Department of Defense
Pharmacoeconomic Center

2421 Dickman Rd., Bldg. 1001, Rm. 310
Fort Sam Houston, TX 78234-5081

MCCS-GPE **13 November 2003**

MEMORANDUM FOR: Executive Director, TRICARE Management Activity (TMA)

SUBJECT: Minutes of the Department of Defense (DoD) Pharmacy and Therapeutics (P&T) Executive Council Meeting

1. The DoD P&T Executive Council convened at 0800 hours on 13 November 2003 at the DoD Pharmacoeconomic Center, Fort Sam Houston, Texas.

2. VOTING MEMBERS PRESENT

COL Daniel D. Remund, MS	DoD P& T Committee Co-chair
COL Joel Schmidt, MC	Army
COL Doreen Lounsbery, MC	Army
MAJ Travis Watson, MS	Army
COL John R. Downs, MC	Air Force
Col Mark Nadeau, MC (For COL Bill Sykora, MC)	Air Force
LtCol George Jones, BSC	Air Force
CAPT Matt Nutaitis, MC	Navy
CDR Mark Richerson, MSC	Navy
CAPT Dennis Alder	Coast Guard
Kathy Kelly (For Mike Valentino)	Department of Veterans Affairs

VOTING MEMBERS ABSENT

CDR Terrance Egland, MC	DoD P& T Committee Co-chair

OTHERS PRESENT

COL William Davies, MS	DoD Pharmacy Program Director, TMA
CAPT Patricia Buss, MC	Chief Medical Officer Representative, TMA
COL Mike Heath, MS	Army Pharmacy Consultant, Chairman Pharmacy Board of Directors
LtCol Phil Samples, BSC (For Col Ardis Meier, BSC)	Air Force Pharmacy Consultant
MAJ John Howe, BSC	Defense Supply Center Philadelphia
LTC Kent Maneval, USA, MS	Joint Readiness Clinical Advisory Board
CAPT Don Nichols, MC	DoD Pharmacoeconomic Center
CDR Denise Graham, MSC	DoD Pharmacoeconomic Center
CDR Jill Pettit, MSC	DoD Pharmacoeconomic Center
CDR Ted Briski, MSC (via TC)	DoD Pharmacoeconomic Center
LtCol Dave Bennett, BSC (via TC)	DoD Pharmacoeconomic Center
LtCol Barb Roach, MC	DoD Pharmacoeconomic Center
CPT Jill Dacus, MC	DoD Pharmacoeconomic Center
Joe Torkildson, MD	DoD Pharmacoeconomic Center
Shana Trice	DoD Pharmacoeconomic Center
Dave Bretzke (via TC)	DoD Pharmacoeconomic Center
Angela Allerman	DoD Pharmacoeconomic Center
Eugene Moore	DoD Pharmacoeconomic Center
MAJ Barbara Hoeben, BSC	UT College of Pharmacy Master's Program
SFC Agustin Serrano	DoD Pharmacoeconomic Center

3. REVIEW MINUTES OF LAST MEETING

The minutes from the last meeting were accepted as written.

4. INTERIM DECISIONS/ADMINISTRATIVE ISSUES

None

5. NATIONAL PHARMACEUTICAL CONTRACTS AND BLANKET PURCHASE AGREEMENT (BPA) AWARDS, RENEWALS AND TERMINATIONS

A. The next option years were exercised for the following contracts: human insulin, and cyclobenzaprine.

B. Option years to be exercised over the next two months include the following contracts: albuterol, colchicine, permethrin, and tretinoin cream.

C. Option years not exercised due to current lower FSS prices than the contract price: rifampin, sucralfate, and salsalate.

D. DSCP signed an incentive agreement with Merck for alendronate (Fosamax) that became effective 1 October 2003. The agreement stipulates that alendronate will be the only bisphosphonate on the BCF. The class remains open on the BCF, so MTFs may have additional bisphosphonates on their formularies. The incentive agreement contains a

confidentiality clause that prohibits disclosure of the specific terms and conditions of the agreement, but it substantially reduces the price of alendronate. Estimated cost avoidance for DoD is $690,000 for the single month of October 2003.

6. PROCUREMENT INITIATIVES

A. Oral Fluoroquinolones – The Oral Fluoroquinolone Solicitation was posted on October 22, 2003. The solicitation offers the addition of a single oral fluoroquinolone to the Basic Core Formulary (BCF) as a workhorse agent to use in the treatment of community acquired pneumonia (CAP) and sinusitis. The solicitation closed on November 11, 2003. The award is pending.

B. Angiotensin Receptor Blockers (ARBs) – The ARB Solicitation was released in August 2003. The solicitation has been protested. DoD/VA is addressing the protest.

C. Cholinesterase Inhibitors – Two companies have offered BPAs on cholinesterase inhibitors. The Council asked the PEC to analyze the proposed BPAs and make recommendations at the next meeting.

D. Brimonidine 0.2% Ophthalmic Solution – The current BCF listing for brimonidine ophthalmic solution specifies the 0.15% formulation (Alphagan P). The Council placed Alphagan P on the BCF in Feb 2002 due to the planned phase-out of the 0.2% formulation by the manufacturer. The difference between the formulations is the preservative used; the 0.15% formulation (Alphagan P) contains a purite preservative, while the 0.2% formulation contains a benzylalkonium (BAK) preservative. Generic equivalents of the 0.2% formulation are now available. As part of the FDA review of generic brimonidine, the FDA determined that differences in intra-ocular pressure (IOP) lowering and adverse events between the two formulations were not clinically significant. Since generic versions of brimonidine 0.2% cost considerably less than brimonidine 0.15% (Alphagan P), the Council expressed interest in a potential sole source contract to compete generic brimonidine products for BCF addition. This issue will be reviewed at the next meeting.

7. REVIEW OF EXISTING PROCUREMENT INITIATIVES

A. LHRH Agonists – Goserelin Acetate Implant (AstraZeneca) was awarded a contract, effective 17 Feb 03, as the sole LHRH agonist on the BCF and VA National Formulary (VANF) for the treatment of prostate cancer. DoD has cost avoided approximately $213,000 since the contract was implemented. Goserelin acetate implants accounted for the following percentages (based on "treatment month equivalents") of LHRH agonist products purchased by MTFs during September 2003:

- DoD: 43%
- AF: 34%
- Army: 40%
- Navy: 59%

The contract reduced the price of goserelin acetate implants by 32%, which would have yielded a potential cost avoidance of $579,564 if goserelin acetate implants had accounted for 100% of the purchases. Since this class of drugs has indications other than

prostate cancer, some utilization of competing products is expected. Goserelin's market share is increasing slightly.

B. Statins – Simvastatin (Merck and Co) was awarded a joint VA/DoD contract, effective 1 May 03, as the sole high-potency statin on the BCF and VANF for the treatment of hyperlipidemia. MTFs may also have lovastatin and either pravastatin or fluvastatin on their formularies. DoD cost avoided approximately $31,652,000 during FY 03 within this class of drugs. The cost avoidance includes the old DoD contract and the first 3 months of the joint VA/DoD contract. Simvastatin accounted for the following percentages (based on tablets/capsules) of statins purchased by MTFs during September 2003:

- DoD: 93.4%
- AF: 95.6%
- Army: 92.8%
- Navy: 90.7%

On average, simvastatin prices are 20% less than they were under the initial DoD statin contract and 45% less than they were prior to the initial contract.

C. Triptans – Zolmitriptan (AstraZeneca) was awarded a contract, effective 11 July 03, as the sole 5HT1 agonist on the BCF. MTFs may have no more than one 5HT1 agonist in addition to zolmitriptan on their formularies. DoD cost avoided $701,843 during the first two months of the contract. Zolmitriptan accounted for the following percentages (based on tablets) of triptans purchased by MTFs during September 2003:

- DoD: 12%
- AF: 12%
- Army: 13%
- Navy: 11%

Zomitriptan prices are 50% less than they were before the contract. Given the large price reduction, MTFs can increase their cost avoidance by maximizing the use of zolmitriptan in lieu of other 5HT1 agonists.

D. Nasal Steroids – An incentive agreement for fluticasone (Flonase) nasal spray became effective 1 January 2003 and stipulated that fluticasone would be the sole aqueous nasal corticosteroid on the BCF. The class remains open on the BCF, so MTFs may have additional nasal corticosteroids on their formularies. The incentive agreement did not reduce the price of fluticasone, but it prevented an increase in price that would have occurred if MTFs had to purchase the product at the Federal Supply Schedule (FSS) price. Fluticasone nasal spray accounted for 87% of the nasal corticosteroid prescription fills at MTF pharmacies in September 2003.

E. Proton Pump Inhibitors (PPIs) – Rabeprazole (Aciphex) and lansoprazole (Prevacid) are the two PPIs on the BCF in accordance with the terms of incentive agreements that took effect 1 April 2003. The class remains open on the BCF, so MTFs may have additional PPIs on their formularies. Rabeprazole and lansoprazole accounted for approximately 75% and 17% respectively of PPI prescription fills at MTFs in September 2003. The weighted average cost per dose for PPIs was $0.80 in September 2003, compared to $0.40 per dose for most of calendar year 2002. The increase in cost is primarily due to a large price increase for rabeprazole. Prices for PPIs may decrease when price competition increases for generic omeprazole.

F. Thiazolidinediones (TZDs, "Glitazones") – Rosiglitazone (Avandia) is the only TZD on the BCF in accordance with the terms of an incentive agreement that took effect in July 2003. The class remains open on the BCF, so MTFs may have additional TZDs on their formularies. Rosiglitazone accounted for 66% of the 30-day equivalent prescriptions for TZDs at MTFs in September 2003. DoD cost avoidance for the first two months of the agreement is approximately $360,000.

G. Second-Generation Antihistamines – Loratadine is available to MTFs through an incentive agreement at less than half the price of other second-generation antihistamines, but loratadine accounted for only 6% of 30-day equivalent prescriptions for second-generation antihistamines at MTFs as of October 2003. The weighted average cost per dose for second-generation antihistamines at MTFs increased from $0.70 in March 2003 to $0.86 in August 2003. The Council encourages MTFs to maximize the use of loratadine (consistent with patients' clinical needs) in lieu of other second-generation antihistamines.

H. Other Blanket Purchase Agreements (BPAs) – The Council reviewed utilization data for ophthalmic prostaglandins, atypical antipsychotics, topical immunomodulators (TIMs), and tolterodine extended release. An estimate of the cost avoidance realized will be reported at the next meeting.

8. PHOSPHODIESTERASE-5 (PDE-5) INHIBITORS FOR ERECTILE DYSFUNCTION

In light of the recent FDA approval of a second PDE-5 inhibitor—vardenafil (Levitra)—the Health Affairs Director of Clinical Program Integration asked the DoD P&T Executive Council to review Health Affairs Policy 98-040, "Practice Guidelines for the Evaluation of Patients Requesting Sildenafil, (Viagra), for the Treatment of Male Impotence" and recommend whether the policy should be continued, modified, or rescinded. The policy mandates that sildenafil will be:

- non-formulary throughout the Military Health System (MHS)
- provided to patients only through a special order or prior authorization process
- subject to a quantity limit of six tablets per month

Based on information provided by the PEC, the Council identified the following concerns with Health Affairs Policy 98-040:

- The mandatory non-formulary status and requirement to special order or prior authorize prescriptions for sildenafil are an administrative hassle for patients, prescribers and pharmacies.
- The mandatory non-formulary status and requirement to special order or prior authorize sildenafil prescriptions inhibits the ability of MTF pharmacies to "recapture" prescription workload from the more expensive retail point of service.
- The mandatory non-formulary status precludes DoD from using formulary or procurement strategies to reduce the acquisition cost of PDE-5 inhibitors.
- One of the goals of the prior authorization process in the TMOP and retail network pharmacies is to identify patients who have psychogenic versus organic erectile

dysfunction because TRICARE does not cover the treatment of psychogenic erectile dysfunction. The prior authorization process is not meeting this goal because providers typically do not attempt to differentiate psychogenic erectile dysfunction from organic erectile dysfunction or mixed psychogenic/organic erectile dysfunction. The diagnostic tests required to confirm the diagnosis of organic erectile dysfunction are generally considered to be excessively expensive, invasive and pose unnecessary risk to the patient.

- The special order or prior authorization process is probably increasing the cost of providing erectile dysfunction therapy. In the TMOP, 27% of the prior authorization requests would have to be denied in order for DoD to break even on the cost of processing the prior authorizations versus the drug costs avoided by denying prescriptions. Over 95% of PA requests are approved in the TMOP. Unless the "sentinel effect" of the prior authorization process is large, DoD is losing money on the prior authorization process. [Note: The "sentinel effect" occurs when the requirement to obtain prior authorization causes a provider to refrain from writing a prescription for the drug.]

The Council voted to recommend that Health Affairs rescind HA Policy 98-040 and allow the DoD P&T Committee to manage the use of PDE-5 inhibitors as follows:

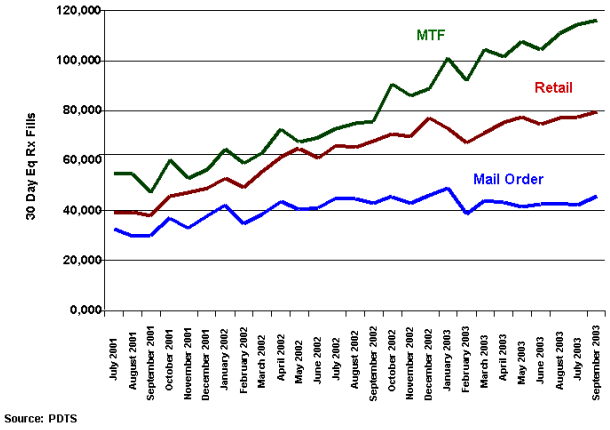
- Retain the quantity limit of six tablets per month.
- Discontinue the requirement for special order or prior authorization.
- Continue to utilize the prospective drug utilization review capabilities of CHCS and PDTS for safety monitoring.
- Consider formulary or contracting strategies to reduce the acquisition cost of PDE-5 inhibitors.

Although Health Affairs Policy 98-040 refers only to sildenafil, all PDE-5 inhibitors will be subject to the provisions of HA Policy 98-040 until Health Affairs rescinds or revises the policy.

9. DRUG/DRUG CLASS EVALUATIONS

A. Cox II Inhibitors – The Council reviewed the utilization and costs of non-steroidal anti-inflammatory drugs (NSAIDs), including the COX-2 selective NSAIDs ("COX-2 inhibitors"), in the three DoD pharmacy points of service. Utilization of COX-2 inhibitors is still increasing in MTFs and the retail network (see Figure 1 below).

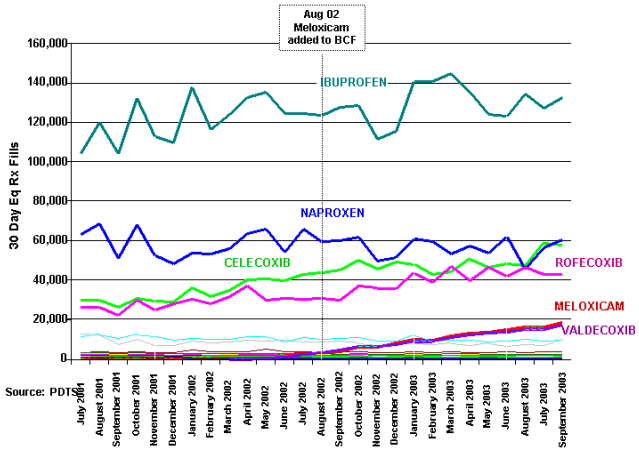
Figure 1: 30-day Equivalent Rxs for COX-2 Selective NSAIDs (Celecoxib, Rofecoxib, Valdecoxib) by Point of Service, Jul 01-Sep 03



Source: PDTS

Utilization of meloxicam (Mobic; Boehringer-Ingelheim), which was added to the BCF in August 2002 as a "relatively" COX-2 selective NSAID, has increased markedly in MTFs, closely tracking utilization of the most recently approved COX-2 inhibitor, valdecoxib (Bextra; Pfizer) (see Figure 2, below). Utilization of non-selective NSAIDs (e.g., ibuprofen, naproxen) remains essentially constant.

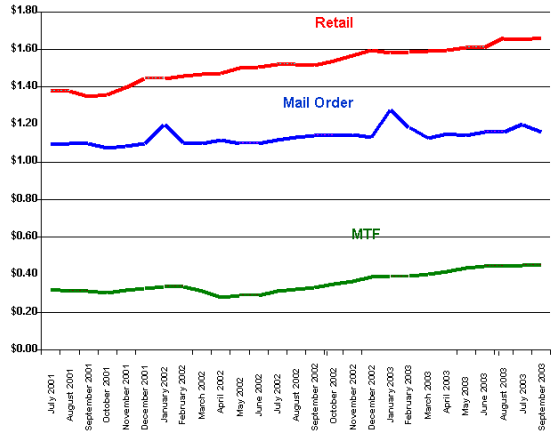
Figure 2: MTF 30-day Equivalent Rxs for NSAIDs, Jul 01 – Sep 03



Source: PDTS

As of Sep 03, monthly costs for NSAID therapy were about $8M in the retail network, $7.5M for MTFs, and $2.5 million in mail order. The cost per unit for NSAID therapy has increased in all points of service since Jul 01 (see Figure 3, below), primarily due to increasing use of COX-2 selective NSAIDs.

Figure 3: NSAID Cost per Unit by Point of Service, Jul 01 – Sep 03



Source: PDTS

Staff members from the PEC and the VA PBM are currently working on a joint DoD/VA NSAID review to support a potential joint procurement initiative for COX-2 selective and/or relatively COX-2 selective NSAIDs.

10. REQUESTS FOR BCF CHANGES

A. Cyclobenzaprine (Flexeril) 5 mg

Cyclobenzaprine tablets are on the BCF. The contract price is $0.02 per 10 mg tablet. The FDA approved a new 5 mg strength of the brand name Flexeril in February 2003. The FSS price of the branded Flexeril 5 mg tablet is $0.54. Due to the high cost of the 5 mg strength, the Council clarified the BCF listing for cyclobenzaprine to exclude Flexeril 5 mg tablets.

B. Zolmitriptan Nasal Spray

Zolmitriptan tablets are on the BCF. Zolmitriptan nasal spray was approved in October 2003. Zolmitriptan nasal spray is not included in the current triptan contract. The FSS price of zolmitriptan 5 mg nasal spray is $15.48/dose ($92.88 per box of 6 spray devices), which is much higher than the contract price of $3.20/2.5 mg or 5 mg tablet. Due to the high cost, the Council agreed that zolmitriptan nasal spray would not be included on the BCF.

C. Lansoprazole Oral Disintegrating Tablets and Delayed Release Suspension

Lansoprazole capsules (Prevacid) are currently on the BCF with an incentive agreement price of $0.65/capsule. Two new formulations of lansoprazole are available, a delayed release oral suspension and an orally disintegrating tablet. The FSS prices for the suspension are $2.00/15 mg packet and $2.28/30 mg packet. The orally disintegrating tablets are $2.80/15 mg tablet and $2.85/30 mg tablet. Although these new formulations could potentially improve ease of use in pediatric and geriatric populations, the existing

capsules are approved for pediatric use in patients 1 year of age or older. They can be opened and sprinkled on soft foods or mixed with liquids and administered enterally. The delayed release suspension comes in packets that must be mixed with water and used immediately upon reconstitution. Since the suspension thickens quickly they should not be used enterally. Due to the high cost and the existence of FDA approved alternative administration options for lansoprazole capsules, the Council clarified the BCF listing for lansoprazole to exclude the oral disintegrating tablets and delayed release suspension.

D. Transdermal Scopolamine Patch

CPT Jill Dacus (PEC) presented a request from a nurse anesthetist for the addition of transdermal scopolamine patch to the BCF. The requestor's rationale was based on two considerations:

1. Transdermal scopolamine would be more cost effective than the majority of serotonin antagonists (e.g., dolasetron, granisetron, ondansetron) for prophylaxis of post-operative nausea and vomiting (PONV).

2. The potential exists for increased use of transdermal scopolamine in ambulatory surgery patients now that droperidol, formerly the most popular antiemetic for PONV, has a black box warning for QT prolongation.

Efficacy/Safety/Tolerability – Transdermal scopolamine has been proven efficacious in the prophylaxis of PONV. In a meta-analysis of 23 trials with scopolamine (N = 979) and placebo (N = 984), the relative risk for vomiting was 0.69 (95% CI 0.58-0.82), with an absolute risk reduction of 17%, and a number needed to treat (NNT) of 5.9. However, the American Society of Anesthesia Task Force on Postanesthetic Care's 2002 Practice Guidelines do not recommend scopolamine patches as first line prophylaxis, stating that the evidence for its use is less robust than for other anti-emetic agents. Scopolamine is contraindicated in children and patients with narrow angle glaucoma. Caution is advised in the elderly due to increased sensitivity to scopolamine's CNS effects, such as confusion, agitation, and hallucinations. The most common side effect is dry mouth, which occurs in 2 out of 3 patients. Administration of scopolamine for prophylaxis of PONV following ambulatory surgery is somewhat cumbersome because the patient would have to obtain the patch and apply it the evening before surgery.

Cost – The MTF average cost per dose for scopolamine is generally lower than the cost for serotonin antagonists, but is higher than the cost for other antiemetics used for PONV (e.g. promethazine). MTFs currently spend about $250K per month on serotonin antagonists, compared to $50,000 per month or less for other perioperative antiemetics.

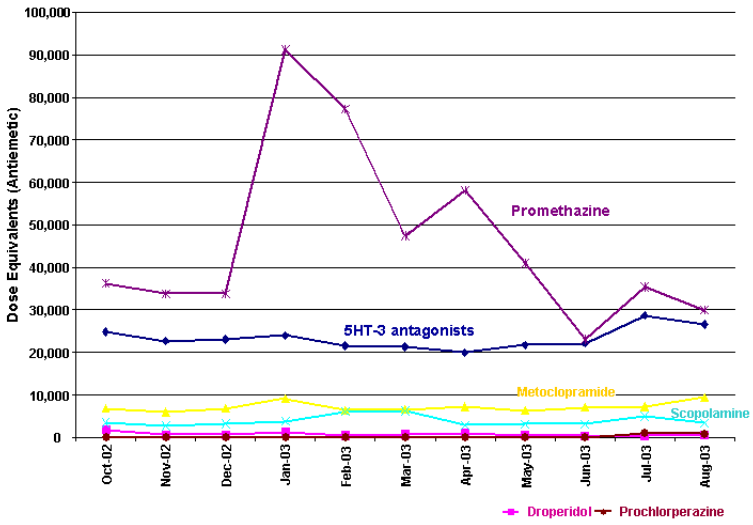
Table 1: Prime Vendor Acquisition Costs (Mean Cost per Dose, Oct 02 – Aug 03)

Antiemetic	Dosage & Route	Mean Cost per Dose
Scopolamine	1.5 mg/24 h TD placed night before surgery	$6.98*
Droperidol	1.25mg IM/IV prior to surgery	$1.63
Prochlorperazine	5-10mg IM/IV 1-2hr before surgery	$3.76-7.56
Promethazine	25-50 mg IM/IV 1-2hr before surgery	$0.05-0.16
Dolasetron	100mg PO, 12.5mg IV, within 2h start of surgery	$5.01, $24.46
Granisetron	1mg IV 30sec before anesthesia induction	$58.24
Ondansetron	16mg PO, 16mg solution PO, 4mg IV, 1hr before anesthesia	$32.46, $38.00, $11.86
Metoclopramide	10-20mg IM injection near end of surgery	$1.92-3.84

*Note: 87% of MTF purchases were for scopolamine patches in boxes of 4 at a cost of $8.59/patch; 23% of purchases were for boxes of 24 at a cost of $2.68/patch.

Utilization –MTFs purchase more dose equivalents of serotonin antagonists, promethazine and metoclopramide than they do scopolamine transdermal patches. However, purchases of scopolamine patches are higher (in terms of dose equivalents) than droperidol, which has a new black box warning, or prochlorperazine, which has not been widely available due to a national drug shortage. Table 4 shows total purchases of all of these agents, which may also be used for indications other than prophylaxis of PONV.

Figure 4: MTF Purchases of Injectable and Transdermal Antiemetics By Dose Equivalents (Oct 02 – Aug 03)



Conclusion: The Council voted unanimously not to add transdermal scopolamine to the BCF based on its high cost, low utilization, cumbersome administration requirements for PONV, and the American Society of Anesthesia Task Force on Postanesthetic Care recommendations.

E. Extended Release Morphine

Due to a lack of raw materials (opium poppy), there is a shortage of 15 mg and 30 mg strengths of MS Contin and generic morphine sulfate extended release products other than Mallincrodt's product. Mallincrodt anticipates no shortages of any strength since it is the principal supplier for all manufacturers of morphine sulfate products. The current BCF listing is for MS Contin or its generic equivalent in strengths of 15, 30, and 60 mg. Mallincrodt has an FDA-approved generic morphine sulfate extended release product that is A-B rated to MS Contin. FSS pricing for Mallinckrodt's product is less than the current FSS price for MS Contin. MTFs should be aware that the generic Mallincrodt product is currently a stable source of supply for oral morphine sulfate extended release.

11. ADJOURNMENT

The meeting adjourned at 1400 hours. The next meeting will be held at Fort Sam Houston, TX at 0800 on Wednesday, 11 February 2004. All agenda items should be submitted to the co-chairs no later than 05 January 2004.

<signed>	<signed>
DANIEL D. REMUND	TERRANCE EGLAND
COL, MS, USA	CDR, MC, USN
Co-chair	Co-chair

Department of Defense
Pharmacoeconomic Center

2421 Dickman Rd., Bldg. 1001, Rm. 310
Fort Sam Houston, TX 78234-5081

MCCS-GPE **6 AUGUST 2003**

MEMORANDUM FOR: Executive Director, TRICARE Management Activity (TMA)

SUBJECT: Minutes of the Department of Defense (DoD) Pharmacy and Therapeutics (P&T) Committee Meeting

1. A meeting of the DoD P&T Committee convened at 0800 hours on 6 August 2003, at the TRICARE Management Activity (TMA), Falls Church, VA.

2. VOTING MEMBERS PRESENT

CDR Terrance Egland, MC	DoD P& T Committee Co-chair
COL Daniel D. Remund, MS	DoD P& T Committee Co-chair
COL Joel Schmidt, MC	Army
COL Doreen Lounsbery, MC	Army
COL Mike Heath, MS (For MAJ Travis Watson, MS)	Army
LtCol Kimberly May, MC (For Col John R. Downs, MC)	Air Force
Col Bill Sykora, MC	Air Force
LtCol Phil Samples, BSC (For LtCol George Jones, BSC)	Air Force
CAPT Matt Nutaitis, MC	Navy
CDR Mark Richerson, MSC	Navy
CAPT Charles Bruner	Coast Guard
Rance Hutchings, Pharm.D. (For Dr. Trevor Rabie)	Uniformed Services Family Health Plans (USFHP)
Francine Goodman (For Mike Valentino)	Department of Veterans Affairs

VOTING MEMBERS ABSENT

None	

OTHERS PRESENT

COL William Davies, MS	DoD Pharmacy Program Director, TMA
Col Ardis Meier, BSC	Air Force Pharmacy Consultant
CAPT Joe Torkildson, MC, USN	DoD Pharmacoeconomic Center
CDR Denise Graham, MSC, USN	DoD Pharmacoeconomic Center
CDR Ted Briski, MSC, USN	DoD Pharmacoeconomic Center
Shana Trice	DoD Pharmacoeconomic Center
LtCol Dave Bennett, USAF, BSC (Via VTC)	DoD Pharmacoeconomic Center
LtCol Barb Roach, USAF, MC (Via VTC)	DoD Pharmacoeconomic Center
CPT Jill Dacus, USA, MC (Via VTC)	DoD Pharmacoeconomic Center
David Bretzke (via VTC)	DoD Pharmacoeconomic Center
Eugene Moore (via VTC)	DoD Pharmacoeconomic Center
Angela Allerman (via VTC)	DoD Pharmacoeconomic Center
Lisa LeGette	Express Scripts
MAJ John Howe, MS	Defense Supply Center Philadelphia
Gene Lakey	TriWest
William Hudson	Humana
Kelly Lenhart	Humana

3. **REVIEW MINUTES OF LAST MEETING/ADMINISTRATIVE ISSUES** – The minutes from the last meeting were accepted as written.

4. **INTERIM DECISIONS**

An interim "email" DoD Executive Council Meeting resulted in the following BCF and TMOP changes:

- Latanoprost (Xalatan) was added to the BCF
- Rosiglitazone (Avandia) was added to the BCF
- Rosiglitazone/metformin (Avandamet) was added to the BCF
- Serevent MDI was removed from the BCF due to market withdrawal. Serevent DPI will be the remaining salmeterol on the BCF.
- Zolmitriptan oral tablets (Zomig) were added to the BCF
- Sumatriptan oral tablets (Imitrex) were removed from the BCF
- Gefitinib (Iressa) was added to the TMOP with quantity limits
- Lovastatin extended release (Altocor) was removed from the TMOP

5. **UNIFORM FORMULARY (UF) PROPOSED RULE**- COL William Davies, DoD Pharmacy Program Director, TMA, stated that the current plan is to implement the Uniform Formulary in conjunction with the TRICARE Retail Pharmacy (TRRx) contract. The TRRx contract is scheduled for implementation in Spring 2004.

6. **BCF AND TRICARE MAIL ORDER PHARMACY (TMOP) FORMULARY ISSUES** – The Committee determined the TMOP formulary status, TMOP or retail network formulary restrictions (quantity limits or prior authorization), and Basic Core Formulary (BCF) status for 11 new drugs or formulations (see Appendix A). The PEC also presented brief information on eleven additional new drugs or formulations not requiring action by the Committee (see Appendix B). The Committee agreed that no further review was required.

7. **MAIL ORDER AND RETAIL NETWORK ISSUES**

   A. *TMOP* – Lisa LeGette from Express Scripts provided a TMOP update to the Committee.

   B. *TMOP Prior Authorizations (PAs)* – Shana Trice provided an update on TMOP PAs.

   C. *Change to TMOP PA for Etanercept* - Etanercept (Enbrel) was recently approved for ankylosing spondylitis, a chronic disease involving inflammation of the sacroiliac, intervertebral, and costovertebral joints. Ankylosing spondylitis affects approximately 350,000 patients in the United States. The Committee unanimously added treatment of ankylosing spondylitis to the PA criteria for etanercept. TMOP PA criteria and forms are available on the PEC website at www.pec.ha.osd.mil/TMOP/TMOPhome.htm#2c-PA.

8. **CONTROLLED DISTRIBUTION OF PRESCRIPTION DRUGS** – Enfuvirtide (Fuzeon) is approved for use in combination with other antiretroviral agents for the treatment of HIV-1 infection in treatment-experienced patients with evidence of HIV-1 replication despite ongoing antiretroviral therapy. Roche Laboratories and Trimeris have contracted the distribution of Fuzeon to the specialty pharmacy operator Chronimed. Fuzeon is available through the TRICARE retail pharmacy benefit through the Fuzeon Progressive Distribution Program established by Chronimed and as described on their website, www.fuzeon.com.

   DoD has made arrangements with Chronimed to make Fuzeon available for MTF pharmacies to purchase and dispense to their patients. The procedure for MTF pharmacies to purchase Fuzeon with their department credit card is outlined on the DoD Fuzeon Procurement Form. The DoD Fuzeon Procurement Form is available for download at the PEC website, http://www.pec.ha.osd.mil/Controlled_Distribution_Drugs.htm, or in the File Library of RxNET, www.dodrxnet.org. Purchases through this mechanism will be billed at federal pricing. Commercial pricing applies to prescriptions filled through the TRICARE retail pharmacy benefit.

   Air Force pharmacies can obtain Fuzeon through the Air Force's High Dollar Program, which is managed out of Wright-Patterson Air Force Base. Air Force facilities wanting to use the High Dollar Program should complete the request forms provided by Wright-Patterson and not the DoD Fuzeon Procurement form described here.

   Questions about the DoD Fuzeon Procurement Form can be directed to David Bretzke or CDR Ted Briski of the DoD Pharmacoeconomic Center at (210) 295-1271.

9. ADJOURNMENT – The meeting adjourned at 1100 hours. The next meeting will be held at Fort Sam Houston, TX at 0800 on Friday, 14 November 2003. All agenda items should be submitted to the co-chairs no later than 06 October 2003.

<signed>
DANIEL D. REMUND
COL, MS, USA
Co-chair

<signed>
TERRANCE EGLAND
CDR, MC, USN
Co-chair

List of Appendices

APPENDIX A: DOD P&T COMMITTEE FORMULARY DECISIONS REGARDING NEWLY APPROVED DRUGS

Generic name (Trade name; manufacturer)	**FDA approval date, drug class, FDA-approved indication**	**TMOP Formulary status**	**TMOP and/or retail network formulary restrictions**	**BCF status**
Moxifloxacin ophthalmic solution 0.5% (Vigamox; Allergan)	16 Apr 03: Fourth generation quinolone ophthalmic antibiotic indicated for treating bacterial conjunctivitis caused by susceptible strains of aerobic gram positive and aerobic gram negative organisms and Chlamydia.	Added to the TMOP Formulary	**Quantity Limits** General rule applies **Prior Authorization:** None	Not added to the BCF **Similar BCF agents:** None
Oxybutynin transdermal system (Oxytrol; Watson)	10 Mar 03: First transdermal formulation of oxybutynin for treatment of overactive bladder with symptoms of urge urinary incontinence, urgency and frequency. Applied every 3-4 days (twice weekly). The product is packaged in 1 carton containing 8 patches, a 30-day supply.	Added to the TMOP Formulary	**Quantity Limits** General rule applies **Prior Authorization** None	Not added to the BCF **Similar BCF agents:** Oxybutynin oral (immediate release tablets) and tolterodine extended release capsules are on the BCF
Influenza intranasal vaccine (FluMist; Medimmune/Wyeth)	17 Jun 03: First nasally administered live influenza virus vaccine. Approved for active immunization for the prevention of disease caused by influenza A and B viruses in healthy children ages 5-17 and healthy adults ages 18-49. FluMist is not to be administered to asthmatics, immunocompromised patients, or patients taking drugs which compromise the immune system (chemo agents, high dose steroids, etc).	Not added to the TMOP Formulary The product is not intended for self-administration and must remain frozen prior to use.	**Quantity Limits** N/A **Prior Authorization** None	Not added to the BCF **Similar BCF agents**: None
Omalizumab injection (Xolair; Genentech/Novartis)	20 Jun 03: First injectable monoclonal antibody that targets the IgE antibody. Approved for treatment of patients 12 years of age and older with moderate to severe allergy-related asthma that is inadequately controlled with inhaled steroid treatments. Eligible patients must have a positive skin test or *in vitro* reactivity to perennial allergies to confirm the diagnosis of allergy-related asthma.	Not added to the TMOP Formulary	**Quantity Limits** N/A **Prior Authorization** None	Not added to the BCF **Similar BCF agents**: None

Note about Omalizumab: Omalizumab injection will not be available from the TMOP due to the following reasons:

1) The product is not labeled or packaged for patient self-administration. No patient instruction information is enclosed in the package insert.
2) The risk of anaphylaxis and lack of clinical experience with omalizumab does not support its use outside of a controlled environment.
3) Reconstitution and administration requirements make patient preparation difficult. (Omalizumab is a lyophilized powder that takes 15-20 minutes to dissolve. Subcutaneous administration of the viscous liquid takes 5-10 seconds, and multiple injection sites may be needed due to the injection volume.)
4) Commercial distribution is limited to a specialty pharmacy network that supplies medications to physicians' offices.

Generic name (Trade name; manufacturer)	**FDA approval date, drug class, FDA-approved indication**	**TMOP Formulary status**	**TMOP and/or retail network formulary restrictions**	**BCF status**
Pravastatin/ buffered aspirin tablets (Pravigard PAC; BMS)	24 Jun 03: This product is not a single tablet formulation, but simply two tablets (pravastatin and buffered aspirin) packaged side-by-side in the same blister pack. Six dosage strengths are available (3 dosages of pravastatin, 20, 40 and 80 mg; with 2 aspirin dosages 81 mg and 325 mg). The product requires a prescription. Indications are to reduce the occurrence of cardiovascular events, including death, MI or stroke in patients who have clinical evidence of cardiovascular and/or cerebrovascular disease. Pravigard PAC is only indicated for secondary prevention of cardiovascular disease; pravastatin is indicated for both primary and secondary prevention.	Not added to the TMOP Formulary	**Quantity Limits** N/A **Prior Authorization** None	Not added to the BCF **Similar BCF agents:** Simvastatin
Notes about Pravigard PAC: • **TMOP**: Pravigard PAC was not added to the TMOP Formulary as it costs a lot more than pravastatin and aspirin that are not packaged together and provides no additional clinical benefit. (Pravigard PAC FSS prices: 20 mg + ASA: $1.84/day; 40 mg +ASA or 80 mg + ASA $2.70/day. Pravastatin FSS prices: 20 mg: $0.75/day; 40 mg: $1.30/day; 80 mg: $1.49/day. Aspirin: Less than $0.01/day.) Pravastatin is available from the TMOP, which will meet the clinical needs of patients with prescriptions for Pravigard PAC. • **BCF & MTF Formularies:** Pravigard PAC was not added to the BCF. The statin contract allows MTFs to have either pravastatin or fluvastatin on their formularies, but not both. MTFs cannot add Pravigard PAC to their local formulary if fluvastatin is on their formulary. MTFs may add Pravigard PAC to their formulary if pravastatin is on their formulary, but MTFs are advised not to add Pravigard PAC to their formulary because it costs too much			
Testosterone buccal system mucoadhesive (Striant; Columbia)	Jun 03: Buccal testosterone mucoadhesive is indicated for replacement therapy in males for conditions associated with a deficiency or absence of endogenous testosterone. Schedule III product.	Added to the TMOP, consistent with inclusion of other non-injectable testosterone products	**Quantity Limits** TMOP: 3 cartons per 90 days Note: although there is a 30-day supply limit on most controlled substances dispensed by the TMOP, other topical androgen replacement products have a 90-day supply limit in the TMOP. Retail: 1 carton per 30 days **Prior Authorization** None	Not added to the BCF. **Similar BCF agents:** None.
Note about Testosterone Buccal System Mucoadhesive: This product is supplied in a blister card of 10 buccal systems, with a total of 6 blister cards (60 buccal systems) in each carton. Anticipated retail cost for one month is $149.35 /60 systems= $4.97/day (need 2 systems/day). As of July 15, there was no FSS listing for this formulation.				

Generic name (Trade name; manufacturer)	**FDA approval date, drug class, FDA-approved indication**	**TMOP Formulary status**	**TMOP and/or retail network formulary restrictions**	**BCF status**
Conjugated estrogen / medroxyprogesterone acetate (Prempro 0.3/1.5; Wyeth)	Jun 03: Lower-dose formulation of Prempro contains 0.45 mg of estrogen, and 1.5 mg of progestin (existing Prempro doses include 0.625 / 2.5 mg, and 0.45 mg / 1.5 mg which was approved in April 2003). Approved for both menopausal vasomotor symptoms and osteoporosis.	Added to the TMOP (line extension)	**Quantity Limits** N/A **Prior Authorization** None	BCF listing for conjugated estrogens / medroxy-progesterone oral (Prempro) will include the 0.3/1.5 mg strength
Conjugated estrogen 0.45 mg (Premarin; Wyeth)	Jun 03: Lower-dose formulation of conjugated estrogens approved for both menopausal vasomotor symptoms and osteoporosis.	Added to the TMOP (line extension)	**Quantity Limits** N/A **Prior Authorization** None	BCF listing for conjugated estrogens will include the 0.45 mg strength.
Clonazepam orally disintegrating tablets (Klonopin Wafers; Solvay)	May 03: Rapidly dissolving formulation of clonazepam, available in 0.125, 0.25, 0.5, 1 and 2 mg sizes. There is no FSS price yet for the new formulation, but it is anticipated to be considerably more costly than generic clonazepam tablets, which cost approximately $0.05 per tab. The Committee agreed that the clinical benefit was unlikely to be sufficient to justify the increased cost for the rapidly dissolving formulation.	Added to the TMOP (line extension)	**Quantity Limits** N/A **Prior Authorization** None	The BCF listing for clonazepam 0.5 mg was clarified to exclude clonazepam orally disintegrating tablets.
Risperidone orally disintegrating tablets (Risperdal Redi-tabs; J&J)	May 03: Rapidly dissolving formulation of risperidone, available in 0.5, 1 and 2 mg strengths. Potential candidates may include psychiatric patients on directly observed therapy, or patients with swallowing difficulties. The cost of the orally disintegrating tablets is somewhat higher than the regular tablets, based on either FSS or BPA pricing. Risperidone is not available generically.	Added to the TMOP (line extension)	**Quantity Limits** N/A **Prior Authorization** None	The BCF listing for risperidone was clarified to exclude the orally disintegrating tablets.
Montelukast oral granules (Singulair; Merck)	May 03: New 4 mg oral granule formulation of montelukast. The new formulation is FDA-approved for treating asthma down to 12 months of age, and for treating seasonal allergic rhinitis down to 2 years of age. Previously, the youngest age for which montelukast was indicated was 2 years (4 mg chewable tablets). The oral granules should be mixed with carrots, applesauce, ice cream or rice; they are not to be mixed with liquids. Montelukast is not available generically. The Committee agreed that the new formulation provides an FDA-approved alternative in this age group and is likely to increase the ease of treatment.	Added to the TMOP (line extension)	**Quantity Limits** N/A **Prior Authorization** None	The BCF listing for montelukast oral was clarified to include the oral granules.

APPENDIX B: FORMULARY STATUS OF NEWLY APPROVED DRUGS NOT REQUIRING FORMAL REVIEW BY THE P&T COMMITTEE

Generic name (Trade name; manufacturer)	**Comments**
Omeprazole magnesium delayed release tablets, OTC (Prilosec OTC; Proctor and Gamble))	Indicated for treatment of frequent heartburn symptoms. Therapy should not be continued beyond 14 days. Available as 20.6 mg tablets in the magnesium salt form, which is equivalent to 20 mg of omeprazole. The over-the counter (OTC) product is not AB rated to Rx omeprazole. Prilosec OTC is anticipated to cost $0.80/tablet, but it will be packaged in blister cards of 14, 28, or 42 tablets, which may limit its usefulness to local MTFs considering formulary addition. Prescription omeprazole will remain on the market. Prices for the prescription products: Rx Prilosec: $2.11/cap (FSS); Rx generic omeprazole: $2.89/cap (retail). Prilosec OTC was not considered for addition to the BCF, since it is an OTC product. Currently there are two proton pump inhibitors (PPIs) on the BCF in an open class: rabeprazole and lansoprazole. Prilosec OTC was not added to the TMOP Formulary, since OTC agents are not a covered TRICARE benefit.
Desloratadine orally disintegrating tablets (Clarinex Redi Tabs; Schering)	Automatically added to the TMOP Formulary as a line extension. Not considered for the BCF because desloratadine (Clarinex) is not a BCF item.
Agalsidase beta (Fabrazyme; Genzyme)	Orphan drug for treating Fabry disease. Administered by IV infusion every 2 weeks. Not considered for the TMOP Formulary because it is not intended for self-administration. Not considered for the BCF due to the specialized nature of the medication.
Laronidase (Aldurazyme; Genzyme))	Orphan drug for treating the Hurler and Hurler-Scheile forms of mucopolysaccharidoses I. Administered by IV infusion q week. Not considered for the TMOP Formulary because it is not intended for self-administration. Not considered for the BCF due to the specialized nature of the medication.
Bortezomib (Velcade; Millennium Pharmaceuticals)	Proteasome inhibitor (new class of anti-cancer drugs). Third-line treatment for multiple myeloma. Administered by IV bolus injection twice/week for two weeks, followed by 10 days off therapy. Not considered for the TMOP Formulary because it is not intended for self-administration. Not considered for the BCF due to the specialized nature of the medication.
Tositumomab & I 131 tositumomab (Bexxar; Corixa Corp)	Monoclonal antibody in combination with radiation for non-Hodgkin's lymphoma. Administered by nuclear medicine. Not considered for the TMOP Formulary because it is not intended for self-administration. Not considered for the BCF due to the specialized nature of the medication.
Carbidopa / levodopa / entacapone (Stalevo; Novartis / Orion)	Combination of Anti-Parkinson's agents carbidopa/levodopa with entacapone (Comtan), a catechol-O-methyltransferase [COMT] inhibitor. Entacapone is always given with carbidopa/levodopa, and never administered by itself. The combination product is indicated for treating Parkinson's Disease patients who experience end-of-dose wearing off. Automatically added to the TMOP Formulary as a new combination of drugs already available. Not considered for the BCF since entacapone is not listed on the BCF.
Ondansetron orally disintegrating tablets (Zofran ODT; GSK)	Automatically added to the TMOP Formulary as a line extension. Not considered for the BCF because ondansetron is not listed on the BCF.
Olmesartan medoxomil /HCTZ tablets (Benicar HCT; Forest/Sankyo)	ARB in combination with HCTZ. Automatically added to the TMOP Formulary as a line extension. Not considered for BCF addition as ARB contracting initiative is in progress.
Atazanavir (Reyataz; BMS)	Protease inhibitor approved for use in combination with other antiretroviral agents for HIV. First once daily protease inhibitor. Automatically added to TMOP as an HIV agent. Not considered for the BCF due to the specialized nature of the medication.
Emtricitabine (Emtriva; Gilead)	NNRTI (non-nucleotide reverse transcriptase inhibitor) for HIV. Automatically added to TMOP as an HIV agent. Not considered for the BCF due to the specialized nature of the medication.

APPENDIX C: COMBINED SUMMARY OF FORMULARY CHANGES FROM THE DOD P&T EXECUTIVE COUNCIL MEETING, THE DOD P&T COMMITTEE MEETING, AND THE JULY 2003 INTERIM "E-MAIL" MEETING OF THE DOD P&T EXECUTIVE COUNCIL

1. **BCF CHANGES**

A. *Additions to the BCF*

1) Polymycin B Sulfate/Trimethoprim Ophthalmic Solution
2) Erythromycin Ophthalmic Ointment
3) Insulin Aspart (Novolog) vials

Interim Meeting Decisions

4) Latanoprost (Xalatan)
5) Rosiglitazone (Avandia)
6) Rosiglitazone/metformin (Avandamet)
7) Zolmitriptan oral tablets (Zomig)

B. Deletions, changes, clarifications or exclusions from the BCF

Interim Meeting Decisions

1) Serevent MDI – removed from the BCF due to market withdrawal. The remaining dry powder salmeterol formulation (Serevent Diskus) will be on the BCF.
2) Sumatriptan oral tablets (Imitrex) – removed from the BCF due to award of the triptan contract.

2. **TMOP FORMULARY CHANGES**

A. *Additions to the TMOP Formulary*

1) Moxifloxacin ophthalmic solution 0.5% (Vigamox)
2) Oxybutynin transdermal system (Oxytrol)
3) Testosterone buccal system mucoadhesive (Striant) – quantity limits apply, see below

Interim Meeting Decisions

4) Gefitinib (Iressa) – quantity limits apply, see below

B. Exclusions from the TMOP Formulary

1) Pravastatin/buffered aspirin (Pravigard PAC)
2) Influenza nasal vaccine (FluMist)

C. Deletions, changes, or clarifications to the TMOP Formulary

Interim Meeting Decisions

1) Lovastatin extended release (Altocor) – Interim Meeting Decision

3. **QUANTITY LIMIT CHANGES (RETAIL NETWORK AND TMOP)**

   A. Quantity limit for testosterone buccal system mucoadhesive (Striant):

   - TMOP: day supply limit of 90 days (same exception to usual 30-day supply limit for controlled substances as other topical testosterone products); quantity limit of 3 cartons (180 systems) per 90 days
   - Retail: 1 carton (60 systems) per 30 days

   B. Quantity limits for gefitinib (Iressa):

   - TMOP: day supply limit of 45 days; quantity limit of 45 tablets per 45 days
   - Retail: day supply limit of 30 days; quantity limit of 30 tablets per 30 days

4. **CHANGES TO THE TMOP PRIOR AUTHORIZATION PROGRAM**

   A. The PA criteria for etanercept (Enbrel) were changed to reflect the recent FDA indication for ankylosing spondylitis. The revised form is available on the PEC website.

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MCCS-GPE **5 August 2003**

MEMORANDUM FOR: Executive Director, TRICARE Management Activity (TMA)

SUBJECT: Minutes of the Department of Defense (DoD) Pharmacy and Therapeutics (P&T) Executive Council Meeting

1. The DoD P&T Executive Council convened at 0800 hours on 5 August 2003 at the TRICARE Management Activity (TMA), Falls Church, VA.

2. VOTING MEMBERS PRESENT

CDR Terrance Egland, MC	DoD P& T Committee Co-chair
COL Daniel D. Remund, MS	DoD P& T Committee Co-chair
COL Joel Schmidt, MC	Army
COL Doreen Lounsbery, MC	Army
COL Mike Heath, MS (For MAJ Travis Watson, MS)	Army
LtCol Kimberly May, MC (For COL John R. Downs, MC)	Air Force
Col Bill Sykora, MC	Air Force
LtCol Phil Samples, BSC (For LtCol George Jones, BSC)	Air Force
CAPT Matt Nutaitis, MC	Navy
CDR Mark Richerson, MSC	Navy
CAPT Chuck Bruner	Coast Guard
Francine Goodman (For Mike Valentino)	Department of Veterans Affairs

VOTING MEMBERS ABSENT

None	

OTHERS PRESENT

COL William Davies, MS	DoD Pharmacy Program Director, TMA
Howard Altschwager	Deputy General Counsel, TMA
CAPT Betsy Nolan, MSC	Navy Pharmacy Specialty Leader
Col Ardis Meier, BSC	Air Force Pharmacy Consultant
MAJ John Howe, BSC	Defense Supply Center Philadelphia
CAPT Joe Torkildson, MC	DoD Pharmacoeconomic Center
CDR Denise Graham, MSC	DoD Pharmacoeconomic Center
CDR (sel) Ted Briski, MSC	DoD Pharmacoeconomic Center
LtCol Dave Bennett, BSC (via VTC)	DoD Pharmacoeconomic Center
LtCol Barb Roach, MC (via VTC)	DoD Pharmacoeconomic Center
CPT Jill Dacus, MC (Via VTC)	DoD Pharmacoeconomic Center
Shana Trice (via VTC)	DoD Pharmacoeconomic Center
Dave Bretzke (via VTC)	DoD Pharmacoeconomic Center
Angela Allerman (via VTC)	DoD Pharmacoeconomic Center
Eugene Moore (via VTC)	DoD Pharmacoeconomic Center

3. REVIEW MINUTES OF LAST MEETING

A. The Council approved the minutes of the last meeting with a correction in Table Two Section 7A: the $7.84 average monthly cost for Estraderm was based on an incorrect dosing frequency of once a week. The correct dosing frequency is twice a week, so the correct average monthly cost for Estraderm is $15.68.

B. The Council approved the minutes of the July interim "email" meeting (Appendix A) with an amendment of the thiazolidinedione (TZD) section.

4. INTERIM DECISIONS/ADMINISTRATIVE ISSUES

The July interim "email" DoD Executive Council Meeting resulted in the following BCF and TMOP changes:

- Latanoprost (Xalatan) was added to the BCF
- Rosiglitazone (Avandia) was added to the BCF
- Rosiglitazone/metformin (Avandamet) was added to the BCF
- Serevent MDI was removed from the BCF due to market withdrawal. Serevent DPI will be the remaining salmeterol on the BCF.
- Zolmitriptan oral tablets (Zomig) were added to the BCF
- Sumatriptan oral tablets (Imitrex) were removed from the BCF
- Gefitinib (Iressa) was added to the TMOP with quantity limits
- Lovastatin extended release (Altocor) was removed from the TMOP

5. NATIONAL PHARMACEUTICAL CONTRACTS AND BLANKET PURCHASE AGREEMENT (BPA) AWARDS, RENEWALS AND TERMINATIONS

A. The next option years were exercised for the following contracts: fluoxetine, indomethacin, digoxin, naproxen, ointment base, captopril, paclitaxel injection, carbidopa/levodopa SA tablets, glyburide, amantadine, buspirone, benztropine.

B. New contracts were awarded for ketoconazole cream, midazolam, pamidronate injection and zolmitriptan.

6. PROCUREMENT INITIATIVES

A. Oral Fluoroquinolones, Angiotensin Receptor Blockers (ARBs), and Bisphosphonates –CDR Briski updated the Council on the progress of the oral fluoroquinolone, ARB and bisphosphonate solicitations.

B. 2nd Generation Antihistamines – Loratadine is available to MTFs at $0.38 per dose compared to fexofenadine at $0.85 per dose and cetirizine at $0.96 per dose. Although fexofenadine currently remains on the BCF, the termination of the fexofenadine contract allows MTFs to have additional non-sedating antihistamines on their formularies. Since loratadine is significantly less expensive than all other second generation antihistamines, MTFs are encouraged to add loratadine to their formularies and maximize the use of loratadine consistent with the clinical needs of patients. [Note: The Council could not add loratadine to the BCF because over-the-counter products are generally not allowed on the BCF.] Loratadine is currently on 52% of MTF formularies.

C. Novo Insulin Products – CAPT Torkildson presented information on two issues regarding the current contract with Novo Nordisk for regular, NPH, lente, and 70/30 insulin products.

1. The Council voted at its last meeting to recommend that DSCP not exercise the final option year on the insulin contract (which covers regular, NPH, 70/30 and lente insulin), and solicit a new contract this year. This recommendation was based on the increasing utilization of both ultra-short acting insulin and alternative insulin delivery systems, neither of which is covered by the current contract. Novo approached the PEC in mid-June with a proposal to lower the FSS price on their FlexPen disposable delivery systems and continue their temporary price reduction for Novolog vials (32% reduction from the FSS price) and Novolog 70/30 vials (53% reduction from FSS) in return for a decision to exercise the final option year of the contract. Since the last meeting the PEC also received information that a third company anticipates approval of their ultra-short acting insulin product early next year.

2. Shortly after its meeting with the PEC in mid-June, Novo notified the PEC that they planned to discontinue distribution of their lente insulin product in October 2003. Novo committed to providing lente insulin to their government clients at current levels through January 2004. An analysis of PDTS data revealed that only 271 patients filled prescriptions for lente insulin at MTFs and only 63 patients filled prescriptions for lente insulin in mail order during the 2nd quarter of FY2003. The number of patient utilizing lente insulin decreased by 50% over

the previous year. Although lente insulin is covered by the current insulin contract, the discontinuation of lente insulin will affect a relatively small number of patients.

The PEC recommended that the council reverse its previous decision and instead recommend that DSCP exercise the final year of the insulin contract and delay a resolicitation of the contract until summer 2004. The Council voted unanimously to exercise the final option year of the insulin contract and defer the resolicitation of insulin contract until next summer.

7. DRUG/DRUG CLASS EVALUATIONS

A. Oral Estropipate Hormone Replacement Therapy – Hormone replacement therapies currently available on the BCF include oral conjugated estrogens (Premarin), oral medroxyprogesterone, combination conjugated estrogen/medroxyprogesterone (Prempro), estrogenic vaginal cream (MTFs select the brand), and estradiol transdermal systems (Esclim). The Council considered oral estropipate for addition to the BCF as an alternative oral estrogen replacement therapy.

Efficacy/Safety/Tolerability – Studies have shown that the various oral estrogen replacement products are equally efficacious in treating postmenopausal symptoms. The labeling for all oral estrogen products contains the same safety warning for the risk of heart disease, stroke, and cancer. There is no evidence that the oral estrogen products differ in tolerability.

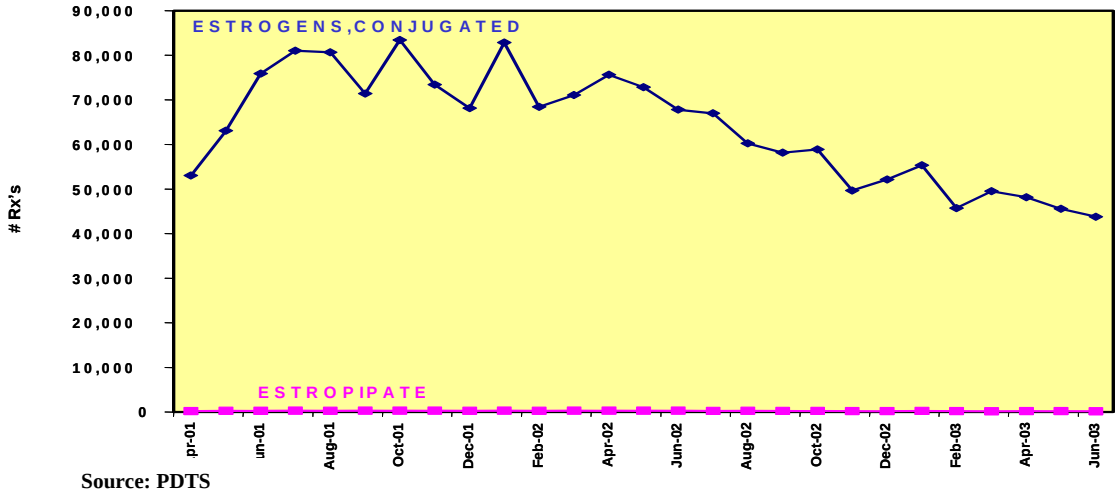
Table 1: Prime Vendor Weighted Average Cost/Tablet for Estropipate and Premarin

	Estropipate (Mylan)	**Estropipate (**Watson)	**Estropipate** (Ogen; Pharmacia & UpJohn	**Estropipate** (Ortho-est; WHFC)	**Conjugated Estrogen** (Premarin; Wyeth-Ayerst)
Prime Vendor Weighted Average Acquisition Cost/Tablet (June 2003)	$0.41	$0.11	$0.18	$0.19 (Was $0.42 prior to BPA initiated in June)	$0.23

Cost – Table 1 displays the prime vendor weighted average cost/tablet for various brands of estropipate and Premarin. Estropipate is available at a significantly lower cost than Premarin.

Other factors – The FDA and American College of Obstetricians and Gynecologists (ACOG) recommend starting women on low doses of estrogen in light of the Women's Health Initiative (WHI) study. Estropipate is not currently available in doses that are equivalent in estrogenic activity to the 0.3 mg and 0.45 mg strengths of Premarin.

Figure 1: MTF Oral Estrogen Rx Fills April 01 – June 03



Source: PDTS

Utilization – Figure 1 shows that MTFs use very little estropipate in comparison to Premarin. Only 20% of MTF formularies include estropipate compared to the 98% that include Premarin. Providers who were surveyed stated that the addition of estropipate to the BCF would not likely cause them to substantially increase their use of estropipate in lieu of Premarin.

The Council voted unanimously to not add an estropipate to the BCF because there is no evidence at this time that prescribers would be willing to use estropipate in lieu of Premarin.

B. *Dopamine Agonists* - The PEC is working with the VA on a joint review of the dopamine agonists. After the review is completed, the PEC will estimate the relative cost-effectiveness of the dopamine agonists and recommend which, if any, dopamine agonists, to add to the BCF.

C. *Isotretinoin*

Isotretinoin, a synthetic analogue of Vitamin-A, is indicated for the treatment of recalcitrant nodular acne. Available from Roche pharmaceuticals as Accutane® since 1982, isotretinoin recently became available as an AB-rated generic from three other manufacturers. The oral isotretinoin products available in the United States as of 1 July 2003 are listed in Table 2.

The Council considered an abbreviated PEC drug class review of isotretinoin for the purpose of deciding whether to pursue a sole-source contract (i.e. a contract to exclusively use a single brand of isotretinoin). Although sole-source contracts for "A-rated" generic equivalents do not typically require the review of the Council, an exception was made for isotretinoin because of its association with severe adverse events.

Table 2: Isotretinoin Products Available in the United States as of July 2003

Brand Name	Dosage Strengths	FDA approval date	Manufacturer
Accutane	10, 20, 40 mg	May 7, 1982	Hoffman – La Roche
Amnesteem	10, 20, 40 mg	Nov 15, 2002	Bertek
Sotret	10, 20, 40 mg	Dec 24, 2002	Ranbaxy labs
Claravis	10, 20, 40 mg	Apr 11, 2003	Barr

An average of 2,500 isotretinoin prescriptions are dispensed each month to DoD beneficiaries. Of these, approximately 1,500 are filled at MTFs and 1,000 through the retail network at costs of $342,000 and $221,000 respectively. The mail order system does not fill isotretinoin prescriptions because of the difficulty in meeting the requirements of the FDA mandated safety programs. The cost of a typical course of therapy for one person (15 weeks) is approximately $1,000 if the medication is dispensed through an MTF and $1,265 if the medication is dispensed through the retail network.

Efficacy/Safety – Isotretinoin has been on the market for over 20 years and remains the most efficacious treatment available for recalcitrant nodular acne. The main issue related to isotretinoin therapy is its potential to cause serious adverse effects, the most serious of which are birth defects and psychiatric disorders. In response to these adverse events, the FDA now requires that all isotretinoin therapy be administered in accordance with its strict risk management criteria.

Contracting Issues – The factors providing the impetus to pursue a sole-source contract for isotretinoin are its high cost, availability from multiple sources, and continued wide use within the MHS. The main issues to be addressed in pursuing a sole-source contract for isotretinoin include: (1) the interchangeability of the products, (2) the interchangeability of the risk management programs, and (3) the interchangeability of the prescription sticker programs.

1. Interchangeability of isotretinoin products: All four isotretinoin products available in the United States are AB-rated. By definition this means they are interchangeable.
2. Interchangeability of risk management programs: The FDA requires that the risk management programs for all isotretinoin manufacturers be the same. This is evident based on a statement by Janet Woodcock, Director of the Center for Drug Evaluation and Research, FDA that was found on the FDA web page: "All generic brands of isotretinoin will utilize the labeling that is alike in all material respects to the name brand, educational tools, and follow-up metrics in place under S.M.A.R.T." S.M.A.R.T. is the risk management program of the innovator company – Roche. To confirm this, written information included in three of the four risk management programs (SMART, SPIRIT, IMPART) were compared by members of the PEC and found to be identical in their wording. The risk management programs for each of the available products are listed in Table 3.
3. Interchangeability of prescription stickers: In a phone discussion with a Roche pharmaceutical representative regarding the interchangeability of isotretinoin

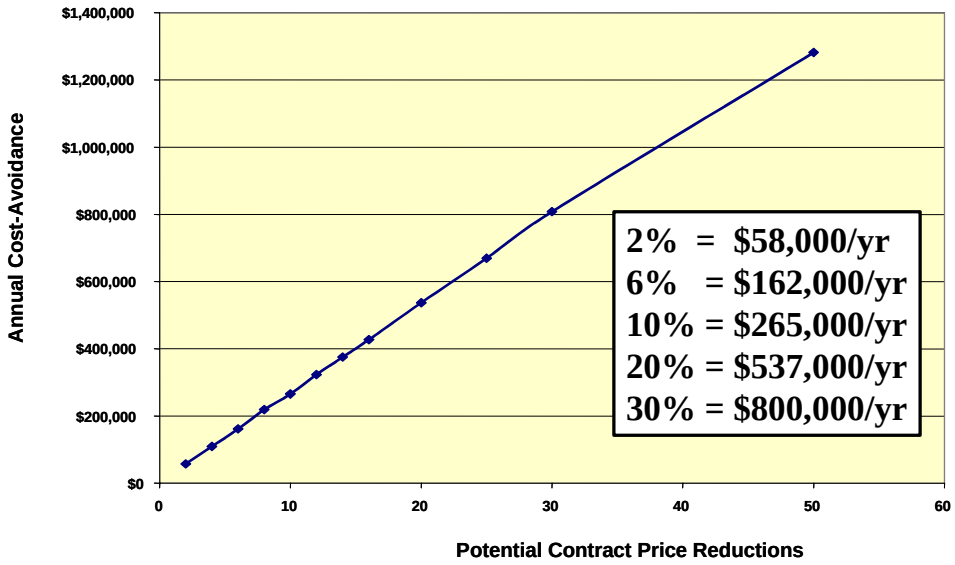
sticker programs, the following oral statement was provided: "Any AB-rated isotretinoin can be substituted for a prescription with an Accutane sticker and Accutane can be substituted for any prescription with an AB-rated isotretinoin sticker." Representatives from a state board of pharmacy (Texas) and the FDA concurred with this statement.

Table 3: Isotretinoin Risk Management Programs

Brand Name	Manufacturer	Safety Program
Accutane	Hoffman-La Roche	S.M.A.R.T. (System to manage Accutane related teratogenicity)
Amnesteem	Bertek	S.P.I.R.I.T. (System to prevent isotretinoin related issues of teratogenicity)
Sotret	Ranbaxy labs	I.M.P.A.R.T. (Isotretinoin medication program alerting you to the risks of teratogenicity)
Claravis	Barr	A.L.E.R.T. (Adverse event learning and education regarding teratogenicity)

Potential Cost-Avoidance – Figure 2 illustrates the cost-avoidance that would result from various price reductions that might be obtained with a sole-source contract for isotretinoin.

Figure 2: Isotretinoin cost avoidance from potential contract price reductions



The Council voted unanimously to support a sole-source contract initiative for isotretinoin that does not mandate addition of isotretinoin to the BCF.

8. REQUESTS FOR BCF CHANGES

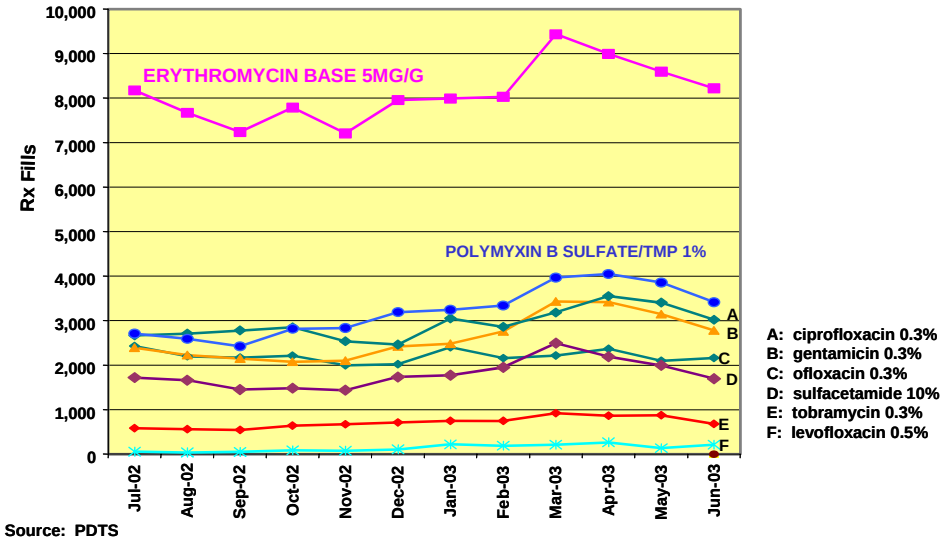
A. Ophthalmic Antibiotics – Polymyxin B Sulfate/Trimethoprim and Erythromycin

CDR Graham presented a recommendation from the PEC that polymyxin B sulfate/trimethoprim and erythromycin ophthalmic antibiotics be added to the BCF. This recommendation was based on two factors: 1) both are cost-effective alternatives compared to ophthalmic fluoroquinolones for primary care treatment of superficial ocular bacterial infections, including acute bacterial conjunctivitis and blepharoconjunctivitis, and 2) high utilization and formulary status in the MTFs.

Efficacy/Safety/Tolerability – Polymyxin B sulfate/trimethoprim and erythromycin have been proven efficacious in the treatment of superficial ocular infections involving the conjunctiva and/or cornea caused by susceptible organisms. Erythromycin is also safe and effective for the prophylactic treatment of ophthalmia neonatorum due to *Neisseria gonorrhoeae* or *Chlamydia trachomatis*. Safety and effectiveness of polymyxin B sulfate/trimethoprim are established down to the age of 2 months.

Cost – Both polymyxin B sulfate/trimethoprim and erythromycin are available as generics with respective costs of $1.19 – 1.52/10 ml vial and $0.99/3.5 gm tube, compared to fluoroquinolones starting around $14.00/5 ml.

Figure 3: MTF Rx Fills Ophthalmic Antibiotics July 02 – June 03



Source: PDTS

Utilization/MTF Formulary Status – Figure 3 shows current MTF utilization of polymyxin B sulfate/trimethoprim and erythromycin compared to other ophthalmic antibiotics. Over 80% of MTFs have both agents on their formulary.

The Council voted unanimously to add polymyxin B sulfate/trimethoprim ophthalmic solution and erythromycin ophthalmic ointment to the BCF.

B. Ultra-Short Acting Insulin Products

CAPT Torkildson and Ms. Angela Allerman presented a recommendation from the PEC that an ultra-short acting insulin product be added to the BCF. This recommendation was based on two factors: 1) the superior outcomes achieved with ultra-short acting insulin compared to regular insulin, and 2) the steadily increasing utilization of ultra-short acting insulin products in DoD.

Data were presented comparing the activity profiles of regular and ultra-short acting insulins. The more rapid onset of action, shorter time to peak activity, and shorter effective duration of action make the profile of ultra-short acting insulin more physiologic. Clinical trials demonstrate improved post-prandial glycemic control, lower HbA1c levels, and fewer episodes of post-prandial hypoglycemia with ultra-short acting insulins.

Data regarding the relative utilization of regular and ultra-short acting insulin at MTFs is presented in Table 4. The projected figures are based on the trend observed over the preceding 12 months. Based on these projections, the number of utilizers of ultra-short acting insulin products will exceed the number of regular insulin utilizers during the first quarter of FY 2004. Based on this information, the Council voted unanimously to accept the PEC's recommendation to add an ultra-short acting insulin to the BCF.

Table 4: Number of Unique Utilizers of Ultra-short Acting and Regular Insulin Products at MTFs

Quarter	Ultra-short Acting	Regular
Historical Figures		
2001, Q4	4,219	13,507
2002, Q1	4,784	13,210
2002, Q2	5,378	12,733
2002, Q3	6,055	12,289
2002, Q4	6,569	11,455
2003, Q1	7,456	11,316
2003, Q2	8,032	10,703
Projected Figures		
2003, Q3	8,638	10,248
2003, Q4	9,280	9,767
2004, Q1	9,922	9,285
2004, Q2	10,564	8,804
2004, Q3	11,206	8,322
2004, Q4	11,848	7,841

The presentation now turned to the question regarding which ultra-short acting insulin represented the most cost-effective choice for the direct care system. Data were first presented that addressed the therapeutic interchangeability, clinical coverage, and provider acceptance of Novolog and Humalog. The available data suggest no clinically relevant difference between the products' activity profiles. Although Novolog has an FDA-approved indication for use in insulin pumps and Humalog does not, several trials including a non-blinded head-to-head trial in pump patients suggest that the products are equally effective in improving post-prandial glucose control in this population. Anecdotal reports exist that suggest Novolog has greater stability and maintenance of potency in pumps, especially in warm climates, but this has not been scientifically evaluated as yet. There is no evidence for a difference in the number, type, or severity of adverse reactions seen with the two products. Therefore, either product appears to be suitable for use in diabetic patients. Either product could reasonably be expected to meet the clinical needs of the majority of patients requiring pre-prandial insulin therapy to control post-prandial hyperglycemia. Conversely, patients who failed to achieve the desired control with one of these products would be unlikely to achieve the desired control with the other.

Assessment of provider acceptance in this case was somewhat complex. As noted previously, Novo Nordisk currently has a contract to provide regular, NPH, and 70/30 mixed insulin to the DoD and VA. DoD compliance with this contract is fairly good, with about 75% of utilizers in each of these market baskets using the Novo product. However, < 3% of utilizers of ultra-short acting insulin use Novolog, despite an $8/vial cost difference in favor of Novolog. Additionally, at the time of the analysis Novolog was on formulary at only 4 MTFs throughout DoD. In a recent *PEC Update*, readers were asked to comment on why this situation existed. Responses indicated that several factors contributed to this: 1) Humalog was first to market and first on formulary (inertia); 2) providers considered the products to be clinically equivalent and were unaware of the price difference; and 3) Novolog was not on formulary at most facilities, and as the products were not seen as having substantial clinical differences providers had no motivation to push for its addition. Both junior and senior level endocrinologists expressed a willingness to change to the less expensive product, and one diabetic educator stated that she had unsuccessfully approached her local P&T Committee on three different occasions with evidence that substantial cost savings could be realized by making Novolog available to providers.

The following cost and utilization data were then presented. During the period 1 May 2002 through 30 April 2003, $3.2 million were spent on ultra-short acting insulin therapy by MTFs. Given the growing utilization of ultra-short acting insulin, it was projected that in FY 2004 MTFs would experience an 18.6% increase in the cost of ultra-short acting insulin therapy, to $3.8 million. However, given the current prices of the two products, if only 10% of the market was moved to Novolog the MTFs would experience instead a 2% decrease in the cost of therapy. If Novolog achieved a 50% market share, the overall cost would decrease by almost 15%, to $2.7 million, despite an almost 20% increase in utilization. The increase in

market share would also ensure that the Novolog prices would remain in place until the awarding of the new insulin contract next fall.

Based on these factors, the Council voted unanimously in favor of the PEC recommendation to add Novolog to the BCF, to have the PEC provide information to providers and facilities encouraging its use for the reasons noted, and to have the PEC provide additional information regarding the opportunity for facilities to achieve additional cost avoidance by evaluating the Novo FlexPen devices as an alternative to Humalog disposable syringes.

9. ADJOURNMENT

The meeting adjourned at 1400 hours. The next meeting will be held at Fort Sam Houston, TX at 0800 on Thursday, 13 November 2003. All agenda items should be submitted to the co-chairs no later than 06 October 2003.

<signed>	<signed>
DANIEL D. REMUND	TERRANCE EGLAND
COL, MS, USA	CDR, MC, USN
Co-chair	Co-chair

APPENDIX A: MINUTES OF THE DEPARTMENT OF DEFENSE (DOD) PHARMACY AND THERAPEUTICS (P&T) "EMAIL" INTERIM EXECUTIVE COUCIL MEETING

NOTE: Amended version (section 4B) approved by the DoD P&T Executive Council at their regularly scheduled meeting, 5 August 2003.

Department of Defense Pharmacoeconomic Center

2421 Dickman Rd., Bldg. 1001, Rm. 310
Fort Sam Houston, TX 78234-5081

MCCS-GPE **14 July 2003**

MEMORANDUM FOR: Executive Director, TRICARE Management Activity (TMA)

SUBJECT: Minutes of the Department of Defense (DoD) Pharmacy and Therapeutics (P&T) "Email" Interim Executive Council Meeting

1. The DoD P&T Executive Council held an interim meeting by email on 9 July 2003 in order to make some decisions that the co-chairs felt should not be delayed until the August meeting. All voting members posted email responses by close of business 14 July 2003.

2. VOTING MEMBERS RESPONDING

CDR Terrance Egland, MC	DoD P& T Committee Co-chair
COL Daniel D. Remund, MS	DoD P& T Committee Co-chair
COL Joel Schmidt, MC	Army
COL Doreen Lounsbery, MC	Army
MAJ Travis Watson, MS	Army
COL John R. Downs, MC	Air Force
COL Bill Sykora, MC	Air Force
LtCol George Jones, BSC	Air Force
CAPT Matt Nutaitis, MC	Navy
CDR Mark Richerson, MSC	Navy
CAPT Robert Rist	Coast Guard

VOTING MEMBERS ABSTAINING

Mike Valentino	Department of Veterans Affairs

3. NATIONAL PHARMACEUTICAL CONTRACT AWARD

The VA National Acquisition Center (NAC) recently awarded a joint VA/DoD triptan contract to Astra Zeneca for zolmitriptan. Per the terms of the contract, zolmitriptan replaces sumatriptan as the only oral triptan on the BCF effective 11 Jul 03. MTFs may have one oral triptan in addition to zolmitriptan on their local formularies. The contract does not affect the formulary status of non-oral triptan dosage forms. The PEC provided guidance to MTFs for implementing the zolmitriptan contract (see the National Contracts page on the PEC website). Sumatriptan injection will remain on the BCF.

4. PROCUREMENT INITIATIVES

A. Ophthalmic Prostaglandins – At the May DoD P&T Executive Council meeting the Council was informed that the VA and DoD would each pursue their own procurement strategies for ophthalmic prostaglandins. Pfizer has proposed a blanket purchase agreement (BPA) that reduces the price of latanoprost by 25% (price decreases from $28.89 to $21.67 per bottle) if latanoprost is added to the BCF and no other ophthalmic prostaglandins are included on the BCF. Latanoprost would be the sole ophthalmic prostaglandin on the BCF, but MTFs could have additional ophthalmic prostaglandins on their local MTF formularies. The Council voted unanimously to add latanoprost to the BCF and advise DSCP to approve the latanoprost BPA.

B. Thiazolidinediones (TZDs, "Glitazones") – The Council had previously authorized the addition of a single thiazolidinedione to the BCF using a procurement strategy that could include up to a joint DoD/VA closed class contracting strategy competing rosiglitazone and pioglitazone. Glaxo Smith Kline (GSK) has proposed a joint VA/DoD BPA that offers tiered pricing for rosiglitazone (Avandia) and the combination of rosiglitazone and metformin (Avandamet) based on their aggregate market share at MTFs if Avandia and Avandamet are the only thiazolidinediones on the BCF. The Avandamet BPA price equals the rosiglitazone BPA price plus the contract price for generic metformin. The BPA pricing will provide a 20% discount to DoD based on the 68% market share that rosiglitazone currently has at MTFs. Based on historical dose distributions, the 20% discount will reduce the average daily cost for rosiglitazone from $2.16 to $1.73. The average daily cost for pioglitazone is $2.41, which is 39% more per day than rosiglitazone.

Although the Council had not previously discussed the inclusion of Avandamet in the TZD procurement strategy, the Council determined that the addition of Avandamet was consistent with previous BCF decisions and would be a rational complement to Avandia on the BCF because:

- Metformin is appropriately and frequently used in combination with rosiglitazone (50% of current rosiglitazone users are also taking metformin).
- The Council has previously concluded that combination products may be more convenient for patients to take and may improve compliance compared to giving the same products separately.
- The Avandamet pricing is cost-neutral compared to the pricing for the separate products. Although DoD currently has a contract for metformin, there have been

supply problems that cause MTFs to make off-contract purchases of metformin at higher prices. To the extent that the use of Avandamet will reduce the use of off-contract metformin, DoD will realize a cost-benefit for those patients needing combination therapy.

The Council voted unanimously to add rosiglitazone (Avandia) and the combination of rosiglitazone and metformin (Avandamet) to the BCF and advise DSCP to approve the rosiglitazone BPA.

5. BCF AND TRICARE MAIL ORDER PHARMACY (TMOP) FORMULARY ISSUES

A. Gefitinib (Iressa) 250 mg tablets – Iressa is a new oral agent approved, 5 May 03, as monotherapy for locally advanced or metastatic non-small cell lung cancer (NSCLC) after failure of both platinum-based and docetaxel (Taxotere) chemotherapies (i.e. third-line treatment).

The Council unanimously voted to not add Iressa to the BCF, but to add Iressa to the TMOP Formulary with a quantity limit of 45 tablets per 45 days, to reduce wastage. Gefitinib is costly ($1168/month based on FSS pricing) and patients are likely to discontinue therapy (2/3 of the patients receiving therapy will be treated for no longer than 3 months), either due to death or lack of response. In addition, since the symptomatic benefit of gefitinib appears to correlate with tumor response rate and occurs early in treatment, it is rational to evaluate the patient within 6 weeks (clinical investigators maintain that four to six weeks of therapy is sufficient to test for response). It also appears reasonable to discontinue therapy in patients who are not benefiting.

B Statins – At the May 03 DoD P&T Executive Council meeting the Council voted to add Altocor to the TMOP Formulary. The PEC has subsequently been advised that the addition of Altocor to the TMOP formulary may violate the provisions of the Zocor contract.

The solicitation for the new stated in part, "The BCF and Mail Order Pharmacy Formulary will also contain a generic form of lovastatin and may contain one of the HMG-CoA agents not extensively metabolized by the cytochrome P450 (CYP) metabolic pathway (i.e. pravastatin or fluvastatin), but not both."

Although the solicitation did not specifically prohibit the inclusion of a brand name version of lovastatin on the TMOP formulary, the specific reference to inclusion of a generic form of lovastatin on the TMOP formulary could reasonably be construed to imply that a brand name version of lovastatin would not be included on the TMOP formulary.

The Council voted unanimously to remove Altocor from the TMOP formulary.

6. NEXT MEETING

The next meeting will be held at TRICARE Management Activity (TMA), conference room 815, Skyline Building 6, 5111 Leesburg Pike, Falls Church, VA at 0800 on Tuesday, 5 August 2003. All agenda items should be submitted to the co-chairs no later than 18 July 2003.

<signed>	<signed>
DANIEL D. REMUND	TERRANCE EGLAND
COL, MS, USA	CDR, MC, USN
Co-chair	Co-chair

NOTE: Amended version (section 4B) approved by the DoD P&T Executive Council at their regularly scheduled meeting, 5 August 2003.

Department of Defense
Pharmacoeconomic Center

2421 Dickman Rd., Bldg. 1001, Rm. 310
Fort Sam Houston, TX 78234-5081

MCCS-GPE **14 July 2003**

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<signed>	<signed>
DANIEL D. REMUND	TERRANCE EGLAND
COL, MS, USA	CDR, MC, USN
Co-chair	Co-chair

Department of Defense
Pharmacoeconomic Center

2421 Dickman Rd., Bldg. 1001, Rm. 310
Fort Sam Houston, TX 78234-5081

MCCS-GPE **7 MAY 2003**

MEMORANDUM FOR: Executive Director, TRICARE Management Activity (TMA)

SUBJECT: Minutes of the Department of Defense (DoD) Pharmacy and Therapeutics (P&T) Committee Meeting

1. A meeting of the DoD P&T Committee convened at 0800 hours on 7 May 2003, at the DoD Pharmacoeconomic Center, Fort Sam Houston, Texas.

2. VOTING MEMBERS PRESENT

CDR Terrance Egland, MC	DoD P& T Committee Co-chair
COL Daniel D. Remund, MS	DoD P& T Committee Co-chair
COL Joel Schmidt, MC	Army
COL Doreen Lounsbery, MC	Army
MAJ Travis Watson, MS	Army
COL John R. Downs, MC	Air Force
COL Mark Nadeau, MC (For COL Bill Sykora, MC)	Air Force
LtCol Ed Zastawny, BSC (For LtCol George Jones, BSC)	Air Force
CDR (sel) Debra Arsenault, MC (For CAPT Matt Nutaitis, MC)	Navy
CDR Mark Richerson, MSC	Navy
CAPT Robert Rist	Coast Guard
Dr. Trevor Rabie	Uniformed Services Family Health Plan
Mark Geraci (For Mike Valentino)	Department of Veterans Affairs

VOTING MEMBERS ABSENT

None	

OTHERS PRESENT

COL William Davies, MS	DoD Pharmacy Program Director, TMA
COL Geoffrey Rake, MC (via TC)	Medical Director, TMA
Howard Altschwager	Deputy General Counsel, TMA
COL Mike Heath, MS (via VTC)	Army Pharmacy Consultant, Chairman Pharmacy Board of Directors
CAPT Betsy Nolan, MSC (VTC)	Navy Pharmacy Specialty Leader
CAPT Joe Torkildson, MC, USN	DoD Pharmacoeconomic Center
LTC Don DeGroff, MS	DoD Pharmacoeconomic Center
CDR Denise Graham, MSC, USN	DoD Pharmacoeconomic Center
LtCol Dave Bennett, USAF, BSC	DoD Pharmacoeconomic Center
LtCol Barb Roach, USAF, MC	DoD Pharmacoeconomic Center
CDR (sel) Ted Briski, MSC, USN	DoD Pharmacoeconomic Center
Shana Trice	DoD Pharmacoeconomic Center
David Bretzke	DoD Pharmacoeconomic Center
Eugene Moore	DoD Pharmacoeconomic Center
Angela Allerman	DoD Pharmacoeconomic Center
LTC Marc Caouette, MS	Joint Readiness Clinical Advisory Board
Lisa LeGette	Express Scripts
Howard Mazzafro	Express Scripts
MAJ John Howe, MS	Defense Supply Center Philadelphia
Gene Lakey	TriWest

3. **REVIEW MINUTES OF LAST MEETING/ADMINISTRATIVE ISSUES** – The minutes from the last meeting were accepted as written.

4. **INTERIM DECISIONS** – No interim decisions.

5. **UNIFORM FORMULARY (UF) PROPOSED RULE**- COL William Davies, DoD Pharmacy Program Director, TMA, stated that the current plan is to implement the Uniform Formulary in conjunction with the TRICARE Retail Pharmacy contract. The proposed date for implementation of the Tricare Retail Pharmacy (TRRx) is April 2004.

6. **BCF AND TRICARE MAIL ORDER PHARMACY (TMOP) FORMULARY ISSUES** – The Committee determined the TMOP formulary status, TMOP or retail network formulary restrictions (quantity limits or prior authorization), and Basic Core Formulary (BCF) status for 6 new drugs or formulations (see Appendix A). The PEC also presented brief information on four additional new drugs or formulations not requiring a complete review by the Committee (see Appendix B). The Committee agreed that no further review was required.

7. MAIL ORDER AND RETAIL NETWORK ISSUES

A. *Statins* – The high potency statin contact was awarded to Merck for simvastatin (Zocor). The contract states that the BCF and Mail Order Pharmacy formulary will also contain a generic form of lovastatin and may contain one of the statins that is not extensively metabolized by the cytochrome P450 3A4 isoenzyme system. The Committee voted unanimously to add generic lovastatin, lovastatin extended release (Altocor), lovastatin/Niaspan (Advicor), and pravastatin (Pravachol) to the TMOP formulary.

B. *Guaifenesin* – At the November 2002 meeting, the P&T Committee was informed that:

> "As of 12 Jul 2002, Mucinex (Adams Labs) became the first single ingredient guaifenesin extended release product to be 1) approved as safe and effective under a New Drug Application (NDA) and 2) to be approved as an over-the-counter (OTC) product. As a consequence of approval, the FDA has sent warning letters to manufacturers of guaifenesin extended release products explaining that currently marketed single ingredient guaifenesin extended release products without an approved application are considered misbranded and in violation of section 505(a) of the Food, Drug, and Cosmetic Act (FDCA). In addition, provisions of the Durham-Humphrey amendment (products cannot be marketed as both Rx and OTC products) effectively mean all single ingredient extended release will be OTC products. At least one affected manufacturer is known to be petitioning this action, but it is not known if any single ingredient guaifenesin extended release product other than Mucinex will continue to be available in the near future. *Since single ingredient guaifenesin extended release products are now OTC products, they will no longer be available from the NMOP and will not be included on the NMOP Formulary. Prescription extended release guaifenesin products will be dispensed by the NMOP as long as current supplies permit.*" (Emphasis added)

The FDA subsequently issued a letter to manufacturers in February 2003 that allowed them to continue manufacturing guaifenesin extended release products until 21May 2003 and continue distribution of such products until 23 October 2003. In the absence of additional actions on this matter, it is expected that legend extended release guaifenesin products will be available until early November 2003.

In light of the FDA's action, the Committee clarified the status of guaifenesin on the TMOP formulary. Single ingredient guaifenesin extended release products will remain on the TMOP formulary and be dispensed from the TMOP as long as they are available as legend drugs.

C. *Legend Vitamins* – Several questions have arisen recently regarding the availability of legend vitamins from the TMOP. According to Chapter 7 of the TRICARE Policy Manual, "Vitamins may be cost-shared only when used as a specific treatment of a medical condition." Operationally, the question is "do all prescriptions for vitamins require an individual determination that they meet the above requirement? Conversely, can prescriptions for certain vitamins be determined to be covered by virtue of their FDA-approved indications and the lack of a potential for off-label use that would not meet the above requirement?" An example of such a product would be a combination of

folic acid, cobalamin (B12) and pyridoxine (B6), indicated as "treatment for hyperhomocysteinemia, homocystinuria, dialysis, end stage renal failure and in conditions associated with cardiovascular disease, cerebrovascular disease, and peripheral vascular disease." The single MCSC pharmacy representative present at the meeting indicated that in his region, phone calls are made on all vitamin prescriptions to verify compliance with the above requirement, except in the case of prenatal vitamins prescribed to women under the age of 45, which are presumed to be medically necessary. This exception is based on a decision made by the DoD P&T Committee in July 1998 to continue to provide prenatal vitamins to females under the age of 45 without a requirement to document pregnancy.

The subsequent discussion focused on how to make the determination that vitamins are being prescribed for a specific medical condition. The TMA General Counsel advised that in general this would be an administrative decision that would be handled as a collaborative effort of Express Scripts, the PEC, and the TMA General Counsel. In most cases the P&T Committee would not be involved in this process, but in some circumstances the Committee might determine that a particular legend vitamin product, by virtue of its FDA-approved indication(s) and a low probability of use that would not be covered by TRICARE, could appropriately be placed on the TMOP formulary. He recommended that in that case a specific statement be included in the minutes stating the specific intended use of the product. The Committee took no further action at this time.

D. "*Line extension" rules for the TMOP* –At the last meeting, the Committee asked for a review of the "line extension" rules for the TMOP, which provide for availability of generic equivalents, new dosage forms, and new formulations of products already on the TMOP formulary without a formal Committee decision. These rules were carried over from the previous National Mail Order Pharmacy (NMOP) program, but there are operational differences between the two programs that affect the manner in which the rules are applied.

For the NMOP program, the mail order contractor (Medco) maintained the file of available items and was responsible for applying line extension rules to determine inclusion or exclusion of new products, along with the NMOP Contracting Officer's Technical Representative (COTR). New molecular entities and other products requiring Committee approval were not added to the file of available items until publication of the minutes of the Committee meeting in which they were approved.

For the TMOP program, the task of maintaining computerized rules defining which items are available through the TMOP now rests with WebMD as a part of the Pharmacy Data Transaction Service (PDTS). Instead of a file of available items, those items not included in the TMOP Formulary are "blocked" using a combination of First Data Bank categories and drug classification codes. Accordingly, it is necessary to review the addition of new products to First Data Bank on an ongoing basis in order to identify new molecular entities and other products that require Committee review. This is now being accomplished by the PEC on a weekly basis, with approval by the TMOP Contracting Officer's Representative (COR).

The Committee approved the line extension rules outlined below. The Committee noted that these are guidelines rather than absolute rules, acknowledging the need for the PEC

and TMOP COR to use their judgment to deal with circumstances not covered by the rules:

- Medications outlined below are added to the TMOP Formulary without formal action by the DoD P&T Committee unless the PEC or TMOP COR identifies a reason for the P&T Committee to be involved in the decision:
  - Generic equivalent, new dosage form, or new formulation of an agent already on the TMOP Formulary
  - New drug entity in a therapeutic class/category for which the Committee has previously approved automatic inclusion for new drug entities. Currently the only drug class to which this applies is AIDS/HIV drugs. The Committee will review drugs automatically included under this provision at the next scheduled meeting.
  - New combination products of medications that are already on the TMOP Formulary.

8. **CONTROLLED DISTRIBUTION OF PRESCRIPTION DRUGS** – Buprenorphine and buprenorphine/naloxone (Subutex/Suboxone) were recently approved for the treatment of opioid dependence and are subject to a controlled distribution process. Subutex/Suboxone are NOT a covered benefit under TRICARE rules. Champus Basic Program benefits; Part 199.4 states: "Drug maintenance programs when one addictive drug is substituted on a maintenance basis (such as methadone substituted for heroin) are not covered. This exclusion applies even in areas outside the United States where addictive drugs are dispensed legally by physicians on a maintenance dosage level."

9. **ADJOURNMENT –** The meeting adjourned at 1030 hours. The next meeting will be held at TRICARE Management Activity (TMA), conference room 815 Skyline Building 6, 5111 Leesburg Pike, Falls Church, VA at 0800 on Wednesday, 6 August 2003. All agenda items should be submitted to the co-chairs no later than 18 July 2003.

<signed>	<signed>
DANIEL D. REMUND	TERRANCE EGLAND
COL, MS, USA	CDR, MC, USN
Co-chair	Co-chair

List of Appendices

APPENDIX A: NEWLY APPROVED DRUGS CONSIDERED FOR THE TRICARE MAIL ORDER PHARMACY (TMOP) FORMULARY AND THE DOD BASIC CORE FORMULARY (BCF)

Generic name (Trade name; manufacturer)	**FDA approval date, drug class, FDA-approved indication**	**TMOP Formulary status**	**TMOP and/or retail network formulary restrictions**	**BCF status**
Estradiol acetate vaginal ring (Femring; Galen)	24 Mar 03: Indicated for the treatment of moderate to severe vasomotor symptoms associated with menopause as well as symptoms of vulvar and vaginal atrophy. The ring is designed for self-insertion and delivers a steady estrogen dose for 3 months. Two doses: 50 or 100 mcg released daily.	Added to the TMOP Formulary	**Quantity Limits** General rule applies **Prior Authorization:** None	Not added to the BCF **Similar BCF agents:** None
Pegvisomant injection (Somavert; Pfizer)	04 Apr 03: Growth hormone receptor antagonist indicated for the treatment of patients with acromegaly who have failed to respond to currently available therapies, such as surgery, radiation therapy, or other medical therapies, or for whom these therapies are not appropriate. Decreases insulin-like growth factor-1 (IGF-1) concentrations As an orphan drug, usage of this product is expected to be infrequent; however, the product is listed in First Data Bank and ESI anticipates no difficulty obtaining it for patients using the TMOP.	Added to the TMOP Formulary & TMOP Covered Injectables List Intended for self-administration; daily subcutaneous injections; must be refrigerated	**Quantity Limits** General rule applies **Prior Authorization** None	Not added to the BCF **Similar BCF agents:** None
Gatifloxacin ophthalmic solution (Zymar; Allergan)	31 Mar 03: 0.3% solution is indicated for treating bacterial conjunctivitis caused by susceptible strains of bacteria	Added to the TMOP Formulary	**Quantity Limits** General rule applies **Prior Authorization** None	Not added to the BCF **Similar BCF agents**: None
Cyclosporine ophthalmic solution 0.05% (Restasis; Allergan)	29 Jan 03: 0.05% solution is indicated to increase tear production in patients whose tear production is presumed to be suppressed due to ocular inflammation associated with keratoconjunctivitis sicca (KCS)	Added to the TMOP Formulary	**Quantity Limits** General rule applies **Prior Authorization** None	Not added to the BCF **Similar BCF agents**: None

Generic name (Trade name; manufacturer)	**FDA approval date, drug class, FDA-approved indication**	**TMOP Formulary status**	**TMOP and/or retail network formulary restrictions**	**BCF status**
Aprepitant capsules (Emend; Merck)	26 Mar 03 (priority review): A substance P / neurokinin 1 (NK1) receptor antagonist indicated for use in combination with other antiemetic agents for preventing acute and delayed nausea and vomiting associated with highly emetogenic cancer chemotherapy (including high-dose cisplatin). First medication specifically labeled for delayed nausea and vomiting. 125 mg dose on day 1 (1 hour prior to chemotherapy), followed by 80 mg QAM on days 2 and 3. Still requires concomitant administration of ondansetron and dexamethasone	Added to the TMOP Formulary	**Quantity Limits** Rationale for the quantity limits includes the potential for inappropriate use and wastage, FDA requirement for the manufacturer to monitor off label uses; and existing quantity limits for 5-HT3 antagonists. Quantity limits are set to provide for the possibility that chemotherapy is on a 3-week cycle, rather than once per month. Most patients will require less. Packaged in convenience packs (one 125 mg; two 80 mg capsules) and in 30-count bottles **Retail:** Convenience packs: 2 packs per 30 days; 125 mg caps: 2 per 30 days; 80 mg caps: 4 per 30 days **TMOP**: Convenience packs: 6 packs per 90 days; 125 mg caps: 6 per 90 days; 80 mg caps: 12 per 90 days **Prior Authorization** None	Not added to the BCF **Similar BCF agents:** None
Enfuvirtide injection (Fuzeon; Roche/ Trimeris)	13 Mar 03 (accelerated approval). New modality for treating HIV (fusion inhibitor) that blocks the interaction of HIV with CD4+ cells. Indicated for use in combination with other antiretroviral agents for treatment-experienced patients with evidence of HIV-1 replication despite ongoing antiretroviral therapy. Product is self-administered SQ BID, and is available in a convenience kit of 60 vials with supplied diluent. Complicated 100-step manufacturing process has resulted in a limited supply for about 12,000-15,000 patients worldwide. Product will be allotted on a first-come, first-serve basis through a sole distributor, Chronimed. Physicians must enroll patients via fax. Details on the Fuzeon Progressive Distribution Program may be found at www.fuzeon.com. Anticipated yearly cost is $20,000.	Not added to the TMOP Formulary & Covered Injectables List. Due to the restricted distribution process, ESI and the PEC will look into the feasibility of supplying enfuvirtide through the TMOP and readdress the issue at the August DoD P&T Committee meeting	**Quantity Limits** Patient needs are established as part of the distribution process; no specific quantity limits are needed. **Prior Authorization** None	Not added to the BCF **Similar BCF agents**: None

APPENDIX B: NEWLY APPROVED DRUGS NOT REQUIRING FULL REVIEW BY THE P&T COMMITTEE

Generic name (Trade name; manufacturer)	**Comments**
Isotretinoin capsules (Claravis; Barr)	AB rated generic to Accutane (Roche brand of isotretinoin). Not added to the TMOP Formulary because isotretinoin is excluded from the TMOP Formulary due to controlled distribution requirements. Generics from Bertek (Amnesteem) and Ranbaxy (Sotret) were evaluated in Mar 2003.
Conjugated estrogen/medroxyprogesterone acetate (Prempro 0.45/1.5; Wyeth)	Low-dose formulation of Prempro contains 0.45 mg of estrogen, and 1.5 mg of progestin (instead of 0.625 / 2.5 mg). Automatically added to TMOP as a line extension. Prempro is on the BCF.
Propranolol extended release capsules (InnoPran XL; Reliant)	Indicated for hypertension; the only beta-blocker formulation specifically indicated for QHS dosing. This product was approved under an NDA and is not a generic equivalent to the other propranolol extended release product, Inderal LA (Wyeth). Generic equivalents to Wyeth's Inderal LA have been discontinued. Innopran XL is available in 80 and 120 mg capsules; Inderal LA in 60, 80, 120 and 160 mg capsules. Automatically added to TMOP as a line extension. Not considered for BCF addition, since the other propranolol extended release product was removed from the BCF in Nov 1999 due both to limited supply (both Inderal LA and generics were manufactured by Wyeth) and low usage in DoD.
Metformin extended release tablets 750 mg (Glucophage XR; Bristol-Meyers Squibb)	Automatically added to TMOP as a line extension. Not considered for the BCF since extended release metformin is specifically excluded from the existing BCF listing for immediate release metformin.

APPENDIX C: COMBINED SUMMARY OF FORMULARY CHANGES FROM THE DOD P&T EXECUTIVE COUNCIL MEETING AND THE DOD P&T COMMITTEE MEETING

1. **BCF CHANGES**

   A. *Additions to the BCF*

      1) Estradiol transdermal system (Esclim)
      2) Risperidone (Risperdal)
      3) Quetiapine (Seroquel)
      4) Pimecrolimus cream (Elidel)
      5) Nitroglycerin patches (Nitrodur) [Schering brand per existing VA/DoD contract]
      6) Isosorbide mononitrate sustained release [Schwarz Pharma brand per existing VA/DoD contract]

   B. *Deletions, changes, clarifications or exclusions from the BCF* - None

2. **TMOP FORMULARY CHANGES**

   A. *Additions to the TMOP Formulary*

      1) Estradiol acetate vaginal ring (Femring; Galen)
      2) Pegvisomant injection (Somavert; Pfizer) – added to the TMOP Covered Injectables List
      3) Gatifloxacin ophthalmic solution (Zymar; Allergan)
      4) Cyclosporine ophthalmic solution (Restasis; Allergan)
      5) Aprepitant capsules (Emend; Merck) – quantity limits apply, see below
      6) Pravastatin
      7) Lovastatin
      8) Lovastatin extended release (Altocor)
      9) Lovastatin/niacin extended release combination (Advicor)

   B. *Exclusions from the TMOP Formulary* - None

   C. *Deletions, changes, or clarifications to the TMOP Formulary* - None

3. **QUANTITY LIMIT CHANGES (RETAIL NETWORK AND TMOP)**

   A. Quantity limit for aprepitant (Emend; Merck):

      - Convenience packs (convenience packs contain one 125 mg capsule and two 80 mg capsules): 2 packs per 30-day supply (Retail); 6 packs per 90-day supply (TMOP)
      - 80 mg capsules: 4 capsules per 30 days (Retail); 12 capsules per 90 supply (TMOP)
      - 125 mg capsules: 2 capsules per 30 days (Retail); 6 capsules per 90-day supply (TMOP)

4. **CHANGES TO THE TMOP PRIOR AUTHORIZATION PROGRAM** - None

Department of Defense
Pharmacoeconomic Center

2421 Dickman Rd., Bldg. 1001, Rm. 310
Fort Sam Houston, TX 78234-5081

MCCS-GPE **6 May 2003**

MEMORANDUM FOR: Executive Director, TRICARE Management Activity (TMA)

SUBJECT: Minutes of the Department of Defense (DoD) Pharmacy and Therapeutics (P&T) Executive Council Meeting

1. The DoD P&T Executive Council met from 0800 to 1500 hours on 6 May 2003 at the DoD Pharmacoeconomic Center, Fort Sam Houston, Texas.

2. VOTING MEMBERS PRESENT

CDR Terrance Egland, MC	DoD P& T Committee Co-chair
COL Daniel D. Remund, MS	DoD P& T Committee Co-chair
COL Joel Schmidt, MC	Army
COL Doreen Lounsbery, MC	Army
MAJ Travis Watson, MS	Army
COL John R. Downs, MC	Air Force
COL Mark Nadeau, MC (For COL Bill Sykora, MC)	Air Force
LtCol Ed Zastawny, BSC (For LtCol George Jones, BSC)	Air Force
CDR (sel) Debra Arsenault, MC (For CAPT Matt Nutaitis, MC)	Navy
CDR Mark Richerson, MSC	Navy
CAPT Robert Rist	Coast Guard
Mike Valentino	Department of Veterans Affairs

VOTING MEMBERS ABSENT

None	

OTHERS PRESENT

COL William Davies, MS	DoD Pharmacy Program Director, TMA
Howard Altschwager	Deputy General Counsel, TMA
CAPT Betsy Nolan, MSC (via VTC)	Navy Pharmacy Specialty Leader
COL Mike Heath, MS (via VTC)	Army Pharmacy Consultant Chair, DoD Pharmacy Board of Directors
COL Ardis Meier, BSC (via VTC)	Air Force Pharmacy Consultant
MAJ John Howe, BSC	Defense Supply Center Philadelphia
CAPT Joe Torkildson, MC	DoD Pharmacoeconomic Center
LTC Don DeGroff, MS	DoD Pharmacoeconomic Center
CDR Denise Graham, MSC	DoD Pharmacoeconomic Center
CDR (sel) Ted Briski, MSC	DoD Pharmacoeconomic Center
LtCol Dave Bennett, BSC	DoD Pharmacoeconomic Center
LtCol Barb Roach, MC	DoD Pharmacoeconomic Center
Shana Trice	DoD Pharmacoeconomic Center
Dave Bretzke	DoD Pharmacoeconomic Center
Angela Allerman	DoD Pharmacoeconomic Center
Eugene Moore	DoD Pharmacoeconomic Center
MAJ Mike Terry, BSC	TRICARE Southwest
Mark Geraci	Department of Veterans Affairs, PBM
LTC Marc Caouette, MS	Joint Readiness Clinical Advisory Board

3. REVIEW MINUTES OF LAST MEETING

The Council approved the minutes of the last meeting with a correction in the last sentence of the fourth paragraph in section 9A:

- Incorrect sentence: MTFs are currently spending nearly $100,000 per month on cholinesterase inhibitors.
- Corrected sentence: MTFs are currently spending nearly $326,000 per month on cholinesterase inhibitors.

4. ADMINISTRATIVE ISSUES

None

5. NATIONAL PHARMACEUTICAL CONTRACTS AND BLANKET PURCHASE AGREEMENT (BPA) AWARD, RENEWALS AND TERMINATIONS

A. The next option years were exercised for the following contracts: oral contraceptives, ticlopidine, valproic acid, nicotine patches, insulin syringes, isosorbide mononitrate, and capsaicin cream.

B. Proposals are being evaluated for the awarding of contracts to procure a sole source of isosorbide dinitrate, tramadol, ketoconazole cream, midazolam, and pamidronate injection.

C. DoD accepted an incentive agreement for methylphenidate (Concerta) that will reduce the price below FSS if performance incentives are met by the government.

6. PROCUREMENT INITIATIVES

A. *Ophthalmic Prostaglandins* – The Council had previously authorized the addition of an ophthalmic prostaglandin to the BCF using a procurement strategy that could include up to a joint DoD/VA closed class contracting strategy competing latanoprost, bimatoprost and travoprost, which would not require patients to be switched from one agent to another. The Federal Pharmacy Executive Steering Committee's (FPESC) subcommittee for contracting determined that a joint DoD/VA closed class contract would not meet the needs of both agencies. Each agency will pursue its own procurement strategy.

B. *Second Generation Antihistamines* –The availability of loratadine to MTFs at $0.38 per dose compared to fexofenadine at $0.60 per dose under a joint DoD/VA contract precipitated the decision to not renew the next option year of the fexofenadine contract. Although fexofenadine currently remains on the BCF, the termination of the fexofenadine contract allows MTFs to have additional non-sedating antihistamines on their formularies. Since loratadine is significantly less expensive than all other second generation antihistamines, MTFs are encouraged to add loratadine to their formularies and maximize the use of loratadine consistent with the clinical needs of patients. [Note: The Council could not add loratadine to the BCF because over-the-counter (OTC) products are generally not allowed on the BCF.]

C. *Thiazolidinediones (TZDs, "Glitazones")* – The Council had previously authorized the addition of a single thiazolidinedione to the BCF using a procurement strategy that could include up to a joint DoD/VA closed class contracting strategy competing rosiglitazone and pioglitazone. The contracting subcommittee of the Federal Pharmacy Executive Steering Committee is evaluating which procurement strategy would be the most cost-effective and meet each agency's requirements.

D. *Oral Fluoroquinolones* – The Council previously voted to support a joint DoD/VA contract for a "workhorse" fluoroquinolone that would compete levofloxacin and gatifloxacin. Two changes have occurred since that time:

1) Ortho McNeil raised the price of levofloxacin by almost 40% effective 1 May 2003, and then repealed the price increase. Levofloxacin has been the only oral fluoroquinolone on the BCF for the past several years.

2) Moxifloxacin recently gained FDA approval for treatment of community acquired pneumonia (CAP).

The Council reviewed the most current clinical data including efficacy and safety/tolerability of levofloxacin, gatifloxacin and moxifloxacin.

Efficacy – CAP and urinary tract infections (UTIs) are the primary indications for which fluoroquinolones are currently used. Gatifloxacin and moxifloxacin have broader gram-positive coverage and reduced gram-negative coverage than levofloxacin. All three agents are indicated for the treatment of CAP, chronic bronchitis, acute sinusitis and uncomplicated skin and skin structure infections. In addition, levofloxacin and gatifloxacin have an FDA indication for UTIs (however gatifloxacin will normally only cover approximately 80% of UTI infections because it has less gram-negative coverage). Moxifloxacin is not indicated for treatment of UTIs, which is attributed to less gram-negative coverage and extensive metabolism prior to excretion.

Safety/Tolerability – Adverse events of note include:

1) QTc prolongation with the subsequent potential for *torsade de pointes*. *Torsade de pointes* has been reported in 2 of 1,300,000 gatifloxacin patients, and 1 of 1,000,000 levofloxacin patients. Phase II-IV studies of moxifloxacin treatment in over 7,900 patients resulted in no cardiovascular morbidity attributable to QTc prolongation.
2) Dysglycemia has been associated with the use of gatifloxacin in diabetic patients receiving oral hypoglycemic agents or insulin, and elderly patients (>75yrs) with underlying disease states that increase the risk for dysglycemia.

Infectious Disease consultants stated the concerns regarding QTc prolongation and dysglycemia are probably "over-stated." However, providers should exercise caution when using fluoroquinolones in specific patients with underlying risk factors.

The Council concluded that fluoroquinolones are not sufficiently interchangeable to support a closed class contract. Differences in coverage and safety/tolerability concerns prevent the use of a single agent for all patients. All three fluoroquinolones will provide adequate clinical coverage for the majority of CAP and acute sinusitis infections.

The Council unanimously voted to authorize a procurement strategy that could include up to a joint DoD/VA open class contract competing moxifloxacin, gatifloxacin, and levofloxacin as a "workhorse" fluoroquinolone for the treatment of CAP and acute sinusitis.

E. *5HT1 Agonists (Triptans)* – The joint DoD/VA solicitation closed on 20 December 2002. The Government Accounting Agency (GAO) resolved a protest by ruling in favor of the Government. Detailed MTF guidance will be available on the PEC website when the contract award is announced.

F. *Angiotensin Receptor Blockers (ARBs)* – The Council had previously authorized the addition of a single ARB to the BCF using a procurement strategy that could include up to a joint DoD/VA closed class contract. The VA has determined that two ARBs should be on the VA National Formulary (VANF). The Council voted unanimously to accept two contracted ARBs for inclusion on the BCF. The change is expected to have minimal economic impact to DoD, while enhancing the ability of MTFs to effectively treat a wider range of patients using formulary ARBs.

G. The Council was updated on the progress of the bisphosphonate and insulin pen procurements.

7. DRUG/DRUG CLASS EVALUATIONS

A. *Transdermal Estrogen Preparations* – Short-term estrogen therapy remains the gold standard for relief of menopausal symptoms. Oral and transdermal routes are the most frequently used, with oral conjugated estrogens as the most popular estrogen formulation in the DoD and United States. Seven estrogen patches, all containing estradiol in varying strengths, are available in the United States (see Table 1). Currently the BCF contains oral conjugated estrogen, medroxyprogesterone, combination conjugated estrogen/medroxyprogesterone (Prempro), and an estrogenic vaginal cream (MTFs' choice). The BCF does not include an estrogen patch.

Table 1: Estradiol Transdermal Systems Available in the U.S.

Product/ Distributor	Release rate (mg/24 hr)	*Surface area (cm^2)	Delivery System/ Frequency of Administration
Vivelle-Dot Novartis	0.025; 0.0375; 0.05; 0.075; 0.1	2.5; 3.75; 5; 7.5; 10	Matrix Twice weekly
Vivelle Novartis;	0.025; 0.0375; 0.05; 0.075; 0.1	7.25; 11; 14.5; 22; 29	Matrix Twice weekly
Esclim Women First Health	0.025; 0.0375; 0.05; 0.075; 0.1	11; 16.5; 22; 33; 44	Matrix Twice weekly
Alora Procter & Gamble	0.05; 0.075; 0.1	18; 27; 36	Matrix Twice weekly
Climara Berlex	0.025; 0.05; 0.075; 0.1	6.5; 12.5; 18.75; 25	Matrix Once a week
♦**Estraderm** Ciba	0.05; 0.1	10; 20	Alcohol reservoir Twice weekly
Estradiol Mylan	0.05; 0.1	15.5; 31	Matrix Once a week
CombiPatch Aventis	0.05 mg estradiol/ 0.14 mg norethindrone acetate; 0.05 mg estradiol/ 0.25 mg norethindrone acetate	16	Twice weekly

*patch size increases with strength;
♦all drug delivery systems are matrix with the exception of Estraderm which uses an alcohol reservoir

Efficacy – All transdermal estrogen systems substantially decrease the number of hot flashes per week. There is no evidence that one estrogen compound is more effective than another. For relief of postmenopausal vasomotor symptoms, any patch can cover the clinical needs of patients; however, those providing the lowest dose with a wide range of dosing options are preferred by providers.

Safety/Tolerability – All estrogen-containing product package inserts carry an identical safety warning for the risk of heart disease, stroke, and cancer. Oral estrogen requires higher doses than transdermal estrogen. A recent trial assessing changes in C-reactive protein (CRP), a marker for inflammation in blood vessels and cardiovascular risk, suggested that transdermal systems might decrease cardiovascular adverse effects of estrogen. Patients using transdermal systems showed no elevation in CRP levels, while oral estrogens increased CRP levels two-fold.

Tolerability issues associated with the systemic effects of estrogen are similar for patches and oral estrogen. Local reactions due to transdermal patches include burning, erythema, irritation, pruritis, and rash. Reactions to the application site occur in about 10% of women who use reservoir (alcohol-based) patches and in 5% of women utilizing the matrix system. The incidence of skin irritation diminishes when the application site is rotated.

Table 2: Prime Vendor Cost for Transdermal Estrogen Systems

	Vivelle-Dot Novartis	**Vivelle** Novartis	**Alora** P&G	**Climara** Berlex	**Estraderm** Ciba	**Estradiol** Mylan
Prime Vendor Weighted Average Acquisition Cost/Patch	$2.20	$1.81	$1.40	$1.92	$1.96	$2.93
Dosage Frequency	Twice a week	Twice a week	Twice a week	Once a week	Twice a week	Once a week
Monthly Cost	$17.60	$14.48	$11.20	$7.68	$7.84	$23.44

Cost – Table 2 displays the prime vendor cost for various transdermal estrogen systems. Women's First Healthcare has offered a blanket purchase agreement that will make their estradiol patch (Esclim) available at a significantly lower monthly cost than other transdermal estrogen products if Esclim is added to the BCF.

Other factors – Esclim has better adhesiveness than Estraderm, which is currently on 75% of MTF formularies. The percentage of transdermal systems that became detached in the Esclim group was 6% compared to 11.3% in the Estraderm group ($p< 0.001$). (Maturitas 1996; 25)

The Council voted unanimously to add Esclim to the BCF. This will result in uniform availability of a transdermal estrogen product at a substantially reduced monthly cost per patient.

B. *Atypical Antipsychotics*

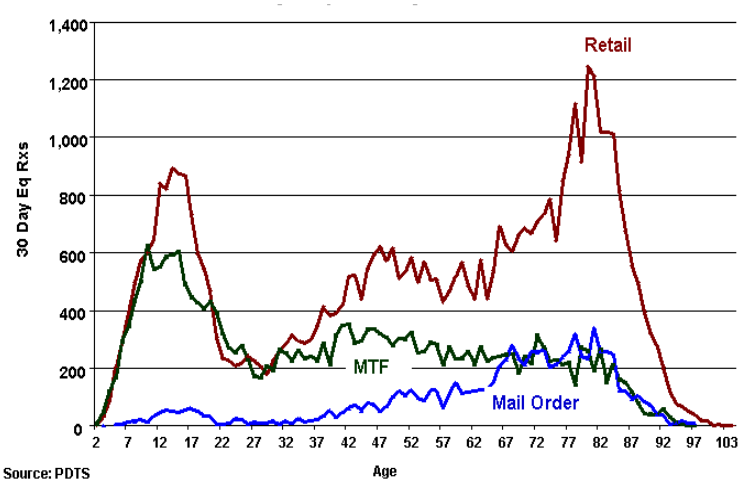
The Council considered a PEC drug class review of five atypical antipsychotics: aripiprazole (Abilify), olanzapine (Zyprexa), quetiapine (Seroquel), risperidone (Risperdal), and ziprasidone (Geodon). The review did not include clozapine (since its significant risk of agranulocytosis and requirement for routine white blood cell monitoring limit its use) or the injectable formulation of ziprasidone (an immediate release medication not intended for chronic use).

All five agents are indicated for schizophrenia; olanzapine is also indicated for acute bipolar mania. Other uses include depression with psychosis; symptoms of dementia including agitation, hyperactivity, hallucinations, suspiciousness, hostility and uncooperativeness; anxiety disorders; developmental disorders; autism; aggression/self injurious behavior; and Tourette's syndrome. Many of the atypical antipsychotics have been studied in pediatric as well as adult populations, although none of the drugs have pediatric indications. The review categorized the uses for atypical antipsychotics into four groups: schizophrenia and related psychoses, behavioral and psychological symptoms of dementia (BPSD), bipolar mania, and psychiatric and behavioral disorders in children and adolescents.

The onset of both schizophrenia and bipolar disorder is typically in early adulthood, between the late teens and mid-30s for schizophrenia, and in the early 20s for bipolar disorder. Based on the age distribution of usage in DoD (see Figure 1) and the likelihood that individuals with severe psychiatric illnesses will be required to leave the military, it

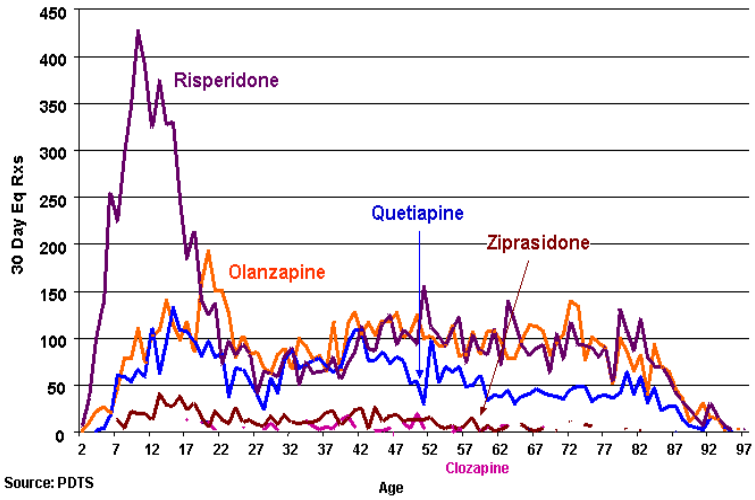
appears probable that uses other than schizophrenia or bipolar disorder represent a substantial proportion of atypical antipsychotic prescriptions in all three points of service.

Figure 1: Age Distribution of Atypical Antipsychotics in DoD
By 30 Day Equivalent Rxs, Oct 02 – Dec 02



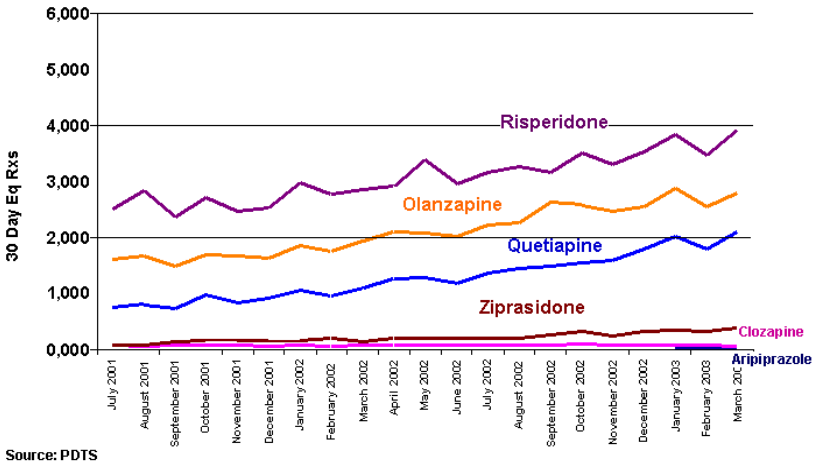
Individual atypical antipsychotics show distinctly different patterns of use at MTFs. As shown in Figure 2 below, risperidone is by far the most commonly prescribed agent in the pediatric population, although there is some usage of other atypical antipsychotics. Olanzapine, quetiapine, and risperidone show similar patterns of use in adult patients, although there is less use of quetiapine overall. Ziprasidone use appears to be less frequent in older patients. Aripiprazole was not yet available during the time period studied.

Figure 2: Age Distribution of Atypical Antipsychotics in MTFs
By 30 Day Equivalent Rxs, Oct 02 – Dec 02



Overall, the most commonly used atypical antipsychotic in MTFs is risperidone, followed by olanzapine and quetiapine (see Figure 3). There is low but increasing use of ziprasidone. Aripiprazole has not been on the market a sufficient period of time to assess its potential use.

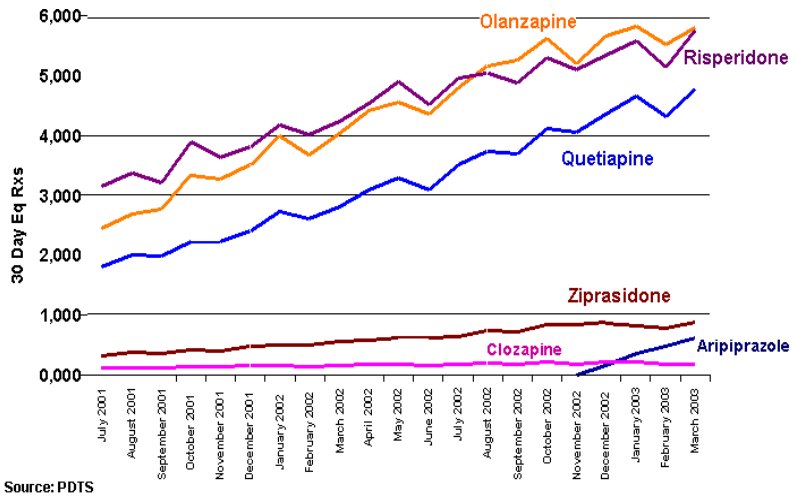
Figure 3: MTF 30 Day Equivalent Prescriptions for Atypical Antipsychotics
Jul 01 – Mar 03



Source: PDTS

In the retail network, olanzapine and risperidone are the most commonly used atypical antipsychotics, followed by quetiapine (see Figure 4). Ziprasidone use is again relatively low, but increasing. Aripiprazole use is increasing at a faster rate than in MTFs.

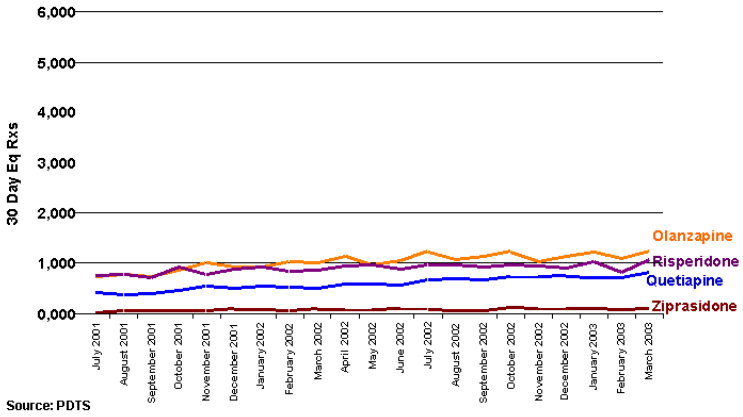
Figure 4: Retail Network 30 Day Equivalent Prescriptions for Atypical Antipsychotics
Jul 01 – Mar 03



Source: PDTS

In the mail order program, olanzapine, risperidone, and quetiapine are the most commonly used atypical antipsychotics (Figure 5). Aripiprazole was not added to the mail order formulary until March 03 and does not show on this graph.

Figure 5: Mail Order 30 Day Equivalent Prescriptions for Atypical Antipsychotics
Jul 01 – Mar 03



Efficacy

- *Schizophrenia and related psychoses* – There do not appear to be any clinically relevant differences among the atypical agents with respect to overall efficacy and treatment of positive symptoms (e.g., delusions and hallucinations), although individual patients may respond better to one than another. There is stronger evidence with olanzapine than with other atypical antipsychotics to support efficacy in treating negative symptoms (e.g., apathy, lack of motivation, lack of interpersonal and social interaction), based on olanzapine's demonstrated superiority to a typical antipsychotic (haloperidol) in reducing negative symptom scores in both individual short-term and long-term trials. Risperidone has also demonstrated superiority to haloperidol in reducing negative symptom scores based on long-term trials and pooled data from short-term trials. Less clinical evidence is available for quetiapine, ziprasidone, and aripiprazole.

  Atypical antipsychotics have also been shown to have positive effects on neurocognitive functioning (e.g., memory and attention) and mood symptoms (e.g., depressed mood) in patients with schizophrenia or related psychoses; however, the relative efficacy of specific atypical antipsychotics in these domains is still unclear.

- *Dementia* – Dementia is generally defined as a progressive decline in intellectual functioning that impedes normal activities; Alzheimer's dementia is the most common type. The FDA has not yet approved any drugs specifically for the "behavioral and psychological symptoms of dementia" (BPSD). Consensus statements from various national groups recommend antipsychotics as the only available pharmacological treatment for psychotic symptoms of *BPSD*. There is no evidence that any one atypical antipsychotic is more efficacious in one type of dementia than another. Risperidone and olanzapine have been shown to be

efficacious in reducing BPSD in published randomized controlled trials. Other atypical antipsychotics lack published data.

- *Bipolar mania* – According to the American Psychiatric Association Guideline for the Treatment of Patients with Bipolar Disorder (2000), first line treatment for more severe manic or mixed episodes of bipolar disorder is the initiation of lithium or valproate plus an antipsychotic. For less ill patients, monotherapy with lithium, valproate, or an antipsychotic may suffice. The guidelines state that atypical antipsychotics are preferred over typical antipsychotics due to their side effect profile. Olanzapine is the only atypical antipsychotic with an FDA-approved indication for the treatment of bipolar mania. It has been shown to be of comparable efficacy to lithium in the reduction of manic symptoms in one clinical trial and superior to divalproex in another. Olanzapine has also been shown to be superior to placebo as adjunctive therapy with a mood stabilizer (lithium or divalproex). Risperidone has been shown to be superior compared to placebo both as monotherapy and as adjunctive therapy with a mood stabilizer. A recently published trial (April 2003) with ziprasidone showed efficacy for monotherapy. Large trials with aripiprazole and quetiapine (either as monotherapy or as adjunctive therapy) have been performed, but results are not yet available as full publications.
- *Psychiatric and behavioral disorders in children and adolescents* – None of the atypical antipsychotics are currently approved for the treatment of children and adolescents. Multiple small trials, uncontrolled trials, case reports, and case series focus on the use of atypical antipsychotics (most commonly risperidone) in pediatric patients for the treatment of a wide variety of conditions. In large ($n \geq 30$) controlled trials, risperidone has been shown to be efficacious for the treatment of conduct disorder in children with mental retardation (two trials) and for the treatment of aggressive behavior in autistic children (one trial). Quetiapine has been shown to be efficacious as adjunctive therapy for bipolar mania with divalproex in adolescents 12-18 years of age.

Safety/Tolerability

Adverse effect profiles differ substantially among atypical antipsychotics. Provider comments with respect to the safety and/or tolerability of specific agents identified the following concerns: olanzapine (weight gain, diabetes, cholesterol/triglyceride elevations, sedation), quetiapine (weight gain, diabetes, cholesterol/triglyceride elevations), risperidone (EPS, prolactin), ziprasidone (cardiac effects, “emerging case reports of EPS”). Providers commented favorably on the ease of dosing olanzapine compared to quetiapine, and their tendency to use once daily drugs first line. Of the agents, olanzapine and aripiprazole are generally dosed once daily, risperidone can be dosed once or twice daily; and ziprasidone and quetiapine are typically dosed twice daily. Aripiprazole was not yet approved when the survey was completed and was not mentioned by survey responders.

- *Extrapyramidal symptoms* (EPS) are abnormal, involuntary movements associated with antipsychotic treatment. Their occurrence is related to D2 receptor binding in the nigrostriatal pathway; atypical antipsychotics have a higher 5-HT-2 / D2

binding ratio than typical antipsychotics, and thus a lower risk of EPS. This lower risk of EPS is considered to be the defining characteristic of "atypicality." Both olanzapine and risperidone may have increased binding affinity for D2 receptors at higher doses, but in the case of olanzapine, high antimuscarinic activity may limit EPS symptoms.

Of the atypical antipsychotics, risperidone in general appears to have a higher risk of EPS than other agents, although at lower doses (<6 mg/day) this may not be true. Tarsy et al (2002) provide a tentative ranking of EPS risk (from highest to lowest) as follows: Risperidone > olanzapine = ziprasidone > quetiapine > clozapine. Aripiprazole was not included in this review; EPS risk appears low in published trials to date. Accurate determination rates of EPS may be complicated by the presence of carryover EPS effects from previous antipsychotic treatment, particularly in short trials with minimal or no washout periods.

- *Tardive dyskinesia* (TD) is a late-appearing and generally irreversible complication of treatment with long-term antipsychotics, consisting of abnormal postures and involuntary movements of the face, eyes, tongue, trunk, or limbs. Up to 25% of patients may develop TD with cumulative use of typical antipsychotics. Sustained EPS is thought to be a risk factor for the development of TD. In general, atypical antipsychotics appear to have a lower risk of TD than typical antipsychotics. Both olanzapine and risperidone have been shown to be associated with a lower risk of TD than haloperidol. There are no long-term head-to-head studies between atypical antipsychotics addressing the risk of TD and limited long-term data with other atypical antipsychotics.
- *Weight gain* has been reported with a number of atypical antipsychotics, including olanzapine, quetiapine, and risperidone. Allison et al (1999) analyzed clinical trials with atypical antipsychotics and made the following estimates of mean weight gain at 10 weeks (6 weeks for quetiapine, which lacked longer trials; all estimates at midpoint of the standard dosing range): 4.15 kg olanzapine, 2.18 kg quetiapine, 2.10 kg risperidone, 1.08 kg haloperidol, 0.04 kg ziprasidone, -0.74 kg placebo. Aripiprazole was not included in this analysis: the mean weight gain in 4- to 6-week placebo-controlled trials with aripiprazole was 0.71 kg. Later studies and other analyses typically show the same rank order; head-to-head studies comparing olanzapine and risperidone typically demonstrate more weight gain with olanzapine. Weight gain is problematic not only because of adverse health consequences, but because it is frequently associated with lack of adherence to medication.
- *Hyperlipidemia* has been reported with atypical antipsychotics, most commonly with olanzapine, but also with risperidone and quetiapine. Olanzapine and risperidone have been most commonly compared. Increases in total cholesterol appear less frequent with risperidone than with olanzapine; there is little published data from large trials focusing on specific lipid effects (e.g., LDL, HDL, or triglycerides).
- *Treatment-emergent diabetes* has also been reported with atypical antipsychotics. The mechanism is unclear, as is the relationship of treatment-emergent diabetes

with weight gain and hyperlipidemia. In general, schizophrenic patients are at increased risk for hyperglycemia and/or diabetes compared to the general population, whether due to lifestyle factors or as a consequence of the disease process. Diabetes appears to occur more frequently in schizophrenic patients receiving atypical antipsychotics than those receiving typical antipsychotics.

Olanzapine has been associated with the greatest increase in risk of hyperglycemia and diabetes among the atypical antipsychotics reviewed, based on epidemiological studies. Risperidone has also been associated with increased risk, but less consistently and at an apparently lower rate than olanzapine. In one large case-control study (19,637 patients diagnosed and treated for schizophrenia between 1987 and 2000) the incidence of treatment-emergent diabetes per 1000 person-years was 10 for olanzapine (95% CI 5.2 – 19.2), 5.4 for risperidone (95% CI 3.0 – 9.8), and 5.1 for typical antipsychotics (95% CI 4.5-5.8) [Koro et al, 2002]. Data with other atypical antipsychotics is limited.

- *QT interval prolongation* – Labeling for ziprasidone contains a warning about the drug's potential for QTc-interval prolongation and risk of *torsade de pointes* (a potentially fatal arrhythmia) based on the occurrence of prolonged QTc intervals in Phase 2/3 clinical trials. Data from an FDA-requested study assessing the effect of maximum recommended doses of oral ziprasidone, risperidone, olanzapine, quetiapine, thioridazine, and haloperidol on the QTc interval in patients with schizophrenia is available from the FDA Psychopharmacological Drugs Advisory Committee Briefing Document for ziprasidone, July 19, 2000 (available at: www.fda.gov/ohrms/dockets/ac/00/backgrd/3619b1.htm). In this open-label, parallel group trial, mean changes in QTc interval occurred in the following rank order, from greatest to least: thioridazine > ziprasidone > quetiapine > risperidone > olanzapine > haloperidol. While ziprasidone was associated with the greatest increase in QTc interval among the atypical antipsychotics studied, no patients had a QTc > 500 msec. The study also included an analysis of the effect of co-administration of metabolic inhibitors for each product. Co-administration of ziprasidone with its metabolic inhibitor, ketoconazole, did not lead to any further prolongation of the QTc despite an increase in serum concentration. According to the manufacturer, there have been no reports of *torsades de pointes* during post-marketing experience with ziprasidone. Ziprasidone has been taken by approximately 150,000 patients since it was approved (Weiden et al, 2002).

  Product labeling for risperidone reports lengthened QTc intervals in some patients but no mean increase even at higher than normal doses. No increases in QTc interval are reported in product labeling for aripiprazole, olanzapine, or quetiapine.

- *Cerebrovascular events* – Results of an analysis of 4 placebo-controlled trials (4-12 weeks in duration) in more than 1200 patients with Alzheimer's disease or vascular dementia receiving risperidone were recently released. The overall risk of cerebrovascular adverse events was 4% in the risperidone-treated group compared to 2% in the placebo group; four patients died in the risperidone group vs. one patient in the placebo group. A further search of postmarketing databases

revealed 37 cases of cerebrovascular adverse events in elderly dementia patients taking risperidone, of which 16 (43%) were fatal.

The manufacturer of risperidone recently stated that it intends to send letters to U.S. physicians advising them of the possibility of increased risk of stroke among elderly patients taking risperidone and to make changes to product labeling more clearly outlining available information about risk in elderly patients. A similar warning was released in Canada last October, with a summary and review of available information published in the November 2002 issue of the Canadian Medical Association Journal (Wooltorton, 2002). The Canadian letter to physicians is available at: http://www.hc-sc.gc.ca/hpb-dgps/therapeut/zfiles/english/advisory/industry/risperdal1_e.pdf.

Whether other atypical antipsychotic agents are associated with similar cerebrovascular risks is unknown.

- *Prolactin elevation* - Blockade of D2 receptors in the hypothalamus can result in increased prolactin secretion, which can lead to breast swelling, tenderness, and discharge; menstrual cycle irregularity or amenorrhea; sexual dysfunction; anovulation; and osteoporosis. Elevated prolactin levels do not always correlate with the presence of symptoms; long-term consequences of elevated prolactin are unclear. Atypical antipsychotics have a lower risk for causing prolactin elevation than typical antipsychotics, due to selectivity in the limbic system and higher 5-HT2 to D2 binding ratios. Of the atypical antipsychotics, risperidone has been associated with the largest increases in prolactin levels.
- *Other adverse effects* considered by the Council included the risk of orthostatic hypotension, anticholinergic effects, somnolence, cataracts, sexual dysfunction, priapism, and seizure.

Cost

MTFs spent about $11.3 million on atypical antipsychotics in FY 02: $5.6M for olanzapine, $3.8M for risperidone, $1.4M for quetiapine, $0.4M for ziprasidone, and $0.1M for clozapine. The average cost per day (tabs/caps only) is given in Table 3 below:

Table 3 - Average cost per tab/cap, tab/caps per day, and average cost per day for atypical antipsychotics in MTFs

	Average cost per tab/cap (PV data Dec 02-Feb 03)	Average tabs/caps per day** (PDTS data Jan 03-Mar 03)	Average cost per day
Aripiprazole*	$7.13	1.01	$7.21
Olanzapine	$4.22	1.33	$5.61
Quetiapine	$1.23	2.14	$2.64
Risperidone	$1.88	1.60	$3.01
Ziprasidone	$2.32	1.97	$4.56

* Limited data for aripiprazole

** Based on days supply. Results are consistent with those calculated for the retail network and mail order and with an older analysis based on directions for use.

The Council considered BPAs or incentive purchase agreement offers from the manufacturers of olanzapine, quetiapine, and risperidone. Offers differed considerably regarding the basis for price discounts and the considerations required by the manufacturers. A cost impact analysis by LCDR Ted Briski showed that annual cost avoidance ranging from $0.7 million to $1 million (based on current usage) could be attained by accepting two of the three offers.

After weighing relative usage, clinical factors, and economic factors, the Council voted to add risperidone and quetiapine to the BCF. The Council noted the following:

- Risperidone is by far the most commonly used atypical antipsychotic in the pediatric population, an age group in which use of this drug class is relatively high. Ensuring uniform availability of this agent across the system may benefit military personnel with children, who commonly move from MTF to MTF.
- The recent reports of an increased incidence of stroke in elderly patients with dementia receiving risperidone may lead to preferential use of other atypical antipsychotics in elderly patients (although there are no data indicating whether the same effect occurs with other atypical antipsychotics). Taken along with the general inter-patient variability in this drug class and the higher incidence of EPS and prolactin elevation with risperidone, this argues for the presence of a second agent on the BCF.
- Data for differences in efficacy among the various agents are not compelling, particularly considering the likelihood of use in conditions other than schizophrenia. However, adverse effect profiles differ considerably. All of the most commonly used medications have adverse effect concerns. Data on the newer agents, ziprasidone and aripiprazole, which may avoid some common adverse affects, are limited, and usage is low.
- Quetiapine and risperidone are the least costly agents on a cost per day basis.
- MTFs are free to add or retain additional atypical antipsychotics on their formularies if required locally.

C. *Topical Immunomodulators (TIMS)*

In November 2002, the DoD P&T Executive Council agreed that TIMS are a unique class and have a substantial place in therapy for the treatment of atopic dermatitis (AD), however there was concern regarding the cost of these agents and the potential for overuse. The Council agreed to consider one or both of these medications for addition to the BCF after procurement options were explored.

Efficacy – Randomized controlled clinical trials demonstrate that both agents are more efficacious than placebo in the treatment of AD. Tacrolimus, an ointment, appears to be as efficacious as a medium potency topical corticosteroid (TCS) whereas pimecrolimus, a cream, is as efficacious as a low potency TCS. Tacrolimus is indicated for moderate to severe AD while pimecrolimus is indicated for mild to moderate AD. Ninety percent of patients have mild to moderate AD and the rest are moderate to severe. Most of the use is in the very young (ages 0-4) and elderly (ages 65+).

Safety/Tolerability – Neither drug has clinically significant adverse effects that cause the patients to discontinue use. The drugs are not systemically absorbed, so they can be used long term without potential problems associated with long-term TCS use. TIMS can also be used on sensitive body areas such as the face and intertriginous regions where one would not want to use a TCS. Because pimecrolimus is a cream and less occlusive, it is preferred over tacrolimus for areas like the face, perioribital eyelids, and flexural and groin areas.

Other – Provider response was markedly positive regarding the prospect of having an alternative to TCSs on MTF formularies. At the same time, providers noted that these would not take the place of the low potency TCSs or other initial therapies for mild AD. Of 68 provider responses, 60 recommended adding one or both agents to the BCF. Of these 60 responses, 33 preferred pimecrolimus, 6 preferred tacrolimus, and the rest either had no preference or wanted both agents on the BCF. Pimecrolimus prescription fills are increasing at all points of service (MTF, TMOP, and retail). Pimecrolimus is currently on 49 percent of all MTF formularies. Tacrolimus is on 25 percent of MTF formularies; tacrolimus prescription fills for all points of service have leveled off at a point well below pimecrolimus.

Cost – Novartis offered an incentive agreement contingent on pimecrolimus being added to the BCF. The agreement provides a discount on all future purchases.

The Council voted unanimously to add pimecrolimus to the BCF. After being reviewed by dermatologists, a place in therapy (PIT) guide will be disseminated to the MTFs as a tool to help reduce potential inappropriate use.

8. REQUESTS FOR BCF CHANGES

A. *Nitroglycerin Products on the BCF*

The American College of Cardiology/American Heart Association currently considers nitroglycerin as third-line treatment for *chronic* symptoms of angina. Despite this third-line consideration for use, nitroglycerin transdermal systems currently account for approximately 8,000 prescriptions monthly in the MHS, second only to the sublingual tablets (approximately 15,000 prescriptions/month). Other nitroglycerin preparations (translingual spray, sustained release capsules, and ointment) combined account for approximately 6,000 prescriptions/month. Current BCF nitroglycerin products include sublingual nitroglycerin tablets, translingual spray, and isosorbide dinitrate oral. The BCF does not contain a long acting nitroglycerin product.

Transdermal nitroglycerin systems are on 75% (86/114) of local MTF formularies. A DoD/VA joint contract for nitroglycerin transdermal systems from Schering provides the patches at a cost of $0.16/day ($4.89/month).

An analysis of MHS prescription data revealed a steadily increasing number of prescriptions for isosorbide mononitrate oral for all three points of service in the MHS (approximately 16,000 prescriptions/month combined). Isosorbide mononitrate oral is on 43% (49/114) of local MTF formularies. The DoD/VA currently has a joint contract for a generic once daily isosorbide mononitrate oral tablet at a cost ranging between $0.04 to $0.06/day, depending on strength.

The Council voted unanimously to add the contracted nitroglycerin transdermal system and the contracted once daily preparation of isosorbide mononitrate oral to the BCF, due to wide usage in the MHS and low cost.

B. *Administrative Changes Concerning the Process for Requests from the Field for BCF Changes*

In order for the PEC to provide support materials for agenda items to the Council members three weeks prior to the meeting, a deadline needs to be established for submission or requests for BCF changes. To allow sufficient time to complete an analysis and prepare a recommendation for any submitted request, the PEC recommended that the deadline for BCF change requests should be 6 weeks prior to the next regularly scheduled meeting. The Executive Council concurred with this recommendation.

A second issue concerned the potential need for individuals requesting the addition of an agent to the BCF to disclose whether they have a financial interest or other relationship with the manufacturer of the product that could be perceived as a conflict of interest. The purpose of this disclosure would not be to prevent the consideration of the request, but to provide the Council with information that would allow it to make a more informed and credible decision. It was initially proposed that a disclosure form should be required to accompany a request for a BCF change. Some Council members suggested that if disclosure forms are required for BCF change requests, the same type of disclosure should be required for input regarding other P&T actions. Council members were concerned that the paperwork burden would degrade the ability of the PEC to obtain input from providers. The Council voted to table this issue and tasked the PEC to clarify the necessary scope and process for obtaining disclosure statements on any input related to formulary decisions making. The PEC is to present a revised recommendation at the next meeting.

9. ADJOURNMENT

The meeting adjourned at 1500 hours. The next meeting will be held at TRICARE Management Activity (TMA), conference room 815, Skyline Building 6, 5111 Leesburg Pike, Falls Church, VA at 0800 on Tuesday, 5 August 2003. All agenda items should be submitted to the co-chairs no later than 18 July 2003.

<signed>	<signed>
DANIEL D. REMUND	TERRANCE EGLAND
COL, MS, USA	CDR, MC, USN
Co-chair	Co-chair

Department of Defense
Pharmacoeconomic Center

2421 Dickman Rd., Bldg. 1001, Rm. 310
Fort Sam Houston, TX 78234-5081

MCCS-GPE **6 MARCH 2003**

MEMORANDUM FOR: Executive Director, TRICARE Management Activity (TMA)

SUBJECT: Minutes of the Department of Defense (DoD) Pharmacy and Therapeutics (P&T) Committee Meeting

1. A meeting of the DoD P&T Committee convened at 0800 hours on 6 March 2003, at the DoD Pharmacoeconomic Center, Fort Sam Houston, Texas.

2. VOTING MEMBERS PRESENT

CDR Terrance Egland, MC	DoD P& T Committee Co-chair
COL Daniel D. Remund, MS	DoD P& T Committee Co-chair
COL Joel Schmidt, MC	Army
MAJ Travis Watson, MS	Army
COL John R. Downs, MC	Air Force
COL Mark Nadeau, MC (for COL Bill Sykora, MC)	Air Force
LtCol George Jones, BSC	Air Force
CAPT Matt Nutaitis, MC	Navy
CDR Mark Richerson, MSC	Navy
CAPT Robert Rist	Coast Guard
Mike Valentino	Department of Veterans Affairs
Dr. Trevor Rabie	Uniformed Services Family Health Plan
COL Doreen Lounsbery, MC	Army

VOTING MEMBERS ABSENT

None	

OTHERS PRESENT

COL William Davies, MS	DoD Pharmacy Program Director, TMA
Howard Altschwager	Deputy General Counsel, TMA
COL Mike Heath, MS	Army Pharmacy Consultant, Chairman Pharmacy Board of Directors
CAPT Betsy Nolan, MSC	Navy Pharmacy Specialty Leader
David Chicoine	Uniformed Services Family Health Plan
CAPT Joe Torkildson, MC, USN	DoD Pharmacoeconomic Center
CDR Denise Graham, MSC, USN	DoD Pharmacoeconomic Center
LtCol Dave Bennett, USAF, BSC	DoD Pharmacoeconomic Center
LtCol Barb Roach, USAF, MC	DoD Pharmacoeconomic Center
CDR (sel) Ted Briski, MSC, USN	DoD Pharmacoeconomic Center
Shana Trice	DoD Pharmacoeconomic Center
David Bretzke	DoD Pharmacoeconomic Center
Eugene Moore	DoD Pharmacoeconomic Center
Angela Allerman	DoD Pharmacoeconomic Center
Lisa LeGette	Express Scripts
Mark Hughes	Express Scripts
MAJ John Howe, MS	Defense Supply Center Philadelphia
Kathy Tortorice	Department of Veterans Affairs
Shannon Rogers	Humana
William Hudson	Humana
Gene Lakey	TriWest
Ray Nan Berry (via T-Con)	Health Net Federal Services
Ron McDonald (via T-Con)	Sierra

3. **REVIEW MINUTES OF LAST MEETING** – The minutes from the last meeting were accepted as written.

4. **INTERIM/ ADMINISTRATIVE DECISIONS** – Trovafloxacin was excluded from the NMOP/TMOP since its use is reserved for "patients with serious, life- or limb-threatening infections who receive their initial therapy in an inpatient health care facility," and is restricted to a two-week period.

5. **UNIFORM FORMULARY (UF) PROPOSED RULE**- COL William Davies, DoD Pharmacy Program Director, TMA, stated that the responses to the public comments on the proposed rule are nearly finalized and will undergo a legal review.

6. **BCF AND TRICARE MAIL ORDER PHARMACY (TMOP) FORMULARY ISSUES** – The Committee determined the TMOP formulary status, TMOP or retail network formulary restrictions (quantity limits or prior authorization), and Basic Core Formulary (BCF) status for 6 new drugs or formulations (see Appendix A). The PEC also presented brief information on fourteen additional new drugs or formulations not requiring a complete review by the Committee (see Appendix B). The Committee agreed that no further review was required.

7. MAIL ORDER AND RETAIL NETWORK ISSUES

A. *Implementation of the TMOP on 1 March 2003* - COL Davies (TMA) and Lisa LeGette from Express Scripts (the contractor for the TMOP program) provided an overview of the implementation of the TRICARE Mail Order Pharmacy program, and the progress of the changeover from the previous National Mail Order Pharmacy (NMOP) program. Shana Trice (PEC) reviewed the new TMOP Formulary page on the PEC website and explained changes from the old NMOP Formulary page. She also discussed revisions to the DoD Quantity Limits page to better reflect implementation of the quantity limits at the TMOP.

The URL for the TMOP Formulary page is: www.pec.ha.osd.mil/TMOP/TMOPhome.htm. Comprehensive benefit information for the TMOP may be found on the TRICARE website at: http://www.tricare.osd.mil/pharmacy/tmop.cfm, while the Express-Scripts website (www.express-scripts.com; click on the DoD seal) provides beneficiaries with the ability to register for the TMOP online, download registration forms, order refills, check order status, etc.

B. *New "line extension" rule for the TMOP* – The Council agreed that newly approved combination products involving addition of a diuretic to another antihypertensive medication may be automatically added to the TMOP Formulary as a line extension, pending confirmation by the Committee at the next scheduled meeting. The Committee asked for a review of "line extension rules" for the TMOP at the next meeting in May 2003. The rules currently in effect are those previously approved for the NMOP; however, there are operational differences between the two programs that affect the manner in which the rules are applied.

8. PRIOR AUTHORIZATIONS (PAs)

The Committee approved prior authorization criteria for adalimumab (Humira) and modifications to prior authorization criteria for etanercept (Enbrel) and anakinra (Kineret) (see Appendix D).

9. CONTROLLED DISTRIBUTION OF PRESCRIPTION DRUGS – Buprenorphine & buprenorphine/naloxone (Subutex/Suboxone) are subject to a controlled distribution process, but it is not clear to the Committee that these medications are covered under TRICARE rules. Enfuvirtide (Fuzeon) a new HIV medication will be manufactured on a limited scale, however the distribution process is unknown. Further information on both these products should be available by the next meeting. Peginterferon-alfa 2b (PEG-Intron) and etanercept (Enbrel) are no longer under controlled distribution.

10. ADJOURNMENT – The meeting adjourned at 1130 hours. The next meeting will be held at Fort Sam Houston, TX at 0800 on Wednesday, 7 May 2003. All agenda items should be submitted to the co-chairs no later than 18 April 2003.

<signed>
DANIEL D. REMUND
COL, MS, USA
Co-chair

<signed>
TERRANCE EGLAND
CDR, MC, USN
Co-chair

List of Appendices

APPENDIX A: NEWLY APPROVED DRUGS CONSIDERED FOR THE TRICARE MAIL ORDER PHARMACY FORMULARY AND DOD BASIC CORE FORMULARY

Generic name (Trade name; manufacturer)	**FDA approval date, drug class, FDA-approved indication**	**TMOP Formulary status**	**TMOP and/or retail network formulary restrictions**	**BCF status**
Nitazoxanide 100 mg/5 mL oral suspension (Alinia; Romark Labs)	22 Nov 02: Treatment of diarrhea caused by *Cryptosporidium parvum* and *Giardia lamblia*, in pediatric patients 1 through 11 years of age. Nitazoxanide is given every 12 hours for 3 days. Nitazoxanide is the first anti-parasitic product approved specifically for treating cryptosporidiosis and the only drug approved for treatment of giardiasis in ages 1-11 years that is available in a suspension formulation. A tablet formulation of nitazoxanide for adults with intestinal parasites is "approvable" at the FDA.	Added to the TMOP Formulary	**Quantity Limits** General rule applies **Prior Authorization:** None	Not added to the BCF **Similar BCF agents:** Metronidazole oral tablets; requires extemporaneous compounding to make a suspension.
Eletriptan tablets (Relpax; Pfizer)	26 Dec 02: Indicated for the acute treatment of migraine attacks with and without aura in adults. This is the 7th 5-HT receptor agonist (triptan) marketed.	Added to the TMOP Formulary	**Quantity Limits** Quantity limits exist for other triptans. Packaged in 12's. **Retail**: 12 tablets/30 days" **TMOP:** 36 tablets/90 days **Prior Authorization** None	Not added to the BCF **Similar BCF agents:** sumatriptan oral tablets and auto-injector. **Note:** A contracting initiative for the triptan class is underway.
Aripiprazole tablets (Abilify; BMS)	15 Nov 02: Atypical antipsychotic indicated for the treatment of schizophrenia. Unlike other atypical antipsychotics, aripiprazole functions as a partial agonist at dopamine D_2 receptors; the clinical significance of this difference is unknown.	Added to the TMOP Formulary	**Quantity Limits** General rule applies **Prior Authorization** None	Not added to the BCF **Similar BCF agents**: None **Note:** Addition of one or more atypical antipsychotics to the BCF is under discussion.
Teriparitide (rDNA origin) injection (Forteo; Lilly)	26 Nov 02: Recombinant parathyroid hormone (PTH); stimulates new bone formation by increasing osteoblast activity. Teriparitide is indicated for the treatment of men and postmenopausal women with osteoporosis who are at high risk for fracture, including those with a history of osteoporotic fracture, multiple risk factors for fracture, or who have failed or are intolerant of previous osteoporosis therapy. Once-daily subcutaneous administration; may be self-injected. The injection device is similar to Lilly's insulin pen. Requires refrigeration. Black box warning for osteosarcoma in rodent studies. Patient medication guide must be dispensed with the product.	Added to the TMOP Formulary & TMOP Covered Injectables List	**Quantity Limits** General rule applies **Prior Authorization** None	Not added to the BCF **Similar BCF agents**: Alendronate tablets are on the BCF. Potential contracting initiative for alendronate or risedronate is under consideration.

Generic name (Trade name; manufacturer)	**FDA approval date, drug class, FDA-approved indication**	**TMOP Formulary status**	**TMOP and/or retail network formulary restrictions**	**BCF status**
Atomoxetine capsules (Strattera; Lilly)	26 Nov 02: Treatment of Attention-Deficit/Hyperactivity Disorder (ADHD) in children (down to age 6 years). Atomoxetine is a highly selective norepinephrine re-uptake inhibitor. It is the only non-controlled medication approved for the treatment of ADHD and the only medication approved for the treatment of ADHD in adults.	Added to the TMOP Formulary	**Quantity Limits** General rule applies **Prior Authorization** None	Not added to the BCF **Similar BCF agents:** Existing products for ADHD are all Schedule II controlled substances: methylphenidate ER (specific brand is Concerta); methylphenidate IR; D,L amphetamine ER (Adderall XR).
Adalimumab injection (Humira; Abbott)	2 Jan 03: Monoclonal antibody that binds to tumor necrosis factor (TNF) alpha. Indicated for reducing the signs and symptoms and inhibiting the progression of structural damage in adults with moderately to severely active RA who have had an inadequate response to one or more disease-modifying anti-rheumatic drugs (DMARDs). Can be used alone or in combination with methotrexate. Administered as a single dose 40 mg subcutaneous (SQ) injection every two weeks (patients not on methotrexate may require weekly administration). May be self-injected. Other similar biologics – etanercept, and infliximab, both TNF inhibitors, and anakinra, an interleukin-1 inhibitor – are also indicated for RA. Etanercept is also indicated for juvenile RA and psoriatic arthritis; infliximab for Crohn's disease. Etanercept (Enbrel) is administered SQ twice a week; infliximab (Remicade) as a monthly IV infusion, and anakinra (Kineret) as a daily SQ injection. Adalimumab contains the same black box warnings as other TNF blockers for emergence of serious infections during treatment, including disseminated or extrapulmonary tuberculosis.	Added to the TMOP Formulary & Covered Injectables List	**Quantity Limits** **TMOP**: 6 syringes per 6 weeks (3 packs of 2 syringes) **Retail:** 4 syringes per 4 weeks (2 packs of 2 syringes) **Note**: the quantity limits allow for the possibility of once weekly administration of adalimumab in some patients. Quantity limits are in place for both etanercept and anakinra. **Prior Authorization** ▪ Yes. See Appendix D for criteria.	Not added to the BCF **Similar BCF agents**: none

APPENDIX B: NEWLY APPROVED DRUGS NOT REQUIRING FULL REVIEW BY THE P&T COMMITTEE

Generic name (Trade name; manufacturer)	**Comments**
Isotretinoin capsules (Amnesteem; Bertek); (Sotret; Ranbaxy)	AB rated generics to Accutane (Roche brand of isotretinoin). Isotretinoin is excluded from the TMOP Formulary.
Ciprofloxacin extended-release tablets (Cipro XR; Bayer)	Approved for uncomplicated UTI caused *by E. coli*, *Proteus*, *Enterococcus*, and *Staphylococcus*; 3-day regimen. Automatically added to TMOP Formulary as a line extension. Ciprofloxacin is not on the BCF.
Stavudine extended release capsules (Zerit XR; BMS)	Nucleoside reverse transcriptase inhibitor for HIV. Automatically added to TMOP Formulary as a line extension. Stavudine is not on the BCF.
Alprazolam extended release capsules (Xanax XR; Pharmacia)	Approved for panic disorder. Automatically added to TMOP Formulary as a line extension. Alprazolam is not on the BCF.
Alpha-1 proteinase inhibitor, human injection (Aralast; Baxter/Alpha)	Orphan drug for hereditary emphysema/alpha 1 antitrypsin deficiency. Requires IV infusion. Not considered for the TMOP Covered Injectables List since it is not designed for self-administration. Not considered for the BCF due to the specialized nature of the indication.
Testosterone gel 1% topical (Testim; Auxilium Pharmaceuticals)	Approved for treatment of primary hypogonadism; 2nd testosterone gel on the market. Not generically substitutable for Androgel; both are reference listed drugs. Automatically added to TMOP Formulary as a line extension. Schedule III controlled medication. Although the general rule limits controlled medications to a 30-day supply at the TMOP, Testim falls under an already established exception to this rule that provides for up to a 90-day supply at the TMOP for commercially available topical testosterone products. Testosterone gel is not on the BCF.
Azelaic acid gel 15% topical (Finacea; Berlex)	Approved for mild to moderate rosacea. A similar product, azelaic acid 20% cream (Fineven; Berlex), approved for acne, is already available from the TMOP. Automatically added to TMOP Formulary as a line extension. Azelaic acid products are not on the BCF.
70% insulin aspart protamine suspension/30% insulin aspart injection (Novolog Mix 70/30 vials & pens; Novo Nordisk)	Biphasic insulin produced by adding protamine to Novolog. Automatically added to TMOP Formulary as a line extension.
Insulin aspart injection (Novolog flex pen; Novo Nordisk)	New packaging for insulin aspart. Automatically added to TMOP Formulary as a line extension.
Alefacept injection (Amevive; Biogen)	Biologic for moderate to severe plaque psoriasis given as a weekly IV bolus or IM injection. Not considered for the TMOP Covered Injectables List since it is not designed for self-administration. Not considered for the BCF due to the specialized nature of the indication.
Ribavirin capsules (Copegus; Roche)	Roche brand of ribavirin for use in combination with pegylated interferon. The Schering brand of ribavirin (Rebetol) is already available from the TMOP. Automatically added to TMOP Formulary as a line extension. Ribavirin is not on the BCF.
Diltiazem graded release tablet (Cardizem LA; Biovail)	New controlled release once-daily formulation of diltiazem; may be dosed in the morning or at bedtime. Not generically substitutable for Cardizem CD or Tiazac. Anticipated availability April 2003. Automatically added to TMOP Formulary as a line extension. Tiazac is the BCF selection for a once-daily diltiazem product.
Cyclobenzaprine tablets (Flexeril; McNeil)	New lower 5 mg dosage form. Automatically added to TMOP Formulary as a line extension. Cyclobenzaprine is not on the BCF.
Eprosartan/HCTZ tablets (Teveten HCT; GSK)	New combination of an angiotensin receptor blocker with hydrochlorothiazide. Automatically added to TMOP Formulary as a line extension. A VA/DoD solicitation for angiotensin receptor blockers is in progress.

APPENDIX C: COMBINED SUMMARY OF FORMULARY CHANGES FROM THE DOD P&T EXECUTIVE COUNCIL MEETING AND THE DOD P&T COMMITTEE MEETING

1. **BCF CHANGES**

   A. *Additions to the BCF*

      1) Chlorthalidone
      2) Benztropine
      3) Trihexyphenidyl
      4) Amantadine
      5) Lansoprazole
      6) Goserelin (Zoladex) 1- and 3-month products for the treatment of prostate cancer

   B. *Deletions, changes, clarifications or exclusions from the BCF* - None

2. **TMOP FORMULARY CHANGES**

   A. *Additions to the TMOP Formulary*

      1) Nitazoxanide oral suspension (Alinia; Romark Labs)
      2) Eletriptan tablets (Relpax; Pfizer) – quantity limits apply, see below
      3) Aripiprazole tablets (Abilify; BMS)
      4) Teriparitide (rDNA origin) injection (Forteo; Lilly) – added to the TMOP Covered Injectables List
      5) Atomoxetine capsules (Strattera; Lilly)
      6) Adalimumab injection (Humira; Abbott) – added to the TMOP Covered Injectables List with prior authorization criteria; quantity limits apply, see below

   B. *Exclusions from the TMOP Formulary*

      1) Trovafloxacin (Trovan; Pfizer) – specifically excluded from the TMOP Formulary, since its use is reserved for "patients with serious, life- or limb-threatening infections who receive their initial therapy in an inpatient health care facility," and is restricted to a two-week period.

   C. *Deletions, changes, or clarifications to the TMOP Formulary* - None

3. **QUANTITY LIMIT CHANGES (RETAIL NETWORK AND TMOP)**

   A. Quantity limit for eletriptan tablets (Relpax; Pfizer): 12 tablets (1 pack) per 30-day supply (retail); 36 tablets (3 packs) per 90-day supply (TMOP); consistent with existing quantity limits for other triptans (within limitations of package size)

   B. Quantity limit for adalimumab injection (Humira; Abbott): 4 syringes (2 packs of 2 syringes) per 4 weeks (retail); 6 syringes (3 packs of 2 syringes) per 6 weeks (TMOP)

4. **CHANGES TO THE TMOP PRIOR AUTHORIZATION PROGRAM**

   A. Prior authorization criteria established for adalimumab injection (Humira; Abbott) – see Appendix D

   B. Prior authorization criteria for etanercept and anakinra modified – see Appendix D

APPENDIX D: PRIOR AUTHORIZATION CRITERIA FOR ADALIMUMAB (HUMIRA) & CHANGES TO PRIOR AUTHORIZATION CRITERIA FOR ETANERCEPT (ENBREL) AND ANAKINRA (KINERET)

Drug	FDA Indications	New TMOP Prior Authorization Criteria
Adalimumab (Humira)	• Reducing signs and symptoms and inhibiting the progression of structural damage in adult patients with moderately to severely active rheumatoid arthritis who have had an inadequate response to one or more DMARDs.	• Coverage provided for the treatment of moderately to severely active rheumatoid arthritis in patients 18 years of age or older when the patient has had an inadequate response to at least one disease-modifying antirheumatic drug (DMARD). • Coverage NOT provided for concomitant use with anakinra (Kineret), etanercept (Enbrel), or infliximab (Remicade).
Anakinra (Kineret)	• Reduction in signs and symptoms of moderately to severely active rheumatoid arthritis, in patients 18 years of age or older who have failed 1 or more disease modifying antirheumatic drugs (DMARDs).	• Coverage provided for the treatment of moderately to severely active rheumatoid arthritis in patients 18 years of age or older when the patient has had an inadequate response to at least one disease-modifying antirheumatic drug (DMARD). • Coverage NOT provided for concomitant use with adalimumab (Humira), etanercept (Enbrel) or infliximab (Remicade). *Changes to previous criteria:* • Listing adalimumab, etanercept, and infliximab as DMARDs. • Adding adalimumab to the statement: "Coverage NOT provided for concomitant use with etanercept (Enbrel) or infliximab (Remicade)." • Making criteria more consistent with package labeling and with criteria for adalimumab by changing the previous requirement that the patient fail (or be unable to take) MTX AND fail at least one other DMARD.
Etanercept (Enbrel)	• Reducing signs and symptoms and inhibiting the progression of structural damage in patients with moderately to severely active rheumatoid arthritis. • Reducing signs and symptoms of moderately to severely active polyarticular-course juvenile rheumatoid arthritis in patients who have had an inadequate response to one or more DMARDs. • Reducing signs and symptoms of active arthritis in patients with psoriatic arthritis.	• Coverage provided for the treatment of moderately to severely active rheumatoid arthritis OR active psoriatic arthritis. • Coverage provided for the treatment of juvenile rheumatoid arthritis when the patient has an inadequate response to at least one disease-modifying antirheumatic drug (DMARD). • Coverage NOT provided for concomitant use with adalimumab (Humira), anakinra (Kineret), or infliximab (Remicade). *Changes to previous criteria:* • Listing adalimumab, anakinra, and infliximab as DMARDs. • Adding the provision that coverage is not provided for concomitant use with adalimumab, anakinra, or infliximab.

For all three prior authorizations:

The following are examples of DMARDs:

- o adalimumab
- o anakinra
- o etanercept
- o infliximab
- o azathioprine
- o hydroxychloroquine
- o gold compounds, oral/injectable (e.g., auranofin, aurothioglucose, gold sodium thiomalate)
- o leflunomide
- o methotrexate
- o d-penicillamine
- o sulfasalazine

Department of Defense
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MCCS-GPE **5 March 2003**

MEMORANDUM FOR: Executive Director, TRICARE Management Activity (TMA)

SUBJECT: Minutes of the Department of Defense (DoD) Pharmacy and Therapeutics (P&T) Executive Council Meeting

1. The DoD P&T Executive Council met from 0800 to 1600 hours on 5 March 2003 at the DoD Pharmacoeconomic Center, Fort Sam Houston, Texas.

2. VOTING MEMBERS PRESENT

CDR Terrance Egland, MC	DoD P& T Committee Co-chair
COL Daniel D. Remund, MS	DoD P& T Committee Co-chair
COL Joel Schmidt, MC	Army
COL Doreen Lounsbery, MC	Army
MAJ Travis Watson, MS	Army
COL John R. Downs, MC	Air Force
COL Mark Nadeau, MC (For COL Bill Sykora, MC)	Air Force
LtCol George Jones, BSC	Air Force
CAPT Matt Nutaitis, MC	Navy
CDR Mark Richerson, MSC	Navy
CAPT Robert Rist	Coast Guard
Mike Valentino	Department of Veterans Affairs

VOTING MEMBERS ABSENT

None	

OTHERS PRESENT

COL William Davies, MS	DoD Pharmacy Program Director, TMA
Howard Altschwager	Deputy General Counsel, TMA
CAPT Betsy Nolan, MSC	Navy Pharmacy Specialty Leader
COL Mike Heath, MS	Army Pharmacy Consultant Chair, DoD Pharmacy Board of Directors
MAJ John Howe, BSC	Defense Supply Center Philadelphia
CAPT Joe Torkildson, MC	DoD Pharmacoeconomic Center
CDR Denise Graham, MSC	DoD Pharmacoeconomic Center
CDR (sel) Ted Briski, MSC	DoD Pharmacoeconomic Center
LtCol Dave Bennett, BSC	DoD Pharmacoeconomic Center
LtCol Barb Roach, MC	DoD Pharmacoeconomic Center
Shana Trice	DoD Pharmacoeconomic Center
Dave Bretzke	DoD Pharmacoeconomic Center
Angela Allerman	DoD Pharmacoeconomic Center
Eugene Moore	DoD Pharmacoeconomic Center
Kathy Tortorice	Department of Veterans Affairs, PBM
Capt Cherie-Anne Mauntel, BSC	USAF AFIT Student
CPT Tamba Dauda, MS	Pharmacy Resident, WHMC/BAMC
Capt Glenn L. Laird, BSC	Pharmacy Resident, WHMC/BAMC
Capt Agnes Kim, BSC	Pharmacy Resident, WHMC/BAMC
CPT Larry Ricks, MS	Pharmacy Resident, WHMC/BAMC

3. REVIEW MINUTES OF LAST MEETING

The minutes from the last meeting were accepted as written.

4. ADMINISTRATIVE ISSUES

A. *Membership and Meeting Frequency*: The Council discussed potential changes in its membership and the need to conduct additional Council meetings via teleconference in order to make timely decisions regarding joint VA/DoD pharmaceutical procurement strategies. The Council concluded that the charter that governs the DoD P&T Committee and Executive Council should be revised. COL Remund will develop an initial draft of a new charter.

The Council welcomed new members COL Doreen Lounsbery and CDR Mark Richerson, taking the place as voting members for COL Rosa Stith and CDR Kevin Cook, respectively.

B. *Clinical Reviews:* A Clinical Workgroup comprised of three members each from the VA PBM and the PEC are working to integrate and standardize the processes for completing clinical reviews of drug classes and drug monographs for new molecular entities.

C. *Rx NET:* RxNET is a web forum that the PEC established to facilitate communication among health care professionals involved in the delivery and management of drug therapy in the Military Health System. Dave Bretzke serves

as the administrator for RxNET. Council members are encouraged to use the forum that has been established for the DoD P&T Council within RxNET.

5. NATIONAL PHARMACEUTICAL CONTRACTS AND BLANKET PURCHASE AGREEMENT (BPA) AWARD, RENEWALS AND TERMINATIONS

A. New joint DoD/VA contracts were awarded for permethrin cream (West-ward), tretinoin topical cream (Allergan), and colchicine tablets (West-ward).

B. Joint DoD/VA contracts for erythromycin topical and clindamycin topical were not awarded because the bid prices were higher than existing FSS prices. The hydrochlorothiazide/triamterene joint contract was not awarded due to lack of offers.

C. New joint DoD/VA blanket purchase agreements were awarded for fluticasone (Flonase; Pharmacia), nisoldipine (Sular; 1st Horizon), tolterodine tartrate extended release capsules (Detrol LA; Pharmacia), lansoprazole (Prevacid; TAP), rabeprazole (Aciphex; Janssen), and levothyroxine (Synthroid; Abbott).

6. PROCUREMENT INITIATIVES

A. The following joint DoD/VA contracts are in various stages of solicitation: isosorbide dinitrate, ketoconazole cream, midazolam injectable, pamidronate injectable, and tramadol tablets.

B. A joint DoD/VA solicitation for a "triptan" closed 20 Dec 02, but the solicitation has been protested to the General Accounting Office (GAO).

C. A joint DoD/VA solicitation for bisphosphonates is being developed. A projected issue date is not yet identified.

D. A joint DoD/VA solicitation for angiotensin receptor blockers (ARBs) has been drafted and is currently being reviewed and edited.

E. A joint DoD/VA solicitation for a thiazolidinedione is being developed. A projected issue date is not yet identified.

F. Levothyroxine (Synthroid) – The price for the Synthroid brand of levothyroxine recently increased from $0.02 per tablet to $0.07 per tablet. In light of the price increase, the Council considered the possibility of a contracting action that would compete various levothyroxine products. Synthroid accounts for 97% of the levothyroxine market at MTF pharmacies. None of the levothyroxine tablets marketed by other companies are "A-rated" to Synthroid. A contracting action that caused patients to be switched from Synthroid to another levothyroxine product would result in therapeutic substitutions requiring additional laboratory tests to monitor thyroid levels. The Council unanimously voted not to pursue a contract for a single levothyroxine product on the BCF.

G. Statins – A joint DoD/VA solicitation for a high potency statin closed 28 February 2003. The solicitation permits (but does not mandate) the addition of generic lovastatin and/or a non-CYP3A4 metabolized statin (pravastatin or fluvastatin) to the BCF. Lovastatin, pravastatin and fluvastatin have not been on

any MTF formularies since the current closed class statin contract was awarded in August 1999.

1) Lovastatin accounts for less than 1% of statin usage at MTFs. Lovastatin costs $0.26 per tablet (joint VA/DoD contract price), so it does not offer any price advantage compared to the current contract prices for the strengths of simvastatin that achieve similar reductions in LDL-cholesterol. The future contract prices for a high potency statin are expected to be even lower. The Council voted to not add lovastatin to the BCF. Individual MTFs may add lovastatin to their local formularies if they determine there is a need to do so.

2) Pravastatin and fluvastatin together account for less than 1% of MTF statin usage. Pravastatin and fluvastatin prices are higher than the contract prices for the strengths of simvastatin that achieve similar reductions in LDL-cholesterol. Since pravastatin and fluvastatin do not offer an economic advantage, their use should be limited to patients who have a clinical need for a non-CYP3A4-metabolized statin. If pravastatin or fluvastatin were added to the BCF, MTFs would no longer be able to use the non-formulary request process to limit usage to patients who have a specific clinical need for these agents. The Council voted to not add a non-CYP3A4 metabolized statin to the BCF and also to not participate in any contracting initiative that would require addition of pravastatin or fluvastatin to the BCF. Individual MTFs may add either pravastatin or fluvastatin to their local formularies if they determine there is a need to do so.

H. LHRH Agonists – The Council voted to add goserelin acetate (Zoladex) 3.6 mg and 10.8 mg implants to the BCF for the treatment of prostate cancer based on a joint DoD/VA contract that was awarded to Astra Zeneca. The contract specifies that Zoladex is the sole LHRH agonist on the Basic Core Formulary (BCF) **for the treatment of prostate cancer**, and that other LHRH agonist dosage forms used for prostate cancer are not allowed on MTF formularies. MTFs are allowed to have additional LHRH agonist products on their formularies for the treatment of conditions other than prostate cancer. Detailed guidance regarding the Zoladex contract is on the PEC website at:

http://www.pec.ha.osd.mil/Contracts/LHRH_Agonist_Contract_Guidance.htm

I. Prostaglandins – The Council voted at the November 2002 meeting to add a prostaglandin to the BCF utilizing a closed class contracting strategy competing latanoprost, bimatoprost and travoprost, which would not require patients to be switched from one agent to another. The ophthalmology consultants for the three services subsequently expressed disagreement with the Council's decision. The consultants' concerns centered on (1) evidence from clinical trials and clinical experience that bimatoprost and travoprost have a higher incidence of hyperemia than latanoprost and (2) less certainty regarding the safety of bimatoprost and travoprost because they have been on the market for less time than latanoprost.

The Council reviewed safety and tolerability data from clinical trials of ophthalmic prostaglandins, data on adverse effects and discontinuation rates from a phase IV study of bimatoprost, VA and DoD usage data, and information about

a switch from latanoprost to bimatoprost by a Kaiser health plan. After a lengthy discussion the Council passed a motion (by an 8 to 3 vote) to reaffirm its decision to seek a contract for a single ophthalmic prostaglandin. Members voting in favor of the motion tended to agree with the argument that differences in the incidence of hyperemia were unlikely to lead to clinical problems of a magnitude that would make bimatoprost or travoprost an unacceptable choice as the sole ophthalmic prostaglandin on the BCF. Members voting in favor of the motion also acknowledged that the longer a drug is on the market the more we generally know about its safety profile, but they concluded that selection of any of the ophthalmic prostaglandins as the sole agent on the BCF would not pose an unacceptable safety risk.

J. Proton Pump Inhibitors (PPIs) – In December 2002 Janssen communicated that Eisai, the manufacturer of rabeprazole (Aciphex), had decided to raise the price of rabeprazole (Aciphex) to the DoD and VA from $0.22 per unit to $0.35 per unit on 1 January 2003, and then to approximately $1.90 per unit on 1 April 2003. The impending price increases caused DoD and the VA to negotiate vigorously with all manufacturers of branded PPIs. Three of the four current manufacturers of branded PPIs submitted proposals to the DoD and VA.

The Council voted unanimously to accept blanket purchase agreements offered by Eisai/Janssen for Aciphex and TAP Pharmaceuticals for lansoprazole (Prevacid). Aciphex will remain on the BCF, and Prevacid will be added to the BCF.

7. Place In Therapy (PIT) Recommendations – PIT recommendations are intended to aid practitioners in the appropriate use of selected medications. The Council reviewed and accepted the revised PIT recommendations for angiotensin II receptor blocker (ARBs). The ARB PIT recommendations will be disseminated to MTFs.

The PEC is developing PIT recommendations for topical immunomodulators (TIMS) and overactive bladder (OAB). The draft PIT recommendations will be disseminated to Council members through RxNET or email. Council members will have a 10-day period to review and comment. The PEC will then modify the PIT recommendations as necessary and disseminate them to MTFs.

8. FORMULARY DECISION FOLLOW-UP

A. *Evista* — Evista was added to the BCF in May 2002. The PEC analyzed prescription data from PDTS to determine the extent to which patients who obtained Evista from retail pharmacies before it was added to the BCF subsequently obtained Evista from MTF pharmacies. An analysis of 11,108 patients who obtained Evista from retail network pharmacies between 1 March 2002 and 1 June 2002 showed that:

- 864 patients (8%) subsequently obtained Evista from MTF pharmacies between 1 September 2002 and 6 December 2002
- 10,244 patients (92%) continued to obtain Evista only from retail network pharmacies between 1 September 2002 and 6 December 2002

The PEC repeated the analysis after dividing the 11,108 patients into two groups. Group 1 included 3,092 patients who obtained prescriptions for drugs other than Evista from MTF pharmacies between 1 March 2002 and 1 June 2002. Group 2 included 8,016 patients who obtained prescriptions for drugs other than Evista at retail network pharmacies only between 1 March 2002 and 1 June 2002. The analysis showed that:

- 693 (22%) of the patients in Group 1 obtained Evista from MTF pharmacies between 1 September 2002 and 6 December 2002
- 171 (2%) of the patients in Group 2 obtained Evista from MTF pharmacies between 1 September 2002 and 6 December 2002

B. *Advair* — Advair was added to the BCF February 2002. The PEC analyzed prescription data from PDTS to determine the extent to which patients who obtained Advair from retail pharmacies before it was added to the BCF subsequently obtained Advair from MTF pharmacies. An analysis of 9,853 patients who obtained Advair from retail network pharmacies between 1 December 2001 and 1 March 2002 showed that:

- 1,874 patients (19%) subsequently obtained Advair from MTF pharmacies between 1 June 2002 and 20 February 2003
- 7,979 patients (81%) continued to obtain Advair only from retail network pharmacies between 1 June 2002 and 20 February 2003

The PEC repeated the analysis after dividing the 9,853 patients into two groups. Group 1 included 2,838 patients who obtained prescriptions for drugs other than Advair from MTF pharmacies between 1 December 2001 and 1 March 2002. Group 2 included 7,015 patients who obtained prescriptions for drugs obtained at retail network pharmacies only between 1 December 2001 and 1 March 2002. The analysis showed that:

- 1,457 (51%) of the patients in Group 1 obtained Advair from MTF pharmacies between 1 June 2002 and 20 February 2003
- 417 (6%) of the patients in Group 2 obtained Advair from MTF pharmacies between 1 June 2002 and 20 February 2003

9. DRUG CLASS EVALUATIONS TO DETERMINE CLINICALLY ACCEPTABLE CONTRACTING/FORMULARY STRATEGIES:

A. *Cholinesterase Inhibitors* — Cholinesterase inhibitors are the primary treatment for cognitive symptoms and functional disability of Alzheimer's disease (AD). Four cholinesterase inhibitors are currently available in the United States: tacrine (Cognex), donepezil (Aricept), rivastigmine (Exelon), and galantamine (Reminyl). The VA plans to conduct a clinical review of the class to determine potential contracting opportunities. The BCF does not include a cholinesterase inhibitor. CDR Graham presented a brief overview of cholinesterase inhibitors to assist the Council in deciding whether or not a cholinesterase inhibitor should be added to the BCF.

Efficacy: Cholinesterase inhibitors have been shown to delay neuropsychiatric, cognitive and functional decline in patients with mild to moderate AD. Long-term studies on outcomes such as patient quality of life, institutionalization, and caregiver burden have not been conducted, but short-term trials have shown that cholinesterase inhibitors delay nursing home placement and reduce costs of care in the home.

Safety/Tolerability: Generally the agents are well tolerated with common adverse effects managed with titration and dose adjustments. Common adverse effects are related to excessive cholinergic activity consisting of nausea, diarrhea, vomiting, and occasionally excessively vivid dreaming. Tacrine (Cognex) use has been limited due to associated risks of hepatotoxicity.

Other factors: The following table displays FSS cost of cholinesterase inhibitors.

	Tacrine	Donepezil	Rivastigmine	Galantamine
FSS Price/Unit	$0.80/cap	$2.54/tab	$1.30/tab	$1.30/tab
Dosage Frequency	QID	QD	BID	BID
Cost/day	$3.20/day	$2.54/day	$2.60/day	$2.60/day
Cost/month	$96.00/month	$76.20/month	$78.00/month	$78.00/month

PDTS data from October 2002 to January 2003 show that donepezil (Aricept) has the majority of the DoD market share in all three points of service, with a steady increase in prescription fills for donepezil, rivastigmine, and galantamine in all three points of service. MTFs are currently spending nearly $100,000 per month on cholinesterase inhibitors.

A Council member expressed the opinion that the cholinesterase inhibitors are very expensive compared to the relatively modest clinical benefits they offer. The Council voted 10 to 1 not to consider the addition of a cholinesterase inhibitor to the BCF.

B. *Parkinson's Disease*

Carbidopa/ levodopa immediate release (Sinemet IR) formulation is currently the only drug on the BCF for the treatment of Parkinson's disease. The Council addressed the following questions:

- Should carbidopa/levodopa controlled release (Sinemet CR) be added to the BCF or replace carbidopa/levodopa immediate release on the BCF?
- Should adjunctive therapy agents (anticholinergic agents and amantadine) be added to the BCF?
- Should one or more of the dopamine agonists (bromocriptine, pergolide, pramipexole, ropinirole) be added to the BCF?

Carbidopa/levodopa controlled release: Carbidopa/levodopa is the most effective drug for the symptomatic treatment of idiopathic Parkinson's disease. There is no

evidence of a clinical advantage for the controlled release (CR) form of carbidopa/levodopa compared to the immediate release (IR). The daily cost of therapy with the CR is substantially higher, ranging from $1.00 to $2.50 vs $0.20 to $0.80 for the immediate release (IR). The Council unanimously voted to not add carbidopa/levodopa CR to the BCF.

Adjunctive therapy: Adjunctive treatment for Parkinson's disease includes anticholinergic agents (trihexyphenidyl, benztropine) and amantadine. Adjunctive therapy agents are effective monotherapy treatment for tremors in patients under the age of 70 in whom akinesia is not a significant problem. Additionally, they may be useful in patients with more advanced disease that have persistent tremor despite treatment with carbidopa/levodopa or dopamine agonists.

- Anticholinergic agents: There is little evidence to suggest that one anticholinergic agent is superior to another. Trihexyphenidyl is the most widely prescribed anticholinergic agent in the MTFs, with benztropine being reserved for use in the management of antipsychotic drug-induced Parkinsonism. The adverse effects of the anticholinergic medications are common and often limit their use, especially in the elderly population.
- Amantadine is an antiviral agent that has mild antiparkinsonian activity with its main advantage being a lower side effect profile than the anticholinergic agents. All three agents are available as generics and are inexpensive.

Since the goal of treatment for Parkinson's is control of symptoms, and no drug gives excellent relief by itself, the Council voted to add these three medications to the BCF.

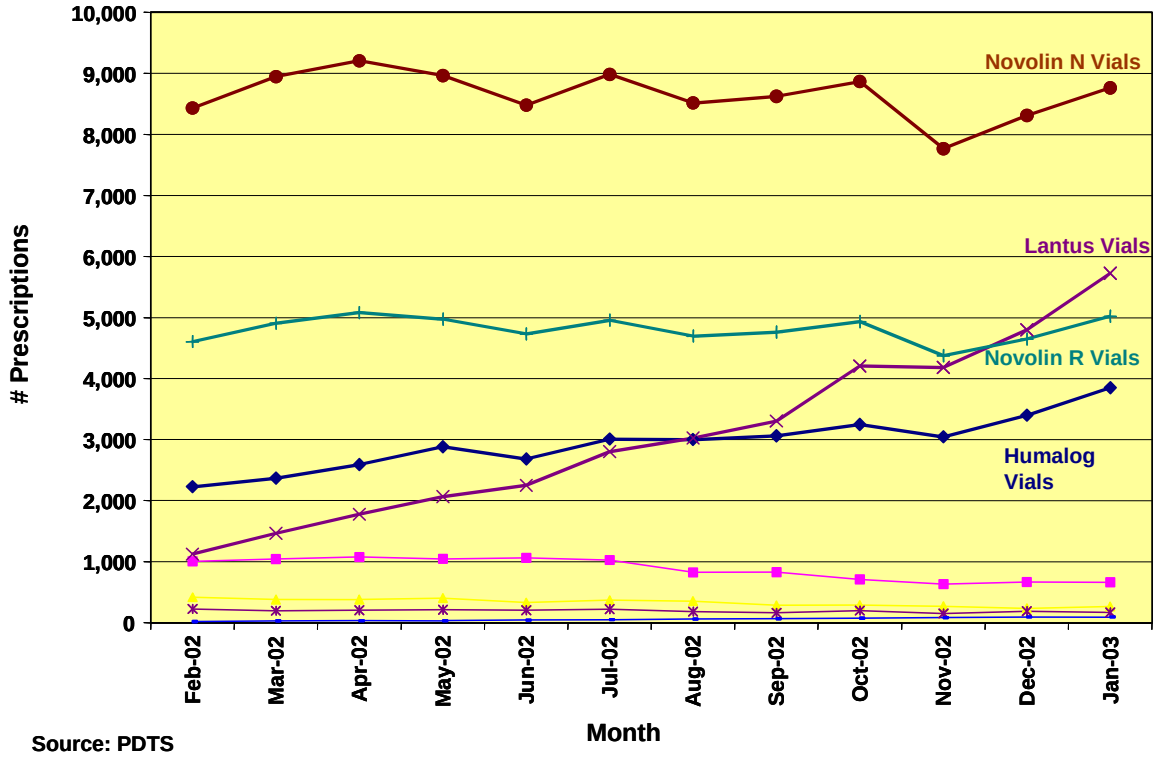
Dopamine agonists: A recent consensus opinion stated that dopamine agents are appropriate for the initial treatment of Parkinson's disease. Controlled trials have shown that bromocriptine (Parlodel), pergolide (Permax), pramipexole (Mirapax), and ropinirole (Requip) are all effective in patients with advanced Parkinson's disease complicated by motor fluctuations and dyskinesias. Dopamine agonists, however, are ineffective in patients who have shown no therapeutic response to carbidopa/levodopa. Side effects caused by dopamine agonists are similar to those of levodopa and patients who are intolerant of one agonist may tolerate another. The Council requested the PEC conduct a drug class review to determine which, if any, dopamine agonists, to add to the BCF.

C. *Insulin Pens* – CAPT Torkildson discussed the need to consider the addition of insulin pens and/or cartridges to the BCF. This question had been raised following the addition of insulin glargine (Lantus) to the BCF in August 2002. A perception had developed that this would result in an increased utilization of these insulin delivery systems, especially for the pre-prandial administration of short-acting and ultra-short-acting insulins. A joint contract was awarded to Novo Nordisk Pharmaceuticals, Inc. in 1999 to provide the DoD and VA with human regular, NPH, lente, and NPH/regular 70/30 mix insulin products. However, this contract included only the 10 ml vial package size of these products. Since the cost per unit of insulin delivered is much higher for the pen and cartridge delivery systems

compared to vials, and these delivery systems are not included in the current insulin contract, the PEC felt it would be prudent to look at this issue in greater detail.

CAPT Torkildson presented current data regarding insulin utilization within the direct care system (see Figure 1). Two of the top four insulin products by prescription volume (Novolin N and Novolin R) are currently under contract, while the other two products (Lantus and Humalog) are not. The other two contracted insulin products, Novolin L and Novolin 70/30, have no appreciable utilization at MTFs. A similar usage pattern exists in the mail order program.

Figure 1: MTF Prescription Volume for Most Commonly Prescribed Insulin Products

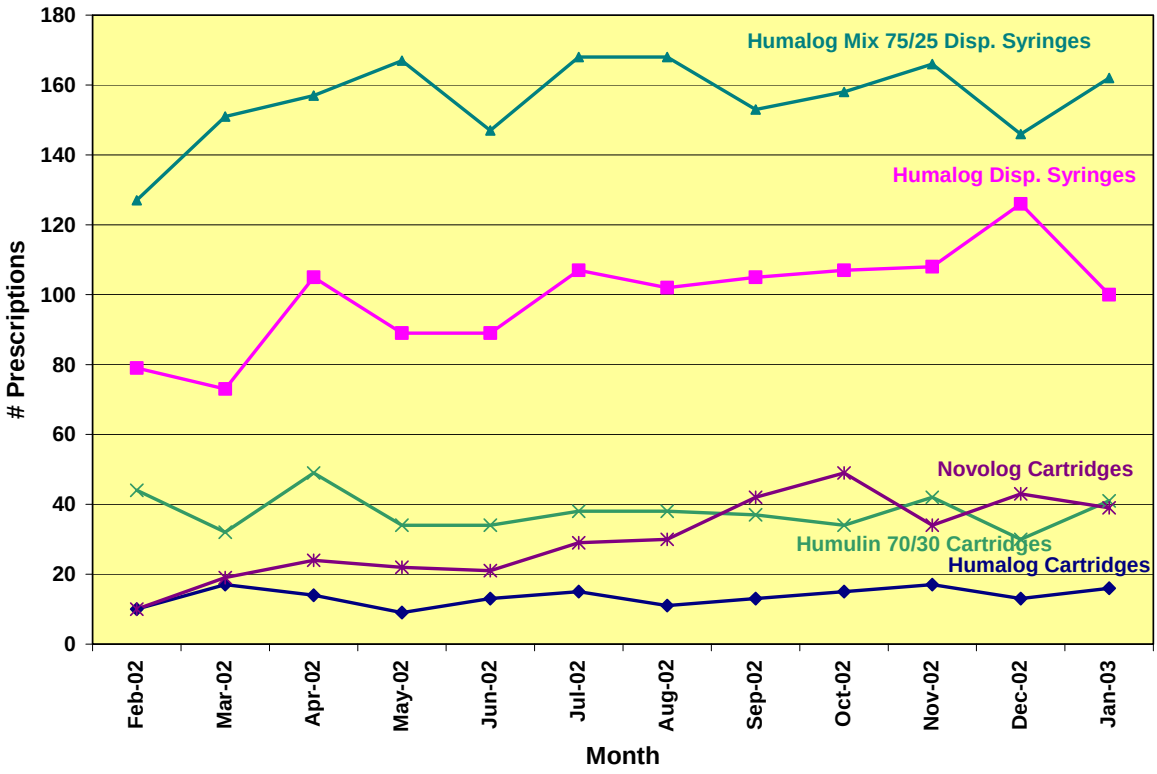


Source: PDTS

The data on utilization of insulin pens and cartridges within the direct care system is presented in Figure 2. Overall, insulin pens and cartridges currently represent a very small fraction of insulin product utilization. For the period 1 March 2002-28 Feb 2003, prescriptions for insulin pens and cartridges represented only 6% of the total number of insulin prescriptions filled in MTFs and the mail order program. However, as can be seen in Figure 2, the number of prescriptions for pen and cartridge delivery systems for ultra-short-acting insulin preparations (Humalog and Novolog) grew by about 50% over this period. In contrast, the prescription volume for other pen and cartridge insulin delivery products remained relatively flat. However, MTF expenditures for insulin pens and cartridges have increased

more rapidly. For example, MTFs spent $15,000 for Humalog pens in January 2003 compared to $5,000 in February 2002.

Figure 2: MTF Prescription Volume for Selected Insulin Disposable Syringe and Cartridge Products



A brief review of the clinical data highlighted the following information: While there are data to support the superiority of the ultra-short-acting insulin products (insulin lispro and insulin aspart) compared to regular insulin in terms of glycemic control, HbA1c levels, and frequency of hypoglycemia; there are currently no data that suggest that one ultra-short-acting insulin product is superior to the other. No data have been published since the award of the current insulin contract to suggest that any significant clinical differences exist between the products that were competed at that time, and no additional manufacturers of the products that are currently under contract have been identified.

From this information, the PEC came to the following conclusions:

- There is substantial and growing use of ultra-short-acting insulin products, primarily Humalog, at MTFs.
- There is almost no utilization of two of the four contracted insulin products, Lente and 70/30.
- There is currently little use of insulin pen devices.

- The monthly MTF expenditures for ultra-short-acting insulin pen devices has more than tripled over the past 12 months, from $6,000 to $20,000/month overall.

The PEC made the following recommendations to the Council:

- The DoD and VA should not exercise the final option year of insulin contract, which would begin on 1 November 2003
- The DoD and VA should instead begin development of a solicitation for a new insulin contract that covers different products than the current contract.
    - Lente insulin and the 70/30 product should not be included in the solicitation
    - The ultra-short-acting products (insulin lispro and insulin aspart) should be included in the solicitation
    - The pen/cartridge delivery system for the ultra-short-acting products only should be included in the solicitation

The Council voted unanimously to accept the PEC's recommendation and forward the above conclusions and recommendations for consideration by the Contracting Officer.

10. DRUG/DRUG CLASS EVALUATIONS TO DETERMINE BCF ADDITION

A. *Atypical antipsychotics* – The PEC is working on a review of the atypical antipsychotics. After the review is completed, the PEC will estimate the relative cost-effectiveness of the atypical antipsychotics and recommend how many of these agents should be added to the BCF.

B. *Ethinyl estradiol 20 mcg / Norelgestromin 150 mcg transdermal system (Ortho Evra)*

A MTF provider requested the addition of Ortho Evra to the BCF due to its unique administration route (topical) and potential for increased compliance.

Efficacy: A head-to-head that trial that compared 812 patients on Ortho Evra to 605 patients on Triphasil (30/40 mcg ethinyl estradiol with 50/75/125 mcg levonorgestrel) found that:

- The mean proportion of each participant's cycles that demonstrated perfect compliance was higher with Ortho Evra than with Triphasil (88.2% vs 77.7%, $p<0.0001$). [Note: Back-up contraception must be used if a patient exceeds a 7-day patch-free interval between Ortho Evra patches.]
- Despite better compliance with Ortho Evra, there was not a statistically significant difference in pregnancies: 5 with Ortho Evra vs 7 with Triphasil; $p=0.57$.

Safety/Tolerability: A higher percentage of patients on Ortho Evra discontinued the study due to adverse events than patients on Triphasil:

- Nausea: 1.8% with Ortho Evra vs 0.8% with Triphasil (p=0.12)
- Headache: 1.5% with Ortho Evra vs 0.3% with Triphasil (p=0.03)
- Dysmenorrhea: 1.5% with Ortho Evra vs 0.2% with Triphasil (p=0.01)
- Breast discomfort 1% with Ortho Evra vs 0.2% with Triphasil (p = 0.09)
- Application site reactions: 2.6% with Ortho Evra—not applicable for Triphasil

Other factors: A pooled analysis of clinical trial data (N=3319, 16,673 cycles) showed that 4.6% of Ortho Evra patches had to be replaced due to complete or partial detachment.

Price and usage: Ortho Evra costs $15.06/cycle, compared to $0.21-$8.00/cycle for oral contraceptives that are on the BCF. Ortho TriCyclen (which is not on the BCF) costs $15.21 per cycle. Ortho TriCyclen is the most commonly used contraceptive in the Military Health System (approximately 32,000 Rxs/month in all 3 points of service), compared to approximately 40,000 Rxs/month for all the oral contraceptives on the BCF combined. As of Jan 03, Ortho Evra had exceeded 10,000 Rxs/month.

The Council concluded that Ortho Evra does not offer any advantages in efficacy or safety/tolerability that justify its higher price compared to oral contraceptives already on the BCF. The Council voted unanimously not to add Ortho-Evra to the BCF.

C. *Topical Immunomodulators (TIMS)*

The PEC is still exploring procurement options for topical immunomodulators, so the Council took no action on these agents.

11. MTF REQUESTS FOR BCF CHANGES

A. *Request to add metoprolol extended release tablets (Toprol XL) to the BCF–* A MTF provider requested the addition of metoprolol succinate extended release tablets (metoprolol XL) to the BCF for congestive heart failure (CHF). The requestor's rationale was that "metoprolol XL is indicated for CHF and is not equivalent to the metoprolol tartrate immediate release preparation (metoprolol IR); additionally the XL formulation provides more dose flexibility by providing low doses to the patient and is the standard of care for CHF patients." No supporting literature was submitted along with the request.

Efficacy: Metoprolol XL is labeled for treating New York Heart Association (NYHA) functional class II/III CHF. A placebo-controlled trial conducted with metoprolol XL (MERIT-HF; Lancet 1999) in approximately 4000 subjects reported that 7.2% of patients receiving the drug died, compared with 11% in the placebo group (34% risk reduction, p<0.00009).

Metoprolol IR lacks an FDA-approved indication for CHF. A placebo-controlled trial conducted with metoprolol IR in approximately 400 patients with dilated idiopathic cardiomyopathy (MDC trial; Lancet 1993) found that 13% of patients

receiving the drug died, compared with 20% in the placebo group. The mortality rate of 13% is within range of the mortality rate seen in other beta blocker trials (7%-16%). Due to the small sample size, the survival benefit did not reach statistical significance ($p<0.058$). However, the risk reduction of 34% achieved with the metoprolol IR is similar to the risk reductions reported in other trials of similar design conducted with the beta blockers bisoprolol, carvedilol, and metoprolol XL.

The metoprolol IR study measured other parameters that showed significant benefits, including a reduced need for cardiac transplantation and improvements in left ventricular ejection fraction and exercise capacity. A head to head mortality study of metoprolol IR in comparison with carvedilol (COMET study) is currently underway in Europe, with results expected in summer 2003.

Safety/Tolerability: The XL formulation produces more consistent blood levels than the IR formulation. More consistent blood levels would theoretically produce more consistent beta-1 receptor blockade and cause fewer adverse events. However, head-to-head trials comparing metoprolol XL and metoprolol IR in small numbers of patients show no difference in safety and tolerability between the two formulations.

Other factors: Metoprolol IR is formulated in tablet strengths required for treating hypertensive patients (50 and 100 mg scored tablets), and is not available in the low doses required for initiating therapy in CHF patients (12.5 –25 mg). Metoprolol IR requires twice daily dosing. Metoprolol XL offers an advantage over metoprolol IR in that it is available in 25 mg scored tablets and is dosed once daily.

An analysis of PDTS prescription data showed that metoprolol XL is responsible for the 2nd highest number of beta blocker prescriptions in the NMOP and Retail Network, second only to atenolol. In the MTF setting, atenolol generates the most beta blocker prescriptions, followed by metoprolol IR, then metoprolol XL.

The Council voted unanimously not to add metoprolol XL to the BCF. Despite the lack of an FDA-approved indication, DoD providers use metoprolol IR for CHF. Although metoprolol XL offers the convenience of once daily administration and dosing flexibility, the absence of a significant difference in efficacy, safety or tolerability compared to metoprolol IR does not justify the higher expense for metoprolol XL ($9.90-$14.70 /month for metoprolol XL vs $0.90-$2.42/month for metoprolol IR). In the absence of a mechanism for MTFs to target the usage of metoprolol XL to patients with CHF, the addition of metoprolol XL to the BCF would likely result in increased use of metoprolol XL for hypertension in lieu of using other less-expensive beta blockers. The Council requested re-evaluation of the use of beta blockers for CHF upon completion of the COMET study.

B. *Request to add chlorthalidone 25 and 50 mg tablets to the BCF–* A MTF provider requested the addition of chlorthalidone, a generic thiazide diuretic, to the BCF in light of the recently completed landmark study (Anti-hypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial; ALLHAT; JAMA 2002). This study showed that the thiazide diuretic chlorthalidone was equally efficacious to a

calcium channel blocker (amlodipine) and an ACE inhibitor (lisinopril) in reducing blood pressure in hypertensive patients, at a much lower cost than the other agents. Efficacy of chlorthalidone was also proven in the Systolic Hypertension in the Elderly Program (SHEP; JAMA 1991), which showed a reduced incidence of stroke and major cardiovascular events in the diuretic arm.

Chlorthalidone has historically has been used more commonly in Europe than the US. Chlorthalidone may have a higher incidence of hypokalemia than hydrochlorothiazide (HCTZ), however, all patients receiving thiazide diuretics require electrolyte monitoring. The incidence of hypokalemia (serum potassium < 3.5 mEq/L) in patients receiving chlorthalidone in both the ALLHAT and SHEP trials was <10% (8.5% and 7.2%, respectively).

Although current DoD utilization of chlorthalidone is low (10,000 chlorthalidone Rxs in all 3 venues, vs 1 million Rxs for HCTZ), the extensive publicity of the results of ALLHAT may cause usage to increase. HCTZ and chlorthalidone are both very inexpensive, with tablet costs as low as $0.01/tablet. Although the current BCF thiazide diuretic HCTZ meets the needs of the majority of DoD patients, practitioners of evidence-based medicine may want to use chlorthalidone, and its availability should be ensured at MTF pharmacies. Providers should be encouraged to take advantage of a low cost drug with excellent evidence of benefit in the treatment of hypertension. The Council voted unanimously to add chlorthalidone to the BCF.

12. ADJOURNMENT

The meeting adjourned at 1530 hours. The next meeting will be held at Fort Sam Houston, TX at 0800 on Tuesday, 6 May 2003. All agenda items should be submitted to the co-chairs no later than 18 April 2003.

<signed>	<signed>
DANIEL D. REMUND	TERRANCE EGLAND
COL, MS, USA	CDR, MC, USN
Co-chair	Co-chair