State and Public School Life and Health Insurance Board Clinical and Fiscal Drug Utilization and Evaluation Committee
Minutes
April 5, 2010

The State and Public Life and Health Insurance Board, Drug Utilization and Evaluation Committee (DUEC) met on Monday, April 5, 2010 at 1:00 p.m., in the EBD Board Room, 501 Woodlane, Little Rock, AR.

Members present:
Dr. William Golden
Mark McGrew
Kat Neill
Larry Dickerson/Proxy
Robert Watson
Dr. Hank Simmons
Dr. Joe Stallings

Members absent:
Dr. James Bethea
Matthew Hadley

Jason Lee, Executive Director, Employee Benefits Division of DFA.

OTHERS PRESENT
Barry Fielder, NMHC; Jill Johnson, Clay Patrick, UAMS College of Pharmacy/EBRx; Leigh Ann Chrouch, Michelle Hazelett , Amy Tustison, Florence Marvin, Lori Eden, Ellen Justus, Sherry Bryant, Cathy Harris, EBD; Barbara Melugin, Health Advantage; Dwight Davis; Jeff Britt, Pfizer; Stein Baughman, GSK; Lance Stewart, Merck; Ronda Walthall, AHTD

CALL TO ORDER
Meeting was called to order by Dr. Golden.

APPROVAL OF MINUTES
The motion was made by Dr Golden to approve the January 11, 2010 minutes. Minutes were approved by consensus.

ANTIHYPERLIPIDEMIC DRUG COVERAGE *by Jill Johnson*
On October 1, 2009, reference based pricing was implemented for the antihyperlipidemic drug class of statins. This applied to equipotent doses of other statins to simvastatin 80mg. The committee reviewed Drug Safety Communication recently presented by the FDA.

Additionally, at the January 2010 DUEC meeting, there was discussion regarding applying the reference based pricing strategy to Vytorin (atorvastatin + ezetimibe). This led to further discussion regarding ezetimibe and its place in therapy. Johnson provided additional information that included the ACC statement on ENHANCE Trial and a comment from an additional study regarding statin therapy with ezetimibe or niacin in high-risk patients.

Vytorin contains a combination of ezetimibe and simvastatin. Both ezetimibe and simvastatin are cholesterol-lowering medicines. Vytorin reduces the amount of cholesterol (a type of fat) absorbed by the body and block the production of cholesterol in the body.

Zetia (ezetimibe) reduces the amount of cholesterol or other sterols that your body absorbs from your diet. Zetia is used to treat high cholesterol, along with a low-fat, low-cholesterol diet. It is sometimes given with other cholesterol-lowering medications. It is also used to treat high blood sitosterol and campesterol along with diet therapy.

Recommendation: Place Zetia at the tier 2 status w/PA requirement 1) intolerance to a statin, and 2) not at LDL goal. Zetia only available if failed high dose statin and niacin or intolerance to either drug or medical problems (severe drug interactions); effective at the beginning of next plan year for existing users and 07/01/2010 for new utilizers. ***Tier status correction made at the Board meeting on April 13TH – Zetia placed on tier 3.***

Vytorin – not covered. Exclude new users effective 7/1/2010. Current users will be grandfathered in at Tier 3 copay for a period of time determined by the Board.

The committee decided by consensus to approve the recommendation for Zetia and Vytorin.

The committee discussed implementing a standard policy for effective dates for incorporating changes to the formulary

Recommendation: Amend the practice and adopt as a policy, plan design changes that includes grandfathering of the drug when it moves through the tiers to occur at the beginning of the plan year

The committee decided by consensus to accept recommendation.

ANTIHYPERTENSIVE DRUGS (ARB's and related products) *by Jill Johnson*
At the January 2010 DUEC meeting, the topic of PA criteria for angiotensin receptor blockers (ARB's) and ARB containing products was tabled. Currently, all ARB's and ARB containing products (ARB/Thiazide combos, ARB/CCB combos, and Valturna (an ARB/Tekturna combo product) require PA if no previous history of an ARB or ARB containing product is seen in claims history.

Recommendation 1: Proposed new PA criteria is 1) intolerance to ACE inhibitor, or 2) in addition to an ACE inhibitor AND WITH the diagnosis of STEMI, or Heart Failure (EF < 40%; from the CHARM-Added trial). Renal disease was removed because the ON-TARGET Renal Outcomes subgroup had worse outcomes and included n>25,000 people, more than the COOPERATE trial. Add in Tekturna and Valturna (an ARB/Tekturna combo product).

Recommendation 2: Move Valturna to Tier 3

The committee decided by consensus to accept recommendation for angiotensin receptor blockers and ARB containing products.

REVIEW OF SELECT PREVIOUSLY EXCLUDED DRUGS *by Jill Johnson*
Stelara (ustekinumab) was previously excluded from coverage under the prescription drug benefit. Shortly after the last DUEC meeting, a trial was published that showed Stelara was superior to Enbrel (etanercept) for patients with moderate to severe plaque psoriasis. The committee reviewed the information from the trial.

Recommendation: cover Stelara at Tier 3 with PA required
Proposed PA criteria is 1) diagnosis of moderate to severe plaque psoriasis (indicated by a PASI score of at least 10 based on 0-72 scale) and involvement of at least 10% BSA, and 2) inadequate response, intolerance, or contraindication to at least one conventional systemic agent for the treatment of psoriases (i.e. methotrexate, cyclosporine, or psoralen plus ultraviolet A), and 3) not on concurrent TNF.

The committee decided by consensus to accept recommendation for Stelara.

TESTOSTERONE REPLACEMENT PRODUCT *by Jill Johnson*
The committee reviewed the Clinical Practice Guideline for Androgen Therapy in Women; a summary of evidence-based guidelines on the therapeutic use of Androgens in women.

Dr. Golden suggested they look at criteria that other insurance plan uses.

No action was taken by the committee.

NEW DRUGS *by Jill Johnson*

Drug Name	Tier

Fanapt **Exclude**

Fanapt is an atypical antipsychotic indicted for the acute treatment of schizophrenia in adults. Fanapt, like all other atypical antipsychotics, has a
Black Box Warning regarding an increased risk of mortality in elderly patients with dementia-related psychosis treated with antipsychotic drugs.

Oforta **T3 with PA**

Oforta™ (fludarabine phosphate tablets) for oral use is indicated as a single agent for the treatment of adult patients with B-cell chronic lymphocytic leukemia (CLL) whose disease has not responded to or has progressed during or after treatment with at least one standard alkylating-agent Containing regimen. (PA criteria: 1) CLL, or 2) Non-Hodgkin's Lymphoma)

Sumavel **Exclude**

Sumavel is a 5-HT receptor agonist indicated for the acute treatment of migraine attacks, with or without aura and the acute treatment of cluster headache episodes. It is a pre-filled, single-dose; needle-free subcutaneous delivery system containing 6mg of sumatriptan succinate

Soriatane **T3**

SORIATANE is indicated for the treatment of severe psoriasis in adults.
Due to the risk of severe birth defects, in females of reproductive potential
SORIATANE should be reserved for nonpregnant patients with severe psoriasis who are unresponsive to other therapies or whose clinical condition contraindicates the use of other treatments.

Wilate **Not applicable**

Wilate is a von Willebrand Factor/Coagulation Factor VIII Complex
(Human) indicated for the treatment of spontaneous and trauma-induced bleeding episodes in patients with severe von Willebrand disease (VWD) as well as patients with mild or moderate VWD in whom the use of desmopressin is known or suspected to be ineffective or contraindicated.

Actemra **T3w/PA**

Actemra is a recombinant humanized anti-human interleukin-6 (IL-6) receptor inhibitor indicated for the treatment of adult patients with moderately-to-severely active Rheumatoid Arthritis (RA) who have had an inadequate response to one or more Tissue Necrosis Factor (TNF) antagoinist therapies.

Victoza **Exclude**

Victoza is a glucagon-like peptide-1 (GLP-1) receptor agonist indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Drug Name	Tier

Zyprexa Relprevv Inj **Exclude**
ZYPREXA® RELPREVV™ is a long-acting atypical antipsychotic for intramuscular injection indicated for the treatement of schizophrenia.

Ampyra **Exclude**
Ampyra is a broad spectrum potassium channel blocker indicated to
Improve walking in patients with multiple sclerosis (MS) demonstrated by an increase in walking speed. It is the first oral therapy approved for MS, the first therapy specifically approved to treat a symptom of MS, and the first new therapy for MS since 2004. Ampyra will likely be used in addition to the biologic MS agents.

Xiaflex inj **Not applicable (medical)**
Xiaflex is indicated for the treatment of adult patients with Dupuytren's contracture with a palpable cord. Xiaflex is designed to reduce collagen deposits and scar tissue in the hands stemming from Dupuytren's contracture.

Cayston Inh **T3w/PA**
Cayston is indicated to improve respiratory symptoms in cystic fibrosis (CF) patients with Pseudomonas aeruginosa. Cayston provides an alternative to Tobi but it does require reconstiatution prior to use as opposed to Tobi's availability in ready to use solution. Also, Cayston is dosed three times per day compared toTobi at twice daily dosing. (PA criteria: 1) DX of cystic fibrosis, and 2) known pulmonary infection with Pseudomonas aeruginosa, and 3) on concurrent bronchodilator therapy.)

Mirapex ER **T3**
Extended release version of pramipexole indicated for the treatment of early idiopathic Parkinson's disease in once daily dosing compared to the 3x per day dosing of the immediate release generic product.

Adrenaclick **T3**
Is a single-dose epinephrine auto-injector used for the treatment of anaphylaxis

Neutrasal Powder **Exclude**
Powder for Supersaturated Calcium Phosphate Rinse is indicated for the dryness of the mouth (hyposalivation, xerostomia)

E-Z-Disk **Exclude**
Barium sulfate is a radiopaque agent. Radiopaque agents are used to help diagnose certain medical problems.

Johnson clarified she proposed in January 2010 DUEC meeting that the drug Valturna be placed on tier 3, but the minutes indicate tier 2 status. Valturna is used to treat high blood pressure (hypertension).

The committee decided by consensus to approve recommendations for new drugs and Valturna.

ELECTION OF DUEC CHAIRMAN *by Jason Lee, EBD Director*
Neill made the motion to nominate Dr. Golden as Chairman of the DUEC. Dickerson seconded. Dickerson made the motion that nominations cease. Stallings seconded and made the motion that Golden be elected by acclamation. Dickerson seconded. By consensus, the motion to cease nominations and elect Dr. Golden passed.

The committee decided by consensus not to appoint a Vice-chairman of the committee. The Chairman will appoint a member of the committee to fill the seat of the chairman in his absence.

Meeting adjourned.

The following pages
were made available to
attendees of the meeting

Arkansas State & Public School Employees

DUEC Meeting

April 5, 2010

AGENDA

State and Public School Life and Health Insurance Board
Clinical and Fiscal Drug Utilization and Evaluation Committee
EBD Board Room, 501 Woodlane, Suite 500
April 5th, 2010

1. Call to Order/Approval of Minutes.....Dr. William Golden
2. Antihyperlipidemic Drug Coverage.....Barry Fielder/Jill Johnson
    a. Vytorin and Zetia Utilization
    b. Simvastatin 80mg
3. Antihypertensive Drugs (ARB's and related products).....Jill Johnson
4. Review of select previously excluded drugs.....Jill Johnson
    a. Stelara
5. Testosterone Replacement Products.....Jill Johnson
6. New Drugs.....Jill Johnson
7. Adjournment

Arkansas State and Public School Employees
Prescription Drug Program
Antihyperlipidemic Drug Coverage

On October 1, 2009, reference based pricing was implemented for the antihyperlipidemic drug class of statins. This applied to equipotent doses of other statins to simvastatin 80mg. An FDA Drug Safety Communication was recently provided by the FDA and is included for your review and discussion.

Additionally, at the January 2010 DUEC meeting, there was discussion regarding applying the reference based pricing strategy to Vytorin (atorvastatin + ezetimibe). This led to further discussion regarding ezetimibe and its place in therapy. Additional information provided includes the ACC statement on ENHANCE Trial and a comment from an additional study regarding statin therapy with ezetimibe or niacin in high-risk patients.

Options for consideration regarding Zetia (ezetimibe) and Vytorin coverage, based on the ENHANCE trial, include:

- exclude Zetia (ezetimibe) in all forms from coverage
- place a PA requirement on Zetia with the criteria of 1) intolerance to a statin, and 2) not at LDL goal
- Apply reference based pricing to Vytorin

FDA Drug Safety Communication: Ongoing safety review of high-dose Zocor* (simvastatin) and increased risk of muscle injury

Safety Announcement

[3-19-2010] Based on review of data from a large clinical trial and data from other sources, the U.S. Food and Drug Administration (FDA) is informing the public about an increased risk of muscle injury in patients taking the highest approved dose of the cholesterol-lowering medication, Zocor (simvastatin) 80 mg, compared to patients taking lower doses of simvastatin and possibly other drugs in the "statin" class.

The clinical trial data being reviewed is from the **S**tudy of the **E**ffectiveness of **A**dditional **R**eductions in **C**holesterol and **H**omocysteine (SEARCH) trial. The agency is also reviewing data from other clinical trials, observational studies, adverse event reports, and data on prescription use of simvastatin to better understand the relationship between high-dose simvastatin use and muscle injury (see Data Summary below).

The muscle injury, also called myopathy, is a known side effect with all statin medications. Patients with myopathy generally have muscle pain, tenderness or weakness, and an elevation of a muscle enzyme in the blood (creatine kinase). The higher the dose of statin used, the greater the risk of developing myopathy. The risk of myopathy is also increased when simvastatin, especially at the higher doses, is used with certain drugs (see Simvastatin Dose Limitations below).

The most serious form of myopathy is called rhabdomyolysis. It occurs when a protein (myoglobin) is released as muscle fibers break down. Myoglobin can damage the kidneys. Patients with rhabdomyolysis may have dark or red urine and fatigue, in addition to their muscle symptoms. Damage to the kidneys from rhabdomyolysis can be so severe that patients may develop kidney failure, which can be fatal.

Known risk factors for developing rhabdomyolysis include age (> 65 years), low thyroid hormone levels (hypothyroidism), and poor kidney function. Myopathy and rhabdomyolysis are listed as possible side effects in the simvastatin and other statin drug labels.

Healthcare professionals should:

- Understand that rhabdomyolysis is a rare adverse event reported with all statins.
- Be aware of the potential increased risk of muscle injury with the 80 mg dose of simvastatin compared to lower doses of simvastatin and possibly other statin drugs.
- Follow the recommendations in the simvastatin label regarding drugs that may increase the risk for muscle injury when used with simvastatin (see Simvastatin Dose Limitations below).

Patients should:

- Not stop taking simvastatin unless told to by their healthcare professional.
- Talk to their healthcare professional about any questions they have about the use of simvastatin.
- Call their healthcare professional if they experience any of the following: muscle pain, tenderness or weakness, urine that is dark or red-colored, or unexplained tiredness.

This communication is in keeping with FDA's commitment to inform the public about its ongoing safety review of drugs. The agency will update the public as soon as this review is complete.

**Simvastatin is sold as a single-ingredient generic medication and as the brand-name, Zocor. It is also sold in combination with ezetimibe as Vytorin; and niacin as Simcor.*

Additional Information for Patients

Patients currently using 80 mg simvastatin should:

- Know that rhabdomyolysis is a rare side effect reported with all statin medications.
- Not stop taking simvastatin unless told to by their healthcare professional.
- Review their medical history and current medications with their healthcare professional to determine if they should continue using simvastatin.
- Talk to their healthcare professional about any questions or concerns they have about simvastatin.
- Call their healthcare professional if they have muscle pain, tenderness or weakness, dark or red colored urine, or unexplained tiredness.
- Report any side effects with simvastatin to FDA's MedWatch program using the information at the bottom of the page in the "Contact Us" box.

Additional Information for Healthcare Professionals

FDA recommends that healthcare professionals should:

- Understand that rhabdomyolysis is a rare adverse event reported with all statins.
- Be aware of the potential increased risk of muscle injury with the 80 mg dose of simvastatin compared to lower doses of simvastatin and possibly other statin drugs.
- Review patients' medical history and medications to determine if simvastatin is clinically appropriate.
- Discuss with patients the benefits and risks, including the risk of myopathy and rhabdomyolysis, of simvastatin therapy.
- Be aware of potential drug-drug interactions with simvastatin.
- Report any adverse events associated with the use of simvastatin to FDA's MedWatch program using the information in the "Contact Us" box at the bottom of the page.

Data Summary

FDA's review of the SEARCH trial is part of the agency's continuing effort to evaluate the risk of muscle injury with simvastatin; this review includes evaluating data from clinical trials, observational studies, and adverse event reports, as well as data on prescription use of simvastatin.

The SEARCH trial evaluated over 6.7 years the number of major cardiovascular events (heart attack, revascularization, and cardiovascular death) in 6031 patients taking 80 mg of simvastatin compared to 6033 patients taking 20 mg of

simvastatin. All patients in the study had previously had a heart attack.

Preliminary SEARCH trial results revealed that more patients in the simvastatin 80 mg group developed myopathy compared to patients in the simvastatin 20 mg group (52 [0.9%] cases compared to 1 case [0.02%]). Further, FDA's preliminary analyses of the primary data suggest that 11 (0.2%) of the patients in the simvastatin 80 mg group developed rhabdomyolysis compared to no patients in the simvastatin 20 mg group.

In 2008, the agency alerted the public about an increased risk of developing rhabdomyolysis when doses greater than 20 mg of simvastatin are given with amiodarone. The agency also included information about this drug interaction in its Summer 2008 issue of the FDA Drug Safety Newsletter[1] and in its November 2008 Patient Safety News broadcast[2].

In March 2010, FDA approved a labeling revision for simvastatin based on interim results from an ongoing clinical trial – the Heart Protection Study 2 (HPS2). The revised label states that patients of Chinese descent should not receive simvastatin 80 mg with cholesterol-modifying doses of niacin-containing products. Further, the revised label recommends caution when such patients are treated with simvastatin 40 mg or less in combination with cholesterol-modifying doses of niacin-containing products. The interim HPS2 results showed that the incidence of myopathy was higher in patients of Chinese descent (0.43%) compared with patients not of Chinese descent (0.03%) taking 40 mg simvastatin plus cholesterol-modifying doses (≥1 g/day) of a niacin-containing product. It is not known if the increased risk for myopathy observed in these patients applies to other patients of Asian descent.

Moreover, FDA has requested that the sponsor of simvastatin change the product labeling to instruct healthcare professionals to avoid prescribing simvastatin doses greater than 40 mg daily when patients are taking the medication diltiazem, due to an increased risk for myopathy.

A 2010 review of prescription drug use data conducted by FDA found that, despite dose limitations and drug-drug interaction precautions included in the simvastatin drug label, patients are continuing to be prescribed higher doses of simvastatin with other medications that are known to increase the risk for rhabdomyolysis (see Simvastatin Dose Limitations below).

It is important for healthcare professionals to consider the potential risks and known benefits of simvastatin compared to

other cholesterol-lowering therapies when deciding to use simvastatin. Healthcare professionals should also carefully review patients' medications for potential drug-drug interactions before prescribing or dispensing simvastatin.

This communication is in keeping with FDA's commitment to inform the public about its ongoing safety review of drugs. The agency will update the public as soon as this review is complete.

Simvastatin Dose Limitations

These limitations apply to ALL patients taking simvastatin.

Do not use simvastatin with these medications: Itraconazole , Ketoconazole , Erythromycin , Clarithromycin , Telithromycin , HIV protease inhibitors , Nefazodone
Do not use more than 10mg of simvastatin with these medications: Gemfibrozil , Cyclosporine, Danazol ,
Do not use more than 20mg of simvastatin with these medications: Amiodarone , Verapamil
Do not use more than 40mg of simvastatin with this medication: Diltiazem

Related Information

- FDA Warns about Increased Risk of Muscle Injury with Zocor[3]
FDA News Release (3/19/2010)
- Simvastatin (marketed as Zocor) Information[4]
- FDA Drug Safety Newsletter - Volume 1, Number 4, Summer 2008[5]
- Patient Safety News, November 2008[6]

ACC Statement on ENHANCE Trial

January 15, 2008
The ENHANCE (Effect of Combination Ezetimibe and High-Dose Simvastatin vs. Simvastatin Alone on the Atherosclerotic Process in Patients with Heterozygous Familial Hypercholesterolemia) trial results were released by Merck and Schering-Plough Pharmaceuticals on January 14, 2008. The results of the trial show no benefit from the combination of ezetimibe (Zetia) and simvastatin (sold together as Vytorin) over simvastatin alone in terms of affecting the rate of atherosclerosis progression.

The study involved 720 patients with heterozygous familial hypercholesterolemia and showed no significant difference in the primary endpoint between patients treated with ezetimibe and simvastatin versus patients treated with simvastatin alone over a two-year period. The study was designed to prove that Vytorin could slow the growth of plaque in carotid arteries supplying the brain more than simvastatin alone. Media reports indicate

that the results of the trial show no benefit from the combination of ezetimibe (Zetia) and simvastatin (sold together as Vytorin) over simvastatin alone.

The American College of Cardiology recommends that major clinical decisions not be made on the basis of the ENHANCE study alone.

According to the American College of Cardiology (ACC), this study deserves serious thought and follow-up. The overall incidence rates of cardiac events were nearly identical between both treatment groups, and both medicines were generally well tolerated. There should no be reason for patients to panic. The difference in IMT changes between the simvastatin group and the Vytorin group was 0.006 mm vs. 0.011 mm.

Health care professionals should speak to their concerned patients using this drug. The ACC is also releasing a public statement explaining that this is not an urgent situation and patients should never stop taking any prescribed medications without first discussing the issue with their health care professional. Further research will be needed in this area to provide conclusive evidence about which lipid lowering strategy is preferred (statin alone vs. statin plus ezetimibe).

Furthermore, the ACC notes that this trial is an imaging study and not a clinical-outcome study. Conclusions should not be made until the three large clinical-outcome trials are presented within the next two to three years. The ACC recommends that Zetia remain a reasonable option for patients who are currently on a high dose statin but have not reached their goal. The ACC also notes that Zetia is a reasonable option for patients who cannot tolerate statins or can only tolerate a low dose statin.

Reports also indicate that the ENHANCE trial has been submitted as an abstract to be presented at the upcoming American College of Cardiology Scientific Session in March, 2008. The late-breaking clinical trial selections by the meeting co-chairs are scheduled to occur in late January.

For more information on the ENHANCE trial, please visit Cardiosource at http://www.cardiosource.com/clinicaltrials/trial.asp?trialID=1640.

ARBITER 6–HALTS trial (Arterial Biology for the Investigation of the Treatment Effects of Reducing Cholesterol 6–HDL and LDL Treatment Strategies; NCT00397657).5 The trial was designed to address the question of whether the addition of ezetimibe (to further reduce LDL cholesterol levels) or the addition of niacin (to improve levels of multiple lipoproteins) is more effective in decreasing
the progression of carotid intima–media thickness in patients receiving statin therapy.

Statin Therapy with Ezetimibe or Niacin in High-Risk Patients

John J.P. Kastelein, M.D., Ph.D., and Michiel L. Bots, M.D., Ph.D., November 2009

"However, to date, only high-dose statin therapy has shown a clear clinical benefit beyond a moderate reduction of the LDL cholesterol level.1 Strategies to lower LDL cholesterol further, through the addition of ezetimibe, are not supported by definitive evidence.2-4 Two studies of clinical end points involving ezetimibe are ongoing: one of patients with renal failure (SHARP [Study of Heart and Renal Protection]; ClinicalTrials.gov number, NCT00125593), and the other of patients with the acute coronary syndrome (IMPROVE-IT [Improved Reduction of Outcomes: Vytorin Efficacy International Trial]; NCT00202878). The large number of hard clinical end points (>5000) required to achieve sufficient statistical power in IMPROVE-IT makes it uncertain whether the trial will ever reach completion."

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RXT3100D - Therapeutic Detail Market Share Cost per Day

Between Jan 1, 2010 and Mar 28, 2010

* Market Share For Selected Filter Criteria

Drug Label Name	Utilizing Members	Number of Rxs	Quantity	Days Supply	AWP Cost	Ingredient Cost Paid	Total Dispensing Fee	Plan Cost Paid Amount	Average Plan Paid Amount	% of Total Plan Cost	Market Share	Average Days Supply	Average Amount Due/ Unit	Cost/ Day
[redacted]														
LIPITOR TAB 80MG	238	680	21,420	21,913	$102,371.07	$91,940.90	$2,394.50	$71,632.44	$105.34	14.2%	2.05%	0.98	$3.34	$3.27
LIPITOR TAB 20MG	454	949	29,368	29,645	$139,158.24	$124,264.91	$3,239.85	$34,040.05	$35.87	6.75%	2.87%	0.99	$1.16	$1.15
LIPITOR TAB 40MG	382	811	24,810	25,201	$117,951.30	$105,909.88	$2,781.32	$28,004.27	$34.53	5.55%	2.45%	0.98	$1.13	$1.11
LIPITOR TAB 10MG	383	1,013	31,469	31,513	$104,903.01	$94,271.29	$3,485.71	$19,589.22	$19.34	3.88%	3.06%	1.00	$0.62	$0.62
CRESTOR TAB 20MG	265	776	23,737	23,662	$107,751.25	$96,881.59	$2,716.03	$75,528.42	$97.33	14.97%	2.34%	1.00	$3.18	$3.19
CRESTOR TAB 10MG	635	1,462	43,920	44,330	$198,199.14	$178,085.42	$5,066.33	$38,750.55	$26.51	7.68%	4.42%	0.99	$0.88	$0.87
CRESTOR TAB 40MG	72	220	6,669	6,669	$30,322.84	$27,264.69	$769.00	$21,114.90	$95.98	4.18%	0.66%	1.00	$3.17	$3.17
CRESTOR TAB 5MG	127	276	8,246	8,417	$37,126.58	$33,410.33	$956.06	$7,575.41	$27.45	1.5%	0.83%	0.98	$0.92	$0.90
SIMVASTATIN TAB 20MG	3308	6,965	233,300	232,724	$1,138,480.94	$96,776.01	$39,069.52	$60,883.20	$8.74	12.07%	21.04%	1.00	$0.26	$0.26
SIMVASTATIN TAB 40MG	4117	8,606	287,297	287,721	$1,400,236.65	$94,307.60	$48,124.93	$50,644.13	$5.88	10.04%	25.99%	1.00	$0.18	$0.18
SIMVASTATIN TAB 80MG	1361	2,787	93,414	95,917	$435,174.94	$36,805.77	$16,008.23	$22,262.34	$7.99	4.41%	8.42%	0.97	$0.24	$0.23
SIMVASTATIN TAB 10MG	488	1,013	35,032	34,936	$97,582.59	$7,959.93	$5,628.93	$2,663.05	$2.63	0.53%	3.06%	1.00	$0.08	$0.08
SIMVASTATIN TAB 5MG	19	46	1,380	1,380	$2,897.61	$114.05	$282.00	$0.00	$0.00	0%	0.14%	1.00	$0.00	$0.00
PRAVASTATIN TAB 40MG	1702	3,210	130,108	119,529	$623,626.80	$60,457.31	$3,969.41	$29,876.65	$9.31	5.92%	9.7%	1.09	$0.23	$0.25
PRAVASTATIN TAB 20MG	854	1,589	58,054	57,829	$189,652.64	$25,110.69	$2,241.68	$14,376.10	$9.05	2.85%	4.8%	1.00	$0.25	$0.25
PRAVASTATIN TAB 80MG	226	429	13,965	14,010	$66,954.34	$20,105.04	$975.99	$5,177.37	$12.07	1.03%	1.3%	1.00	$0.37	$0.37
PRAVASTATIN TAB 10MG	127	238	8,225	8,165	$26,443.18	$1,284.58	$1,197.46	$578.55	$2.43	0.11%	0.72%	1.01	$0.07	$0.07
LOVASTATIN TAB 20MG	481	941	40,938	34,516	$97,035.86	$12,552.98	$1,357.90	$9,346.34	$9.93	1.85%	2.84%	1.19	$0.23	$0.27
LOVASTATIN TAB 40MG	328	651	25,416	22,188	$108,400.21	$25,690.23	$1,450.99	$8,958.69	$13.76	1.78%	1.97%	1.15	$0.35	$0.40
LOVASTATIN TAB 10MG	93	178	6,541	6,421	$8,800.81	$651.10	$856.98	$184.02	$1.03	0.04%	0.54%	1.02	$0.03	$0.03
LESCOL XL TAB 80MG	25	65	1,952	1,952	$7,900.77	$7,105.21	$222.96	$1,756.71	$27.03	0.35%	0.2%	1.00	$0.90	$0.90
PRAVACHOL TAB 10MG	2	2	180	180	$773.08	$491.40	$0.00	$311.40	$155.70	0.06%	0.01%	1.00	$1.73	$1.73
PRAVACHOL TAB 80MG	2	3	90	90	$576.41	$518.79	$10.50	$245.36	$81.79	0.05%	0.01%	1.00	$2.73	$2.73
PRAVACHOL TAB 20MG	2	5	210	210	$916.53	$503.06	$14.00	$130.54	$26.11	0.03%	0.02%	1.00	$0.62	$0.62
LESCOL CAP 20MG	4	14	480	480	$1,542.26	$1,171.23	$45.50	$238.42	$17.03	0.05%	0.04%	1.00	$0.50	$0.50
LESCOL CAP 40MG	4	9	300	270	$947.48	$852.75	$31.50	$158.32	$17.59	0.03%	0.03%	1.11	$0.53	$0.59

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RXT3100D - Therapeutic Detail Market Share Cost per Day

Between Jan 1, 2010 and Mar 28, 2010

* Market Share For Selected Filter Criteria

	Drug Label Name	Utilizing Members	Number of Rxs	Quantity	Days Supply	AWP Cost	Ingredient Cost Paid	Total Dispensing Fee	Plan Cost Paid Amount	Average Plan Paid Amount	% of Total Plan Cost	Market Share	Average Days Supply	Average Amount Due/ Unit	Cost/ Day
ZOCOR	TAB 20MG	2	3	90	90	$504.96	$454.47	$10.50	$119.99	$40.00	0.02%	0.01%	1.00	$1.33	$1.33
ZOCOR	TAB 40MG	1	3	90	90	$504.96	$454.47	$10.50	$119.99	$40.00	0.02%	0.01%	1.00	$1.33	$1.33
ZOCOR	TAB 80MG	1	1	30	30	$168.31	$151.48	$3.50	$94.98	$94.98	0.02%	0%	1.00	$3.17	$3.17
SIMCOR	TAB 500-20MG	55	138	4,525	4,165	$11,480.92	$10,297.97	$481.03	$258.66	$1.87	0.05%	0.42%	1.09	$0.06	$0.06
SIMCOR	TAB 1000-20	5	9	360	330	$1,615.48	$1,453.93	$31.50	$0.00	$0.00	0%	0.03%	1.09	$0.00	$0.00
ADVICOR	TAB 1000-20	1	2	60	60	$250.15	$225.14	$7.00	$0.00	$0.00	0%	0.01%	1.00	$0.00	$0.00
ADVICOR	TAB 1000-40	2	6	180	180	$855.74	$768.67	$21.00	$0.00	$0.00	0%	0.02%	1.00	$0.00	$0.00
ADVICOR	TAB 500-20MG	2	9	270	270	$978.99	$881.10	$31.50	$0.00	$0.00	0%	0.03%	1.00	$0.00	$0.00
Total for Drug Class: 3940 - HMG-COA REDUCTASE INHIBITORS*		**15,768**	**33,109**	**1,132,126**	**1,115,083**	**$5,062,086.07**	**$1,159,173.97**	**$143,493.81**	**$504,620.07**	**$15.24**	**100%**	**100%**	**1.02**	**$0.45**	**$0.45**
Total for Drug Group: 39 - ANTIHYPERLIPIDEMICS*		**15,768**	**33,109**	**1,132,126**	**1,115,083**	**$5,062,086.07**	**$1,159,173.97**	**$143,493.81**	**$504,620.07**	**$15.24**	**100%**	**100%**	**1.02**	**$0.45**	**$0.45**

Selected Filters

Client: State of Arkansas, Account: ALL; Group: ALL; For: Select Date Range;Date Submitted:Jan 1, 2010 and Mar 28, 2010; Pharmacy Type: All; Drug Type: All; Report Description: No

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RXT3100D - Therapeutic Detail Market Share Cost per Day

Between Jan 1, 2010 and Mar 28, 2010 *

* Market Share For Selected Filter Criteria

	Drug Label Name	Utilizing Members	Number of Rxs	Quantity	Days Supply	AWP Cost	Ingredient Cost Paid	Total Dispensing Fee	Plan Cost Paid Amount	Average Plan Paid Amount	% of Total Plan Cost	Market Share	Average Days Supply	Average Amount Due/ Unit	Cost/ Day
Drug Group: 39 - ANTIHYPERLIPIDEMICS															
Drug Class: 3999 - ANTIHYPERLIPIDEMICS - COMBINATIONS															
VYTORIN	TAB 10-40MG	379	1,091	34,113	34,019	$137,784.11	$123,851.02	$3,818.00	$59,421.07	$54.46	48.36%	48%	1.00	$1.74	$1.75
VYTORIN	TAB 10-20MG	255	753	23,210	23,237	$93,870.25	$84,351.30	$2,638.50	$40,367.81	$53.61	32.85%	33.13%	1.00	$1.74	$1.74
VYTORIN	TAB 10-80MG	123	371	11,413	11,443	$46,098.94	$41,464.39	$1,297.50	$19,834.02	$53.46	16.14%	16.32%	1.00	$1.74	$1.73
VYTORIN	TAB 10-10MG	17	58	1,860	1,860	$7,529.96	$6,765.30	$203.00	$3,248.30	$56.01	2.64%	2.55%	1.00	$1.75	$1.75
Total for Drug Class: 3999 - ANTIHYPERLIPIDEMICS - COMBINATIONS*		774	2,273	70,596	70,559	$285,283.27	$256,432.01	$7,957.00	$122,871.20	$54.06	100%	100%	1.00	$1.74	$1.74
Total for Drug Group: 39 - ANTIHYPERLIPIDEMICS*		774	2,273	70,596	70,559	$285,283.27	$256,432.01	$7,957.00	$122,871.20	$54.06	100%	100%	1.00	$1.74	$1.74

Selected Filters

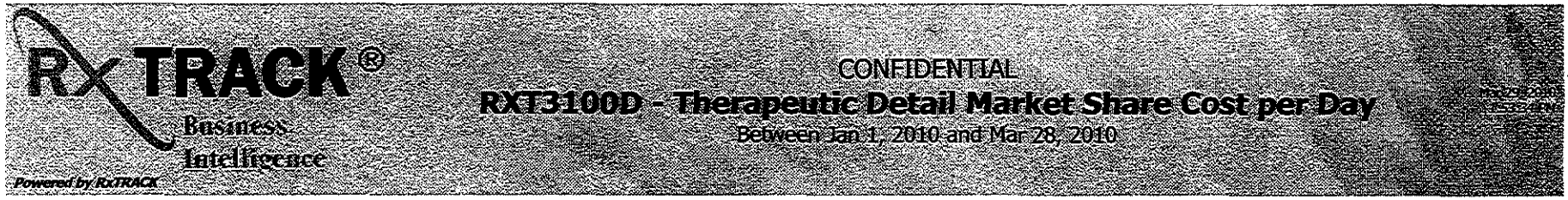
Client: State of Arkansas, Account: ALL; Group: ALL; For: Select Date Range;Date Submitted:Jan 1, 2010 and Mar 28, 2010; Pharmacy Type: All; Drug Type: All; Report Description: No

RXT3100D - Therapeutic Detail Market Share Cost per Day

Between Jan 1, 2010 and Mar 28, 2010

* Market Share For Selected Filter Criteria

	Drug Label Name	Utilizing Members	Number of Rxs	Quantity	Days Supply	AWP Cost	Ingredient Cost Paid	Total Dispensing Fee	Plan Cost Paid Amount	Average Plan Paid Amount	% of Total Plan Cost	Market Share	Average Days Supply	Average Amount Due/ Unit	Cost/ Day
[redacted]															
ZETIA	TAB 10MG	535	1,622	51,102	50,573	$203,817.80	$182,403.93	$5,663.50	$86,839.24	$53.54	100%	100%	1.01	$1.70	$1.72
[redacted]															
Total for Drug Class: 3930 - INTESTINAL CHOLESTEROL ABSORPTION INHIBITORS*		535	1,622	51,102	50,573	$203,817.80	$182,403.93	$5,663.50	$86,839.24	$53.54	100%	100%	1.01	$1.70	$1.72
Total for Drug Group: 39 - ANTIHYPERLIPIDEMICS*		535	1,622	51,102	50,573	$203,817.80	$182,403.93	$5,663.50	$86,839.24	$53.54	100%	100%	1.01	$1.70	$1.72



Selected Filters

Client: State of Arkansas, Account: ALL; Group: ALL; For: Select Date Range;Date Submitted:Jan 1, 2010 and Mar 28, 2010; Pharmacy Type: All; Drug Type: All; Report Description: No

Arkansas State and Public School Employees
Prescription Drug Program
Antihypertensive Drug Review

At the January 2010 DUEC meeting, the topic of PA criteria for angiotensin receptor blockers (ARB's) and ARB containing products was tabled. Currently, all ARB's and ARB containing products (ARB/Thiazide combos, ARB/CCB combos, and Valturna (an ARB/Tekturna combo product) require PA if no previous history of an ARB or ARB containing product is seen in claims history. The one exception is Tekturna, which is addressed below.

Current PA criteria for an ARB is 1) past use or side effect of ACE inhibitor (no automatic lookback) or 2) if the patient requires initial combination therapy of ACE Inhibitor + ARB including a diagnosis of ST elevation MI (Anterior, Renal Disease, or Heart Failure (EF $\leq$ 40%).

Proposed new PA criteria is 1) intolerance to ACE inhibitor, or 2) in addition to an ACE inhibitor AND WITH the diagnosis of STEMI, or Heart Failure (EF $\leq$ 40%; from the CHARM-Added trial). Renal disease was removed because the ON-TARGET Renal Outcomes subgroup had worse outcomes and included n>25,000 people, more than the COOPERATE trial.

COOPERATE trial – losartan + trandolapril vs either alone 1` composite doubling srCr or ESRD. 1` combo 11% vs 23% losartan vs 23% trandolapril, p 0.016, BP reduction similar.

	Ramipril n (%)	Telmisartan n (%)	Ramipril+ telmisartan n (%)	Telmisartan vs ramipril HR (95% CI)	p	Ramipril+ telmisartan vs ramipril HR (95% CI)	p
All dialysis doubling death)	1150 (13·4)	1147 (13·4)	1233 (14·5)	1·00 (0·92–1·09)	0·968	1·09 (1·01–1·18)	0·037
All dialysis and doubling	174 (2·03)	189 (2·21)	212 (2·49)	1·09 (0·89–1·34)	0·420	1·24 (1·01–1·51)	0·038
All dialysis	48 (0·56)	51 (0·60)	63 (0·74)	1·07 (0·72–1·58)	0·747	1·33 (0·92–1·94)	0·133
All death	1014 (11·8)	989 (11·6)	1065 (12·5)	0·98 (0·90–1·07)	0·641	1·07 (0·98–1·16)	0·144
Doubling	140 (1·63)	155 (1·81)	166 (1·95)	1·11 (0·88–1·39)	0·378	1·20 (0·96–1·50)	0·110
Acute dialysis	13 (0·15)	20 (0·23)	28 (0·33)	1·55 (0·77–3·11)	0·221	2·19 (1·13–4·22)	0·020
Chronic dialysis	33 (0·39)	31 (0·36)	34 (0·40)	0·94 (0·58–1·54)	0·817	1·05 (0·65–1·69)	0·854

Additionally, a PA requirement is recommended for Tekturna (aliskiren) as well, to keep coverage rules consistent.

Antihypertensive drug utilization is provided for reference.

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* Market Share For Selected Filter Criteria

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RXT3100D – Therapeutic Detail Market Share Cost per Day

Between Jan 1, 2010 and Mar 28, 2010

Drug Label Name	Utilizing Members	Number of Rxs	Quantity	Days Supply	AWP Cost	Ingredient Cost Paid	Total Dispensing Fee	Plan Cost Paid Amount	Average Plan Paid Amount	% of Total Plan Cost	Market Share	Average Days Supply	Average Amount Due/ Unit	Cost/ Day
DIOVAN HCT TAB 160/12.5	651	2,175	72,830	68,125	$227,080.74	$203,039.48	$7,613.97	$142,524.62	$65.53	7.98%	7.96%	1.07	$1.96	$2.09
DIOVAN HCT TAB 160/25MG	416	1,365	44,223	42,223	$156,472.98	$140,209.12	$4,777.55	$102,346.21	$74.98	5.73%	5%	1.05	$2.31	$2.42
DIOVAN HCT TAB 320/25MG	296	974	30,312	30,312	$135,825.34	$122,090.33	$3,411.52	$95,141.64	$97.68	5.33%	3.57%	1.00	$3.14	$3.14
DIOVAN HCT TAB 80/12.5	395	1,309	43,412	41,492	$124,523.55	$111,826.96	$4,579.50	$74,524.21	$56.93	4.17%	4.79%	1.05	$1.72	$1.80
DIOVAN HCT TAB 320/12.5	194	612	18,838	18,838	$74,571.03	$67,024.27	$2,142.00	$50,341.78	$82.26	2.82%	2.24%	1.00	$2.67	$2.67
AMLOD/BENAZP CAP 5-20MG	679	1,555	62,134	50,460	$177,622.47	$125,638.52	$8,832.00	$117,640.52	$75.65	6.59%	5.69%	1.23	$1.89	$2.33
AMLOD/BENAZP CAP 10-20MG	689	1,564	51,943	50,092	$172,502.70	$121,496.08	$9,138.34	$113,719.74	$72.71	6.37%	5.72%	1.04	$2.19	$2.27
AMLOD/BENAZP CAP 5-10MG	387	888	30,618	28,275	$82,885.99	$58,482.43	$5,092.50	$53,946.92	$60.75	3.02%	3.25%	1.08	$1.76	$1.91
AMLOD/BENAZP CAP 2.5-10MG	17	34	1,260	1,260	$3,344.67	$2,371.71	$191.00	$2,142.71	$63.02	0.12%	0.12%	1.00	$1.70	$1.70
LOTREL CAP 10-40MG	219	694	21,742	21,562	$108,942.31	$97,846.27	$2,425.50	$78,731.77	$113.45	4.41%	2.54%	1.01	$3.62	$3.65
LOTREL CAP 5-40MG	67	232	7,352	7,082	$30,291.61	$27,231.64	$812.00	$20,884.77	$90.02	1.17%	0.85%	1.04	$2.84	$2.95
LOTREL CAP 10-20MG	11	30	1,020	1,020	$4,643.85	$4,165.33	$101.50	$2,226.83	$74.23	0.12%	0.11%	1.00	$2.18	$2.18
LOTREL CAP 5-20MG	6	16	543	543	$2,110.29	$1,899.33	$56.00	$875.33	$54.71	0.05%	0.06%	1.00	$1.61	$1.61
LOTREL CAP 5-10MG	1	4	120	120	$449.58	$404.61	$14.00	$178.61	$44.65	0.01%	0.01%	1.00	$1.49	$1.49
AVALIDE TAB 300-12.5	152	494	15,902	15,692	$53,920.42	$48,510.36	$1,731.25	$34,581.61	$70.00	1.94%	1.81%	1.01	$2.17	$2.20
AVALIDE TAB 300-25MG	115	386	11,797	11,797	$44,102.57	$39,657.10	$1,359.50	$29,213.33	$75.68	1.64%	1.41%	1.00	$2.48	$2.48
AVALIDE TAB 150-12.5	133	417	13,710	13,085	$42,768.62	$38,422.98	$1,456.00	$26,686.58	$64.00	1.49%	1.53%	1.05	$1.95	$2.04
HYZAAR TAB 100-25	226	752	23,139	22,951	$85,723.29	$77,096.01	$2,632.00	$33,916.60	$45.10	1.9%	2.75%	1.01	$1.47	$1.48
HYZAAR TAB 50-12.5	104	322	10,764	9,714	$29,302.22	$26,268.79	$1,128.00	$8,325.10	$25.85	0.47%	1.18%	1.11	$0.77	$0.86
HYZAAR TAB 100-12.5	47	142	4,325	4,325	$16,062.85	$14,455.03	$497.00	$6,312.03	$44.45	0.35%	0.52%	1.00	$1.46	$1.46
BENICAR HCT TAB 40-25MG	176	519	15,806	15,820	$55,641.34	$50,050.34	$1,816.50	$20,239.40	$39.00	1.13%	1.9%	1.00	$1.28	$1.28
BENICAR HCT TAB 40-12.5	121	367	11,457	11,277	$36,739.33	$32,955.04	$1,281.88	$11,545.02	$31.46	0.65%	1.34%	1.02	$1.01	$1.02
BENICAR HCT TAB 20-12.5	114	310	10,194	9,474	$27,768.46	$24,986.91	$1,085.00	$7,165.27	$23.11	0.4%	1.13%	1.08	$0.70	$0.76
LISINOP/HCTZ TAB 20-12.5	1501	3,049	131,521	106,420	$160,618.23	$22,375.00	$15,602.88	$12,096.44	$3.97	0.68%	11.16%	1.24	$0.09	$0.11
LISINOP/HCTZ TAB 10-12.5	704	1,398	50,715	49,439	$56,932.35	$10,833.71	$7,126.55	$6,228.13	$4.46	0.35%	5.12%	1.03	$0.12	$0.13
LISINOP/HCTZ TAB 20-25MG	1091	2,242	83,088	78,987	$103,265.99	$11,697.55	$11,502.31	$4,798.33	$2.14	0.27%	8.21%	1.05	$0.06	$0.06
EXFORGE TAB 10-320MG	47	129	3,874	3,874	$17,525.28	$15,772.60	$451.50	$8,303.86	$64.37	0.47%	0.47%	1.00	$2.14	$2.14
EXFORGE TAB 5-320MG	36	114	3,420	3,420	$13,657.26	$12,291.52	$399.00	$6,000.70	$52.64	0.34%	0.42%	1.00	$1.75	$1.75
EXFORGE TAB 5-160MG	45	127	4,234	4,054	$13,335.54	$11,974.32	$444.50	$4,318.82	$34.01	0.24%	0.46%	1.04	$1.02	$1.07
EXFORGE TAB 10-160MG	27	75	2,250	2,250	$8,047.94	$7,242.70	$262.50	$3,005.20	$40.07	0.17%	0.27%	1.00	$1.34	$1.34
ATACAND HCT TAB 16-12.5	33	105	3,855	3,510	$12,461.99	$11,207.28	$366.50	$8,035.50	$76.53	0.45%	0.38%	1.10	$2.08	$2.29
ATACAND HCT TAB 32-12.5	33	120	3,692	3,662	$12,192.86	$10,973.18	$420.00	$7,733.18	$64.44	0.43%	0.44%	1.01	$2.09	$2.11

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* Market Share For Selected Filter Criteria

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RX13100D - Therapeutic Detail Market Share Cost per Day

Between Jan 1, 2010 and Mar 26, 2010

Drug Label Name	Utilizing Members	Number of Rxs	Quantity	Days Supply	AWP Cost	Ingredient Cost Paid	Total Dispensing Fee	Plan Cost Paid Amount	Average Plan Paid Amount	% of Total Plan Cost	Market Share	Average Days Supply	Average Amount Due/ Unit	Cost/ Day
ATACAND HCT TAB 32-25MG	5	13	510	510	$1,814.57	$1,620.70	$45.50	$1,156.20	$88.94	0.06%	0.05%	1.00	$2.27	$2.27
AZOR TAB 10-40MG	50	147	4,710	4,700	$20,234.16	$18,109.94	$507.50	$9,413.54	$64.04	0.53%	0.54%	1.00	$2.00	$2.00
AZOR TAB 5-40MG	22	63	2,025	1,965	$7,978.68	$7,130.26	$219.50	$3,395.39	$53.90	0.19%	0.23%	1.03	$1.68	$1.73
AZOR TAB 5-20MG	14	30	990	900	$3,124.44	$2,806.57	$105.00	$1,111.57	$37.05	0.06%	0.11%	1.10	$1.12	$1.24
AZOR TAB 10-20MG	8	22	676	676	$2,295.70	$2,066.06	$77.00	$633.42	$28.79	0.04%	0.08%	1.00	$0.94	$0.94
MICARDIS HCT TAB 80/12.5	48	167	5,464	5,138	$17,031.36	$15,319.92	$584.50	$5,781.06	$34.62	0.32%	0.61%	1.06	$1.06	$1.13
MICARDIS HCT TAB 80/25MG	40	109	3,245	3,245	$10,151.16	$9,125.90	$379.72	$3,176.60	$29.14	0.18%	0.4%	1.00	$0.98	$0.98
MICARDIS HCT TAB 40/12.5	25	64	1,920	1,920	$5,950.08	$5,330.69	$220.55	$1,711.24	$26.74	0.1%	0.23%	1.00	$0.89	$0.89
TARKA TAB 4-240 CR	46	154	4,776	4,626	$15,897.87	$14,269.18	$539.00	$5,561.02	$36.11	0.31%	0.56%	1.03	$1.16	$1.20
TARKA TAB 2-240 CR	10	34	1,140	991	$3,794.72	$3,403.14	$119.00	$1,482.14	$43.59	0.08%	0.12%	1.15	$1.30	$1.50
TARKA TAB 2-180 CR	11	36	1,088	1,088	$3,621.63	$3,257.82	$126.00	$1,223.82	$34.00	0.07%	0.13%	1.00	$1.12	$1.12
TARKA TAB 1-240 CR	1	5	300	150	$998.61	$898.75	$17.50	$616.25	$123.25	0.03%	0.02%	2.00	$2.05	$4.11
QNAPRIL/HCTZ TAB 20-12.5	58	133	5,547	4,405	$6,783.15	$5,215.52	$778.50	$4,524.02	$34.02	0.25%	0.49%	1.26	$0.82	$1.03
QNAPRIL/HCTZ TAB 20-25MG	27	61	2,223	2,083	$2,718.65	$2,121.83	$374.50	$1,786.33	$29.28	0.1%	0.22%	1.07	$0.80	$0.86
QNAPRIL/HCTZ TAB 10-12.5	16	32	1,176	1,086	$1,438.18	$1,178.40	$191.00	$1,009.40	$31.54	0.06%	0.12%	1.08	$0.86	$0.93
MOEXIPR/HCTZ TAB 15-25MG	37	90	2,974	2,819	$3,966.16	$2,456.97	$507.00	$2,023.97	$22.49	0.11%	0.33%	1.05	$0.68	$0.72
MOEXIPR/HCTZ TAB 15-12.5	22	46	1,847	1,562	$2,464.15	$1,527.79	$263.00	$1,234.51	$26.84	0.07%	0.17%	1.18	$0.67	$0.79
MOEXIPR/HCTZ TAB 7.5-12.5	14	36	1,101	1,087	$1,469.10	$909.23	$211.00	$740.23	$20.56	0.04%	0.13%	1.01	$0.67	$0.68
EXFORGE HCT TAB	31	50	1,518	1,518	$6,100.64	$5,452.65	$171.50	$2,595.55	$51.91	0.15%	0.18%	1.00	$1.71	$1.71
EXFORGEH/10- TAB 320-25	10	10	300	300	$1,397.60	$1,257.80	$35.00	$692.80	$69.28	0.04%	0.04%	1.00	$2.31	$2.31
EXFORGEH/5- TAB 160-12.5	4	4	150	120	$485.30	$436.76	$14.00	$210.76	$52.69	0.01%	0.01%	1.25	$1.41	$1.76
EXFORGEH/10- TAB 160-25	2	2	60	60	$220.20	$198.18	$7.00	$85.18	$42.59	0%	0.01%	1.00	$1.42	$1.42
EXFORGEH/5- TAB 160-25	2	2	60	60	$194.12	$174.70	$7.00	$61.70	$30.85	0%	0.01%	1.00	$1.03	$1.03
EXFORGEH/10- TAB 160-12.5	1	1	30	30	$110.10	$99.09	$3.50	$42.59	$42.59	0%	0%	1.00	$1.42	$1.42
ENALAPR/HCTZ TAB 10-25MG	181	403	13,952	12,755	$17,566.50	$5,055.70	$2,419.20	$3,263.50	$8.10	0.18%	1.48%	1.09	$0.23	$0.26
ENALAPR/HCTZ TAB 5-12.5MG	34	76	2,670	2,340	$3,062.90	$511.92	$377.75	$329.72	$4.34	0.02%	0.28%	1.14	$0.12	$0.14
TEKTURNA HCT TAB 300-25MG	20	57	1,635	1,710	$5,895.91	$5,307.60	$196.61	$2,126.65	$37.31	0.12%	0.21%	0.96	$1.30	$1.24
TEKTURNA HCT TAB 300-12.5	4	14	420	420	$1,507.34	$1,356.55	$49.00	$565.55	$40.40	0.03%	0.05%	1.00	$1.35	$1.35
TEKTURNA HCT TAB 150-12.5	9	23	750	750	$2,152.48	$1,937.31	$80.50	$517.81	$22.51	0.03%	0.08%	1.00	$0.69	$0.69
TEKTURNA HCT TAB 150-25MG	4	13	390	390	$1,107.22	$996.54	$45.50	$262.04	$20.16	0.01%	0.05%	1.00	$0.67	$0.67
METOPRL/HCTZ TAB 100-25MG	14	34	1,115	1,025	$1,976.34	$1,738.29	$186.00	$1,584.29	$46.60	0.09%	0.12%	1.09	$1.42	$1.55
METOPRL/HCTZ TAB 50-25MG	15	32	1,218	1,023	$1,381.21	$1,212.66	$190.73	$1,063.39	$33.23	0.06%	0.12%	1.19	$0.87	$1.04
METOPRL/HCTZ TAB 100-50MG	2	4	150	120	$281.92	$253.72	$22.00	$235.72	$58.93	0.01%	0.01%	1.25	$1.57	$1.96

Drug Label Name	Utilizing Members	Number of Rxs	Quantity	Days Supply	AWP Cost	Ingredient Cost Paid	Total Dispensing Fee	Plan Cost Paid Amount	Average Plan Paid Amount	% of Total Plan Cost	Market Share	Average Days Supply	Average Amount Due/ Unit	Cost/ Day
FOSINOP/HCTZ TAB 10/12.5	12	28	1,020	900	$1,574.78	$1,318.24	$143.00	$1,161.24	$41.47	0.07%	0.1%	1.13	$1.14	$1.29
FOSINOP/HCTZ TAB 20/12.5	11	24	840	780	$1,220.57	$1,079.85	$132.00	$951.85	$39.66	0.05%	0.09%	1.08	$1.13	$1.22
BENAZEP/HCTZ TAB 20-25MG	48	107	3,668	3,503	$3,806.61	$1,291.84	$632.97	$773.06	$7.22	0.04%	0.39%	1.05	$0.21	$0.22
BENAZEP/HCTZ TAB 20-12.5	83	187	7,826	5,914	$8,100.11	$1,525.03	$1,109.50	$697.12	$3.73	0.04%	0.68%	1.32	$0.09	$0.12
BENAZEP/HCTZ TAB 10-12.5	35	76	2,466	2,466	$2,560.87	$898.22	$462.00	$530.87	$6.99	0.03%	0.28%	1.00	$0.22	$0.22
ZIAC TAB 2.5/6.25	4	10	480	300	$1,617.02	$1,455.28	$35.00	$890.28	$89.03	0.05%	0.04%	1.60	$1.85	$2.97
ZIAC TAB 5/6.25MG	4	10	420	300	$1,414.90	$1,271.78	$35.00	$706.78	$70.68	0.04%	0.04%	1.40	$1.68	$2.36
ZIAC TAB 10/6.25	1	3	90	90	$303.18	$272.85	$10.50	$103.35	$34.45	0.01%	0.01%	1.00	$1.15	$1.15
VALTURNA TAB 300-320	13	15	450	450	$1,536.90	$1,383.15	$52.50	$985.65	$65.71	0.06%	0.05%	1.00	$2.19	$2.19
VALTURNA TAB 150-160	2	2	60	60	$162.44	$146.20	$7.00	$93.20	$46.60	0.01%	0.01%	1.00	$1.55	$1.55
NADOLOL/BEND TAB 40-5MG	5	12	360	360	$886.53	$724.68	$75.00	$679.68	$56.64	0.04%	0.04%	1.00	$1.89	$1.89
TEVETEN HCT TAB 600-12.5	2	7	210	210	$735.50	$652.42	$24.50	$256.92	$36.70	0.01%	0.03%	1.00	$1.22	$1.22
TEVETEN HCT TAB 600-25MG	1	4	120	120	$420.29	$378.24	$14.00	$152.24	$38.06	0.01%	0.01%	1.00	$1.27	$1.27
CORZIDE TAB 40-5MG	1	4	180	180	$589.22	$530.31	$14.00	$184.31	$46.08	0.01%	0.01%	1.00	$1.02	$1.02
CORZIDE TAB 80-5MG	1	3	90	90	$380.06	$342.05	$10.50	$172.55	$57.52	0.01%	0.01%	1.00	$1.92	$1.92
ZESTORETIC TAB 20-12.5	7	28	963	753	$1,827.68	$1,644.93	$98.00	$321.86	$11.50	0.02%	0.1%	1.28	$0.33	$0.43
ZESTORETIC TAB 10-12.5	3	8	240	240	$420.79	$378.72	$28.00	$0.00	$0.00	0%	0.03%	1.00	$0.00	$0.00
ZESTORETIC TAB 20-25MG	2	6	180	180	$345.73	$311.16	$21.00	$0.00	$0.00	0%	0.02%	1.00	$0.00	$0.00
CAPTOPR/HCTZ TAB 25-15MG	12	33	1,410	990	$1,101.13	$270.61	$182.00	$127.65	$3.87	0.01%	0.12%	1.42	$0.09	$0.13
CAPTOPR/HCTZ TAB 50-25MG	6	11	685	479	$895.26	$184.18	$69.50	$96.66	$8.79	0.01%	0.04%	1.43	$0.14	$0.20
CAPTOPR/HCTZ TAB 25-25MG	4	9	360	300	$277.15	$75.00	$45.50	$22.25	$2.47	0%	0.03%	1.20	$0.06	$0.07
CAPTOPR/HCTZ TAB 50-15MG	1	1	60	30	$81.97	$9.00	$5.50	$4.50	$4.50	0%	0%	2.00	$0.08	$0.15
BISOPRL/HCTZ TAB 5/6.25MG	316	660	24,658	23,119	$28,124.36	$1,450.28	$3,250.17	$88.01	$0.13	0%	2.42%	1.07	$0.00	$0.00
BISOPRL/HCTZ TAB 10/6.25	261	583	21,855	20,119	$24,929.98	$1,442.84	$2,968.86	$55.88	$0.10	0%	2.13%	1.09	$0.00	$0.00
BISOPRL/HCTZ TAB 2.5/6.25	98	208	8,143	7,287	$9,288.30	$553.98	$1,091.00	$29.01	$0.14	0%	0.76%	1.12	$0.00	$0.00
VASERETIC TAB 10-25MG	2	4	150	120	$421.95	$379.77	$14.00	$153.77	$38.44	0.01%	0.01%	1.25	$1.03	$1.28
TENORETIC TAB 100	1	4	120	120	$349.32	$314.40	$14.00	$88.40	$22.10	0%	0.01%	1.00	$0.74	$0.74
METHYLD/HCTZ TAB 250/25	5	14	750	480	$432.75	$155.00	$71.00	$76.20	$5.44	0%	0.05%	1.56	$0.10	$0.16
METHYLD/HCTZ TAB 250/15	1	3	90	90	$46.30	$17.85	$16.50	$4.35	$1.45	0%	0.01%	1.00	$0.05	$0.05

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Between Jan 1, 2010 and Mar 28, 2010

* Market Share For Selected Filter Criteria

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ATENOL/CHLOR TAB 100-25MG	89	182	6,142	6,084	$8,179.77	$512.35	$916.23	$60.32	$0.33	0%	0.67%	1.01	$0.01	$0.01
ATENOL/CHLOR TAB 50-25MG	254	538	18,295	18,203	$17,291.07	$1,241.93	$2,743.36	$18.69	$0.03	0%	1.97%	1.01	$0.00	$0.00
QUINARETIC TAB 20-12.5	2	3	90	90	$110.04	$86.01	$13.50	$69.51	$23.17	0%	0.01%	1.00	$0.77	$0.77
PROPRAN/HCTZ TAB 80/25	6	12	694	541	$453.95	$98.74	$73.00	$25.30	$2.11	0%	0.04%	1.28	$0.04	$0.05
PROPRAN/HCTZ TAB 40/25	4	9	340	280	$181.08	$31.83	$50.50	$4.24	$0.47	0%	0.03%	1.21	$0.01	$0.02
ACCURETIC TAB 20-12.5	1	1	30	30	$55.42	$49.88	$3.50	$0.00	$0.00	0%	0%	1.00	$0.00	$0.00
CLORPRES TAB 0.1-15MG	1	2	60	60	$80.50	$72.46	$7.00	$0.00	$0.00	0%	0.01%	1.00	$0.00	$0.00
HYDRAL/HCTZ CAP 25/25	2	2	47	39	$36.74	$6.18	$12.00	$0.00	$0.00	0%	0.01%	1.21	$0.00	$0.00
PRINZIDE TAB 10-12.5	1	4	120	120	$153.30	$138.00	$14.00	$0.00	$0.00	0%	0.01%	1.00	$0.00	$0.00
PRINZIDE TAB 20-12.5	1	1	30	30	$41.49	$37.34	$3.50	$0.00	$0.00	0%	0%	1.00	$0.00	$0.00
TENORETIC TAB 50	1	4	120	120	$248.88	$224.00	$14.00	$0.00	$0.00	0%	0.01%	1.00	$0.00	$0.00
UNIRETIC TAB 15-12.5	1	5	120	120	$235.34	$206.46	$17.39	$0.00	$0.00	0%	0.02%	1.00	$0.00	$0.00
UNIRETIC TAB 15-25MG	2	7	210	210	$414.32	$372.91	$24.50	$0.00	$0.00	0%	0.03%	1.00	$0.00	$0.00
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
DIOVAN TAB 160MG	548	1,766	60,771	55,650	$174,267.52	$155,702.64	$6,182.89	$105,814.13	$59.92	5.93%	21.64%	1.09	$1.74	$1.90
DIOVAN TAB 320MG	316	1,028	32,473	32,618	$117,741.05	$105,900.39	$3,600.12	$76,891.84	$74.80	4.31%	12.6%	1.00	$2.37	$2.36
DIOVAN TAB 80MG	421	1,358	46,814	43,163	$124,777.99	$112,039.58	$4,757.50	$73,051.87	$53.79	4.09%	16.64%	1.08	$1.56	$1.69
DIOVAN TAB 40MG	25	72	2,400	2,220	$5,348.95	$4,814.07	$252.00	$2,846.07	$39.53	0.16%	0.88%	1.08	$1.19	$1.28
AVAPRO TAB 150MG	210	668	22,988	21,502	$59,285.24	$53,199.00	$2,334.50	$33,778.69	$50.57	1.89%	8.19%	1.07	$1.47	$1.57
AVAPRO TAB 300MG	151	513	15,909	15,878	$49,384.34	$44,368.01	$1,792.00	$30,119.41	$58.71	1.69%	6.29%	1.00	$1.89	$1.90
AVAPRO TAB 75MG	10	26	780	780	$1,894.06	$1,704.69	$91.00	$1,015.69	$39.06	0.06%	0.32%	1.00	$1.30	$1.30
COZAAR TAB 100MG	141	468	15,262	14,751	$51,116.31	$45,746.58	$1,638.00	$18,179.89	$38.85	1.02%	5.73%	1.03	$1.19	$1.23
COZAAR TAB 50MG	146	452	16,170	14,055	$39,810.44	$35,750.57	$1,575.00	$9,427.05	$20.86	0.53%	5.54%	1.15	$0.58	$0.67
COZAAR TAB 25MG	20	56	1,681	1,665	$3,142.53	$2,823.79	$196.00	$44.45	$0.79	0%	0.69%	1.01	$0.03	$0.03
BENICAR TAB 40MG	198	542	16,561	16,530	$50,807.23	$45,561.51	$1,948.96	$14,918.30	$27.52	0.84%	6.64%	1.00	$0.90	$0.90
BENICAR TAB 20MG	169	492	15,509	15,075	$36,916.75	$33,161.93	$1,723.25	$5,582.32	$11.35	0.31%	6.03%	1.03	$0.36	$0.37
BENICAR TAB 5MG	6	10	420	300	$896.76	$807.07	$35.00	$242.07	$24.21	0.01%	0.12%	1.40	$0.58	$0.81

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Between Jan 1, 2010 and Mar 28, 2010

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ATACAND TAB 32MG	41	135	4,158	4,158	$13,458.01	$12,113.76	$471.00	$8,429.57	$62.44	0.47%	1.65%	1.00	$2.03	$2.03
ATACAND TAB 16MG	43	140	4,562	4,366	$10,926.49	$9,815.20	$497.50	$5,742.71	$41.02	0.32%	1.72%	1.04	$1.26	$1.32
ATACAND TAB 8MG	17	45	1,665	1,710	$3,960.86	$3,564.67	$157.50	$2,012.17	$44.71	0.11%	0.55%	0.97	$1.21	$1.18
ATACAND TAB 4MG	6	24	720	720	$1,729.08	$1,556.09	$84.00	$920.09	$38.34	0.05%	0.29%	1.00	$1.28	$1.28
MICARDIS TAB 80MG	60	176	5,535	5,490	$17,248.68	$15,516.41	$616.00	$5,445.74	$30.94	0.31%	2.16%	1.01	$0.98	$0.99
MICARDIS TAB 40MG	63	170	5,190	5,220	$16,131.60	$14,514.72	$595.00	$4,913.76	$28.90	0.28%	2.08%	0.99	$0.95	$0.94
MICARDIS TAB 20MG	3	7	240	210	$737.28	$663.56	$24.50	$268.06	$38.29	0.02%	0.09%	1.14	$1.12	$1.28
TEVETEN TAB 600MG	4	13	420	390	$1,387.05	$1,248.38	$45.50	$513.88	$39.53	0.03%	0.16%	1.08	$1.22	$1.32
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
RAMIPRIL CAP 10MG	489	1,165	47,165	37,466	$101,010.14	$70,551.24	$6,644.53	$64,781.82	$55.61	3.63%	6.15%	1.26	$1.37	$1.73
RAMIPRIL CAP 5MG	327	741	26,417	24,058	$48,257.45	$35,009.80	$4,152.20	$31,125.39	$42.00	1.74%	3.91%	1.10	$1.18	$1.29
RAMIPRIL CAP 2.5MG	161	377	12,648	11,957	$22,063.17	$15,577.84	$2,087.82	$13,516.01	$35.85	0.76%	1.99%	1.06	$1.07	$1.13
RAMIPRIL CAP 1.25MG	6	10	513	423	$757.06	$581.02	$48.00	$489.02	$48.90	0.03%	0.05%	1.21	$0.95	$1.16
QUINAPRIL TAB 20MG	214	487	18,804	16,139	$24,437.61	$10,386.80	$2,810.81	$7,745.39	$15.90	0.43%	2.57%	1.17	$0.41	$0.48
QUINAPRIL TAB 40MG	215	494	19,061	16,257	$24,289.39	$8,114.70	$2,839.40	$5,579.10	$11.29	0.31%	2.61%	1.17	$0.29	$0.34
QUINAPRIL TAB 10MG	86	205	7,385	6,500	$9,467.43	$4,471.60	$1,172.81	$3,477.87	$16.97	0.19%	1.08%	1.14	$0.47	$0.54
QUINAPRIL TAB 5MG	23	45	2,039	1,592	$2,545.32	$1,276.62	$256.50	$1,003.12	$22.29	0.06%	0.24%	1.28	$0.49	$0.63
LISINOPRIL TAB 40MG	925	1,941	73,897	66,168	$110,594.29	$15,174.59	$11,145.58	$5,720.52	$2.95	0.32%	10.25%	1.12	$0.08	$0.09
LISINOPRIL TAB 20MG	2176	4,241	179,245	153,641	$185,277.50	$18,094.28	$21,828.72	$4,327.35	$1.02	0.24%	22.4%	1.17	$0.02	$0.03
LISINOPRIL TAB 10MG	2016	4,003	151,827	141,324	$149,087.13	$9,857.59	$20,328.14	$433.84	$0.11	0.02%	21.14%	1.07	$0.00	$0.00
LISINOPRIL TAB 5MG	705	1,337	50,941	48,028	$40,037.59	$3,316.84	$6,738.35	$190.81	$0.14	0.01%	7.06%	1.06	$0.00	$0.00
LISINOPRIL TAB 30MG	79	156	5,470	5,380	$8,082.88	$879.47	$924.98	$172.63	$1.11	0.01%	0.82%	1.02	$0.03	$0.03
LISINOPRIL TAB 2.5MG	140	257	9,473	9,059	$6,087.88	$434.99	$1,262.47	$0.00	$0.00	0%	1.36%	1.05	$0.00	$0.00
FOSINOPRIL TAB 10MG	76	160	6,043	5,622	$7,210.15	$3,270.98	$899.00	$2,300.74	$14.38	0.13%	0.85%	1.07	$0.38	$0.41
FOSINOPRIL TAB 20MG	59	125	5,479	4,237	$6,531.64	$2,966.22	$726.95	$2,228.93	$17.83	0.12%	0.66%	1.29	$0.41	$0.53
FOSINOPRIL TAB 40MG	34	65	2,795	2,528	$3,333.97	$1,504.55	$378.50	$1,044.47	$16.07	0.06%	0.34%	1.11	$0.37	$0.41
ENALAPRIL TAB 20MG	269	546	26,037	18,985	$39,586.27	$3,458.71	$2,843.15	$1,608.85	$2.95	0.09%	2.88%	1.37	$0.06	$0.08
ENALAPRIL TAB 10MG	285	612	26,844	20,599	$28,768.50	$3,193.43	$3,264.53	$1,139.98	$1.86	0.06%	3.23%	1.30	$0.04	$0.06
ENALAPRIL TAB 5MG	198	401	18,110	13,484	$18,510.56	$1,647.83	$2,101.37	$354.57	$0.88	0.02%	2.12%	1.34	$0.02	$0.03
ENALAPRIL TAB 2.5MG	46	105	4,500	3,405	$3,616.05	$198.88	$511.98	$20.70	$0.20	0%	0.55%	1.32	$0.00	$0.01
MOEXIPRIL TAB 15MG	30	72	2,658	2,403	$3,841.33	$1,973.87	$375.00	$1,548.87	$21.51	0.09%	0.38%	1.11	$0.58	$0.64
MOEXIPRIL TAB 7.5MG	14	36	1,166	1,076	$1,605.78	$1,293.85	$208.00	$1,141.85	$31.72	0.06%	0.19%	1.08	$0.98	$1.06

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TRANDOLAPRIL TAB 4MG	44	99	3,861	3,276	$4,668.45	$2,122.94	$566.40	$1,599.34	$16.15	0.09%	0.52%	1.18	$0.41	$0.49
TRANDOLAPRIL TAB 2MG	22	48	1,642	1,565	$1,987.12	$906.94	$264.00	$650.94	$13.56	0.04%	0.25%	1.05	$0.40	$0.42
TRANDOLAPRIL TAB 1MG	8	17	480	510	$577.75	$265.11	$108.50	$203.61	$11.98	0.01%	0.09%	0.94	$0.42	$0.40
ALTACE CAP 10MG	7	18	840	660	$2,472.12	$2,224.98	$63.00	$967.98	$53.78	0.05%	0.1%	1.27	$1.15	$1.47
ALTACE CAP 5MG	5	17	720	510	$1,794.30	$1,614.88	$59.50	$654.38	$38.49	0.04%	0.09%	1.41	$0.91	$1.28
ALTACE CAP 2.5MG	3	9	360	270	$863.58	$777.23	$31.50	$268.73	$29.86	0.02%	0.05%	1.33	$0.75	$1.00
VASOTEC TAB 10MG	4	14	780	420	$2,168.13	$1,951.32	$49.00	$1,160.32	$82.88	0.06%	0.07%	1.86	$1.49	$2.76
VASOTEC TAB 5MG	3	10	511	301	$1,292.62	$1,120.35	$35.00	$572.57	$57.26	0.03%	0.05%	1.70	$1.12	$1.90
BENAZEPRIL TAB 20MG	160	328	12,992	11,014	$13,502.19	$1,586.48	$1,693.68	$732.67	$2.23	0.04%	1.73%	1.18	$0.06	$0.07
BENAZEPRIL TAB 40MG	136	274	10,676	9,596	$11,118.32	$1,337.06	$1,364.96	$505.30	$1.84	0.03%	1.45%	1.11	$0.05	$0.05
BENAZEPRIL TAB 10MG	88	177	6,585	6,058	$6,783.48	$628.45	$914.85	$143.12	$0.81	0.01%	0.93%	1.09	$0.02	$0.02
BENAZEPRIL TAB 5MG	16	32	1,112	1,022	$1,143.50	$70.50	$163.92	$3.90	$0.12	0%	0.17%	1.09	$0.00	$0.00
PERINDOPRIL TAB 4MG	4	10	604	364	$1,336.47	$829.50	$36.00	$745.50	$74.55	0.04%	0.05%	1.66	$1.23	$2.05
PERINDOPRIL TAB 8MG	1	3	180	90	$503.35	$453.00	$16.50	$439.50	$146.50	0.02%	0.02%	2.00	$2.44	$4.88
ACCUPRIL TAB 10MG	2	9	570	270	$1,075.08	$967.59	$31.50	$480.59	$53.40	0.03%	0.05%	2.11	$0.84	$1.78
ACCUPRIL TAB 20MG	1	5	450	150	$847.87	$763.09	$17.50	$480.59	$96.12	0.03%	0.03%	3.00	$1.07	$3.20
ACCUPRIL TAB 40MG	5	19	690	570	$1,313.36	$1,182.06	$66.50	$182.96	$9.63	0.01%	0.1%	1.21	$0.27	$0.32
ACEON TAB 4MG	6	14	601	420	$1,530.61	$1,377.53	$49.00	$586.53	$41.90	0.03%	0.07%	1.43	$0.98	$1.40
ACEON TAB 8MG	3	7	330	270	$1,021.28	$919.15	$24.50	$403.65	$57.66	0.02%	0.04%	1.22	$1.22	$1.50
ZESTRIL TAB 20MG	4	12	641	364	$1,088.48	$979.64	$42.00	$365.54	$30.46	0.02%	0.06%	1.76	$0.57	$1.00
ZESTRIL TAB 10MG	2	4	210	120	$333.06	$299.74	$14.00	$87.42	$21.86	0%	0.02%	1.75	$0.42	$0.73
PRINIVIL TAB 20MG	3	9	383	274	$469.52	$422.59	$31.50	$47.64	$5.29	0%	0.05%	1.40	$0.12	$0.17
PRINIVIL TAB 10MG	3	10	300	300	$343.53	$309.20	$35.00	$0.00	$0.00	0%	0.05%	1.00	$0.00	$0.00
CAPTOPRIL TAB 50MG	38	76	5,439	2,702	$4,985.36	$190.96	$400.02	$4.99	$0.07	0%	0.4%	2.01	$0.00	$0.00
CAPTOPRIL TAB 100MG	2	3	240	150	$444.53	$27.65	$16.50	$0.00	$0.00	0%	0.02%	1.60	$0.00	$0.00
CAPTOPRIL TAB 12.5MG	19	41	2,379	1,323	$1,247.82	$55.54	$180.88	$0.00	$0.00	0%	0.22%	1.80	$0.00	$0.00
CAPTOPRIL TAB 25MG	34	69	4,645	2,405	$2,330.95	$65.35	$334.17	$0.00	$0.00	0%	0.36%	1.93	$0.00	$0.00
LOTENSIN TAB 10MG	1	2	60	60	$109.10	$98.19	$7.00	$0.00	$0.00	0%	0.01%	1.00	$0.00	$0.00
LOTENSIN TAB 20MG	1	4	120	120	$223.34	$201.01	$14.00	$0.00	$0.00	0%	0.02%	1.00	$0.00	$0.00
MAVIK TAB 1MG	1	3	90	90	$128.74	$108.09	$10.50	$0.00	$0.00	0%	0.02%	1.00	$0.00	$0.00
MAVIK TAB 2MG	2	6	180	180	$256.21	$230.58	$21.00	$0.00	$0.00	0%	0.03%	1.00	$0.00	$0.00

RxTRACK® Business Intelligence

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RXT3100D – Therapeutic Detail Market Share Cost per Day

Between Jan 1, 2010 and Mar 28, 2010

* Market Share For Selected Filter Criteria

Drug Label Name	Utilizing Members	Number of Rxs	Quantity	Days Supply	AWP Cost	Ingredient Cost Paid	Total Dispensing Fee	Plan Cost Paid Amount	Average Plan Paid Amount	% of Total Plan Cost	Market Share	Average Days Supply	Average Amount Due/ Unit	Cost/ Day
MAVIK TAB 4MG	1	2	60	60	$84.14	$75.72	$7.00	$0.00	$0.00	0%	0.01%	1.00	$0.00	$0.00
MONOPRIL TAB 10MG	1	1	30	30	$49.40	$44.46	$3.50	$0.00	$0.00	0%	0.01%	1.00	$0.00	$0.00
[redacted]														
CLONIDINE DIS 0.3/24HR	12	18	66	466	$4,440.64	$3,625.82	$103.00	$3,548.82	$197.16	0.2%	0.48%	0.14	$53.77	$7.62
CLONIDINE DIS 0.2/24HR	10	23	87	603	$4,219.28	$3,532.86	$109.50	$2,744.00	$119.30	0.15%	0.62%	0.14	$31.54	$4.55
CLONIDINE DIS 0.1/24HR	14	24	96	652	$2,765.52	$2,206.57	$148.50	$2,115.07	$88.13	0.12%	0.64%	0.15	$22.03	$3.24
CLONIDINE TAB 0.3MG	62	132	9,052	4,267	$4,495.62	$1,315.09	$805.47	$727.73	$5.51	0.04%	3.54%	2.12	$0.08	$0.17
CLONIDINE TAB 0.2MG	281	565	37,420	18,545	$12,815.19	$2,409.69	$3,155.28	$498.12	$0.88	0.03%	15.15%	2.02	$0.01	$0.03
CLONIDINE TAB 0.1MG	555	1,037	63,204	32,445	$14,490.74	$3,520.32	$5,607.68	$484.32	$0.47	0.03%	27.81%	1.95	$0.01	$0.01
CLONIDINE POW	2	4	140	120	$13,860.00	$329.97	$17.50	$157.97	$39.49	0.01%	0.11%	1.17	$1.13	$1.32
CATAPRES-TTS DIS 0.3/24HR	14	43	172	1,225	$13,033.67	$11,730.26	$150.50	$9,300.76	$216.30	0.52%	1.15%	0.14	$54.07	$7.59
CATAPRES-TTS DIS 0.2/24HR	16	37	148	1,018	$8,153.58	$6,923.82	$129.50	$4,833.32	$130.63	0.27%	0.99%	0.15	$32.66	$4.75
CATAPRES-TTS DIS 0.1/24HR	17	34	136	946	$4,474.00	$4,023.62	$119.00	$2,102.62	$61.84	0.12%	0.91%	0.14	$15.46	$2.22
DOXAZOSIN TAB 4MG	168	333	15,541	12,394	$14,987.42	$1,684.89	$1,782.84	$516.18	$1.55	0.03%	8.93%	1.25	$0.03	$0.04
DOXAZOSIN TAB 2MG	103	216	8,556	7,260	$7,911.01	$1,022.38	$1,140.27	$321.30	$1.49	0.02%	5.79%	1.18	$0.04	$0.04
DOXAZOSIN TAB 8MG	110	202	8,754	7,915	$8,558.53	$815.48	$1,034.00	$203.35	$1.01	0.01%	5.42%	1.11	$0.02	$0.03
DOXAZOSIN TAB 1MG	31	59	2,365	1,820	$2,151.31	$129.89	$280.30	$21.78	$0.37	0%	1.58%	1.30	$0.01	$0.01
TERAZOSIN CAP 5MG	124	276	10,738	9,474	$17,206.37	$1,554.18	$1,411.86	$592.43	$2.15	0.03%	7.4%	1.13	$0.06	$0.06
TERAZOSIN CAP 1MG	33	60	2,566	2,018	$4,098.12	$476.28	$318.80	$191.98	$3.20	0.01%	1.61%	1.27	$0.07	$0.10
TERAZOSIN CAP 2MG	88	191	8,021	6,337	$12,851.04	$824.62	$976.47	$182.65	$0.96	0.01%	5.12%	1.27	$0.02	$0.03
TERAZOSIN CAP 10MG	74	157	6,226	5,744	$9,971.34	$479.28	$837.43	$11.13	$0.07	0%	4.21%	1.08	$0.00	$0.00
METHYLDOPA TAB 500MG	37	61	3,833	1,833	$2,532.96	$630.67	$362.00	$418.39	$6.86	0.02%	1.64%	2.09	$0.11	$0.23
METHYLDOPA TAB 250MG	33	59	4,782	1,895	$1,748.75	$447.03	$314.50	$251.53	$4.26	0.01%	1.58%	2.52	$0.05	$0.13
PRAZOSIN HCL CAP 2MG	10	24	1,610	760	$792.01	$325.08	$135.50	$226.58	$9.44	0.01%	0.64%	2.12	$0.14	$0.30
PRAZOSIN HCL CAP 5MG	3	8	600	240	$468.00	$206.82	$39.50	$184.32	$23.04	0.01%	0.21%	2.50	$0.31	$0.77
PRAZOSIN HCL CAP 1MG	8	20	1,582	600	$560.96	$198.80	$101.00	$99.80	$4.99	0.01%	0.54%	2.64	$0.06	$0.17
GUANFACINE TAB 2MG	20	48	1,771	1,534	$2,151.12	$526.59	$285.00	$308.17	$6.42	0.02%	1.29%	1.15	$0.17	$0.20
GUANFACINE TAB 1MG	37	77	3,478	2,545	$3,032.82	$412.05	$413.50	$138.37	$1.80	0.01%	2.06%	1.37	$0.04	$0.05
MINIPRESS CAP 2MG	1	5	450	150	$494.07	$444.67	$17.50	$162.17	$32.43	0.01%	0.13%	3.00	$0.36	$1.08

Drug Label Name	Utilizing Members	Number of Rxs	Quantity	Days Supply	AWP Cost	Ingredient Cost Paid	Total Dispensing Fee	Plan Cost Paid Amount	Average Plan Paid Amount	% of Total Plan Cost	Market Share	Average Days Supply	Average Amount Due/ Unit	Cost/ Day
RESERPINE TAB 0.1MG	1	2	210	63	$174.95	$157.45	$11.00	$138.45	$69.22	0.01%	0.05%	3.33	$0.66	$2.20
GUANABENZ TAB 4MG	1	1	100	30	$97.99	$62.66	$6.50	$59.16	$59.16	0%	0.03%	3.33	$0.59	$1.97
CATAPRES TAB 0.1MG	2	4	180	120	$269.45	$236.71	$17.00	$51.16	$12.79	0%	0.11%	1.50	$0.28	$0.43
CARDURA TAB 2MG	1	4	120	120	$200.32	$180.29	$14.00	$0.00	$0.00	0%	0.11%	1.00	$0.00	$0.00
CARDURA TAB 8MG	2	5	151	151	$278.34	$250.52	$17.50	$0.00	$0.00	0%	0.13%	1.00	$0.00	$0.00
Total for Drug Class: 3820 - ANTIADRENERGIC ANTIHYPERTENSIVES**	1,870	5,729	192,153	125,290	$770,283.12	$50,684.36	$19,862.40	$30,591.03	$16.36	1.71%	6.37%	1.56	$0.16	$0.25
Drug Class: 3827 - DIRECT RENIN INHIBITORS**														
TEKTURNA TAB 300MG	74	220	6,606	6,606	$23,648.42	$21,277.22	$770.00	$8,886.62	$40.39	0.5%	56.41%	1.00	$1.35	$1.35
TEKTURNA TAB 150MG	61	170	5,508	5,058	$15,647.71	$14,044.81	$598.00	$4,595.43	$27.03	0.26%	43.59%	1.09	$0.83	$0.91
Total for Drug Class: 3827 - DIRECT RENIN INHIBITORS**	135	390	12,114	11,664	$39,296.13	$35,322.03	$1,368.00	$13,482.05	$34.57	0.76%	0.66%	1.04	$1.11	$1.16
Drug Class: 6547 - VASODILATORS**														
HYDRALAZINE TAB 50MG	51	102	9,702	3,199	$5,457.55	$2,748.05	$571.89	$2,244.78	$22.01	0.13%	25%	3.03	$0.23	$0.70
HYDRALAZINE TAB 100MG	16	33	2,736	1,053	$2,771.24	$1,609.49	$193.50	$1,452.99	$44.03	0.08%	8.09%	2.60	$0.53	$1.38
HYDRALAZINE TAB 25MG	52	99	9,804	3,196	$4,979.32	$1,737.84	$584.88	$1,286.90	$13.00	0.07%	24.26%	3.07	$0.13	$0.40
HYDRALAZINE TAB 10MG	17	30	3,150	1,080	$1,293.30	$401.34	$157.50	$228.17	$7.61	0.01%	7.35%	2.92	$0.07	$0.21
MINOXIDIL TAB 10MG	50	106	6,770	3,442	$9,388.38	$3,086.16	$594.00	$2,530.16	$23.87	0.14%	25.98%	1.97	$0.37	$0.74
MINOXIDIL TAB 2.5MG	21	38	3,374	1,264	$2,099.58	$858.05	$210.50	$648.55	$17.07	0.04%	9.31%	2.67	$0.19	$0.51
Total for Drug Class: 6547 - VASODILATORS**	207	408	15,536	13,724	$25,989.36	$10,440.93	$2,312.27	$8,391.55	$20.57	0.47%	3.69%	1.59	$0.24	$0.53
Drug Class: 6548 - ALDOSTERONE RECEPTOR ANTAGONISTS**														
EPLERENONE TAB 25MG	10	24	870	780	$3,566.77	$3,011.49	$127.00	$2,878.49	$119.94	0.16%	41.38%	1.12	$3.31	$3.69
EPLERENONE TAB 50MG	4	9	390	270	$1,598.78	$1,302.53	$56.50	$1,269.03	$141.00	0.07%	15.52%	1.44	$3.25	$4.70
INSPRA TAB 50MG	2	10	600	300	$2,811.93	$2,530.74	$35.00	$1,965.74	$196.57	0.11%	17.24%	2.00	$3.28	$6.55
INSPRA TAB 25MG	4	15	600	450	$2,806.40	$2,525.79	$52.50	$1,678.29	$111.89	0.09%	25.86%	1.33	$2.80	$3.73
Total for Drug Class: 6549 - SELECTIVE ALDOSTERONE RECEPTOR ANTAGONISTS (SARAS)	20	58	2,460	1,800	$10,783.91	$9,370.55	$274.00	$7,791.55	$134.34	0.44%	0.1%	1.57	$3.17	$4.33
Drug Class: 6830 - AGENTS FOR PHEOCHROMOCYTOMA**														
PHENTOLAMINE INJ MESYLATE	1	1	1	1	$64.80	$58.32	$6.50	$54.82	$54.82	0%	100%	1.00	$54.82	$54.82
Total for Drug Class: 6830 - AGENTS FOR PHEOCHROMOCYTOMA**	1	1	1	1	$64.80	$58.32	$6.50	$54.82	$54.82	0%	0%	1.00	$54.82	$54.82
Total for Drug Group: 36 - ANTIHYPERTENSIVES*	24,861	59,001	2,230,734	1,950,969	$4,311,319.69	$2,740,661.96	$275,045.35	$1,785,243.38	$30.26	100%	100%	1.14	$0.80	$0.92

Selected Filters

Client: State of Arkansas, Account: ALL; Group: ALL; For: Select Date Range;Date Submitted:Jan 1, 2010 and Mar 28, 2010; Pharmacy Type: All; Drug Type: All; Report Description: No

Arkansas State and Public School Employees
Prescription Drug Program
Stelara Drug Review

Stelara (ustekinumab) was previously excluded from coverage under the prescription drug benefit. Shortly after the last DUEC meeting, a trial was published that showed Stelara was superior to Enbrel (etanercept) for patients with moderate to severe plaque psoriasis. Information from this trial is provided below.

Proposal: cover Stelara at Tier 3 with PA required

PA criteria include 1) diagnosis of moderate to severe plaque psoriasis (indicated by a PASI score of at least 10 based on 0-72 scale) and involvement of at least 10% BSA, and 2) inadequate response, intolerance, or contraindication to at least one conventional systemic agent for the treatment of psoriasis (i.e. methotrexate, cyclosporine, or psoralen plus utltraviolet A).

Dosing for patients weighing < 100kg is 45mg at week 0 and 4, and then every 12 weeks thereafter. For patients weighing > 100kg, dosing is 45mg or 90mg at the same intervals.

Consider initiating all patients at 45mg at weeks 0 and 4. At week 12 their dose could be increased if they are an inadequate responder. The initial PA would be for 4 weeks (2 doses at weeks 0 and 4). Subsequent PA approval would be annually and the dose would be determined by response to the 45mg dose. All those weighing 100 kg or less would have the 45mg dose.

Table 2. Clinical Responses at Week 12.*

Variable	Etanercept (N=347)	Ustekinumab	
		45 mg (N=209)	90 mg (N=347)
Improvement in PASI score			
At least 75% — no. (%)	197 (56.8)	141 (67.5)	256 (73.8)
P value		0.01	<0.001
Treatment difference (95% CI)		10.7 (2.4–19.0)	17.0 (10.0–24.0)
At least 90% — no. (%)	80 (23.1)	76 (36.4)	155 (44.7)
P value		<0.001	<0.001
Treatment difference (95% CI)		13.3 (5.8–20.7)	21.6 (14.6–28.5)
Physician's global assessment			
Cleared or minimal disease — no. (%)	170 (49.0)	136 (65.1)	245 (70.6)
P value		<0.001	<0.001
Treatment difference (95% CI)		16.1 (7.6–24.4)	21.6 (14.4–28.6)
Cleared disease — no. (%)	30 (8.6)	34 (16.3)	91 (26.2)
P value		0.006	<0.001
Treatment difference (95% CI)		7.7 (2.2–13.2)	17.6 (11.6–23.7)

* P values are for the comparison of rates between each ustekinumab group and the etanercept group. Treatment differences are percentage-point differences between each ustekinumab group and the etanercept group. CI denotes confidence interval, and PASI psoriasis area-and-severity index.

The infromation below was provided by the pharmacy consultant at the January 2010 meeting.

Stelara	Ustekinumab	From Pharmacist's Letter: first of a new class. It inhibits the inflammatory proteins interleukin-12 and -23 instead of TNF. Some evidence suggests that Stelara might be more effective than Enbrel for psoriasis. But this isn't proven yet. And ther are concerns about long-term safety. Stelara is given SC q12w compared to q2 for Enbrel and qOW for Humira. But Stelara is NOT approved for self-inj. the FDA wants pts to get it from a healthcare provider for closer monitoring. Expect pricing to be similar to Enbrel and Humira. But it will be twice as much for patients over 100 kg because they will need two 45mg vials instead of one. REcommend TB testing before starting Stelara and counsel pts to watch for signs of infection. Cancer might be a bigger concern with Stalara than with TNF inhibitors. Consider it an option to Enbrel or Humira especially in pt who can't take TNF inhibitors due to demyelinating disease (MS, etc) or heart failure.; May be useful in Crohn's and psoriatic arthritis; no comparative trial results yet.	e x c l u d e

Enbrel ($28,525 per year)	Humira ($23,774 per year)	Amevive ($13,104 - $26,208 per year)	AWP/unit $5,595.60 per vial	AWP/month $27,97($55,956 per year

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CLINICAL PRACTICE GUIDELINE

Androgen Therapy in Women: An Endocrine Society Clinical Practice Guideline

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Objective: The objective was to provide guidelines for the therapeutic use of androgens in women.

Participants: The Task Force was composed of a chair, selected by the Clinical Guidelines Subcommittee (CGS) of The Endocrine Society, six additional experts, a methodologist, and a medical writer. The Task Force received no corporate funding or remuneration.

Evidence: The Task Force used systematic reviews of available evidence to inform its key recommendations. The Task Force used consistent language and graphical descriptions of both the strength of recommendation and the quality of evidence, using the recommendations of the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) group. The strength of a recommendation is indicated by the number **1** (strong recommendation, associated with the phrase "we recommend") or **2** (weak recommendation, associated with the phrase "we suggest"). The quality of the evidence is indicated by cross-filled circles, such that ⊕◯◯◯ denotes very-low-quality evidence, ⊕⊕◯◯ low quality, ⊕⊕⊕◯ moderate quality, and ⊕⊕⊕⊕ high quality. Each *recommendation* is followed by a description of the *evidence*.

Consensus Process: Consensus was guided by systematic reviews of evidence and discussions during one group meeting, several conference calls, and e-mail communications. The drafts prepared by the task force with the help of a medical writer were reviewed successively by The Endocrine Society's CGS, Clinical Affairs Committee (CAC), and Executive Committee. The version approved by the CGS and CAC was placed on The Endocrine Society's web site for comments by members. At each stage of review, the Task Force received written comments and incorporated needed changes.

Conclusions: We recommend against making a diagnosis of androgen deficiency in women at present because of the lack of a well-defined clinical syndrome and normative data on total or free testosterone levels across the lifespan that can be used to define the disorder. Although there is evidence for short-term efficacy of testosterone in selected populations, such as surgically menopausal women, we recommend against the generalized use of testosterone by women because the indications are inadequate and evidence of safety in long-term studies is lacking. A review of the data currently available is presented, and areas of future research are outlined. To formulate clinical guidelines for use of testosterone in women, additional information will be necessary. This includes defining conditions that, when not treated with androgens, have adverse health consequences to women; defining clinical and laboratory parameters that distinguish those with these conditions; and assessing the efficacy and long-term safety of androgen administration on outcomes that are important to women diagnosed with these conditions. This necessary clinical research cannot occur until the biological, physiological, and psychological underpinnings of the role of androgens in women and candidate disorders are further elucidated. (***J Clin Endocrinol Metab* 91: 3697–3710, 2006**)

SUMMARY OF EVIDENCE-BASED GUIDELINES ON THE THERAPEUTIC USE OF ANDROGENS IN WOMEN

1. Diagnosis

1.1 We recommend *against* making a diagnosis of androgen deficiency in women at this time because there is neither a well-defined clinical syndrome nor normative data on testosterone or free testosterone levels in women across their lifespans that can be used to define the disorder (1|⊕◯◯◯).

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Abbreviations: BMD, Bone mineral density; CAIS, complete androgen insensitivity syndrome; CVD, cardiovascular disease; DHEA, dehydroepiandrosterone; DHEAS, DHEA sulfate; DHT, dihydrotestosterone; FAI, free androgen index; Kd, dissociation constant; MT, methyltestosterone; OCP, oral contraceptive pill.

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2. Treatment

2.1 Although evidence exists for short-term efficacy of testosterone in selected populations, such as surgically menopausal women, we recommend *against* the generalized use of testosterone by women because the indications are inadequate and evidence of safety in long-term studies is lacking (1|⊕◯◯◯).

To formulate clinical recommendations, the task force would require additional data 1) defining conditions that, when not treated with androgens, have adverse health consequences to women; 2) defining clinical and laboratory parameters that distinguish those with these conditions; and 3) assessing the efficacy and long-term safety of androgen administration on outcomes that are important to women diagnosed with these conditions.

This necessary clinical research cannot occur until the biological, physiological, and psychological underpinnings of the role of androgens in women and candidate disorders are further elucidated. Thus, the task force makes the following recommendations to the clinical and research community.

3. Needed Assays

3.1 We recommend the development of sensitive and specific assays to accurately measure testosterone and free testosterone in women across their lifespans (1|⊕⊕⊕◯).

4. Needed Research

4.1 We recommend additional research in the following human model systems to define the clinical syndrome of androgen deficiency and to study the benefits and risks of androgen therapy (1|⊕◯◯◯):

- Surgical menopause is a condition in which the ovarian, but not adrenal androgen, precursors are removed abruptly independent of age.
- Hypopituitarism can be used to study the physiological replacement of ovarian and adrenal androgens precursors.
- Anorexia nervosa may be used as a model of androgen deficiency secondary to dysfunction of the hypothalamic-pituitary and adrenal axes.
- Primary adrenal insufficiency allows for the investigation of the loss of adrenal androgen precursors in the presence of intact ovarian androgen function.
- Ablation-replacement models in normal women using GnRH analogs to eliminate ovarian androgens, with or without suppression of adrenal androgen precursors, offer another way to assess the effects of androgen withdrawal and replacement.
- Subjects with complete androgen insensitivity syndrome offer a way to investigate target tissue effects that are dependent on the androgen receptor but are independent of aromatization.
- There are studies in patients with low weight and HIV and with natural aging; however, these systems are too complex to recommend as initial models to understand the potential therapeutic role of androgens in women.

4.2 We recommend additional investigation using rodents and primates to further define the specific targets of androgen action (1|⊕◯◯◯).

4.3 We recommend additional research into the role of local androgen production, action, and metabolism in tissues (1|⊕◯◯◯).

4.4 We recommend the further study of physiological targets of androgen action such as (1|⊕◯◯◯):

- Sexual dysfunction
- Cognition
- Mood
- Bone
- Cardiovascular function
- Body composition
- Muscle strength and function

4.5 We recommend the following endpoints be considered for safety and risk assessment of androgen administration (1|⊕◯◯◯):

- Appearance of or change in hirsutism, acne, male pattern balding, clitoromegaly, and deepening of the voice.
- Cardiovascular and metabolic evaluation, with and without estrogen replacement, should include fasting lipid profiles, vascular reactivity, markers of insulin sensitivity, and markers of inflammation.
- Effects on the breast, with or without estrogen replacement, should be measured. Breast biopsy studies with *in vitro* markers of cell proliferation and apoptosis should be considered.
- Alterations in the endometrium with and without estrogen coadministration.
- Alterations in mood using validated instruments.

METHOD OF DEVELOPMENT OF EVIDENCE-BASED GUIDELINES

The CGS of The Endocrine Society identified "androgens in women" as a topic of importance for practice guidelines and appointed a six-member expert panel to formulate evidence-based recommendations. The Task Force elected to use the approach recommended by the GRADE group, an international group with expertise in development and implementation of evidence-based guidelines (1). The Task Force reviewed the available literature to inform its key recommendations and used consistent language and graphical descriptions of both the strength of recommendation and the quality of evidence. The strength of a recommendation is indicated by the number **1** (strong recommendation, associated with the phrase "we recommend") or **2** (weak recommendation, associated with the phrase "we suggest"). The quality of the evidence is indicated by cross-filled circles, such that ⊕◯◯◯ denotes very-low-quality evidence, ⊕⊕◯◯ low quality, ⊕⊕⊕◯ moderate quality, and ⊕⊕⊕⊕ high quality. Each *recommendation* is followed by a description of the *evidence.*

Although high-quality evidence measuring patient-important outcomes is lacking to allow for broadly applicable recommendations for diagnosis and treatment of androgen deficiency in women in clinical practice at this time, the panel felt strongly that this is an important area of clinical and scientific interest. On the basis of this review, the panel has outlined recommendations for needed research to allow future recommendations on diagnosis and treatment.

1. Diagnosis

1.1.A RECOMMENDATION

We recommend against making a diagnosis of androgen deficiency in women at this time because there is neither a well-defined clinical syndrome nor normative data on testosterone or free testosterone concentrations in blood in women across their lifespan that can be used to define the disorder.

1.1.B EVIDENCE

Research related to therapeutic use of androgens in women has been hampered by a lack of a clear definition of a syndrome and by inadequate endocrine measurements and poor outcome tools. Neither a clear definition nor clear clinical syndromes are attributable to androgen deficiency in women. In addition, the assays to measure androgens have not been optimized to measure the low levels found in premenopausal or postmenopausal women. Because total testosterone concentrations are modulated by SHBG, which in turn is modulated by estrogens, free testosterone levels would be a better measure of androgen status. However, to date, few assays have the sensitivity or specificity to measure free testosterone levels in women, especially menopausal women. Thus, if normative data are lacking across the lifespan, it is difficult to use an endocrine assay to define "deficiency." Moreover, serum levels may not reflect intracellular testosterone production from adrenal and ovarian prohormones.

2. Treatment

2.1.A RECOMMENDATION

Although evidence exists for short-term efficacy of testosterone in selected populations, such as surgically menopausal women, we recommend against the generalized use of testosterone by women because the indications are inadequate and evidence of safety in long-term studies is lacking (1⊕○○○).

2.1.B EVIDENCE

In the United States, testosterone therapy is not approved for use in women for "androgen deficiency." Some compounding pharmacies and over-the-counter products, however, have bypassed this restriction by providing personalized androgen replacement. Problems with this approach include the lack of quality assurance for the androgenic substances sold in compounding pharmacies or products at health food stores. The adrenal and ovarian precursor hormones dehydroepiandrosterone (DHEA) and androstenedione are not considered true androgens because they do not bind to and activate the androgen receptor. In addition, the metabolism and actions of these precursors is complex. Because both DHEA and androstenedione are prohormones, and can be converted to testosterone and/or dihydrotestosterone (DHT), as well as to estrogens, the tissue-specific actions may be androgenic and/or estrogenic. Studies using a nonaromatizable androgen would more directly assess androgen *vs.* estrogen action at various targets. Studies using depot formulations of testosterone in pellets and injectable forms showed pharmacological plasma androgen levels that are neither approved nor safe for women. Furthermore, most interventional studies to date have been in estrogen-replete subjects; dose-response characteristics of testosterone in the absence of endogenous estrogens are needed. Finally, there are no data on the safety and efficacy of physiological testosterone administration in women beyond 24 wk. The data concerning administration of prohormones such as DHEA or androstenedione are even weaker and will not be discussed in detail. Because of these deficiencies, the Task Force recommends against the use of testosterone therapy in women until further research is completed. In this document, we summarize the available research to date and areas where investigation is needed.

3. Needed Assays

3.1.A RECOMMENDATION

We recommend the development of sensitive and specific assays to measure testosterone and free testosterone in women across their lifespans (1⊕⊕⊕○).

3.1.B EVIDENCE

Androgens in plasma

All assays of analytes in plasma must meet criteria of sensitivity, specificity, and reproducibility. The problem in the measurement of testosterone in plasma is the difficulty of quantifying very small concentrations in the presence of steroids with closely related structures. The issue is compounded when evaluating the very low levels of free testosterone. In women, only about 1–3% of testosterone is free in the blood, the remainder being bound to SHBG (~65–75%) and albumin (~25–35%) (2).

Measurement of total testosterone

The advent of RIA for testosterone (3, 4) addressed the problems of sensitivity and specificity in the measurement of this hormone in biological fluids. The creation of high-affinity antibodies and the use of radioactive labels allowed detection of extraordinarily small concentrations of testosterone. However, barring the use of an extraction step, which increases sensitivity, the achieved sensitivity is inadequate for measurement of levels in women. Furthermore, when the same sample is analyzed using a number of different proprietary assays, some of which use unextracted serum, significantly different answers are obtained for both men and women (5, 6). At the low concentration of testosterone in the plasma of women, the values have little utility (5, 6). Realization of this problem has fostered the development of nonimmunoassay technology that involves chromatography, followed by sequential mass spectroscopy (MS/MS) (7, 8).

Free testosterone

In plasma, testosterone circulates bound to two proteins, SHBG and albumin (9). That which is unbound, free testosterone, is often thought of as being the moiety that has access to the cell and results in androgenic effects. In truth, the situation is more complicated (10, 11); but, as a practical matter, free testosterone often correlates better with the androgenic state of the patient than does total testosterone. In addition, there exists the concept of bioavailable testosterone,

defined as the concentration of testosterone that is free together with that which is weakly bound, *e.g.* the albumin-bound fraction, or simply non-SHBG-bound testosterone. It must be realized that any measure of free testosterone, or its surrogates, depends on the quality of the assay for total testosterone. Assuming that the total testosterone assay is at optimal sensitivity and specificity, there are several alternative approaches to estimate free testosterone. Still, one is attempting *ex vivo* to approximate an *in vivo* concept.

Measurement of free testosterone. There are three general ways to measure free testosterone *in vitro* (8, 12): 1) separate free testosterone and assay it; 2) add radiolabeled testosterone to plasma *in vitro*, separate the free radioactivity from that which is bound, and multiply the fraction free by the assayed total testosterone done in a separate assay; and 3) perform a direct immunoassay. The first two methods are technically difficult but can give reproducible and accurate answers—limited mainly by the ability to measure total testosterone accurately and specifically (13). These methods depend neither on having an accurate assay for SHBG nor on knowing the dissociation constant (Kd) for the testosterone-SHBG interaction. However, neither method allows approximation of so-called bioavailable testosterone. The third method, direct immunoassay, although simple and relatively inexpensive, should *not* be used because the values it generates are extraordinarily inaccurate (13, 14). Under development are methods based on chromatography followed by tandem mass spectrometry sensitive enough to measure free testosterone (7).

Measurement of bioavailable testosterone. Bioavailable testosterone refers to that fraction of testosterone in plasma that can enter cells. This fraction is widely defined as the free plus albumin-bound testosterone. The SHBG-bound testosterone is not "bioavailable." However, the concept is too simplistic, because in some tissues SHBG-bound testosterone is available and in others it is not (10), an issue that is a concern with any method used. The method depends on the precipitation *in vitro* of radiolabeled testosterone bound to SHBG and the multiplication of the fraction in the supernatant (albumin-bound and free) by total testosterone. The main difficulty with this process is that it is poorly standardized (15).

Free testosterone index (testosterone/SHBG). Because free testosterone depends heavily on testosterone and SHBG, there is a reasonable correlation between this measurement and free testosterone. However, free testosterone depends not only on the ratio, but also on the absolute concentration of both testosterone and SHBG (16).

Calculation of free testosterone. One can use the law of mass action to calculate free testosterone and the concentration that is bound to SHBG and albumin (17, 18). The calculation depends on the measurement of total testosterone, total SHBG, and total albumin and on the use of the Kd between SHBG and testosterone and between albumin and testosterone. There is no difficulty with the albumin portion of the calculation (18). Although the Kd for SHBG-testosterone is about 10^{-9} M, this number needs to be verified and universally agreed upon. SHBG is an abundant protein that is not difficult to measure; however, different kits and methods use a different standard, thus yielding discrepant results. A universal standard is needed so that results between labs can be compared. With those caveats, calculation of free testosterone is a practical estimate of free testosterone in plasma (18, 19), and it can be performed using the published equations (17, 18). Again, the major obstacle is the ability to measure total testosterone to use in the equation.

4. Needed Research

There is currently no established definition of androgen deficiency in women on which to base clinical care. Such definitions presuppose standard, valid assays and normative data that are only now being developed (see 3. *Needed Assays*). Additional data are necessary to establish a definition of a clinically relevant androgen deficiency syndrome—one that is based on measurable deleterious clinical effects attributable to androgen deficiency, in association with low androgen levels in women.

4.1.A RECOMMENDATIONS

We recommend additional research in the following human model systems to define the clinical syndrome of androgen deficiency and to study the benefits and risks of androgen therapy (1⊕○○○):

- *Surgical menopause is a condition in which ovarian androgens, but not adrenal androgen precursors, are removed abruptly, independent of age.*
- *Hypopituitarism, although uncommon, can be used to study the physiological replacement of both ovarian androgens and adrenal androgen precursors.*
- *Women with anorexia nervosa have altered hypothalamic-pituitary suppression of ovarian and adrenal androgen precursors.*
- *Primary adrenal insufficiency allows the investigation of adrenal androgen precursor replacement with intact ovarian androgen function.*
- *Subjects with complete androgen insensitivity syndrome offer a way to investigate target tissue effects which are dependent on the androgen receptor but are independent of aromatization.*
- *Patients with HIV and low body weight have been used to evaluate the impact of androgen deficiency.*
- *Glucocorticoid- and oral contraceptive (OCP)-induced suppression of endogenous androgens are additional paradigms to examine the effects of androgen deficiency.*
- *Ablation-replacement models in normal women using GnRH analogs to remove ovarian androgens, with or without inhibition of adrenal secretion, offer another way to assess the effects of androgen withdrawal and replacement.*
- *Normal aging represents the ultimate relevant clinical scenario; there have been some cross-sectional and a few longitudinal studies, but the complexities of aging make it an unsuitable model for initial studies to carefully dissect the physiological role of androgens in women.*

4.1.B EVIDENCE

Surgical menopause

Bilateral oophorectomy results in the loss of ovarian androgen and androgen precursor production (20) in both post-

menopausal and premenopausal women. The plasma concentrations of the major androgenic products of the ovaries are lower in postmenopausal oophorectomized women than in postmenopausal nonoophorectomized women (21). Thus, women with surgical menopause provide a model in which to study the efficacy of androgen therapy in women deprived of ovarian androgens. To optimize such studies, several issues should be considered. Investigators must ensure that women are matched by age and years since oophorectomy, as these factors may affect the clinical response to the intervention. Use of physiological estrogen therapy, by a parenteral route, should be considered in studies of estrogen with and without androgen to avoid the biochemical perturbations induced by oral estrogen therapy. Finally, subanalyses based on the initial indication for oophorectomy should be performed, as these factors may affect the ultimate efficacy of hormonal therapy. A recent study confirmed that perimenopausal women choosing elective hysterectomy and bilateral salpingo-oophorectomy over hysterectomy alone for benign disease did not show any deterioration in sexual function (22).

Hypopituitarism

Hypopituitarism in women results in compromised adrenal and ovarian function and is associated with very low plasma concentrations of androgens, including testosterone, free testosterone, androstenedione, and DHEA sulfate (DHEAS) (23). Hypopituitarism is therefore a useful condition in which to study the effects of replacement strategies on severe androgen deficiency in women. There is only a single randomized, placebo-controlled study of the effects of testosterone administration in women with hypopituitarism. In estrogen-replete, androgen-deficient women receiving testosterone patch compared with placebo, Miller *et al.* (24) showed an increase in hip and radial, but not spine, bone density. Thigh muscle mass, fat-free mass, mood, and sexual function as well as some aspects of quality of life improved, but there was no improvement in cognitive function (24). Arlt *et al.* (25) demonstrated improvements in sexual function, libido, and mood in a small randomized placebo-controlled study of DHEA, 50 mg daily, in women with adrenal insufficiency of primary or secondary origin. Three subsequent small, randomized, placebo-controlled studies of DHEA replacement (20–50 mg/d) in women with hypopituitarism (26–28) also reported improvements in quality of life; one (27) also found improved sexual function and another (28) found improved mood. However, these effects were generally small, and two other studies of women with adrenal insufficiency demonstrated no improvements in well-being (29, 30) with DHEA administration. Changes in body composition (29, 31) and bone density (27) have been investigated in a few studies of DHEA therapy, with only one demonstrating a statistically significant decrease in percentage of fat mass (29).

Anorexia nervosa

There are few data on androgen deficiency in women with anorexia nervosa. One 3-wk placebo-controlled trial in 33 androgen-deficient women with anorexia nervosa demonstrated increases in procollagen I carboxy-terminal propeptide (PICP), a bone formation marker, as well as improvements in mood and spatial cognition (32). In this same pilot study, mood also improved in depressed women with anorexia nervosa (32). DHEAS levels were decreased in women with anorexia nervosa (33). There have been no long-term placebo-controlled studies of the effects of testosterone administration in this population.

Adrenal insufficiency

Adrenal insufficiency is characterized by low DHEA and its metabolites, including testosterone (34). Arlt *et al.* (34) demonstrated a beneficial effect of DHEA in women with adrenal insufficiency (see *Hypopituitarism*). Several subsequent randomized, placebo-controlled studies of DHEA replacement in adrenal insufficiency have shown less consistent results (see *Hypopituitarism*) (28–31, 35).

Subjects with complete androgen insensitivity syndrome (CAIS)

Patients who have estrogens but are androgen resistant represent an uncommon but informative group. If androgens have a significant physiological role at various targets independent of estrogens, individuals with this syndrome would be predicted to have significant deficits. To date, little information is available. In one study of 22 subjects with CAIS, psychosexual adjustment did not differ from that of control women (36). In a long-term follow-up of subjects with CAIS, patients reported satisfaction with the female gender and sexual function (37); however, a recent assessment of 66 women with CAIS, who had had vaginal reconstruction, reported that 90% had sexual complaints, including infrequent intercourse and difficulties with vaginal penetration (38). The latter problem may be due to lack of adequate surgical vaginal reconstruction in such women, rather than an effect of androgen status.

Low-weight subjects with HIV

Lower mean androgen levels were observed in two studies of HIV-positive women compared with healthy controls (39, 40). However, placebo-controlled trials failed to demonstrate substantial increases in weight or muscle mass or alterations in neuropsychological endpoints in women with AIDS wasting who were given transdermal testosterone (150–300 μg daily) (41, 42). One randomized, placebo-controlled trial demonstrated an increase in strength in women receiving testosterone, compared with those receiving placebo, after 6 months of treatment (43).

Exogenous suppression of androgens

Glucocorticoid administration is associated with a rapid and marked suppression of DHEA, DHEAS, androstenedione, testosterone, and DHT in women (25). Such women are potential candidates for the study of androgen replacement. Administration of testosterone to glucocorticoid-treated men (44) has beneficial effects on measures of bone and body composition, but no data regarding women are available.

It has been suggested that some OCPs suppress ovarian

androgen production sufficiently to cause decreases in libido (45). However, it may not be the contraceptive alone that is responsible for a woman's decreased libido; psychological factors may contribute. It therefore becomes challenging to tease apart the role of other factors from androgen suppression in the alteration in libido of women taking OCPs (46, 47). Nonetheless, OCPs suppress total and free testosterone levels in women with polycystic ovarian syndrome to those seen in eumenorrheic women without polycystic ovarian syndrome (48), and in normal women levels are suppressed to below normal (23). Women on OCPs might provide a useful, albeit complex, group for studying effects of androgens. The androgenicity of the progestin in the OCP studied, as well as the effects of certain OCPs on body composition and SHBG (49), would need to be considered as confounding issues in this model.

Ablation-replacement paradigms in normal subjects

Women can have their ovarian steroid production suppressed with GnRH analogs with or without blockade of adrenal hormone secretion. The administration of aromatizable and nonaromatizable androgens to such subjects would provide a more precise definition of the dose-response relationships of androgens, as well as the possible role of conversion to estrogens in the responses in various target tissues. Aromatization by adipose tissue may increase with age and, thus, may affect plasma and cellular concentrations of estrogens (50, 51); controls for these variables should be included in future investigation.

Aging

DHEAS in plasma decreases with increasing age (52–54). Cross-sectional data indicate an approximately 80% decline from age 20 to age 80 yr. Because DHEAS is a stable marker of adrenal prohormone production, it typically has been used as the "gold standard" single measure. However, in the limited investigations performed to date, DHEA and other adrenal metabolites appeared to undergo an identical trajectory (53). Recent data from the Study of Women's Health Across the Nation (SWAN) (55), as well as data from nonhuman primates (56), indicate that natural menopause was associated with a brief rise in DHEA and DHEAS, although this finding was not shown in other databases.

Ovarian androgens do not decline dramatically with natural menopause. The data on circulating and bioavailable testosterone during the menopausal transition are not uniform. Four cohort studies have examined androgens in detail in naturally menopausal women. Rannevik *et al.* (57) studied 160 Swedish women longitudinally through the menopausal transition. Small but significant decreases in testosterone were observed. Decreases in SHBG were associated with increasing body mass index. DHEAS decreased over time, without acceleration at menopause.

The Massachusetts Women's Health Study (58), derived from a population-based sample of largely Caucasian women, reported results in 88 women sampled at 4- to 6-month intervals over a 10-yr period. A significant decline in DHT and DHEAS was observed, with a rise in androstenedione associated with traversal of the menopause (58). Similar results were seen in a smaller longitudinal study of 32 women (59). The Melbourne Healthy Women's Study (60) sampled blood across the menopausal transition in 172 of 450 women. There was no annual decrease in testosterone over the course of the transition, but an increase in free androgen index (FAI) was observed as was a decreasing SHBG. No support for a menopause-related decrease in ovarian androgens was found. SWAN, a multicenter, community-based cohort of 3302 women of five different ethnicities, reported baseline and 2-yr follow-up data on androgens (61). Women in SWAN were aged 42–52 yr at baseline, and all were relatively estrogen replete, with at least one menstrual period within the past 3 months. Initial and 2-yr follow-up of serum testosterone found no correlation of testosterone with menopausal status. Testosterone and FAI were noted to be strongly positively correlated to the presence of the metabolic syndrome at baseline and were less strongly correlated to self-rated health, well-being, and sexual desire and arousal. Testosterone and FAI were negatively correlated to Center for Epidemiological Studies-Depression Scale (CES-D) scores; DHEAS was directly correlated to higher physical functioning and self-rated health (62). Most of these population studies used commercially available kit assays for the measurement of total testosterone; these assays are known to have limited sensitivity and accuracy at lower values. Thus, interpretation of the normative data in the literature must be viewed as preliminary until more sensitive assays are validated.

The published data indicate a progressive, substantial, age-related decline in DHEAS. There is minimal evidence to support a decline in testosterone associated with the menopause transition *per se*; only one of the four cohorts described above reported a slight but statistically significant decline (57). If circulating hormones are meaningful indicators of biological activity, then the natural menopause cannot be conceptualized as an ovarian androgen-deficiency state. However, testosterone levels do decline substantially from the mid-reproductive years (21, 63) such that, relative to women in their twenties, women in their forties have an approximately 50% reduction in plasma testosterone. This process occurs before the menopausal transition, and its etiology is unclear. Because of the complexities of the process and the limitations of current testosterone and free testosterone assays, women with natural menopause would not be an optimal model in which to initially investigate testosterone replacement, yet this is the population to which most investigational data are intended to be applied.

4.2.A RECOMMENDATION

We recommend additional investigation using rodent and primate models to further define the specific targets of androgen action (1|⊕○○○).

4.2.B EVIDENCE

Animal or cell models are needed to define potential markers of androgen action. Although certain endpoints of androgen action [*e.g.* bone mineral density (BMD) or turnover, body composition, *etc.*] are relatively easy to assess in humans, potential effects of androgens on brain function or

sexual responses are much more subjective and difficult to evaluate. The development of potential markers of such responses (*e.g.* using specialized brain-imaging techniques) in these animal models would greatly aid further research in the area of androgen's effects on brain and sexual function in women.

4.3.A RECOMMENDATION

We recommend additional research into the role of local androgen production, action, and metabolism in tissues (1|⊕○○○).

4.3.B EVIDENCE

Steroids are secreted and may act as such or be converted in target tissues to an active principle. For example, testosterone is both a hormone (*i.e.* acts as such in tissues such as muscle) and a prohormone (*i.e.* is converted into DHT) (64), which is the active principle in tissues such as skin. This situation is further complicated by the occurrence of small fractional conversions of steroids, present in high concentrations in plasma, *e.g.* DHEA and DHEAS, to yield biologically relevant amounts of active hormones, *e.g.* testosterone (65–67). Furthermore, if the testosterone that arises in cells from plasma precursors is additionally metabolized within those cells, without passing through the plasma, then we have no current measure of these effects. In addition, this tells us that hormone action may be influenced not only by the secretion, clearance, and plasma binding of testosterone, but also by the activity of enzymes within cells that convert it into an active metabolite that may change with physiology, pathology, and age. That these events occur is unquestionable. How relevant they are to our understanding of androgen therapy for women is unclear. There are pathological states, *e.g.* androgenic alopecia in women, with normal plasma testosterone, where we assume the hypersensitivity of the scalp to normal concentrations of circulating testosterone is based on such mechanisms, *e.g.* increased activity of 5α-reductase. We currently have no method to evaluate such mechanisms in the normal woman who is hypothesized to be hypoandrogenic and, therefore, for the moment, we must proceed in clinical decision making with the use of plasma-based assays.

4.4.A RECOMMENDATION

We recommend further study of physiological targets of androgen action (1|⊕○○○) *such as:*

- *Sexual dysfunction*
- *Cognition*
- *Mood*
- *Bone*
- *Cardiovascular function*
- *Body composition*
- *Muscle strength and function*

4.4.B EVIDENCE

Sexual dysfunction

Testosterone therapy at supraphysiological dosing in animals and humans is associated with increased arterial flow-mediated dilatation (68), vaginal blood flow (69, 70), and vaginal smooth muscle contractility (71). Large clinical studies, which included 2961 and 1021 women across the lifespan, indicate that serum levels of testosterone using current assays (free, calculated free, total, or bioavailable) do not correlate with sexual function (52, 62). Difficulties in interpretation arise from the lack of accuracy of the assays, a lack of consensus on the optimal time for measuring testosterone during the menstrual cycle, and a lack of consensus on the definition of sexual function and measurement instruments. Finally, the inability to measure testosterone produced within target cells from precursors is an issue that cannot be addressed with current methodology.

Women's sexual dysfunctions result from the interplay of many personal, interpersonal, contextual, and medical factors (77–80). In any one woman, changes in androgens may or may not be relevant. Apparent "dysfunction" frequently results from adaptation to a nonconducive psychosocial milieu, often with no defect in the woman's physical sexual response system (77, 81, 82). Four factors have been shown to correlate robustly with women's sexual function/satisfaction: the woman's mental and emotional health including her sexual self-image (77, 78, 83); her feelings for her partner both at the time of sexual interaction and in general (77, 84); her expectations regarding the future of the relationship (85, 86); and her past sexual experiences (84). Other factors showing strong correlation include the woman's perception of her general health (87), her perceived level of stress (85), her partner's sexual function (88), and the duration of the relationship (84, 89).

Studies of testosterone therapy to date have excluded women with depression, problematic relationships, poor health, and partners with sexual dysfunction, yet these comorbidities are common. Studies are needed in which, along with optimal hormonal evaluation, these psychosocial factors are carefully examined. The interaction between these underlying issues and response to exogenous testosterone warrants exploration.

To date, the main evidence that testosterone has a role in women's sexual function comes from the benefit of testosterone supplementation in surgically menopausal women complaining of sexual dysfunction. Of the 24 separate trials before November 2003 addressing testosterone treatment, five recruited women with sexual dysfunction, nine reported effects on sexual function, and only three provided data suitable for meta-analysis—two of these involved methyl testosterone and one involved testosterone implants (reviewed in Ref. 90). Two of the reviewed studies involved transdermal testosterone, and the remainder used either methyl testosterone or injectable testosterone to achieve plasma levels exceeding the upper limits of normal in younger women (91–98).

Four subsequent studies used transdermal testosterone given to estrogen-replete oophorectomized women and achieved testosterone levels at the upper end of the normal range for young healthy women in the assay used (99–102). One trial of transdermal testosterone in naturally menopausal women has been reported (103). Using validated unpublished questionnaires, all five studies showed a significant increase in desire and response scores, and four showed significant reductions in distress scores. After 24 wk of trans-

dermal testosterone patch therapy, there were small but significant correlations observed among changes in serum total, bioavailable, and free testosterone and the frequency of satisfying sexual activity (Spearman's rank correlation of 0.16 to 0.18; $P < 0.05$). For sexual desire, the correlations with total and free testosterone were 0.20 to 0.25 ($P < 0.05$), and for personal distress the correlation was −0.11 to −0.17 ($P < 0.05$) (100). Only one study was dose ranging, and the data suggest a dose-response relationship (100). Similarly, in the trial in which all women used transdermal estradiol patches, serum total and free testosterone and DHT correlated with desire, arousal, orgasm, pleasure responsiveness, and the number of satisfying sexual events (101). Although modest, there were also statistically significant correlations between testosterone levels and multiple aspects of sexual response in the study of naturally menopausal women (103). The overall size of the effect is small in these studies, resulting in approximately one more episode of satisfying sexual activity per month compared with controls. However, after exclusion of women using conjugated equine estrogens from the analysis, the effect size was increased to a mean of two more episodes per month compared with controls (Procter & Gamble Pharmaceuticals, FDA Advisory Committee Briefing Document NDA 21-769; available at http://www.fda.gov/OHRMS/DOCKETS/AC/04/briefing/2004-4082B1_01_A-P&G-Intrinsa.pdf). The benefit over placebo was observed with the 300-μg, but not the 150- or 450-μg, patch administered biweekly.

Despite the documented benefit of transdermal testosterone in estrogen-replete women, there are two major factors precluding its recommendation for broad use. Because women initiating therapy may wish to remain sexually active indefinitely (104), the lack of long-term safety data of testosterone therapy and the reservations about long-term estrogen therapy preclude recommendation. There are no data regarding the sexual benefit of transdermal testosterone in estrogen-deficient women at present.

The second major reason is the lack of a clear definition of the "disorder." The recent trials recruited women diagnosed with "hypoactive sexual desire disorder." The definition of this entity assumes that sexually satisfied women initiate or accept sexual activity for reasons of desire. This is not evidence based (73, 105–108). Thus, further work is ongoing to reassess the official definitions of women's sexual dysfunction (81, 82, 109–112).

Definitions of women's sexual dysfunction

"Hypoactive sexual desire disorder" is defined in the *American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders*, Text Revised (DSM-IV-TR) (113) as follows: "Persistently recurrently deficient (or absent) sexual fantasies and desire for sexual activity. The judgment of deficiency or absence is made by the clinician, taking into account factors that affect sexual functioning, such as age and context of the person's life, the disturbance causes marked distress or interpersonal difficulty." Of note, the DSM-IV-TR definition is the same for women as for men. However, lack of desire at the outset of sexual engagement is common for sexually content women and sexual thoughts are infrequent in many women without sexual complaints (77). Furthermore, the frequency of sexual fantasies has little correlation with women's sexual satisfaction (77, 86).

Randomized controlled trials have not yet been conducted in women using the recently revised definition of sexual desire/interest disorder defined as "absent or diminished feelings of sexual interest or desire, absence of sexual thoughts or fantasies, *and a lack of responsive desire.* Motivations (here defined as reasons/incentives) for attempting to become sexually aroused are scarce or absent. The lack of interest is considered to be beyond the normative lessening with lifecycle and relationship duration" (81). The revised definition clarifies that lack of spontaneous or initial desire is not of itself dysfunctional; rather, it is the additional inability to become aroused, to sense pleasure and trigger *responsive* desire during the sexual encounter that constitutes disorder. Of note, the recent testosterone-patch trials reported increases not only in desire but also in arousal, pleasure, and orgasmic response. It would, therefore, be important to study women recruited on the basis of the new definitions of desire/interest disorder: the focus would be on restoring subjective arousal and pleasure such that desire is triggered during the sexual experience and not on "spontaneous/initial" desire. The latter is more typically present at the beginning of new relationships (89) and is known to have a broad range of frequency across sexually satisfied women (72) as well as to lessen gradually with age. Because all recent randomized controlled trials have used testosterone rather than a nonaromatizable androgen, it is unclear whether the sexual benefit is ultimately conferred by an androgen or an estrogen. However, one recently published study indicates that the effect may not require aromatization (101).

Need for industry-independent studies of female sexual dysfunction

There is a need for non-industry-funded research into female sexual health, the physiological role of androgenic steroids, and the efficacy and safety of pharmacotherapy. Such industry-independent randomized placebo-controlled trials should recruit women diagnosed with sexual desire/interest and arousal disorders consonant with the current definitions of women's sexual disorders. The focus would then be on women for whom no sexual experiences are satisfying. Given the confirmed multifactorial nature of women's sexual function and dysfunction, both hormonal and nonhormonal factors should be carefully investigated. Women receiving testosterone therapy must receive long-term follow-up, with the expectation that therapy will be open-ended.

Cognition

Tests of cognition should be sensitive to subtle changes that fall within the average range of performances. Unfortunately, most tests of cognition were not developed to measure subtle changes in cognitively intact persons. In addition, the repeated administration of the same tests leads to some improvement in performance in healthy participants. For example, improvement in total learning over five trials of the California Verbal Learning Test (CVLT) is well documented

(115). Only tests shown to have minimal practice effects can be readministered repeatedly, yet few validated tests of cognition meet this requirement. Finally, if aromatizable androgens are administered, the effects on specific cognitive outcome measures change across the day as the androgen is converted into estrogens (116).

Few studies have investigated the effects of exogenous testosterone on cognition. Of these, several did not randomize for estrogen replacement in postmenopausal women, although testosterone was given randomly. Many of the studies have been underpowered, and cognitive measurement used only subscales of validated instruments. It is highly likely, therefore, that the finding of a single improvement in score on one test was a chance finding. Androgen doses typically have been large, resulting in supraphysiological plasma levels. Thus, the available evidence does not demonstrate a consistent effect, the methodology often has been invalid, and the generalizability of the data is unknown.

In two studies of premenopausal women, improvements in specific aspects of cognitive function have been reported after a single supraphysiological dose of testosterone (117, 118). Specifically, improvements in visuospatial memory were reported after a dose of 0.5 mg testosterone was administered sublingually; the assessment was undertaken shortly thereafter. Although testosterone levels were not measured in either study, the authors report that this dose was associated with a 10-fold increase in total testosterone levels within 15 min of intake. Such levels are supraphysiological for women and approximate those in men.

In postmenopausal women, two studies of methyltestosterone (MT) reported improvements in isolated cognitive tasks (119, 120). Wisniewski *et al.* (120) reported no statistically significant difference between treatments for visuospatial memory but reported maintenance of the Building Memory Task score for the MT-treated group. In a double-blind cross-over study, Regestein *et al.* (119) reported a significant benefit of MT on the Switching Attention Test.

In a cross-over study, there was no effect on cognitive function of supraphysiological intramuscular injections of estrogen plus testosterone *vs.* estrogen alone (121). A 3-wk randomized placebo-controlled study demonstrated that transdermal testosterone (150–300 μg) resulted in improvements in spatial cognition in women with anorexia nervosa (32). In a subset of these subjects, positron emission tomography (PET) scans showed improvements in brain hypometabolism in the posterior cingulate cortex after testosterone administration. These salutary changes were associated with improvements in spatial cognitive testing (32). Such experiments provide an example of a quantifiable outcome that is amenable to serial measurement.

Mood

No studies using validated psychiatric tools have specifically investigated the effects of testosterone or DHEA administration on mood in depressed women. Mood has been investigated as a secondary endpoint in several small studies in other populations. These populations include women of reproductive age with bilateral oophorectomy (122), sexual dysfunction (123), or anorexia nervosa (32).

Bone

With the use of new, high-sensitivity testosterone assays, both trabecular and cortical BMD have been recently shown to be associated with serum bioavailable testosterone levels, particularly in late postmenopausal women (124). There are no data on the effects of androgen replacement in women on the risk of fracture. Relatively small studies, using BMD as a fracture surrogate, are inconsistent. Two studies comparing oral estrogens or estrogens plus androgens (125) or estradiol and estradiol plus testosterone implants (126) in postmenopausal women found no significant effect of added testosterone on spine or hip BMD. By contrast, three studies comparing oral estrogens and oral estrogens plus androgens (127), sublingual estradiol with estradiol plus testosterone (128), or estradiol implants with estradiol plus testosterone implants (94) showed that the addition of testosterone therapy to estrogen replacement enhanced increases in spine and/or hip BMD. One study in estrogen-replete women with androgen deficiency associated with hypopituitarism showed increased BMD at the hip and radius but not spine (24). Bone resorption markers decrease similarly with estrogen alone or combined with testosterone (128, 129); there may be a short-term (over 9 wk) maintenance (or increase) of bone formation markers with the addition of testosterone (129) as compared with estrogen alone (128, 129). The clinical relevance of this difference in terms of changes in BMD or fracture risk remains unknown. Only one randomized placebo-controlled study investigated the effect of transdermal testosterone on bone markers in the absence of estrogen administration. Procollagen I carboxy-terminal propeptide (PICP), a bone formation marker, increased over 3 wk in women with anorexia nervosa (32). The clinical relevance of the differences in the markers, in terms of changes in BMD or fracture risk, remains unknown.

Cardiovascular function

Effects on lipoproteins. Dissecting the possible role of sex steroids in cardiovascular disease (CVD) due to alterations in lipoproteins is complex. Understanding the relationships between SHBG and the CVD risk factors is critical in determining whether androgens in women contribute to CVD risk. SHBG is produced by the liver and is a pivotal determinant of the concentration of free sex steroids (130). Estrogens increase, whereas androgens and insulin decrease, SHBG concentration in plasma (131). Insulin has been shown to be a strong independent marker of insulin resistance (132, 133). Several studies have demonstrated that low SHBG is associated with increased CVD risk and coronary disease mortality in women and men (134–137).

Numerous studies have reported an association among the FAI, CVD risk factors, and the metabolic syndrome (135, 137–139). The nature of the underlying relationships and mechanisms for them remain unknown. In a study of 200 women not using hormone therapy, lower SHBG and higher FAI levels were noted among postmenopausal women who developed CVD events; however, this was not statistically significant after adjusting for body mass index and other cardiovascular risk factors (140). Additional outcome studies are needed to identify the strength of the relationship be-

tween SHBG, insulin resistance, and CVD end points in women, as well as mechanistic studies capable of teasing out the independent contributions of androgens, should they exist.

Other surrogate markers for vascular function. Studies of the effects of exogenous androgens on lipids have involved the administration of oral MT or transdermal testosterone. These different modes of testosterone administration result in different effects on lipoproteins. Oral MT (2.5 mg) has consistently been associated with a reduction in high-density lipoprotein cholesterol (90, 141), whereas this has not been observed with transdermal testosterone (32, 42, 122, 142). MT also has been associated with reductions in triglycerides but with inconsistent findings with respect to total cholesterol and low-density lipoprotein cholesterol (90).

Other surrogate markers for the effects of testosterone on the cardiovascular system include effects on endothelial function, carotid intima-media thickness, and coronary artery calcification, among others. Research on these surrogate vascular markers in women has been mostly limited to studies of women with polycystic ovarian syndrome. Because this is not simply a condition of androgen excess but also involves an intrinsic insulin resistance, findings from these studies cannot be extrapolated to the use of exogenous androgens or endogenous androgen effects in otherwise healthy women. One open-label study of flow-mediated blood vessel dilation in women, with and without testosterone implants with or without pharmacologically induced testosterone levels, showed no adverse effects of testosterone treatment on this measure of endothelial function (68). Additional data are needed on the effects of physiological testosterone administration on vascular markers in women.

Body composition

Three studies have found that addition of testosterone to conjugated estrogen replacement resulted in greater increases in fat-free mass (143, 144). Davis *et al.* (143) found that fat-free mass increased by 12.5% in the estrogen plus testosterone group but remained unchanged in the estrogen alone group, and Dobs *et al.* (144) found that lean body mass increased by 1.2 kg with estrogen plus testosterone therapy as compared with only a 0.4-kg increase with estrogen alone. In one of these studies (143), testosterone appeared to attenuate the reduction observed in central body fat with estrogen alone. Thus, although estrogen administration decreased the ratio of fat mass to fat-free mass in a region directly over the abdomen (as measured by dual-energy x-ray absorptiometry), this effect was lost in the group treated with estrogen plus testosterone. Miller *et al.* (24) demonstrated increases in thigh muscle area by cross-sectional computed tomography.

Muscle strength and function

In two studies, transdermal testosterone treatment (300 μg) in women with AIDS led to no increase in fat-free or muscle mass (41, 43); one (43) showed increases in strength. One randomized, placebo-controlled study of 40 postmenopausal women demonstrated increases in fat-free mass and increased strength in those receiving esterified estrogen plus MT (1.25 mg estrogen + 2.5 mg MT/d) compared with esterified estrogen alone (1.25 mg/d; Ref. 144). One randomized, placebo-controlled study demonstrated an increase in lean body mass with nandrolone decanoate plus caloric restriction compared with caloric restriction alone in obese postmenopausal women (145). More data are needed.

4.5.A RECOMMENDATION

We recommend the following endpoints be considered for safety and risk assessment in future studies (1|⊕○○○):

- *Alterations in the endometrium after androgen administration, with and without estrogen coadministration.*
- *Effects of androgen therapy on the breast with or without estrogen replacement should be measured, including mammographic density. Breast biopsy studies with in vitro markers of cell proliferation and apoptosis should be considered.*
- *Cardiovascular and metabolic end points should include fasting lipid profiles, vascular reactivity, fasting glucose and insulin levels, and inflammatory markers such as adiponectin and C-reactive protein.*
- *Hirsutism, acne, male pattern balding, and change in voice should be monitored.*

4.5.B EVIDENCE

Endometrium

It is widely believed that androgens, acting through classical androgen receptor mechanisms, are antiproliferative in the human endometrium. In support of this hypothesis, evidence from a study using mixed progesterone agonists suggests that these agents mediate endometrial atrophy by up-regulating the androgen receptor (146). Endometrial adenocarcinoma growth is prevented by androgens, and the presence of androgen receptors appears to be associated with reduced proliferation (147). Although endometrial hyperplasia would appear to be unlikely in women taking exogenous androgens, the endometrium should be monitored in an adequately powered randomized control trial.

Breast

Androgens, acting through the androgen receptor, oppose estradiol-induced proliferation of human breast cancer cell lines (148). Zhou *et al.* (149) have demonstrated androgen-induced down-regulation of mammary epithelial proliferation and estrogen receptor expression in primates. Clinically, women with elevated androgen levels, either endogenous or exogenous, experience breast atrophy, consistent with the notion that androgens *per se* are antiproliferative for the breast. However, advanced proliferative premalignant breast lesions are known to have enhanced local aromatase (150, 151), and the possibility exists that aromatization of exogenous androgens could contribute to breast cancer risk for women taking them.

If one looks at polycystic ovarian syndrome as a model of androgen excess, the risk of breast cancer is not increased despite hyperandrogenism and long-term exposure to unopposed estrogens (74, 75). In fact, Gammon and Thompson (75) reported an age-adjusted odds ratio for breast cancer in women with this syndrome of 0.52 (95% confidence interval,

0.32 to 0.87). In postmenopausal women, there are inconsistent results as to the relation of testosterone levels to breast cancer risk in both cross-sectional studies and prospective studies. Limitations of the studies include use of insensitive assays, measurement of only total testosterone, and failure to take into consideration the diurnal variation of testosterone when drawing blood (114). Thus, the evidence pertaining to the use of testosterone therapy and breast cancer risk has significant methodological limitations and inconclusive results (114).

Cardiovascular and metabolic function

Metabolic safety parameters that should be evaluated in future clinical trials include lipids, fasting glucose, and insulin. Effects on inflammatory markers such as C-reactive protein should be assessed.

Side effects on skin and voice

Hirsutism, acne, male pattern balding, and deepening of voice should be monitored. Most recent studies using doses of testosterone that result in free testosterone in or near the normal range for women report no increase in hirsutism, acne, or virilizing side effects with short-term administration (42, 99, 100, 102, 122). However, data in this regard are limited by sample size, the failure of many studies to report the presence or absence of side effects, lack of objective measures, and short study duration. Monitoring of facial and body hair is limited by the common use of depilatory techniques. Therefore, frequency of depilation may be a more sensitive end point to detect increases in hirsutism. For example, Shifren *et al.* (122) found no increases in hirsutism when measured by the Lorenzo scale but detected an increase in depilatory rates, compared with baseline, in women receiving transdermal testosterone at 300 μg daily. Importantly, long-term effects (>1 yr) of androgen administration in women on these outcomes have not been established.

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DUEC New Drugs January - March 2010

Fanapt	iloperidone	Fanapt is an atypical antipsychotic indicted for the acute treatment of schizophrenia in adults. Fanapt, like all other atypical antipsychotics, has a Black Box Warning regarding an increased risk of mortality in elderly patients with dementia-related psychosis treated with antipsychotic drugs.	EXCLUDE. One 4w trial iloperidone, ziprasidone, or placebo in n=593 acute schizophrenia exacerbations. Ilop was better than placebo (P<0.01). Zip was better than placebo (p<0.05), NS ilop vs zip.J Clin Psychopharmacol. 2008 Apr;28(2 Suppl 1):S20-8.		
Oforta	fludarabine phosphate	Oforta™ (fludarabine phosphate tablets) for oral use is indicated as a single agent for the treatment of adult patients with B-cell chronic lymphocytic leukemia (CLL) whose disease has not responded to or has progressed during or after treatment with at least one standard alkylating-agent containing regimen.	T3 with PA: 1. CLL, or 2. Non-Hodgkin's Lymphoma		
Sumavel	sumatriptan succinate inj	Sumavel is a 5-HT receptor agonist indicated for the acute treatment of migraine attacks, with or withoiut aura and the acute treatment of cluster headache episodes. It is a pre-filled, single-dose, needle-free subcutaneous delivery system containing 6mg of sumatriptan succinate.	T3 or exclude (would be like a mandatory generic). But a generic is available. $400 vs $250/m		
Soriatane	acitretin	SORIATANE is indicated for the treatment of severe psoriasis in adults. Due to the risk of severe birth defects, in females of reproductive potential SORIATANE should be reserved for nonpregnant patients with severe psoriasis who are unresponsive to other therapies or whose clinical condition contraindicates the use of other treatments.	T3; may look at utilization in 6 m. I doubt this drug would be used inappropriately and thus a PA would likely have 100% approval.		
Wilate	antihemophilic factor /VWF (Human)	Wilate is a von Willebrand Factor/Coagulation Factor VIII Complex (Human) indicated for the treatment of spontaneous and trauma-induced bleeding episodes in patients with severe von Willebrand disease (VWD) as well as patients with mild or moderate VWD in whom the use of desmopressin is known or suspected to be ineffective or contraindicated. Wilate is not indicated for the prophylaxis of spontaneous bleeding episodes, or the prevention of excessive bleeding during and after surgery in VWD patients. Wilate is also not indicated for Hemophilia A	T3 PA. PA criteria: 1. requires TREATMENT of spontaneous or trauma-induced bleeding episodes (NOT for prevention of bleeding during/after surgery), AND 2. has the dx of severe von Willebrand disease, OR has the dx of mild-mod VWD and desmopressin is ineffective or contraindicated.		
Actemra	tocilizumab	Actemra is a recombinant humanized anti-human interleukin-6 (IL-6) receptor inhibitor indicated for the treatment of adult patients with moderately-to-severely active Rheumatoid Arthritis (RA) who have had an inadequate response to one or more Tissue Necrosis Factor (TNF) antagoinist therapies.	Superior to MTX in MTX naïve pts. But FDA-approved for RA adults who have failed antiTNF drugs. T3 PA: 1. Dx of RA, 2. Failed anti-TNF therapy, 3. Not on concomitant anti-TNF therapy, IL-1R antagonists (ex. anakinra), anti-CD 20 monoclonal a		

Victoza	liraglutide	Victoza is a glucagon-like peptide-1 (GLP-1) receptor agonist indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. Important limitations of use associated with Victoza include: 1) not recommended as first-line therapy for patients inadequately controlled on diet and exercise, 2) has not been studied sufficiently in patients with a history of pancreatitis, caution is recommended in this patient population; 3) not for treatment of type 1 diabetes mellitus; and 4) has not been studied in combination with insulin.	Exclude. (see package insert)		
Zyprexa Relprevv inj	olanzapine pamoate for ext release IM	ZYPREXA® RELPREVV™ is a long-acting atypical antipsychotic for intramuscular injection indicated for the treatement of schizophrenia.	No info yet.		
Ampyra	dalfampridine	Ampyra is a broad spectrum potassium channel blocker indicated to improve walking in patients with multiple sclerosis (MS) demonstrated by an increase in walking speed. It is the first oral therapy approved for MS, the first therapy specifically approved to treat a symptom of MS, and the first new therapy for MS since 2004. Ampyra will likely be used in addition to the biologic MS agents.	Approved 3/25/10. No peer-reviewed and published trials in PUBMED. The PI summarizes 3 trials. One showed that 55% alf and 30% placebo improved their 25 feet walking test by at least 10%. To qualify for the trial, pts had to be able to walk 25 feet in 8-45 seconds. This drug helped 20% more patients walk it 10% faster. EXCLUDE at this time.		
Xiaflex inj	collagenase clostridium histolyticum	Xiaflex is indicated for the treatment of adult patients with Dupuytren's contracturewith a palpable cord. Xiaflex is designed to reduce collagen deposits and scar tissue in the hands stemming from Dupuytren's contracture. Auxillium Pharmaceuticals estimates that there are 240,000 annual candidates for Xiaflex in the U.S. and Europe.	XIAFLEX is only available through a managed distribution program called XIAFLEX Xperience™. This program was developed as part of Auxilium's commitment to patient safety. Only enrolled, qualified healthcare providers may have access to XIAFLEX. Physicians must complete the XIAFLEX Xperience™ training and enrollment process before their healthcare facility may receive XIAFLEX orders. Only enrolled healthcare sites may receive XIAFLEX orders. Healthcare site enrollment requires an authorized site representative (physician, administrator, pharmacist, nurse, or staff member) to coordinate activities internally and assure compliance with the XIAFLEX Xperience™ program . T3 (or with PA. I am unsure this drug would be used inappropriately.)		
Cayston Inh	aztreonam for inhalation	Caystonis indicated to improve respiratory symptoms in cysticfibrosis (CF) patients with *Psedomonas aeruginosa*. Cayston provides an alternative to Tobi but it does require reconstiatution prior to use as opposed to Tobi's availability in ready tp use solultoin. Also, Cayston is dosed three times per day compared to Tobi at twice daily dosing.	Cayston is administered with the Altera Nebulizer System, a new device that allows patients to take the medicine in less than 5 minutes, reducing the burden of the typical treatment regimen that may take 3 to 4 hours per day. T3 PA. PA Criteria: 1. Dx of cystic fibrosis, and 2. known pulmonary infection with Pseudomonas aeruginosa, and 3. on concurrent bronchodilator therapy.		
Mirapex ER	pramipexole SR	Extended release version of pramipexole indicated for the treatment of early idiopathic Parkinson's disease in once daily dosing compared to the 3x per day dosing of the immediate release generic product.	T3		

Revatio inj	sildenafil citrate IV soln 10mg/12.5ml	REVATIO® is indicated for the treatment of pulmonary arterial hypertension (WHO Group I) to improve exercise ability and delay clinical worsening. The injectable version is given as an IV bolus of 10mg three times daily It is intended for patients already taking oral Revatio who are temporarily unable to take oral medication.	N/A for outpatient.		
Endal CD	codeine/diphenhydramine/phenylephrine		No info in Facts & Comparisons. OTC alternatives available. Exclude		
Folivane OB	prenatal multivitamine without Vit A with Minerals, Iron, and Folate capsules and tablets		No info in Facts & Comparisons. OTC alternatives available. Exclude		
Welchol Pak	COLESEVELAM HYDROCHLORIDE 3.75g powder packet for suspension		This is the reference listed drug. It would be used only in those 10 and over and there are tablets available. Exclude.		
Adrenaclick	epinephrine 0.15mg or 0.3mg auto-injector		Adrenaclick 0.15mg or 0.3mg, AWP = $73.15/syr; Epipen 0.15mg or 0.3mg, AWP = $74.58/syr; Twinject 0.15mg or 0.3mg, AWP = $100.13/syr. Include same place as Epipen.		
Pacnex MX Liq	benzoyl peroxide 4.5% liquid wash		Exclude. Generics available at approximately the same strengths.		
Respa C&C IR			Exclude. No info in Facts & Comparisons.		
Sumaxin Wash Liq	sulfacetamide sodium 10% and sulfur 4%)		Exclude. Cheaper generics available.		
Accuhist Drops			Exclude. No info in Facts & Comparisons.		
Accuhist drops PDX syrup	dextromethorphan 5mg, guaifenesin 50mg, phenylephrine 5mg, brompheniramine 2mg		Exclude. This is not novel. OTC alternatives. For ages 2 and up. Follow our Cough & Cold policy.		
Citranatal Mis 90 DHA			Exclude. Many generic alternatives		
Citranatal Mis B-Calm			Exclude. Many generic alternatives		
Drymax Syp			Exclude. No information in Facts & Comparisons.		
Ferralet 90			Exclude. carbonyl iron (Ferralet 90, Feosol Carbonyl Iron) is pure elemental iron, absorbed slowly so may be preferred if accidental ingestion is a concern.		

Giltuss TR	dextromethorphan, guaifenesin, phenylephrine		Exclude.		
Marnatal-F cap			Exclude. No info in Facts & Comparisons.		
Neutrasal Pow	Saliva Substitute		**Powder**; **oral** : 50 mg calcium chloride, 10 mg dibasic sodium phosphate, 10 mg monobasic sodium phosphate, 2 mg silicon dioxide, 450 mg sodium chloride, 16 mg sodium bicarbonate		
Rescon – JR			Exclude. No info in Facts & Comparisons.		
Salvax Duo Kit Plus	**Foam**: 6% salicylic acid, 40% urea, glycerin, parabens		Exclude. No info, not indexed.		
DUET DHA	prenatal vitamin		Exclude. No info in Fact & Comparisons.		
Pramosone E cream	hydrocortisone, pramoxine, vit E?		Exclude. No info on the FDA website.		
Prenexa cap	prenatal vitamin		Exclude. No info in Facts & Comparisons.		
Prolex DMX Liq			Exclude. No info in Facts & Comparisons.		
Carbapehn 12			Exclude. No info in Facts & Comparisons.		
Cleanse/Trea			?		
Ultravate Kit	halobetasol cream + kit		Exclude. Generic cream available not part of a kit.		
V-Cof Sus			Exclude.		
V-Hist Sus			Exclude. Not indexed.		
Avar LS Liq Cleanser	sulfacetamide sodium and sulfur		Exclude. Alternatives available. No info on this specific product.		
Avar-E LS			Exclude. Alternatives available. No info on this specific product.		
Donatuss XP			Exclude. Not indexed.		
E-Z-Disk tab	Barium Tablet		T3 or exclude. EZ disk 700mg tab AWP=$2.15/tab. Esopho-CAT 3%, $2.20/d. 30G Jar AWP=$0.22/g		
TL G-Fol OS			Exclude. Not even indexed in Facts & Comparisons.		
Zonatuss cap			Exclude. No info.		
Prefera OB cap	prenatal vitamin		Exclude. Alternatives available. No info on this specific one.		