Uniform Formulary Beneficiary Advisory Panel Handout
September 2005

PURPOSE: The purpose of this handout is to provide BAP Committee members with a reference document for the relative clinical-effectiveness presentations for each Uniform Formulary Class Review.

TABLE 1: UNIFORM FORMULARY RECOMMENDATIONS FOR THE ACE INHIBITORS, CALCIUM CHANNEL BLOCKERS, AND ALPHA BLOCKERS*

ACE inhibitors	
Uniform Formulary	Benazepril and combo with HCTZ
	Captopril and combo with HCTZ
	Enalapril and combo with HCTZ
	Fosinopril and combo with HCTZ
	Lisinopril and combo with HCTZ
	Trandolapril (Mavik)
Non-Formulary	Moexipril (Univasc) and combo with HCTZ
	Perindopril (Aceon)
	Quinapril (Accupril) and combo with HCTZ
	Ramipril (Altace)
Calcium Channel Blockers	
Uniform Formulary	**Verapamil products**
	Verapamil immediate release
	Verapamil sustained release
	Diltiazem products
	Diltiazem sustained release
	Diltiazem extended release (various products CD/XR/XT)
	DHP products
	Felodipine
	Nifedipine immediate release
	Nifedipine extended release (various products CC/XL/CR)
	Nimodipine
	Nisoldipine (Sular)
Non-Formulary	**Verapamil products**
	Verapamil extended release (Verelan)
	Verapamil extended release for bedtime dosing (Verelan PM)
	Verapamil extended release for bedtime dosing (Covera HS)
	Diltiazem products
	Diltiazem extended release for bedtime dosing (Cardizem LA)
	DHP products
	Amlodipine (Norvasc)
	Isradipine immediate release (DynaCirc)
	Isradipine controlled release (DynaCirc CR)
	Nicardipine immediate release
	Nicardipine sustained release (Cardene SR)
Alpha Blockers	
Uniform Formulary	Terazosin
	Doxazosin
	Alfuzosin (Uroxatral)
Non-Formulary	Tamsulosin (Flomax)

Note: Drugs with a trade name listed in parentheses are not available in generic formulations
***These classes do not have prior authorization criteria or quantity limits that apply.**

ANGIOTENSIN CONVERTING ENZYME INHIBITOR (ACE INHIBITOR)

Table 2: ACE Inhibitor Generic and Brand Names

Generic	Brand (Manufacturer)	Generics available	Available with HCTZ	FDA approval date
Benazepril	Lotensin	Yes	Yes	06/1991
Captopril	Capoten	Yes	Yes	1981
Enalapril	Vasotec	Yes	Yes	12/1985
Fosinopril	Monopril	Yes	Yes	1991
Lisinopril	Prinvil; Zestril	Yes	Yes	12/1987
Moexipril	Univasc (Schwarz)	None as of Jan 2005	Yes	04/1995
Perindopril	Aceon (Solvay)	No	No	12/1993
Quinapril	Accupril (Pfizer)	None as of April 2005	Yes	11/1991
Ramipril	Altace (King/Monarch)	No	No	01/1991
Trandolapril	Mavik (Abbott)	No	No	04/1996

Figure 1: MHS ACE inhibitor Utilization, Prescriptions Filled

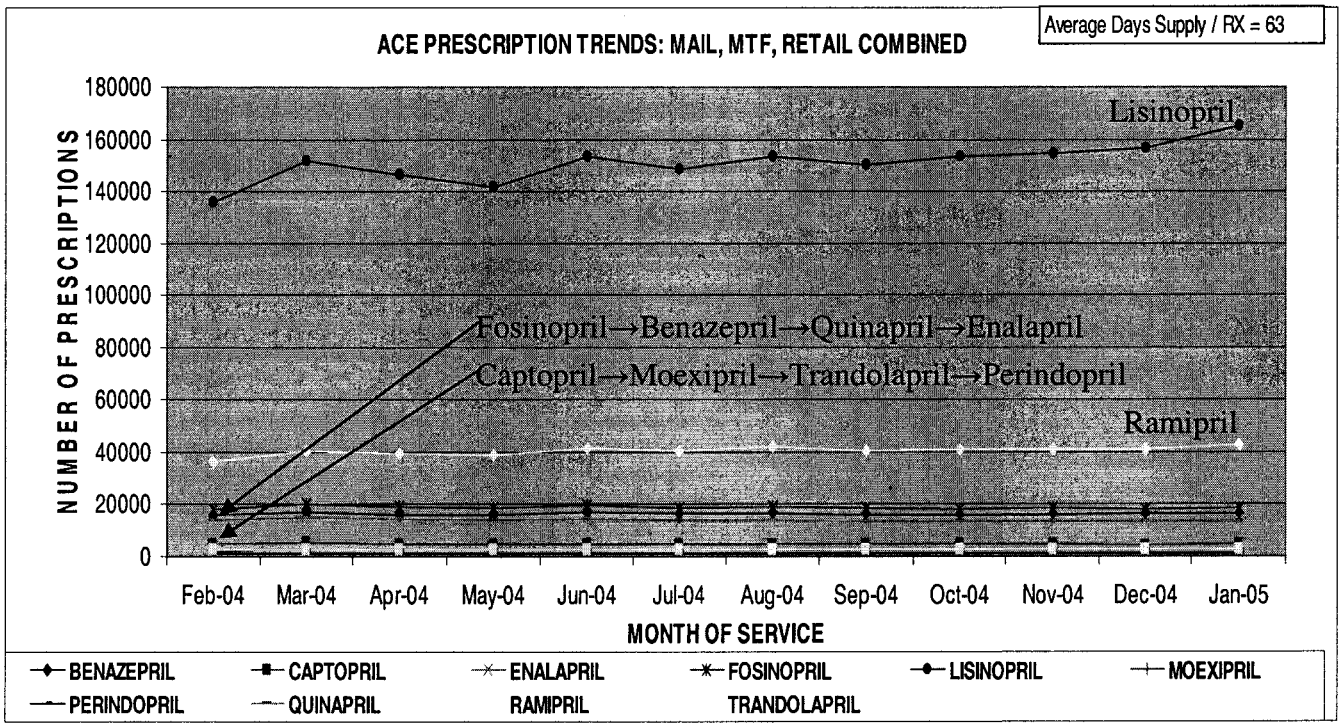

Table 3: ACE Inhibitor FDA Approved Indications

	FDA Approved Indications				
Drug	**Hypertension**	**Heart Failure**	**Post-Myocardial Infarction**	**Diabetic Nephropathy**	**↓ risk of heart attack / stroke / cardiac death in high-risk patients**
Benazepril	X				
Captopril	X	X	X	X (type 1 DM)	
Enalapril	X	X			
Fosinopril	X	X			
Lisinopril	X	X	X		
Moexipril	X				
Perindopril	X				b
Quinapril	X	a			
Ramipril	X	X	X		X
Trandolapril	X	X	X		

a: quinapril data is not based on a mortality benefit; only showed an improvement in exercise tolerance.
b: perindopril reduced the risk of combined endpoint of cardiovascular death, heart attack, and cardiac arrest, but the primary benefit was due to a reduction in the risk of heart attack in patients at high cardiovascular risk

Table 4: Summary of Three Trials of ACE Inhibitors Used in Patients at High Risk of Cardiovascular Events

ACE inhibitor	Study population	Results
Ramipril 10 mg over 5 years **HOPE** 9,287 patients	Unstable patients with history of heart disease, peripheral vascular disease, or myocardial infarction, plus at least one of the following risk factors (diabetes, high blood pressure, smokers, high cholesterol), but no history of heart failure	Significant reduction in death due to any cause, death due to cardiovascular causes, heart attack, or stroke, compared to patients not receiving ramipril. Background medications: aspirin 76%, lipid drugs 29%
Perindopril 8 mg over 4 years **EUROPA** 12, 218 patients	Stable patients with heart disease, but not heart failure. 66% had a history of heart attack, and 55% had a history of a procedure (bypass or balloon angioplasty).	Significant difference in risk of death due to cardiovascular causes/heart attack/cardiac arrest when these 3 endpoints were lumped together. But when the endpoints were split out separately, there was no difference in cardiovascular death, or death due to any cause. There was a significant reduction in the risk of non-fatal heart attack. Background medications: aspirin 92%, lipid drugs 59%
Trandolapril 4 mg over 5 years **PEACE** 8,290 patients	Stable patients with heart disease but without heart failure. Heart disease was defined as history of heart attack, previous cardiac bypass surgery or balloon angioplasty surgery, or >50% obstruction of one coronary artery.	No significant difference seen in mortality or cardiovascular events (non-fatal heart attack, need for repeat coronary procedure). Background medications: aspirin 90%, lipid drugs 70%

Ranking of ACE inhibitors based on FDA-approved indications, mortality data, avoidance of duplication of therapy, existing DOD utilization, and generic availability:

ramipril, lisinopril, captopril, fosinopril, benazepril, enalapril higher clinical utility than quinapril, perindopril, trandolapril, moexipril

Ranking of ACE inhibitors from #1 to #10 based on evidence for use FDA-approved indications, dosing schedule, and elimination route:
(1) ramipril, (2) trandolapril, (3) enalapril, (4) perindopril, (5) captopril, (6) lisinopril, (7) fosinopril, (8) quinapril, (9) benazepril, (10)moexipril

CALCIUM CHANNEL BLOCKER (CCBS)

Table 5: Calcium Channel Blocker Brand and Generic Names

Generic Name	Brand (Manufacturer)	Generics products available
Non-dihydropyridines (non-DHPs): Verapamil products		
Verapamil	**Immediate Release**	
	Isoptin (FSC); Calan (Searle)	Yes, to Isoptin
	Sustained Release	
	Calan SR; Isoptin SR (Par)	Yes to Isoptin SR
	Extended Release	
	Verelan (Elan)	Yes
	Verelan (Elan)	**No**
	Verelan PM (Elan) *(bedtime dosing)*	**No**
	Covera HS (Searle) *(bedtime dosing)*	**No**
Non-dihydropyridines (non-DHPs): Diltiazem products		
Diltiazem	**Immediate Release**	
	Cardizem (Kos)	Yes
	Sustained Release	
	Diltiazem HCL (Cardizem SR)	Yes
	Extended Release	
	Cardizem CD (Biovail)	No (360 mg does not have generics)
	Dilacor XR (Watson)	Yes
	Cardizem CD; Cartia XT (Andrx)	Yes
	Tiazac (Biovail), Taztia XT (Andrx),	Yes
	Tiazac (Forest, Inwood)	Yes, except 420 mg does not have generics
	Cardizem LA (Kos) *(bedtime dosing)*	**No**
Dihyrdopyridines (DHPs)		
Amlodipine	***Norvasc (Pfizer)***	**No**
Felodipine	Plendil (AstraZeneca)	Yes
Isradipine	***DynaCirc (Reliant)***	**No**
	DynaCirc CR (Reliant) *[GITS]*	**No**
Nicardipine	Cardene (Roche)	Yes
	Cardene SR (Roche) [granules/powder mix]	**No**
Nifedipine	Procardia (Pfizer)	Yes
	Adalat CC (Bayer) [core coat]	Yes
	Procardia XL (Pfizer) *[GITS]*	Yes
Nimodipine	Nimotop	No
Nisoldipine	***Sular (First Horizon)*** [core coat]	**No**

Figure 2: MHS CCB Inhibitor Utilization, Prescriptions Filled

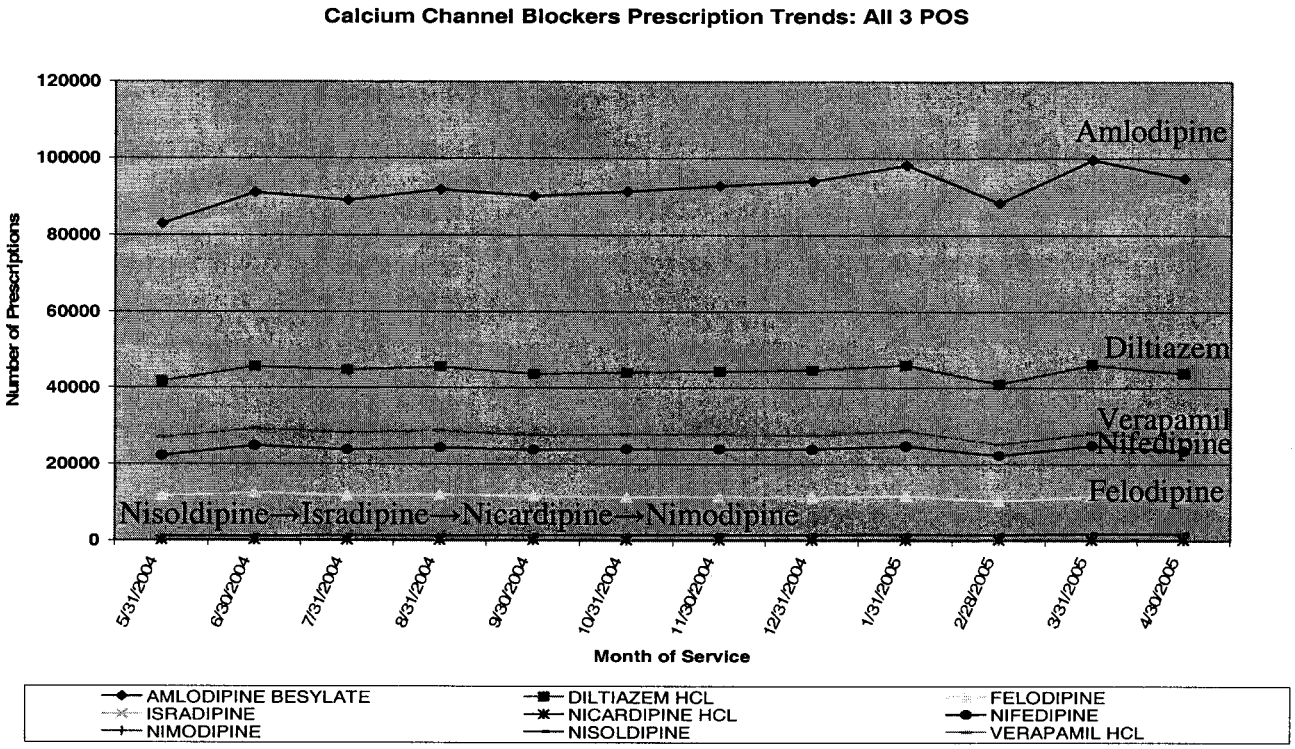

Table 6: Calcium Channel Blockers Approved Indications

Drug	Formulation	Hypertension	Angina	Other
Non-dihydropyridines: Verapamil products				
Verapamil	**Covera HS**	X		
	IR	X	X	Arrhythmias (IV)
	SR	X		
	Verelan	X		
	Veralan PM	X		
Non-dihydropyridines: Diltiazem products				
Diltiazem	IR		X	Arrhythmias (IV)
	SR	X		
	Cardizem CD	X	X	
	Dilacor XR	X	X	
	Tiazac	X	X	
	Cardizem LA	X	X	
Dihydropyridines				
Amlodipine (Norvasc)	N/A	X	X	
Felodipine (Plendil)	N/A	X		
Isradipine (Dynacirc)	**IR**	X		
	CR	X		
Nicardipine **(Cardene)**	IR	X		
	SR	X		
Nifedipine	IR		X	
	Procardia XL	X	X	
	Adalat CC	X		
Nimodipine (Nimotop)	N/A			Subarachnoid hemorrhage
Nisoldipine (Sular)	N/A	X		

Note: bolded drugs designate that there are no generics on the market
IR = immediate release
SR = sustained release
ER = extended release
CR = controlled release

ALPHA-BLOCKERS

Figure 3: MHS Alpha-Blocker Utilization, Prescriptions Filled

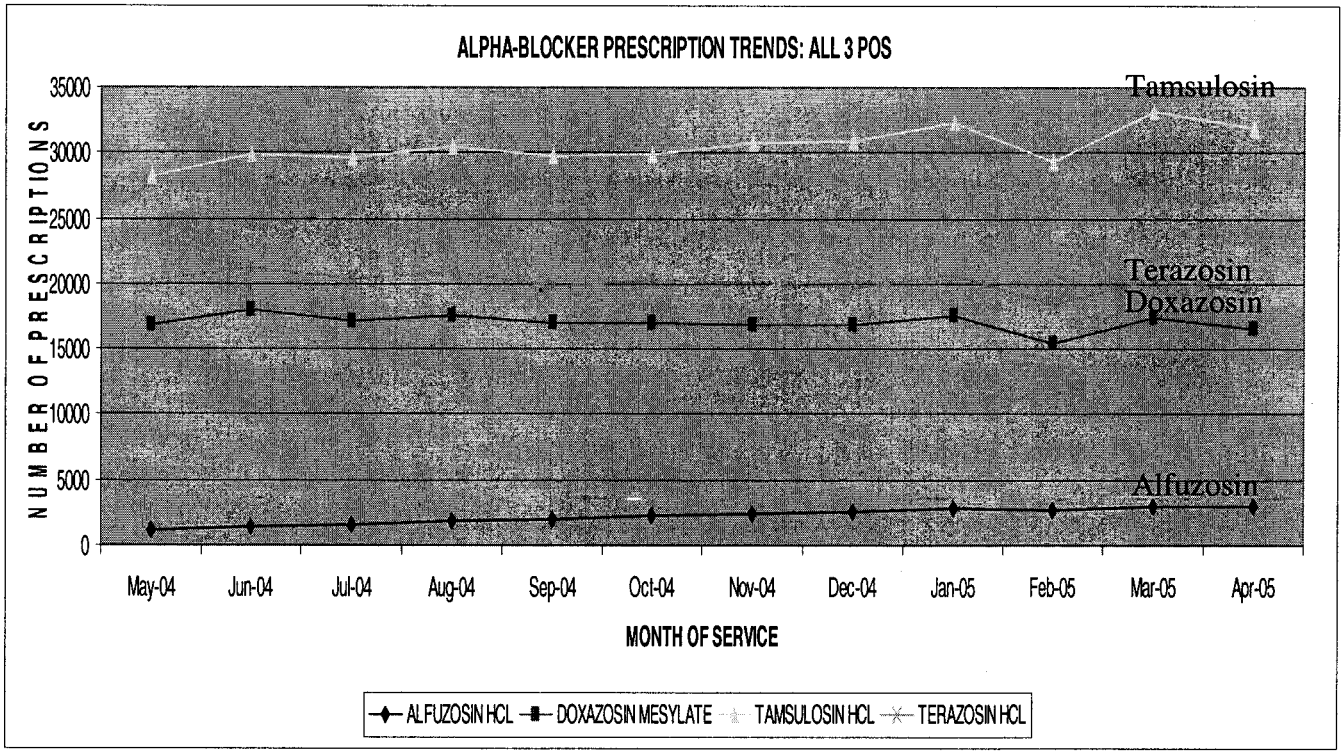

Table 7: Alpha-Blockers Used In Benign Prostatic Hyperplasia (BPH) Available In the United States

Generic Name	Brand Name (Manufacturer)	Selectivity (Generation)	Availability	FDA Approval Date	Uniform Formulary Recommendation
Terazosin	Hytrin (Abbott, generic)	Non-uroselective (2nd generation)	1 mg, 2 mg, 5 mg, 10 mg tablets and capsules generic tabs/caps available	08/07/1987 tablets 12/14/1995 capsules	Formulary
Doxazosin	Cardura (Pfizer, generic)	Non-uroselective (2nd generation)	1 mg, 2 mg, 4 mg, 8 mg tablets (generics available) 4 mg, 8 mg XL tablets (no generics available)	11/02/1990 tablets 02/22/2005 XL tablets	Formulary
Tamsulosin	Flomax (Boehringer Ingelheim)	Uroselective (3rd generation)	0.4 mg capsule no generics available	4/15/1997	Non-Formulary
Alfuzosin	Uroxatral (Sanofi-Synthelabo)	Uroselective (3rd generation)	10 mg ER tablet no generics available	06/12/2003	Formulary

UNIFORM FORMULARY IMPLEMENTATION PLAN SUMMARY

Table 7: Uniform Formulary Implementation Plan Summary

Drug Class	Total Number of Beneficiaries Affected	Beneficiaries Affected by POS	Implementation Plan (First Wednesday after X days after the final decision date)	Justification
Proton Pump Inhibitors	138,739 (13% of patients receiving PPIs)	MTF: 6,691 Retail: 117,520 Mail: 14,528	90-Days	Based on the substantial number of beneficiaries
Angiotensin Receptor Blockers	2,184 (0.5% of patients receiving ARB)	MTF: 13 Retail: 1,644 Mail: 527	90-Days	Recommended 30-day implementation overturned; 90-day BAP recommendation accepted
Phosphodiesterase Inhibitors	128,007 (90% of patients receiving a PDE-5 Inhibitor)	MTF: 55,161 Retail: 49,850 Mail: 22,996	90-Days	Based on the substantial number of beneficiaries
Topical Antifungals	49,743 (13 % of patients receiving a Topical Antifungal)	MTF: 14,266 Retail: 33,430 Mail: 2,047	30-Days	Medication used to treat acute (rather than chronic) infections, not likely to require therapy change
Multiple Sclerosis Disease Modifying Drugs	0	MTF: 0 Retail: 0 Mail: 0	N/A	No medications moved to the non-formulary status on UF.
Angiotensin Converting Enzyme Inhibitors	158,101 (21% of patients receiving a ACE Inhibitor)	MTF: 77,159 Retail: 57,982 Mail: 22,959	120-Days	Based on the substantial number of beneficiaries
Calcium Channel Blockers	274,616 (73% of patients receiving a CCB)	MTF: 133,794 Retail: 101,345 Mail: 39,477	150-Days	Based on the substantial number of beneficiaries
Alpha-Blockers	89,926 (46 % of patients receiving an Alpha-Blocker)	MTF: 26,692 Retail: 47,674 Mail: 15,560	120-Days	Based on the substantial number of beneficiaries