

May/June 2003

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 met in May and **added** the following medications to the Formulary:

- + clotrimazole vaginal 1% cream
- + cyclosporine ophthalmic emulsion (*Restasis*) — **indicated for the treatment of keratoconjunctivitis sicca**
- + albuterol/ipratropium unit dose nebulizer solution for inhalation (*DuoNeb*) — **for inpatient and clinic use only**
- + miconazole 200mg vaginal suppositories
- + progesterone vaginal 8% gel (*Crinone*)

The following medications were **added** to the **Basic Core Formulary (BCF)** by the DoD Formulary Committee (some medications already on Evans' Formulary):

- + amantadine (*Symmetrel*) 100mg capsules
- + benztropine (*Cogentin*) 0.5mg, 1mg, 2mg tablets
- + carbinoxamine 1mg/pseudoephedrine 15mg (*Cardec*) drops — **equivalent to *Rondec* drops**
- + chlorthalidone (*Hygroton*) 25mg, 50mg tablets — **added due to the extensive publicity of the results of the ALLHAT study**
- + goserelin (*Zoladex*) 3.6, 10.8mg implants — **as the sole LHRH agonist on the BCF for the treatment of prostate cancer**
- + lansoprazole (*Prevacid*) 15mg, 30mg capsules
- + triamterene 50mg/HCTZ 25mg (*Maxzide-25*) tablets
- + trihexyphenidyl (*Artane*) 2mg, 5mg tablets

The following medications were **deleted** from the Formulary:

- *Maalox* suspension — **deleted due to significant price increase**
- guaifenesin 300mg/pseudoephedrine 60mg (*Guaifed-PD*) capsules — **deleted due to very low usage at all three MTFs**

The next Formulary Committee Meetings will be held in July 2003. New Drug Requests must be received by the Chief, Pharmacy Service, no later than **23 June 2003** to be considered at the next meetings.



FAREWELL to...

LTC Torkilson who will be retiring soon and will remain in the area. He promises he will check in now and again to make sure things are running smoothly.

MAJ Vitt who will be leaving to attend the University of Colorado College of Pharmacy for his Doctor of Pharmacy (PharmD) degree.



Best Wishes!!

MAJ Ford and **CPT Lueg** will be on board soon to replace them.

Q & A

What are the 2003 primary changes and updates to the CDC's *Prevention and Control of Influenza?*



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In this issue....

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The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7) will be published in the 21 May 2003 issue of *JAMA*. The key messages listed in the article's abstract include:

- In persons older than 50 years, systolic blood pressure (BP) of more than 140 mmHg is a much more important cardiovascular disease (CVD) risk factor than diastolic BP.
- The risk of CVD, beginning at 115/75 mmHg, doubles with each increment of 20/10 mmHg; individuals who are normotensive at 55 years of age have a 90% lifetime risk for developing hypertension.
- Individuals with a systolic BP of 120 to 139 mmHg or a diastolic BP of 80 to 89 mmHg should be considered as pre-hypertensive and require health-promoting lifestyle modifications to prevent CVD.
- Thiazide-type diuretics should be used in drug treatment for most patients with uncomplicated hypertension, either alone or combined with drugs from other classes. Certain high-risk conditions are compelling indications for the initial use of other antihypertensive drug classes.
- Most patients with hypertension will require 2 or more antihypertensive medications to achieve goal BP (<140/90 or <130/80 for patients with diabetes or chronic kidney disease).
- If BP is more than 20/10 mmHg above goal BP, consideration should be given to initiating therapy with 2 agents, 1 of which usually should be a thiazide-type diuretic.
- The most effective therapy prescribed by the most careful clinician will control hypertension only if patients are motivated.

New Drug Requests

All New Drug Requests submitted for a patient require **adequate justification** for need of the specific medication. Please include, if applicable, indication for use, previous therapy/treatment failures, adverse events with formulary agents, etc. Examples of inappropriate justification for need that have been received include: "topical therapy", "increased cholesterol", "allergies".

RECENT FDA APPROVALS

Premarin (conjugated estrogens) ... for new low dose strength of 0.45mg per tablet

Zosyn (piperacillin/tazobactam) ... for new dosing regimen of four times a day for patients with nosocomial pneumonia (previously dosed six times per day for nosocomial pneumonia)

Fabrazyme (agalsidase beta) ... an enzyme replacement therapy for Fabry disease

Velcade (bortezomib) ... for the treatment of multiple myeloma patients who have received at least two prior therapies and have demonstrated disease progression on the last therapy

Viracept (nelfinavir mesylate) ... for new tablet strength of 625mg to be taken 2 tablets twice a day (versus the 250mg tablet taken as five tablets twice a day)

Aldurazyme (laronidase) ... a biotechnology product which is a version of the human form of the deficient enzyme in patients with certain forms of a rare genetic disease called MPS I, which includes Hurler Syndrome

Iressa (gefitinib) ... for the treatment of advanced non-small-cell lung cancer

Somavert (pegvisomant for injection) ... for the treatment of acromegaly in patients who have had an inadequate response to surgery and/or radiation therapy and/or other medical therapies, or for whom these therapies are not appropriate

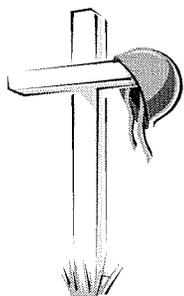
Coreg (carvedilol) ... new indication for patients who have had a myocardial infarction and who have left ventricular dysfunction

Emend (aprepitant) ... for use in combination with other anti-nausea and anti-vomiting drugs for prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of chemotherapy known to cause these adverse events

Valtrex (valacyclovir) ... new indication for the suppression of recurrent genital herpes in HIV-infected individuals

Factive (gemifloxacin) ... for the treatment of mild-to-moderate community-acquired pneumonia and acute bacterial exacerbation of chronic bronchitis

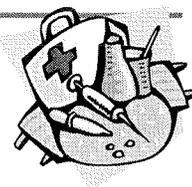
Lantus (insulin glargine) ... new indication for flexible administration at any time of day (previously once daily at bedtime)



" It is rather for us to be here dedicated to the great task remaining before us. . . that from these honored dead we take increased devotion to that cause for which they gave the last full measure of devotion. . . that we here highly resolve that these dead shall not have died in vain. . . that this nation, under God, shall have a new birth of freedom. . . and that government of the people. . .by the people. . .for the people. . . shall not perish from the earth. "

— Abraham Lincoln, Gettysburg Address

ADVERSE DRUG REACTION REPORT



There were 65 adverse drug reactions (ADRs) reported for March (n=34; 16 involving anthrax and/or smallpox vaccine) and April (n=31; 8 involving anthrax and/or smallpox vaccine), of which 20 (31%) were reported **spontaneously** (8 from outpatient pharmacy; 4 from Family Practice; 2 each from clinical pharmacy, Dermatology, and TMC#9; and 1 each from Pediatrics and 5E. The most prevalent adverse events reported involved the vaccines; if the anthrax/smallpox vaccines are not included, then the analgesic agents (n=14), the anti-infective agents (n=13), and the cardiovascular agents (n=7) were the most prevalent classes of drugs involved in the reported adverse events (consistent with past months).

Two events (3%) were deemed preventable — **patient error/contraindicated**:

- 1) A 29 year old male presented to the Emergency Department with flushing, head-to-toe hives, and urticaria after taking *Advil*. Patient had a history of allergy to ibuprofen. He was treated with IV *Benadryl*, *SoluMedrol*, and *Zantac* and discharged on oral prednisone, *Atarax*, and *Zantac*.
- 2) A 2 year old male was brought to the Emergency Department by his father with a slight erythematous rash on his back after taking his brother's amoxicillin. The father gave ipecac at home. The patient was seen in the ER and discharged on oral *Benadryl*.

One event (1.5%) was deemed **moderate** in severity:

- 1) A 20 year old male was hospitalized for 3 days with erythema multiforme, almost Stevens-Johnson syndrome, due to the smallpox vaccine, with oral, eye, and skin involvement. Treatment included IV *SoluMedrol*, acyclovir, *Percocet*, and ophthalmic antibiotic.

The anthrax and smallpox vaccine adverse events were reported to the FDA through the VAERS system.

Thanks to all who continue to report adverse drug events.



**"Pay any price, bear any burden,
meet any hardship, support any friend, oppose any foe
to assure the survival and success of liberty.."**

— John F. Kennedy



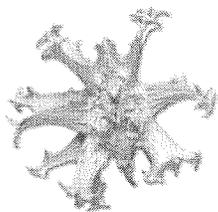
To Report an ADR...

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.



Devil's Claw (*Harpagophytum procumbens*), named for the peculiar appearance of its fruit (curved, covered with numerous small claw-like appendages), is a native plant to south and southwestern Africa, growing naturally in the Kalahari desert and Namibian steppes. Numerous tribes native to southern Africa have used devil's claw as a folk remedy for a wide variety of diseases, ranging from liver and kidney disorders to allergies, headaches, and most commonly rheumatism. European colonists brought devil's claw back home where it became a popular treatment for arthritis. In modern Europe, devil's claw is used to treat all types of joint pain, including osteoarthritis, rheumatoid arthritis, and gout.

The major active chemical component of devil's claw is harpagoside. Other important compounds include harpagide, procumbide, stigmasterol, fatty acids, aromatic acids, triterpenes, and flavonoids. Harpagoside, found primarily in the roots, produces negative chronotropic and positive inotropic effects due to alteration in the mechanisms that regulate calcium influx in smooth muscles. Dose-dependent reductions in blood pressure, decreased heart rate, and antiarrhythmic activity have been reported in animals. In contrast, harpagide possesses only slight negative chronotropic properties but considerable negative inotropic properties. The results of a German clinical study indicated that devil's claw has anti-inflammatory activity comparable to that of phenylbutazone; analgesia was observed along with reductions in abnormally high uric acid and cholesterol levels.

Devil's claw is claimed to be useful as an antiarthritic, antirheumatic, and appetite stimulant. Although one study showed findings of an anti-inflammatory effect, other studies have failed to replicate the effect in either humans or animals. Other therapeutic claims, which lack scientific support, include treatment of allergies, arteriosclerosis, boils, climacteric problems, dysmenorrhea, GI disturbances, headaches, heartburn, liver and kidney disorders, lumbago, malaria, neuralgia, nicotine poisoning, and skin cancer.

The dose of devil's claw tested in humans for decreased eicosanoid production was 2,000mg orally daily. A typical dosage of devil's claw is 750mg three times daily of a standardized preparation containing 3% iridoid glycosides.

Adverse effects in human trials have been rare, generally consisting of headache, tinnitus, or anorexia. Although no drug interactions have been reported, cautious use is recommended in patients also on antiarrhythmic agents. Devil's claw is contraindicated in patients with gastric and duodenal ulcers (it promotes the secretion of stomach acid) and in pregnant patients (it may stimulate uterine contractions).

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

"All of life is a constant education."

~ Eleanor Roosevelt

A Bit of History...

- 1976 ... Filovirus *Ebola zaire* is discovered.
- 1974 ... Dr. Henry Heimlich introduces his now famous maneuver.
- 1946 ... Dr. Benjamin Spock publishes *The Common Sense Book of Baby and Child Care*.
- 1928 ... Alexander Fleming discovers penicillin.
- 1897 ... Ronald Ross discovers mosquito-borne protozoa that cause malaria.
- 1890 ... Rubber gloves are used during surgery for the first time at Johns Hopkins University.
- 1885 ... Dr. Mules creates the first glass eye for a patient whose eye he has just eviscerated.
- 1846 ... Ether is discovered by William T. G. Morton.
- 1835 ... James Paget, a London pathologist, first detects the parasite *Trichinella spiralis*.
- 1821 ... Caffeine is discovered by Pierre-Joseph Pelletier. It is known to contribute to irritability, depression, diarrhea, insomnia, and other disorders.
- 1816 ... French physician Rene Laennec develops the first stethoscope.



Drug Interaction Corner

Drugs that interact with corticosteroids

*from "Common Errors in Internal Medicine", Federal Practitioner, Oct02

- ◇ Cardiac glycosides — effect enhanced by corticosteroids (corticosteroids reduce serum K⁺ level, thereby sensitizing the myocardium to the effect of the cardiac glycosides)
- ◇ Loop diuretics — diminish effect of corticosteroids; increase risk of hypokalemia (loop diuretics increase K⁺ loss, further reducing serum K⁺ level)
- ◇ Rifampin, phenytoin, barbiturates, primidone, anticholinesterase agents — diminish effect of corticosteroids (these drugs elevate level of cytochrome P450)
- ◇ Estrogen — enhances effect of corticosteroids (estrogen alters binding of globulin)
- ◇ NSAIDs — increase risk of GI bleeding (NSAIDs exacerbate the risk of gastric mucosal impairment)
- ◇ Angiotensin converting enzyme inhibitors — elevate risk of leukopenia (mechanism unknown)
- ◇ Cloroquin, mefloquin — elevate risk of cardiomyopathies (catabolic effects)
- ◇ Warfarin — corticosteroids alter the INR (competitive inhibition of CYP3A3/4 substrate)

MEDICATION USE REVIEW COMMITTEE REPORT

MEDICATION USE EVALUATION — *LOVENOX* (enoxaparin); March 2003

conducted/report prepared by: Connie Stroll, CPhT and Jo Vickers, PharmD

Purpose: To review the use of Low Molecular Weight Heparins approved for use with the Outpatient DVT Protocol through the Anticoagulation Monitoring Service (AMS)

Patient Population: Those receiving *Lovenox* identified from CHCS for time period 1 May 2002 through 22 January 2003

Results: n = 70; 3 patients with multiple usage; 40 patients followed by AMS

Indications:

Bridge treatment	28 patients
DVT treatment	17 patients
PE treatment	2 patients
Atrial fibrillation	1 patient
Undocumented	2 patients
ACS (in ER)	23 patients

Total Doses Used:

Acute Coronary Syndrome (ACS)	27 doses
All other indications	1018 doses

Documentation of Lovenox dosage 1mg/kg:

15 patients documented in medical record
42 patients documented in medical record or AMS

Estimated Cost Comparison:

<i>Lovenox</i> 1mg/kg q12h	\$26,931
<i>Fragmin</i> 100 IU/kg q12h	\$24,850
<i>Innohep</i> 175 IU/kg qd	\$51,550

- Conclusions:**
1. *Lovenox* use for Acute Coronary Syndrome (ACS) hasn't been approved by the P&T Committee
 2. Poor documentation of patient weight and/or mg/kg dose for *Lovenox*
 3. Providers using outside of current formulary guidelines
 4. Some cost savings if use *Fragmin* (manufacturer is seeking DVT treatment indication – fast track)

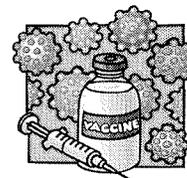
- Recommendations:**
1. Approve use of *Lovenox* for ACS use — done at March 2003 P&T Committee meeting
 2. Use *Fragmin* for patients who have burning with *Lovenox*

Q & A

From the CDC website: <http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5208a1.htm>

The five primary changes and updates for 2003 in the *Prevention and Control of Influenza* include:

- ❖ The optimal time to receive influenza vaccine continues to be October and November. However, because of vaccine distribution delays during 2000 to 2002, the Advisory Committee on Immunization Practices (ACIP) recommends that vaccination efforts in October focus on persons aged ≥ 50 years and those aged 6 to 23 months, persons aged 2 to 49 years with certain medical conditions that place them at increased risk for influenza-related complications, children aged < 9 years receiving influenza vaccine for the first time, health-care workers, and household contacts of persons at high risk, and that vaccination of other groups begin in November.
- ❖ Because young, otherwise healthy children are at increased risk for influenza-related hospitalization, influenza vaccination of healthy children aged 6 to 23 months continues to be encouraged when feasible. Vaccination of children aged ≥ 6 months who have certain medical conditions continues to be strongly recommended.
- ❖ The 2003/2004 trivalent inactivated vaccine virus strains are A/Moscow/10/99 (H3N2)-like, A/New Caledonia/20/99 (H1N1)-like, and B/Hong Kong/330/2001-like antigens (for the A/Moscow/10/99 [H3N2]-like antigen, manufacturers will use the antigenically equivalent A/Panama/2007/99 [H3N2] virus, and for the B/Hong Kong/330/2001-like antigen, manufacturers will use either B/Hong Kong/330/2001 or the antigenically equivalent B/Hong Kong/1434/2002).
- ❖ A limited amount of influenza vaccine with reduced thimerosal content, including 0.25ml single-dose syringe preparations for children aged 6 to 35 months, should be available for the 2003/2004 influenza season.
- ❖ Influenza vaccine for the U.S. market will be available from two manufacturers in 2003/2004, compared with three manufacturers in 2002/2003.



MEDICATION USE REVIEW COMMITTEE REPORT (CONTINUED)

MEDICATION USE EVALUATION — *LEVAQUIN* (levofloxacin); March 2003

conducted/report prepared by: Connie Stroll, CPhT and Jo Vickers, PharmD

Purpose: To review the use of *Levaquin*, a broad-spectrum antibiotic with increased resistance patterns

Patient Population: Those receiving *Levaquin* identified from CHCS for time period 1 August 2002 through 31 January 2003

Results:

	#	
EACH providers	99	
Prescriptions	730	
C&S done	344	*** 47% of patients receiving <i>Levaquin</i> had culture done
Urine C&S	270	*** 50% of patients receiving <i>Levaquin</i> who had urine culture had no pathogen identified
Pathogen identified	137	

MEPERS	# Providers	# RXs	# C&S	% cultured
IMC	13	132	51	39%
FP	26	122	76	62%
ER	11	146	69	47%
OB	6	6	2	33%
GI	1	8	2	25%
Urology	3	150	65	43%
PACC	3	27	15	56%
TMC	15	82	36	44%
EENT/Allergy	2	15	5	33%
Orthopedics	3	5	2	40%
Podiatry	3	12	10	83%
Miscellaneous	13	25	11	44%

Providers who wrote > 20 RXs in 6 months:

MEPERS	# Providers	# RXs	# C&S	% cultured
IMC	2	52	8	15%
FP	1	24	13	54%
ER	5	106	53	50%
Urology	3	150	65	43%

Dosing: one provider dosed drug BID

Cost: 5661 tablets X \$1.95/tab = \$11,050.65

- Conclusions:**
1. > 50% of patients receiving broad-spectrum antibiotic were not cultured
 2. Eleven providers accounted for > 60% of prescriptions (urology used pre/post surgical therapy)
 3. BID dosing doubles cost
 4. 50% of urine cultures were negative for pathogens

- Recommendations:**
1. Inform 12 outlying providers of how they compare to other providers in their clinics
 2. Recommend each provider group have reorientation of UTIs: signs & symptoms, early diagnosis, and alternative therapy
 3. Re-evaluate and compare to alternative therapy (i.e. SMX/TMP) in the future