has been our ability,  
foremost among nations,  
to preserve our lasting values  
by making change work for us  
rather than against us."

~ Ronald Reagan

### RECENT FDA APPROVALS

*Betaseron* (interferon beta-1b) ... for expanded labeling for the treatment of relapsing forms of multiple sclerosis to reduce the frequency of clinical exacerbations

*Avonex* (interferon beta-1a) ... for the treatment of first multiple sclerosis attack if brain MRI scan abnormalities characteristic of MS are shown

*Fuzeon* (enfuvirtide), the first HIV fusion inhibitor ... for the treatment of HIV-1 infection in treatment-experienced patients with evidence of HIV-1 replication despite ongoing antiretroviral therapy

*InnoPran XL* (propranolol extended release) ... for the treatment of hypertension; administered in the evening; can be used alone or in combination with other antihypertensives

*Prempro 0.45/1.5* ... a new lower dose of 0.45mg conjugated estrogen and 1.5mg medroxyprogesterone acetate

*Avelox* (moxifloxacin) ... for the treatment of community-acquired pneumonia due to penicillin-resistant *Strep pneumoniae*

*Avandia* (rosiglitazone) ... for use in combination with insulin for the treatment of type 2 diabetes

*Oxytrol* (oxybutynin transdermal system) ... as the first transdermal therapy for the treatment of overactive bladder

*Eligard 30mg* (leuprolide acetate injectable suspension), four-month prostate cancer product ... for the palliative treatment of advanced prostate cancer

*Effexor XR* (venlafaxine) ... for the treatment of social anxiety disorder

*Zoloft* (sertraline) ... for the acute and long-term treatment of social anxiety disorder

*Flexeril* (cyclobenzaprine) ... for a new lower, less sedating dose of 5mg

*Azasan* (azathioprine) ... for new doses of 75mg and 100mg tablets for more flexible dosing options

### NEW CONTRAINDICATION

In a letter sent to health care providers, the manufacturer of products containing ergotamine or dihydroergotamine cautioned that these medications must not be taken with drugs that can result in increased levels of ergotamine. The new contraindication applies to *Migranal* (dihydroergotamine mesylate) nasal spray, *DHE* (dihydroergotamine mesylate) injection, *Cafergot* (ergotamine tartrate and caffeine) suppositories and tablets, *Cafergot-PB* (ergotamine tartrate, caffeine, belladonna alkaloids, and pentobarbital) suppositories, and *Bellergal Spacetabs* (belladonna alkaloids, ergotamine tartrate, and phenobarbital). These five products must not be taken at the same time as drugs that strongly inhibit CYP 3A4 enzymes because the resulting high levels of ergotamine can cause serious decreases in blood flow to the brain or to the limbs. Cases of stroke and gangrene have been reported from ergot toxicity, with some cases resulting in death or amputation.

Strong CYP 3A4 inhibitors include protease inhibitors (ritonavir, nelfinavir, indinavir, saquinavir), macrolide antibiotics (erythromycin, clarithromycin), and antifungal agents (ketoconazole, itraconazole, fluconazole, clotrimazole). Other medications that are not contraindicated but may pose a potential risk of ischemia when taken with ergotamine-containing products include antidepressant medications (nefazodone, fluoxetine, fluvoxamine) as well as grapefruit juice. Additionally, the manufacturer stresses that ergotamine or dihydroergotamine products should not be taken every day nor taken to prevent symptoms.



### Drug Interaction Corner

#### **SepralBactim (TMP-SMZ) Drug Interactions**

- ❖ *Anticoagulants* – prothrombin time of warfarin may be prolonged
- ❖ *Cyclosporine* – decrease in the therapeutic effect of cyclosporine and an increased risk of nephrotoxicity have occurred
- ❖ *Dapsone* – increase serum levels of both dapsone and TMP may occur
- ❖ *Diuretics* – in elderly patients, concomitant use has increased the incidence of thrombocytopenia with purpura
- ❖ *Hydantoin*s – phenytoin's hepatic clearance may be decreased and the half-life prolonged
- ❖ *Methotrexate* – sulfonamides can displace MTX from plasma protein binding sites increasing free MTX concentration
- ❖ *Sulfonylureas* – hypoglycemic response may be increased
- ❖ *Zidovudine* – serum levels of zidovudine may be increased due to decreased renal clearance