Division of Medicaid

Office of the Governor

State of Mississippi

DUR Board Meeting

June 23, 2005

DIVISION OF MEDICAID
OFFICE OF THE GOVERNOR
DRUG UTILIZATION REVIEW BOARD
AGENDA

June 23, 2005

Welcome — **Tim Alford, MD**

Old Business

Reading and Approval of March 31, 2005 DUR Board Meeting Minutes — **Lew Anne Snow, RN**

CNS Update — **Frankie Rutledge**

Updates — **Dennis Smith, RPh**

- **Antibiotic Utilization in Children**
- **Hydroxyurea Use in Sickle Cell Therapy**
- **NSAID/Celebrex® Utilization Analysis**
- **Cost Management Analysis**

Pharmacy Program Update — **Judith Clark, RPh**

New Business

DUR Intervention — **Dennis Smith, RPh**

- **Overview of DUR Intervention Process**
- **Osteoporosis Targeted Intervention**
- **Prevention of Cardiovascular Events**
  Leigh Ann Ross, PharmD
- **Suggested Interventions**
- **Second Quarter Criteria Recommendations**

Black Box Warnings or Boxed Warning Update — **Dennis Smith, RPh**

Next Meeting Information — **Tim Alford, MD**

Minutes of the March 31, 2005
Drug Utilization Review (DUR) Board Meeting

Members Attending: Billy Brown , PharmD, Randy Calvert, RPh., Montez Carter, RPh., John Mitchell, M.D., Lee Montgomery, M.D., Joe McGuffee, RPh., Lee Anne Ross, PharmD., Rudy Runnels, M.D., Cynthia Undesser, M.D.,

Members Absent: Tim Alford, M.D., Clarence Dubose, RPh., Andrea Phillips, M.D.

Also Present: Judith Clark, RPh., Gay Gibson, R.N., Phillip Meredith, M.D., Sharon Barnett-Myers, Rich Robertson – DOM
Lew Anne Snow, R.N., Kathleen Burns, R.N., Sam Warman, RPh., HID

Dr John Mitchell called the meeting to order at 2:05p.m.

Approval of the minutes of last meeting (November 18, 2004): Dr. Undesser made a motion to accept the minutes as written. Montez Carter seconded the motion. All voted in favor of the approval.

Reports:
Update on Inappropriate Therapy for the Elderly
Sam Warman presented information about the following interventions regarding inappropriate therapy for the elderly:

- Inappropriate Therapy for the elderly: Ambien and Sonata
- Inappropriate Therapy for the elderly: long half-life Benzodiazepine Anxiolytics and Sedatives
- Inappropriate Therapy for elderly: Barbiturate Sedative/Hypnotics
- Inappropriate Therapy for elderly: certain Tertiary Tricyclic Amines

There were 697 educational intervention letters with attached response forms mailed to prescribers for the identified recipients. There were 919 fewer prescriptions written for the identified beneficiaries after intervention letters were mailed to physicians. This reduction in prescriptions resulted in a cost savings of about $98.32 per beneficiary. No vote was taken on the recommendations at this time due to the implementation of a CNS program approved by DOM.

Effect of Recent News on Cox-2 Inhibitor Utilization:
Sam Warman presented a review on the utilization of COX-2 Inhibitors following the voluntary removal of Vioxx from the market in September 2004. The information presented showed that prescriptions for Celebrex and Bextra remained almost equal in number as prior to September 2004. There was a significant increase in the NSAID therapeutic class as well as narcotic analgesics. Judith Clark explained that the P&T Committee voted to leave the COX-2 inhibitors on prior authorization pending the FDA review of COX-2 inhibitors.

Antibiotic Utilization in Children:
Sam Warman presented a report regarding antibiotic and antihistamine utilization in children. Data from December 2003 through November 2004 for children 0-20 years of age was reviewed for total prescriptions per month for both antibiotic and antihistamine therapy. Using data from December 1, 2003 through December 31, 2003 as an example, there were 2,617 beneficiaries who received Zithromax and another antibiotic during this time period. After much general discussion the board asked that further review be done regarding duplicate antibiotic therapy in children. The DUR Board asked that the following information be included in the review:

- Specific geographical areas
- Review areas of care – i.e. ER visits vs. clinic or physician office visits
- ICD-9 codes assigned to visit
- Specific time frame of 72 hours to 5 days after initial antibiotic RX

Montez Carter made a motion that these interventions be revisited following an enhanced review. Dr. Undesser seconded the motion. All voted in favor of the motion.

Retrospective DUR Criteria Recommendations:
Sam Warman presented the following retrospective DUR criteria recommendations for the first quarter 2005:

- Narcotic/Sickle Cell/Hydroxyurea- The patient has sickle cell anemia and appears to be receiving only narcotics for associated pain. The patient may benefit from the addition of hydroxyurea for pain prevention.
  - Cynthia Undesser made a motion to accept this criteria recommendation. Leigh Ann Ross seconded the motion. All voted in favor of the motion.
- Estazolam/Azole Antifungals-Concomitant use of estazolam with CYP3A4 enzymes inhibitors, ketoconazole or itraconazole may result in estazolam toxicity.
  Estazolam/ 3A4 inhibitors-Concomitant use of estazolam with drugs that exhibit significant inhibition of 3A4 metabolism may result in elevated estazolam concentrations.
  Estazolam/certain CYP3A4 inducers-Concomitant use of estazolam with potent CYP3A4 enzyme inducers would decrease estazolam concentrations.
  - Dr. Montgomery motioned that the DUR Board recommend to the P&T Committee that estazolam be removed from the preferred drug list due to the extensive list of interactions/dangers associated with the medication. Dr. Montgomery also recommended that a list of the prescribers using this group of medications in the last 60 days be sent an appropriate letter. Joe McGuffee seconded the motion. All voted in favor of the motion.
- Valdecoxib/therapeutic appropriateness-serious skin reactions have been reported in patients receiving Bextra. Valdecoxib should be discontinued at the first appearance of a skin rash, mucosal lesions, or any sign of hypersensitivity. Valdecoxib contains sulfa, and patients with a history of allergic reactions to sulfa may be at a greater risk of skin reactions.
  Valdecoxib/therapeutic appropriateness –Bextra is contraindicated for treatment of postoperative pain immediately coronary artery bypass surgery (CABG). Patients treated with valdecoxib for pain following CABG have a higher risk for cardiovascular/thromboembolic events, deep surgical infections or sternal wound complications.

- Dr Montgomery motioned that the recommendations be approved. Dr. Montgomery also asked that DOM consider adding the following questions to the PA process for Bextra:
    - Does patient have an allergy to Sulfa?
    - Has patient had a CABG procedure within the last 6 months?

  Dr. Ross seconded the motion. All voted in favor of the motion.

- Celecoxib/ Overutilization- Recent clinical trials involving the use of this category to prevent colon polyps were halted due to an increased risk of CV events. Patients taking 400 mg of celecoxib twice a day have a 3.4 times greater risk of CV events compared to placebo and 2.5 times greater for 200 mg twice a day. The FDA is advising that all physicians prescribing celecoxib consider the evolving information in evaluating the risks and benefits for the individual patient. Ms. Clark stated the P&T Committee asked that the DUR Board consider placing a maximum dose allowed on all COX-2 inhibitors.
    - Dr. Montgomery made a motion to change the maximum quantity currently allowed by DOM from 150% of the recommended dose to 100% of the recommended dose. Joe McGuffee seconded the motion. Dr. Mitchell asked for a review of all NSAIDS and COX2 inhibitor prescriptions where the quantity dispensed was over the recommended maximum dose. Dr. Mitchell requested that the report include diagnosis information as well as physician specialty information.

Black Box Warnings and Updates:

Sam Warman presented black box warnings issued by the FDA concerning the following:

- Crestor- FDA issued a public health advisory describing revisions to the WARNINGS, DOSAGE AND ADMINISTRATION, CLINICAL PHARMACOLOGY, and PRECAUTIONS sections of the labeling. The revisions include results from a Phase 4 pharmacokinetic study in Asian-Americans and highlight important information on the safe use of Crestor to reduce the risk for serious muscle toxicity (myopathy/rhabdomyolysis), especially at the highest approved dose of 40 mg. At this time, the FDA is also making statements about the muscle and kidney safety of Crestor based on extensive review of available information.

- Agrylin- Shire and FDA notified healthcare professionals about changes to the CONTRAINDICATIONS and WARNINGS sections of the prescribing information for Agrylin (anagrelide hydrochloride), a medication approved for the treatment of thrombocythemia secondary to myeloproliferative disorders to reduce platelet count and the risk of thrombosis and to ameliorate associated symptoms including thrombohemorrhagic events. Pharmacokinetic studies have revealed an 8-fold increase in total exposure (AUC) to anagrelide hydrochloride in patients with moderate hepatic impairment. Use of anagrelide hydrochloride has not been studied in patients with severe hepatic impairment. Labeling changes include the contraindication to the use of Agrylin in patients with severe hepatic impairment. The WARNINGS section describes the need for dosage reduction in patients with moderate hepatic impairment and the necessity of monitoring these patients carefully for cardiovascular effects.

- Gabitril- FDA and Cephalon, Inc. notified healthcare professionals and the public that a Bolded Warning has been added to the labeling for Gabitril (tiagabine) to warn

prescribers of the risk of seizures in patients without epilepsy being treated with Gabitril. FDA has received reports of the occurrence of seizures in more than 30 patients prescribed Gabitril for conditions other than epilepsy. Most of these uses were in patients with psychiatric illnesses. Such off label prescribing is a common practice among physicians. Because of the risk of seizures, however, in addition to adding the Bolded Warning to product labeling, the sponsor has agreed to undertake an educational campaign, targeted to healthcare professionals and patients, in which such off-label use will be discouraged.

- Phenergan- FDA and Wyeth notified healthcare professionals of revisions to the CONTRAINDICATIONS, WARNINGS/Use in Pediatric Patients, and DOSAGE AND ADMINISTRATION sections of the prescribing information for Phenergan. Phenergan is contraindicated for use in pediatric patients less than two years of age because of the potential for fatal respiratory depression. Post marketing cases of respiratory depression including fatalities, have been reported with use of Phenergan in pediatric patients less than two years of age. Caution should also be exercised when administering Phenergan to pediatric patients two years of age and older. Dr. Mitchell asked if DOM was covering Phenergan prescriptions for children after this warning was issued by the FDA. Ms. Clark explained that DOM does not deny for Black Box Warnings.
  - Dr. Montgomery made a motion to send intervention letters containing the FDA black box warning to physicians who continue to prescribe Phenergan for children less than 24 months of age. Joe McGuffee requested that this information also be included in the DOM Bulletin as an educational alert. A motion was made by Dr. Undesser to accept both Dr. Montgomery's motion and to also include the request made by Joe McGuffee. Dr. Ross seconded the motion. All voted in favor of the motion.

- Estraderm-The Women's Health Initiative (WHI) study reported increased risks of myocardial infarction, stroke, invasive breast cancer, pulmonary emboli, and deep vein thrombosis in postmenopausal women (50-79 years of age) during 5 years of treatment with oral conjugated equine estrogens (CE 0.625 mg) combined with medroxyprogesterone acetate (MPA 2.5 mg) relative to placebo. The Women's Health Initiative Memory Study (WHIMS), a substudy of WHI, reported increased risk of developing probable dementia in postmenopausal women 65 years of age or older during 4 years of treatment with oral conjugated equine estrogens plus medroxyprogesterone acetate relative to placebo. It is unknown whether this finding applies to younger postmenopausal women or to women taking estrogen alone. Other doses of oral conjugated estrogens with medroxyprogesterone acetate, and other combinations and dosage forms of estrogens and progestins were not studied in the WHI clinical trials and, in the absence of comparable data, these risks should be assumed to be similar.

Suggested Interventions:
Sam Warman presented several intervention recommendations. Each suggested intervention included the number of recipients identified during profile review as being at risk for the specific intervention. These suggested intervention included.

- Inappropriate Therapy for Elderly-long half-life benzodiazepine anxiolytics
- Inappropriate Therapy for Elderly-barbiturate sedative/hypnotic
- Inappropriate Therapy for Elderly- certain tertiary TCA's
- Inappropriate Therapy for Elderly- famotidine
- Inappropriate Therapy for Elderly- Sonata and Ambien
- Drug (actual) disease precaution – adverse cardiovascular effects COX-2 inhibitors
- Celecoxib/overutilization
- Valdecoxib/therapeutic appropriateness

After much discussion, the DUR Board decided to postpone approval of the suggested interventions until after implementation of the CNS/DOM program.

Cost Analysis:
Sam Warman presented a brief cost management analysis report from January 1, 2005 through January 31, 2005. This report included the top 15 therapeutic classes by total cost of claims, the top 25 drugs based on number of claims and the top 25 drugs based on total claims cost for this time period. Dr Montgomery asked that the board be given a list of specific medications included under miscellaneous therapeutic agents and miscellaneous anticonvulsants for the next DUR Board meeting.

Academic Detailing:
Lew Anne Snow gave an overview of the new Academic Detailing program. Three new Medicaid Pharmacy Specialists, representing all areas of the state, were introduced to the DUR Board. Under the direction of the Division of Medicaid, the Medicaid Pharmacy Specialists will provide education regarding all aspects of the Mississippi Division of Medicaid pharmacy program to prescribing providers throughout the state

Pharmacy Updates:
Judith Clark, Director of Pharmacy Bureau, gave a brief report on recent pharmacy program expenditures. Mrs. Clark distributed a copy of the preferred drug list to the board members. She also provided the board members with a list of preferred vs. non-preferred antihistamines and antihistamine/decongestant combination products. A copy of the DUR Board by-laws was given to every Board member. Mrs. Clark reminded the board members of the attendance requirement addressed in the by-laws.

CNS presentation:
Judith Clark introduced Billy E. Jones, M.D., Medical Director and Frankie Rutledge, account manager for Comprehensive NeuroScience, Inc. Dr. Billy Jones gave the board an overview of the behavioral pharmacy management system. Supported by a grant from Eli Lilly, CNS will partner with the MS Division of Medicaid to encourage appropriate utilization of behavioral drugs.

There being no other business, Dr. Mitchell asked for a motion to adjourn the meeting. Joe McGuffee made a motion to adjourn. Leigh Ann Ross seconded the motion. All voted in favor of the motion. The meeting was adjourned at 4:15 p.m.

Respectfully submitted:
Health Information Designs

Antibiotic Utilization in Children

Introduction

The following analysis is presented in response to a request from the board for additional information regarding antibiotic duplication in children. The DUR board asked that the following information be included in the review: specific geographic areas, areas of care (e.g. ER, clinic, etc.), and ICD-9 codes assigned to the visits. Also, the Board asked that the time frame be decreased to 72 hours.

Method

Pharmacy claims data were analyzed by the HID clinical staff. In order to get a more accurate depiction of therapeutic duplication, a more recent 90-day period (October 2004-December 2004) was analyzed. Beneficiaries 0-20 years of age were the only population included in the analysis.

Results

Zithromax® topped the list as the most duplicated antibiotic with 2,474 total duplications. Table 1 lists the top 10 antibiotics involved in therapeutic duplications as the first agent dispensed.

Table 1

MISSISSIPPI MEDICAID	
Therapeutic Duplication of Antibiotics	
Top 10 Antibiotics Filled First	
Drug Name	**Count**
ZITHROMAX	889
CEPHALEXIN	741
AMOXICILLIN	699
SULFAMETHOXAZOLE/TRIMETHOPRIM	679
LEVAQUIN	675
CIPROFLOXACIN HCL	568
AMOX TR-POTASSIUM CLAVULANATE	494
OMNICEF	368
NITROFURANTOIN MONOHYD MACRO	293
CLINDAMYCIN HCL	265

NOTE: Data covers Oct. 2004 - Dec. 2004

Table 2 lists the top 10 antibiotics involved in therapeutic duplications as the agent filled within 72-hours of the agents in Table 1.

Table 2

MISSISSIPPI MEDICAID Therapeutic Duplication of Antibiotics Top 10 Antibiotics Filled within 72 Hours of Original	
Drug Name	**Count**
ZITHROMAX	1,585
SULFAMETHOXAZOLE/TRIMETHOPRIM	884
LEVAQUIN	696
ROCEPHIN	591
UROGESIC-BLUE	577
CEPHALEXIN	456
OMNICEF	420
AMOX TR-POTASSIUM CLAVULANATE	413
DOXYCYCLINE HYCLATE	318
CIPROFLOXACIN HCL	286

NOTE: Data covers Oct. 2004 - Dec. 2004

The agents listed in table 2 are not necessarily only the second antibiotic. It is possible that some of these agents were actually a 3rd or 4th agent prescribed within the 72 hours time frame. The remaining tables address the top prescribers associated with antibiotic therapeutic duplication.

Table 3

MISSISSIPPI MEDICAID Therapeutic Duplication of Antibiotics Top Prescribers of Antibiotics with Duplication within 72 Hours			
Provider Name*	**Count**	**City**	**State**
UMC – Dummy prescriber ID 1	394	Jackson	MS
Unknown - Dummy prescriber ID	261	Unknown	MS
Prescriber 1	213	Jackson	MS
Prescriber 2	145	Clarksdale	MS
Prescriber 3	120	Memphis	TN
Prescriber 4	111	Oxford	MS
UMC – ER	97	Jackson	MS
Prescriber 5	92	Corinth	MS
Prescriber 6	89	Morton	MS
Prescriber 7	87	Marks	MS

NOTE: Data cover Oct. 2004 - Dec. 2004

* For confidentiality reasons, the names of the providers have been deleted.

The following table lists the top prescribers, with frequency, involved in duplications within 72 hours of the original who were not the prescriber of the initial prescription.

Table 4

MISSISSIPPI MEDICAID			
Therapeutic Duplication of Antibiotics			
Top Second Prescribers of Antibiotics with Duplication within 72 Hours			
Provider Name*	**Count**	**City**	**State**
UMC – Dummy prescriber ID 1	25	Jackson	MS
Dummy prescriber ID	22	Unknown	MS
Prescriber 2	17	Clarksdale	MS
UMC - ER	13	Jackson	MS
NMMC	8	Tupelo	MS
Prescriber 3	8	Memphis	TN
Prescriber 8	7	Hattiesburg	MS
UMC – Dummy prescriber ID 2	6	Jackson	MS
Prescriber 9	6	Columbus	MS
Prescriber 10	6	Biloxi	MS

NOTE: Data cover Oct. 2004 - Dec. 2004
* For confidentiality reasons, the names of the providers have been deleted.

Although not directly addressed by tables 5 and 6, the incidence of therapeutic duplication of antibiotics appears to be similar across Mississippi and not isolated to a particular geography. While central Mississippi seems most-implicated, this area traditionally has the highest Medicaid participation by number.

Conclusion

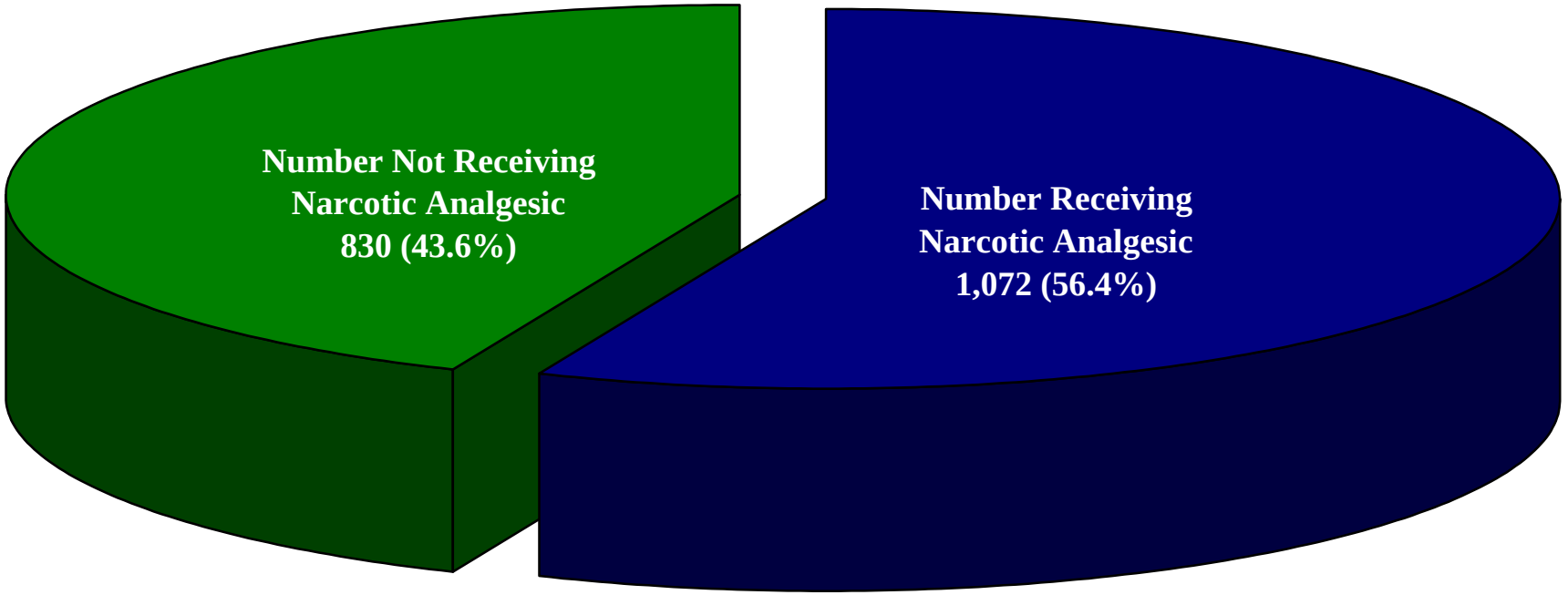
Upon analyzing the data, a few observations can be made.

Over half of the incidences of antibiotic duplication involved a hospital setting. In fact, almost all of the second prescribers were either identified as a medical center or a dummy number was used.

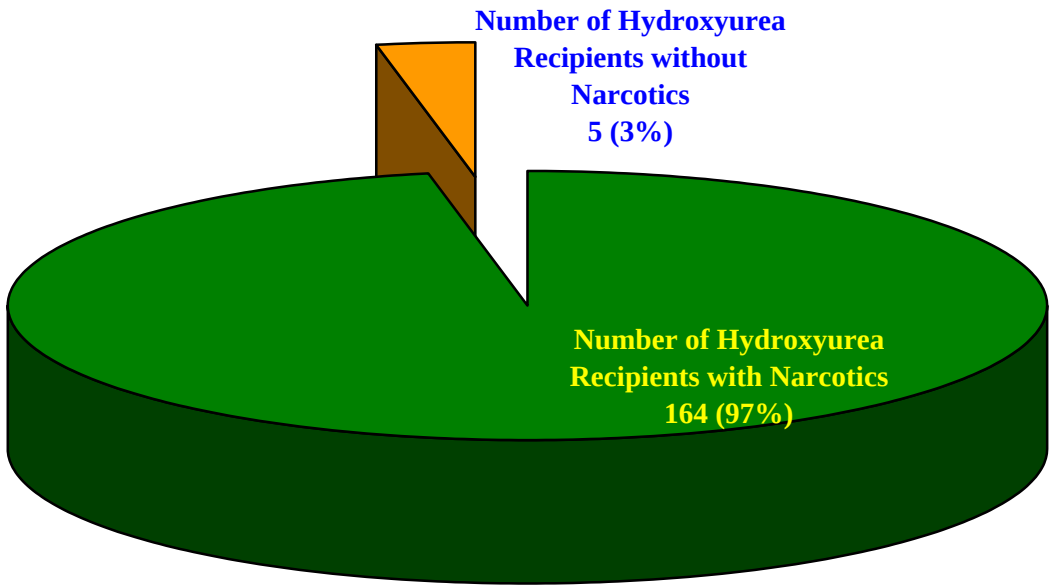
Also of note, the data seems to suggest that in few cases is the subsequent prescriber different from the initial prescriber. In other words, the same prescriber is involved in both prescriptions.

In light of this information and the anticipated impact of the new prescription limits soon to be implemented, a therapeutic duplication edit or prior authorization requirement is not recommended at this time.

MISSISSIPPI MEDICAID
Number of Sickle Cell Recipients who Received at Least One Prescription for a Narcotic Analgesic Between Jan. 2004 and Mar. 2005
[Total Group = 1,902]



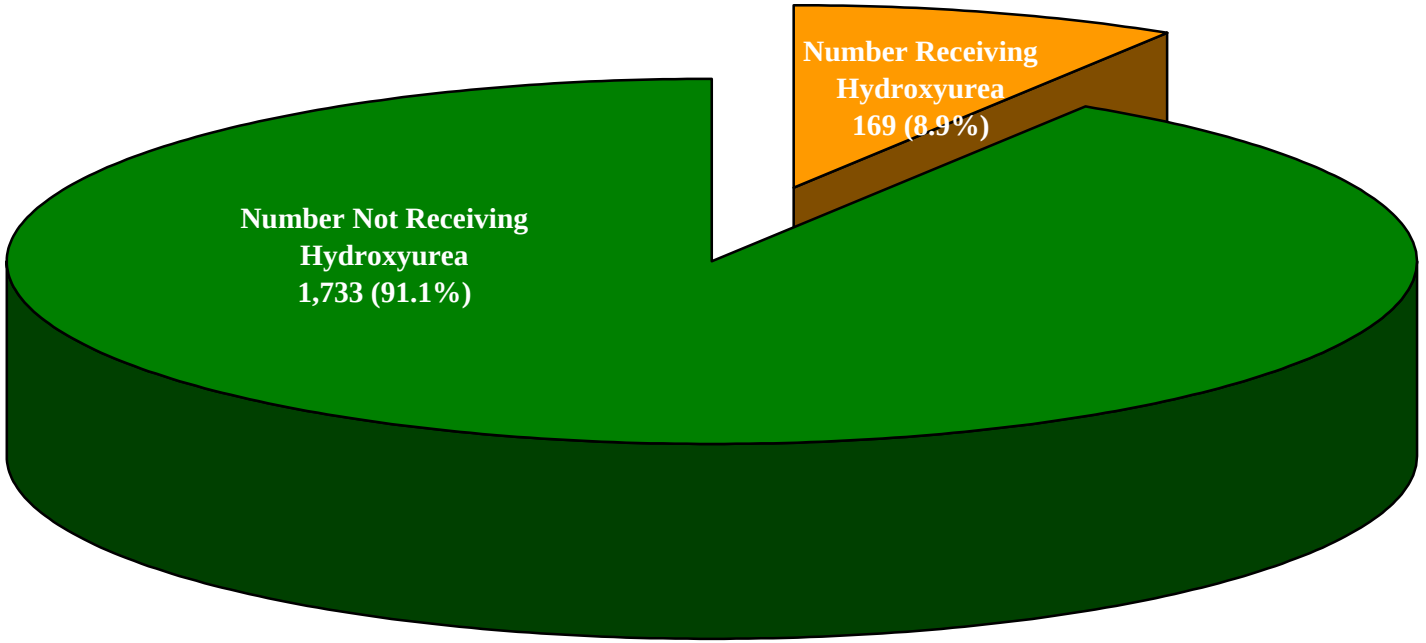
MISSISSIPPI MEDICAID
For Sickle Cell Recipients Receiving at Least One Prescription for Hydroxyurea, Number who Also Received at Least One Prescription for a Narcotic Analgesic Between Jan. 2004 and Mar. 2005 [Total Group = 169]



MISSISSIPPI MEDICAID

Number of Sickle Cell Recipients who Received at Least One Prescription of Hydroxyurea Between Jan. 2004 and Mar. 2005

[Total Group = 1,902]



MISSISSIPPI MEDICAID
NSAID Prescriptions Above Maximum Daily Dose
Oct. 2004 - Dec. 2004

NSAID	Diagnosis	Total Prescriptions	Total Prescriptions Above Max. Daily Dose	Percent Above Max. Daily Dose
ARTHROTEC	OA	19	3	15.79%
	RA	35	3	8.57%
	Other DX*	1,209	4	0.33%
DICLOFENAC	OA	18	2	11.11%
	RA	55	0	0.00%
	Other DX*	1,459	2	0.14%
ETODOLAC	OA	9	0	0.00%
	RA	22	0	0.00%
	Other DX*	862	22	2.55%
FENOPROFEN	OA	2	0	0.00%
	RA	1	0	0.00%
	Other DX*	246	1	0.41%
FLURBIPROFEN	OA	3	0	0.00%
	RA	8	3	37.50%
	Other DX*	454	190	41.85%
IBUPROFEN	OA	44	1	2.27%
	RA	113	11	9.73%
	Other DX*	24,458	2,985	12.20%
INDOMETHACIN	OA	23	0	0.00%
	RA	53	3	5.66%
	Other DX*	2,209	40	1.81%
KETOPROFEN	OA	10	0	0.00%
	RA	28	0	0.00%
	Other DX*	826	9	1.09%
MECLOFENAMATE	OA	1	0	0.00%
	RA	9	0	0.00%
	Other DX*	430	12	2.79%
MOBIC	OA	47	2	4.26%
	RA	172	2	1.16%
	Other DX*	3,841	45	1.17%
NABUMETONE	OA	44	0	0.00%
	RA	91	0	0.00%
	Other DX*	2,453	0	0.00%
NAPROXEN	OA	114	0	0.00%
	RA	192	7	3.65%
	Other DX*	11,831	195	1.65%
OXAPROZIN	OA	15	0	0.00%
	RA	23	1	4.35%
	Other DX*	983	4	0.41%
PIROXICAM	OA	9	0	0.00%
	RA	19	0	0.00%
	Other DX*	955	12	1.26%
SULINDAC	OA	20	0	0.00%
	RA	35	3	8.57%
	Other DX*	1,139	32	2.81%
TOLMETIN	OA	1	0	0.00%
	RA	2	0	0.00%
	Other DX*	35	7	20.00%

* Other DX include: dysmenorrhea, fever, pain, ankylosing spondylitis

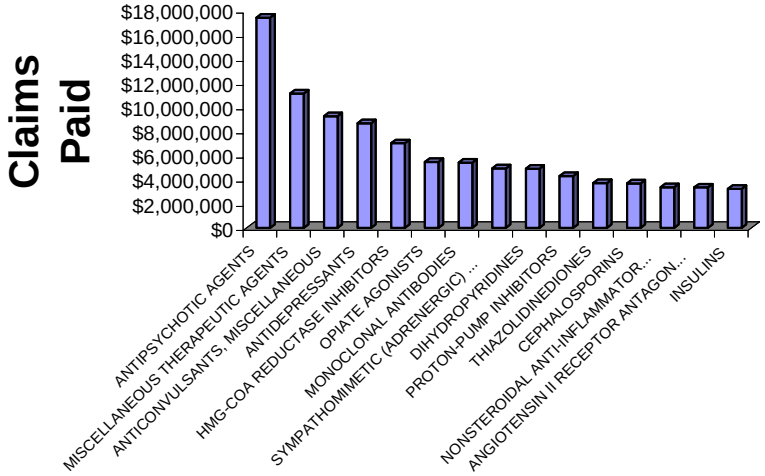
MISSISSIPPI MEDICAID
Cost Management Analysis

TOP 15 THERAPEUTIC CLASSES BY TOTAL COST OF CLAIMS FROM 01/01/2005 - 03/31/2005

AHFS Therapeutic Class	Rx	Paid	Paid/Rx
ANTIPSYCHOTIC AGENTS	73,536	$ 17,418,536.62	$ 236.87
MISCELLANEOUS THERAPEUTIC AGENTS	93,501	$ 11,139,550.05	$ 119.14
ANTICONVULSANTS, MISCELLANEOUS	63,789	$ 9,242,451.46	$ 144.89
ANTIDEPRESSANTS	129,037	$ 8,662,962.70	$ 67.14
HMG-COA REDUCTASE INHIBITORS	67,043	$ 7,011,044.10	$ 104.58
OPIATE AGONISTS	161,871	$ 5,456,969.58	$ 33.71
MONOCLONAL ANTIBODIES	4,430	$ 5,411,099.51	$ 1,221.47
SYMPATHOMIMETIC (ADRENERGIC) AGENTS	69,745	$ 4,939,477.26	$ 70.82
DIHYDROPYRIDINES	73,011	$ 4,909,538.42	$ 67.24
PROTON-PUMP INHIBITORS	42,101	$ 4,299,301.38	$ 102.12
THIAZOLIDINEDIONES	25,932	$ 3,717,262.34	$ 143.35
CEPHALOSPORINS	65,917	$ 3,684,756.76	$ 55.90
NONSTEROIDAL ANTI-INFLAMMATORY AGENTS	84,616	$ 3,373,326.84	$ 39.87
ANGIOTENSIN II RECEPTOR ANTAGONISTS	57,354	$ 3,352,720.86	$ 58.46
INSULINS	35,711	$ 3,233,039.03	$ 90.53
TOTAL TOP 15	1,047,594	$ 95,852,036.91	$ 91.50

Total Rx Claims From 01/01/2005 - 03/31/2005	2,714,835

Top 15 Therapeutic Classes
Based on Total Cost of Claims



Health Information Designs, Inc.

MISSISSIPPI MEDICAID
Cost Management Analysis

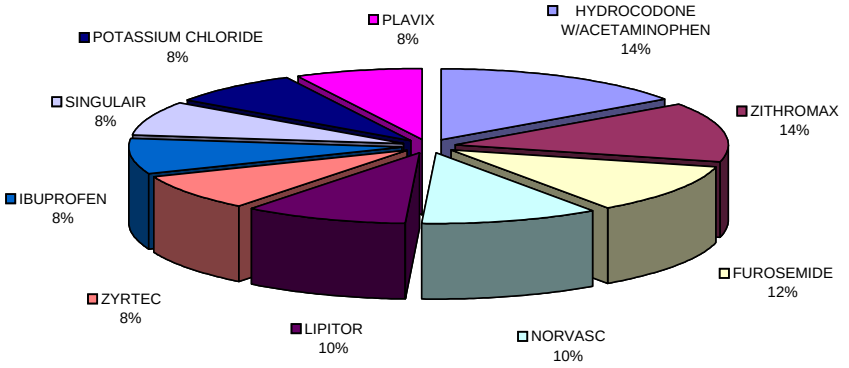
05/25/2005

TOP 25 DRUGS BASED ON NUMBER OF CLAIMS FROM 01/01/2005 - 03/31/2005

Drug	AHFS Therapeutic Class	Rx	Paid	Paid/Rx	% Total Claims
HYDROCODONE W/ACETAMINOPHEN	OPIATE AGONISTS	55,626	$ 795,544.64	$ 14.30	2.05%
ZITHROMAX	MACROLIDES	49,241	$ 2,201,561.21	$ 44.71	1.81%
FUROSEMIDE	DIURETICS	41,940	$ 251,415.83	$ 5.99	1.54%
NORVASC	DIHYDROPYRIDINES	38,094	$ 2,286,083.21	$ 60.01	1.40%
LIPITOR	HMG-COA REDUCTASE INHIBITORS	34,959	$ 3,280,049.27	$ 93.83	1.29%
ZYRTEC	SECOND GENERATION ANTIHISTAMINES	30,026	$ 1,530,965.81	$ 50.99	1.11%
IBUPROFEN	NONSTEROIDAL ANTI-INFLAMMATORY AGENTS	29,207	$ 266,090.32	$ 9.11	1.08%
SINGULAIR	MISCELLANEOUS THERAPEUTIC AGENTS	28,630	$ 2,600,801.33	$ 90.84	1.05%
POTASSIUM CHLORIDE	REPLACEMENT PREPARATIONS	27,843	$ 530,053.05	$ 19.04	1.03%
PLAVIX	MISCELLANEOUS THERAPEUTIC AGENTS	27,690	$ 3,547,081.49	$ 128.10	1.02%
TOPROL XL	BETA-ADRENERGIC BLOCKING AGENTS	26,690	$ 911,705.54	$ 34.16	0.98%
AMOXICILLIN	PENICILLINS	26,477	$ 223,671.06	$ 8.45	0.98%
RANITIDINE HCL	HISTAMINE H2-ANTAGONISTS	23,790	$ 757,272.83	$ 31.83	0.88%
PROMETHAZINE HCL	PHENOTHIAZINE DERIVATIVES	22,158	$ 405,265.80	$ 18.29	0.82%
PROPOXYPHENE NAPSYLATE W/APAP	OPIATE AGONISTS	21,925	$ 259,682.80	$ 11.84	0.81%
CEPHALEXIN	CEPHALOSPORINS	21,359	$ 420,876.59	$ 19.70	0.79%
LOTREL	DIHYDROPYRIDINES	21,126	$ 1,768,012.18	$ 83.69	0.78%
AMOX TR-POTASSIUM CLAVULANATE	PENICILLINS	20,964	$ 1,323,556.23	$ 63.13	0.77%
GABAPENTIN	ANTICONVULSANTS, MISCELLANEOUS	20,888	$ 2,658,613.62	$ 127.28	0.77%
OMNICEF	CEPHALOSPORINS	20,685	$ 1,575,620.01	$ 76.17	0.76%
ALBUTEROL	SYMPATHOMIMETIC (ADRENERGIC) AGENTS	20,496	$ 418,966.88	$ 20.44	0.75%
ZOLOFT	ANTIDEPRESSANTS	20,195	$ 1,935,834.07	$ 95.86	0.74%
HYDROCHLOROTHIAZIDE	DIURETICS	20,014	$ 134,232.16	$ 6.71	0.74%
LEXAPRO	ANTIDEPRESSANTS	19,390	$ 1,382,197.91	$ 71.28	0.71%
SEROQUEL	ANTIPSYCHOTIC AGENTS	18,341	$ 4,114,759.62	$ 224.35	0.68%
TOTAL TOP 25		687,754	$ 35,579,913.46	$ 51.73	25.33%

Total Rx Claims From 01/01/2005 - 03/31/2005	2,714,835

Top 10 Drugs
Based on Number of Claims



Health Information Designs, Inc.

MISSISSIPPI MEDICAID
Cost Management Analysis

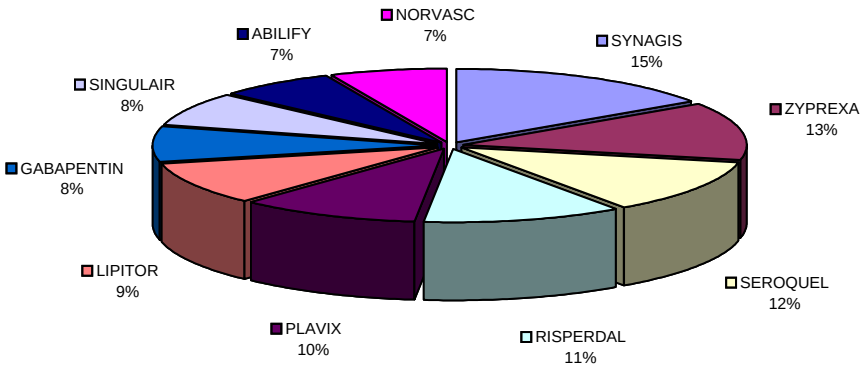
05/25/2005

TOP 25 DRUGS BASED ON TOTAL CLAIMS COST FROM 01/01/2005 - 03/31/2005

Drug	AHFS Therapeutic Class	Rx	Paid	Paid/Rx	% Total Claims
SYNAGIS	MONOCLONAL ANTIBODIES	4,430	$ 5,411,099.51	$ 1,221.47	0.16%
ZYPREXA	ANTIPSYCHOTIC AGENTS	12,527	$ 4,422,761.29	$ 353.06	0.46%
SEROQUEL	ANTIPSYCHOTIC AGENTS	18,341	$ 4,114,759.62	$ 224.35	0.68%
RISPERDAL	ANTIPSYCHOTIC AGENTS	17,651	$ 3,894,003.08	$ 220.61	0.65%
PLAVIX	MISCELLANEOUS THERAPEUTIC AGENTS	27,690	$ 3,547,081.49	$ 128.10	1.02%
LIPITOR	HMG-COA REDUCTASE INHIBITORS	34,959	$ 3,280,049.27	$ 93.83	1.29%
GABAPENTIN	ANTICONVULSANTS, MISCELLANEOUS	20,888	$ 2,658,613.62	$ 127.28	0.77%
SINGULAIR	MISCELLANEOUS THERAPEUTIC AGENTS	28,630	$ 2,600,801.33	$ 90.84	1.05%
ABILIFY	ANTIPSYCHOTIC AGENTS	6,469	$ 2,343,371.83	$ 362.25	0.24%
NORVASC	DIHYDROPYRIDINES	38,094	$ 2,286,083.21	$ 60.01	1.40%
ZITHROMAX	MACROLIDES	49,241	$ 2,201,561.21	$ 44.71	1.81%
ZOLOFT	ANTIDEPRESSANTS	20,195	$ 1,935,834.07	$ 95.86	0.74%
ZOCOR	HMG-COA REDUCTASE INHIBITORS	13,985	$ 1,832,690.28	$ 131.05	0.52%
ADVAIR DISKUS	SYMPATHOMIMETIC (ADRENERGIC) AGENTS	11,973	$ 1,774,957.21	$ 148.25	0.44%
LOTREL	DIHYDROPYRIDINES	21,126	$ 1,768,012.18	$ 83.69	0.78%
ACTOS	THIAZOLIDINEDIONES	10,865	$ 1,728,533.89	$ 159.09	0.40%
TOPAMAX	ANTICONVULSANTS, MISCELLANEOUS	6,675	$ 1,613,504.20	$ 241.72	0.25%
ARICEPT	PARASYMPATHOMIMETIC (CHOLINERGIC AGENTS)	10,931	$ 1,595,835.80	$ 145.99	0.40%
OMNICEF	CEPHALOSPORINS	20,685	$ 1,575,620.01	$ 76.17	0.76%
ZYRTEC	SECOND GENERATION ANTIHISTAMINES	30,026	$ 1,530,965.81	$ 50.99	1.11%
PREVACID	PROTON-PUMP INHIBITORS	10,946	$ 1,447,215.73	$ 132.21	0.40%
PULMICORT	ADRENALS	7,414	$ 1,438,401.11	$ 194.01	0.27%
LEXAPRO	ANTIDEPRESSANTS	19,390	$ 1,382,197.91	$ 71.28	0.71%
LEVAQUIN	QUINOLONES	15,251	$ 1,376,751.78	$ 90.27	0.56%
AMOX TR-POTASSIUM CLAV	PENICILLINS	20,964	$ 1,323,556.23	$ 63.13	0.77%
TOTAL TOP 25		479,346	$ 59,084,261.67	$ 123.26	17.66%

Total Rx Claims From 01/01/2005 - 03/31/2005	2,714,835

Top 10 Drugs
Based on Total Claims Cost



Miscellaneous Anticonvulsants

Generic Name	Brand Example
Carbamazepine	Tegretol
Epsom Salt	
Felbamate	Felbatol
Gabapentin	Neurontin
Tiagabine	Gabitril
Levetiracetam	Keppra
Lamotrigine	Lamictal
Magnesium Citrate/D5W	
Magnesium Chloride	
Topiramate	Topamax
Oxcarbazepine	Trileptal
Valproate	Depakote
Valproic Acid	Depakene
Zonisamide	Zonegran

Miscellaneous Therapeutic Agents

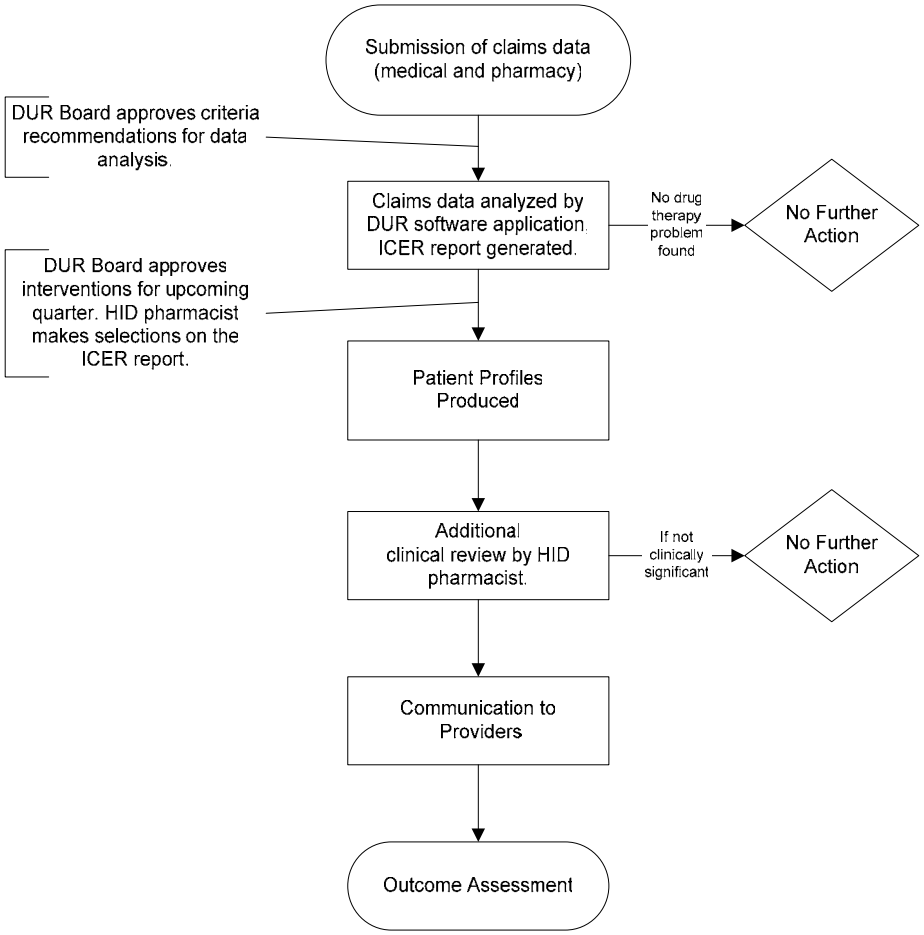
DRUG NAME

ACCOLATE 10 MG TABLET
ACCOLATE 20 MG TABLET
ACCOLATE 20MG TABLET
ACTONEL 30 MG TABLET
ACTONEL 35 MG TABLET
ACTONEL 5 MG TABLET
AGRYLIN 0.5 MG CAPSULE
AGRYLIN 1 MG CAPSULE
ALLOPURINOL 100 MG TABLET
ALLOPURINOL 100MG TABLET
ALLOPURINOL 300 MG TABLET
ALLOPURINOL 300MG TABLET
ALTERRA 450 MG TABLET SA
AMINO ACID CERVICAL CREAM
AMINOBENZOATE POT 500 MG CAP
AMINOBENZOATE POT ENVULE 2 GM
AMINOBENZOATE POT PACKET 2G
AMINO-CERV CREAM
ANTABUSE 250MG TABLET
ANTABUSE 500MG TABLET
ARAVA 10 MG TABLET
ARAVA 100 MG TABLET
ARAVA 20 MG TABLET
AREDIA 30 MG VIAL
AREDIA 60MG VIAL
AREDIA 90 MG VIAL
ARTHX DS CAPSULE
ARTHX SS CAPSULE
ASTRAGALUS 250 MG CAPSULE
AVODART 0.5 MG CAPSULE
AVODART 0.5 MG SOFTGEL
AVONEX ADMIN PACK
AZASAN 100 MG TABLET
AZASAN 75 MG TABLET
AZATHIOPRINE 50 MG TABLET
BROMOCRIPTINE 2.5 MG TABLET
BROMOCRIPTINE 5 MG CAPSULE
CELLCEPT 200 MG/ML ORAL SUSP
CELLCEPT 250 MG CAPSULE
CELLCEPT 500 MG TABLET
CELLSURE SOFTGEL
COLCHICINE 0.5 MG TABLET
COLCHICINE 0.6MG TABLET
CYCLOSPORINE 100 MG CAPSULE
CYCLOSPORINE 100 MG/ML SOLN
CYCLOSPORINE 25 MG CAPSULE
CYCLOSPORINE 50 MG SOFTGEL
DHEA 25 MG CAPSULE
DHEA 50 MG CAPSULE
DHEA TABLET
DIDRONEL 200 MG TABLET
DIDRONEL 400MG TABLET
DISULFIRAM 250MG TABLET
DISULFIRAM 500MG TABLET

ELMIRON 100 MG CAPSULE
FLOMAX 0.4 MG CAPSULE SA
FOSAMAX 10MG TABLET
FOSAMAX 35 MG TABLET
FOSAMAX 40 MG TABLET
FOSAMAX 5 MG TABLET
FOSAMAX 70 MG ORAL SOLUTION
FOSAMAX 70 MG TABLET
FOSAMAX PLUS D 70 MG/2,800 IU
GENGRAF 100 MG CAPSULE
GENGRAF 100 MG/ML SOLUTION
GENGRAF 25 MG CAPSULE
GLUCOSAMINE/CHONDR/MSM TAB
GLUCOSAMINE/CHONDROIT SFTGL
IMURAN 50MG TABLET
LEUCOVORIN CALCIUM 10 MG TAB
LEUCOVORIN CALCIUM 15 MG TAB
LEUCOVORIN CALCIUM 25 MG TAB
LEUCOVORIN CALCIUM 5 MG TAB
LURIDE DROPS
LURIDE LOZI-TAB 1MG TAB CHEW
LURIDE LOZI-TABS 0.25MG CHW
LURIDE LOZI-TABS 0.5 MG CHEW
LURIDE LOZI-TABS 1 MG TAB CHEW
LURIDE-SF LOZI-TABS 0.25MG
MELATONIN TABLET
NEORAL 100 MG GELATN CAPSULE
NEORAL 100 MG/ML SOLUTION
NEORAL 25 MG GELATIN CAPSULE
PARLODEL 2.5 MG TABLET
PARLODEL 5 MG CAPSULE
PERIGEL ORAL CARE SYSTEM
PERIO MED DENTAL RINSE
PERIO-RINSE 0.63% SOLUTION
PERIOSELECT 0.4% DENTAL GEL
PERIOSELECT 0.63% RINSE
PLAVIX 75 MG TABLET
PLETAL 100 MG TABLET
PLETAL 50 MG TABLET
PROGRAF 0.5 MG CAPSULE
PROGRAF 1 MG CAPSULE
PROGRAF 5 MG CAPSULE
PROSCAR 5 MG TABLET
RAPAMUNE 1 MG TABLET
RAPAMUNE 1 MG/ML ORAL SOLN
RAPAMUNE 2 MG TABLET
SANDIMMUNE 100 MG CAPSULE
SANDIMMUNE 100 MG/ML SOLN
SANDIMMUNE 25 MG CAPSULE
SANDIMMUNE 50 MG/ML AMPUL
SANDIMMUNE 50MG CAPSULE
SENSIPAR 30 MG TABLET
SENSIPAR 60 MG TABLET
SENSIPAR 90 MG TABLET
SINGULAIR 10 MG TABLET
SINGULAIR 4 MG GRANULES
SINGULAIR 4 MG TABLET CHEW
SINGULAIR 5 MG TABLET CHEW
SOD FLUORID 0.25MG(.55MG)TB

SOD FLUORIDE 0.5 MG (1.1MG)
SOD FLUORIDE 1 MG (2.2MG)TAB
SOD FLUORIDE 1.1MG(0.5MG)TB
SODIUM FLOURIDE DROPS
SODIUM FLUORIDE GEL
SODIUM FLUORIDE POWDER
THALOMID 100 MG CAPSULE
THALOMID 200 MG CAPSULE
THALOMID 50 MG CAPSULE
THYROID LIQUID
TICLID 250 MG TABLET
TICLOPIDINE 250 MG TABLET
TILADE INHALER
UROXATRAL 10 MG TABLET
VASOFLEX FORTE CAPSULE
VASOFLEX HD CAPLET
VASOFLEX TABLET
ZYFLO 600 MG FILMTAB
ZYLOPRIM 100 MG TABLET
ZYLOPRIM 300 MG TABLET

Overview of Drug Utilization Review (DUR) Intervention Process



Steps:

- Paid Medicaid claims are submitted to HID on magnetic media by the client's drug benefit administrator.
- The full set of therapeutic DUR criteria are applied to each recipient record. The DUR Board reviews and approves these criteria.
- Initial Criteria Exception Report (ICER) is generated to aid in the selection of high risk profiles.
- Patient profiles are generated for the most clinically significant drug therapy conflicts. The types of interventions generated are based on the recommendations and approval of the DUR Board.
- Profiles are reviewed by pharmacist to verify clinical significance.
- Intervention letters and profiles are sent to appropriate providers.
- Activity and impact reports are delivered to DOM monthly and to the DUR board quarterly.

Targeted Disease Intervention
"Osteoporosis and Corticosteroid Use"

The Problem

Osteoporosis is the reduction in bone mass and deterioration in bone architecture after age 40 that results in an increase in the fragility of bone and its susceptibility to fractures.[1] This disorder is recognized as a major public health problem because of its physical and socioeconomic consequences. In the United State, it is estimated that 16.8 million postmenopausal women have lost more than 10% of their peak adult bone mass, another 9.4 million have lost more than 25%, and 4.8 million have already suffered an osteoporotic fracture.[2] Statistics have shown that for every 10% of bone that is lost, the risk of fracture doubles. [2] These alarming statistics solidify the need for targeted education initiatives to better educate patients and providers of the potential health hazards associated with osteoporosis.

Bone mass increases during the first three decades of life; it approaches maximal (peak) levels in the late teen years, increases slightly during the third decade of life, and reaches its peak around 30 years.[2] Pathological conditions causing bone loss are estrogen or androgen deficiency, multiple myelomatosis, hyperparathyroidism, and hyperthyroidism.[1] Dual x-ray absorptiometry of lumbar spine and proximal femur provides reproducible values at important sites of osteoporosis-associated fracture. [2] These central sites are also more likely than peripheral sites to show a response to treatment and are preferred for baseline and serial management. [2] In order for these tests to be most reliable, the same instrument and technologist should be used to reduce variation.

In order to have effective preventive strategies, recognition of age-related and secondary causes of bone loss need to be addressed. Osteoporosis induced by glucocorticoid treatment results from suppression of osteoblast activity and decreased bone formation, with the possible contribution of an increase in bone resorption. [1]

The intent of this targeted intervention is to alert prescribers of recipients at increased risk for adverse outcomes and to provide them with information, in the form of a complete drug history profile, to aid in the review of current medication therapy.

While the purpose of an Osteoporosis Targeted Disease Intervention Program is first to increase the appropriate use of medications that treat bone diseases, another purpose is to prevent age-related and secondary causes of bone loss. This can be achieved by identifying beneficiaries with diagnosis codes (ICD-9) for osteoporosis that are currently on chronic oral corticosteroid therapy. Educating providers and beneficiaries on methods to better ensure outcomes will be instrumental in a successful program.

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[1] Rodan GA, Martin JT. Therapeutic Approaches to Bone Diseases. The American Association for the Advancement of Science 2000. 289:1508-14.
[2] American Association of Clinical Endocrinologists 2001 Medical Guidelines for Clinical Practice. The Prevention and Management of Osteoporosis. Endocrine Practice 2001. 7:293-312.

Methodology
Health Information Designs, Inc. (HID) has developed criteria for the evaluation. Recipients have to meet all criteria listed below in order to be selected for review and evaluation.

Osteoporosis and Oral Corticosteroid Criteria

1. Beneficiary must have a diagnosis at any time in their history of osteoporosis. The following ICD-9 diagnoses will be used:
   733.00 Osteoporosis Unspecified
   733.01 Senile Osteoporosis
   733.02 Idiopathic Osteoporosis
   733.03 Disuse Osteoporosis
   733.09 Other Osteoporosis

2. Beneficiaries must have NOT received any of the following drugs for the treatment of osteoporosis during the most recent 90 days:

   Alendronate (Fosamax®)
   Calcitonin ((Miacalcin®)
   Estrogen replacement therapy (excluding oral contraceptives)
   Etidronate (Didronel®
   Raloxifene (Evista®)
   Risedronate (Actonel®)
   Teriparatide (Forteo®)
   Ibandronate (Boniva®)

3. The beneficiary must have received a 30-day supply of an oral corticosteroid drug during the most recent 90 days.

For the targeted intervention, the most recent 90-day period will be reviewed. Claims data will be evaluated against the criteria and cases will be identified for review. Beneficiary drug history profiles, along with any available diagnosis data, will be reviewed by an HID clinical pharmacist.

A complete drug history profile, along with any available diagnosis data, will be included with an intervention letter. The drug history profile will contain the following alert message:

The profile history indicates that the patient has a diagnosis of osteoporosis and is receiving corticosteroid therapy. Corticosteroid therapy in patients with osteoporosis may increase the risk of fractures due to decreased bone density

associated with corticosteroid use. This patient may be particularly at risk since they are not currently receiving treatment for osteoporosis.

Each educational letter will have a physician response form, which will ask the prescriber to indicate any action taken in response to the intervention letter and to rate the usefulness of the information. The response form will also contain a question asking if the recipient is currently taking calcium and vitamin D supplements, since these agents are used for prevention and treatment of osteoporosis. Response forms will be returned to HID for review and evaluation. A sample copy of the education letter and response form can be found at the end of this section.

A follow-up evaluation will be performed four months or 120 days after the educational letters are sent to determine if any recipients had therapy for osteoporosis added to their drug regimen or if oral corticosteroid therapy was discontinued.

Dr. John Doe July 1, 2005

1 Medical Lane
Suite 1
Smalltown, MS 39000

Dear Dr. Doe,

Health Information Designs, Inc. in association with the Mississippi Division of Medicaid has recently implemented a targeted disease management program designed to improve medical outcomes. The program's goal is to share information with treating physicians about medication usage patterns that could potentially increase the risk of adverse outcomes. One way to achieve this goal is to identify potential drug therapy problems that may place patients at risk, particularly if multiple providers are identified. This program is educational in nature and allows you to incorporate the information provided into your continuing assessment of the patient's drug therapy requirements.

During a recent review of the enclosed drug history profile, *it appears your patient* Jane Doe *is receiving* **Prednisone** *and also has a diagnosis of osteoporosis.* Corticosteroid therapy in patients with osteoporosis may increase the risk of fractures due to decreased bone density associated with corticosteroid use. This patient may be particularly at risk since they are not currently receiving treatment for osteoporosis. In presenting this information to you, we recognize that the management of each patient's drug therapy depends upon an assessment of the patient's entire clinical situation about which we are not fully aware. The enclosed historical drug profile is provided for your review and evaluation and contains all prescription claims from all prescribers for the patient.

The success of this program is enhanced by the two-way exchange of information. Therefore, at your convenience, we would appreciate learning of your assessment of this information and of any action taken in response to this notice. Although participation is this program is voluntary, we find your feedback helpful in adjusting our program to address clinically important problems. Please complete the response form on the reverse side of this letter and return it in the enclosed envelope or fax it to the number at the bottom of the response form.

At the bottom of this letter are the specific prescriptions attributed to you by the dispensing pharmacy. In addition, if multiple prescribers are involved in the therapy identified above, each will receive this information. Thank you for your professional consideration.

RX#(s): [rx_no_a]

Sincerely,

W. Murray Yarbrough, M.D.
Medical Director
Health Information Designs

Case#: [case_no]
Enclosures

PRESCRIBER RESPONSE

Your response is voluntary, implies no penalty or liability, and is reviewed with strict confidentiality.

All information used to generate the enclosed letter, including prescriber identification, was obtained from pharmacy claims data. If there appears to be an error in the information provided, please note the discrepancy. Thank you for your cooperation.

1. This patient:
   ___is under my care, however, I did not prescribe the following medication(s) that were attributed to my provider number.
   ___ has an appointment to discuss drug therapy.
   ___ is under my care, however, has not seen me recently.
   ___ is no longer under my care.
   ___ has never been under my care.
   ___ has recently expired.
   ___ is currently taking calcium and Vitamin D supplements.

2. I have reviewed the information provided and, I:
   ___ discontinued the following medication(s) _____.
   ___ initiated drug therapy with the following medication(s) _____.
   ___ reassessed and modified drug therapy.
   ___ have not modified patient's drug therapy because the benefits outweigh the risks.
   ___ have not modified patient's drug therapy because the potential interactions are not clinically significant.
   ___ have tried to modify the drug therapy, however, patient refuses to change medications.
   ___ have tried to modify the drug therapy, however, recurrence of symptom necessitates continuation of the medication.

3. I have reviewed the enclosed information and found it:
   _____ Very useful _____useful ____neutral ____ somewhat useful ____ not useful.

4. ___ Please check here if you would like to receive an updated historical drug profile for the patient in the future.

Comments: _____
_____
_____

[adress1] Case# [case_no]
Letter Type [letter_type]
[criteria]

Health Information Designs, Inc.
513 Liberty Rd. Suite 2A
Flowood, MS 39232
(800) 355-0486 ext 100
Fax (800) 459-2135

Patient Information
"Osteoporosis"

Risk Factors

Certain facts play a part in the development of osteoporosis or contribute to a person's likelihood of developing the disease. These are called "risk factors". Many people with osteoporosis have several of these risk factors, but others with osteoporosis have no identified risk factors. There are some risk factors that you cannot change, and others that you can.

Risk factors you cannot change:

- *Gender*- Your chances of developing osteoporosis are greater if you are a woman. Women have less bone tissue and lose bone more rapidly than men because of the changes involved in menopause.
- *Age*- the older you are, the greater your risk of osteoporosis. Your bones become less dense and weaker as you age.
- *Body size*- small, thin-boned women are at greater risk.
- *Ethnicity*- Caucasian and Asian women are at highest risk. African-American and Latino women have a lower but significant risk.
- *Family History*- Susceptibility to fracture may be, in part, hereditary. People whose parents have a history of fractures also seem to have reduced bone mass and may be at risk for fractures.

Risk factors you can change:

- *Sex Hormones*- abnormal absence of menstrual periods (amenorrhea), low estrogen level (menopause), and low testosterone levels in men.
- *Anorexia*
- A lifetime diet low in calcium and vitamin D.
- Use of certain medications, such as glucocorticoids or some anticonvulsants.
- An inactive lifestyle or extended bed rest.
- Cigarette smoking.
- Excessive use of alcohol.

Osteoporosis

Osteoporosis is known as the “silent disease” because it happens without symptoms.

Things to Avoid!

- Do Not Smoke
- Do Not Drink a lot of alcohol

Things to Do!

- Exercise regularly
- Increase Calcium and Vitamin D intake

Sources of Calcium

- Low fat dairy products, such as milk, yogurt, cheese, and ice cream
- Dark green leafy vegetables, such as broccoli, collard greens, and spinach
- Sardines and salmon with bones
- Tofu
- Almonds
- Foods fortified with calcium, such as orange juice, cereals, and breads

Sources of Vitamin D

- Vitamin D supplementation to ensure a daily intake of between 400-800 IU of vitamin D is recommended

Fall prevention is a special concern for people with osteoporosis.
Some tips to help eliminate factors that lead to falls:

- Wear rubber-soled shoes for traction
- Use a can or walker if needed for added stability
- Walk on grass when sidewalks are slippery
- Keep rooms free of clutter
- Avoid walking indoors with just socks
- Use a rubber bath mat in the shower

A DUR Approach to Prevention of Cardiovascular Events

Mortality and morbidity associated with cardiovascular disease continues to be a challenge in the Medicaid population of Mississippi. Few would dispute that aggressive treatment in line with the currently accepted standards of care and recommendations could have a significant positive impact on this problem.

For example, the JNC-7 report states that undiagnosed, untreated, and uncontrolled hypertension clearly places a substantial strain on the health care delivery system. Treatment of hypertension to goal could no doubt decrease this strain.

Following are several suggested DUR interventions which could play a role in encouraging optimal treatment aimed at preventing cardiovascular events.

1. Diabetes/Hypertension/Cardiovascular Drugs (Negating) Criteria #1536

Alert Message: This patient has a history of diabetes and hypertension and may benefit from the addition of an anti-hypertensive agent to reduce cardiovascular morbidity and mortality. The coexistence of these conditions imposes a need for a significantly lower goal blood pressure (130/80 mm Hg) than the goal recommended for a non-diabetic patient with hypertension (140/90 mm Hg). If lifestyle modifications alone are no longer effective consider JNC-7 pharmacologic treatment recommendations for the selection of the optimal anti-hypertensive therapy.

Util A	Util B	Util C (Negating)
Insulin	Hypertension	ACEIs
Oral Hypoglycemic Agts.	(ICD9)	ARBs
		Beta Blockers
		Calcium Channel Blockers
		Anti-adrenergic - Centrally & Peripherally Acting Agents
		Alpha/Beta Adrenergic Blockers
		Diuretics

References:
The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure, NIH Publication No. 03-5233, May 2003.
Arauz-Pacheco C, Parrott MA, Raskin P: The treatment of hypertension in adult patients with diabetes (Technical Review). *Diabetes Care* 25:134–147, 2002.

2. Certain Antihypertensive Agents/Post MI/Beta-blockers, ACEI & Aldosterone Antagonists Criteria#1607

Alert Message: This patient has a diagnosis of myocardial infarction and is on an anti-hypertensive medication. The current JNC-7 report recommends a beta-blocker, ACE inhibitor or an aldosterone antagonist as optimal antihypertensive therapy for hypertensive post myocardial infarction patients, if no contraindications are present.

Util A	Util B	Util C(Negating)
Calcium Channel Blockers	Post MI	ACEIs
Anti-adrenergic:		Aldosterone Antagonists
Centrally & Peripherally Acting Agents		Beta Blockers
Alpha/Beta Adrenergic Blockers		
Diuretics		

References:
The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure, NIH Publication No. 03-5233, May 2003.

3. Certain Antihypertensive Agents/Stroke/Thiazide diuretics & ACEI Criteria #1608

Alert Message: This patient has a history of stroke and is on an anti-hypertensive medication. The current JNC-7 report suggests that recurrent stroke rates are lowered by the combination of an ACE inhibitor and a thiazide-type diuretic, if no contraindications are present.

Util A	Util B	Util C(Negating)
Calcium Channel Blockers	Stroke	ACEIs
Anti-adrenergic:		Diuretics
Centrally & Peripherally Acting Agents		
Alpha/Beta Adrenergic Blockers		
ARBs		
Beta Blockers		

References:
The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure, NIH Publication No. 03-5233, May 2003.

4. Certain Antihypertensive Agents/Chronic Kidney Disease/ACEI & ARB Criteria #1609

Alert Message: This patient has a diagnosis of chronic kidney disease and is on an anti-hypertensive medication. The current JNC-7 report recommends an ACE inhibitor or angiotensin II receptor antagonist as optimal antihypertensive therapy in these patients, if no contraindications are present.

Util A	Util B	Util C(Negating)
Calcium Channel Blockers	Chronic Kidney Disease	ACEIs
Anti-adrenergic:		ARBs
Centrally & Peripherally Acting Agents		
Alpha/Beta Adrenergic Blockers		
Diuretics		
Beta Blockers		

References:
The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure, NIH Publication No. 03-5233, May 2003.

5. Diabetes/Proteinuria/Negating ACEI & ARB
Criteria #541

Alert Message: Diabetics (hypertensive and normotensive) with microalbuminuria may benefit from the addition of an ACE inhibitor or an ARB to their therapy to reduce the rate of progression of renal disease.

Util A	Util B	Util C
Diabetes	Proteinuria	ACEI
		ARB
		Pregnancy
		Renal Artery Stenosis

References:
The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: The JNC 7 Report. JAMA. 2003;289(19):2560-71.
Standards of Medical Care for Patients with Diabetes Mellitus. Diabetes Care 2003;26:S33-S50.

6. Diabetes/Hypertension/Negating ACEI & ARB
Criteria #1493

Alert Message: Diabetics with hypertension and nephropathy may benefit from the addition of an ACE inhibitor or angiotensin receptor antagonist to their therapy to reduce the rate of progression to renal disease.

Util A	Util B	Util C (Negating)
Insulins	Hypertension (ICD-9's)	ACE Inhibitors
Diabetic Agents		ARB's
		Pregnancy
		Renal Artery Stenosis

References:
Micromedex Healthcare Series, Drugdex Drug Evaluations.
AHFS Drug Information, 2003
American Diabetes Association. Clinical Practice Recommendations. Position Statement. Diabetic Nephropathy. Diabetes Care. 26:(Suppl 1):S94-S98, 2003.

7. Diabetes/Hypertension or Diabetic Nephropathy/Negating ACEI & ARB
Criteria #1439

Alert Message: According to the JNC 7 report, the hypertension treatment goal for patients with diabetes is a blood pressure of < 130/80-mm Hg. In order to achieve this goal, multiple antihypertensive agents may be required. Adding an ACEI or an ARB should be considered if no contraindications are present. These agents also have been shown to delay the progression of nephropathy in diabetic patients with microalbuminuria.

Util A	Util B	Util C (Negating)
Insulins	Hypertension (ICD-9's)	ACE Inhibitors
Diabetic Agents	Diabetic Nephropathy	ARB's

References:
The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: The JNC 7 Report. JAMA. 2003; 289(19):2560-71.
Standards of Medical Care for Patients with Diabetes Mellitus. Diabetes Care 2003;26:S33-S50.

Summary of Suggested Interventions
June 23, 2005

1. Criteria #1536 ICER count: 689 beneficiaries
   Diagnosis of DM and hypertension - May benefit from an antihypertensive agent.

2. Criteria #1607 ICER count: 66 beneficiaries
   Diagnosis of MI and on an antihypertensive agent – Recommend a BB, ACEI or aldosterone antagonist.

3. Criteria # 1608 ICER count: 130 beneficiaries
   History of stroke and on an antihypertensive agent – Recommend ACEI and thiazide diuretic.

4. Criteria # 1609 ICER count: 1,227 beneficiaries
   Diagnosis of chronic kidney disease and on an antihypertensive agent – Recommend ACEI or ARB.

5. Criteria #541 ICER count: 8,590 beneficiaries (403 medium and high risk)
   Diabetes with proteinuria – recommend ACEI or ARB.

6. Proposed Criteria #1493
   Diabetes with hypertension and nephropathy – recommend ACEI or ARB.

7. Proposed Criteria #1439
   Diabetes with hypertension and/or diabetic nephropathy – recommend ACEI or ARB.

8. Additionally, the Osteoporosis Targeted Intervention, if approved by the Board, will be reviewed within the same 90-day period.

MISSISSIPPI MEDICAID
RETROSPECTIVE DUR
CRITERIA RECOMMENATIONS
SECOND QUARTER 2005

Recommendations ***Approved*** ***Rejected***

1. Tizanidine / Fluvoxamine _____ _____

Alert Message: Concurrent use of tizanidine with fluvoxamine, a potent CYP1A2 inhibitor, is contraindicated. Significant alterations of pharmacokinetic parameters of tizanidine including AUC, t1/2, Cmax, increased oral bioavailability and decreased plasma clearance have been observed with concomitant fluvoxamine administration. Coadministration of these agents has resulted in profound hypotension, bradycardia and excessive drowsiness.
Conflict Code: DD – Drug/Drug Interaction
Drug/Disease:

Util A	Util B	Util C
Tizanidine	Fluvoxamine	

References:
Zanaflex Prescribing Information, April 2005, Athena Neurosciences.
Micromedex Healthcare Series, Drugdex Drug Evaluations, 2005.

2. Tizanidine / CYP1A2 Inhibitors _____ _____

Alert Message: Caution is recommended when considering concomitant use of tizanidine with other inhibitors of CYP1A2, such as antiarrhythmics (amiodarone, mexiletine, propafenone), cimetidine, fluoroquinolones (ciprofloxacin, norfloxacin) and ticlopidine. The concurrent use of these agents may increase the risk of profound hypotension, somnolence and dizziness.
Conflict Code: Drug/Drug Interaction
Drug/Disease:

Util A	Util B		Util C
Tizanidine	Amiodarone	Ciprofloxacin	
	Mexiletine	Norfloxacin	
	Propafenone	Ticlopidine	
	Cimetidine		

References:
Granfors MT, Backman JT, Neuvonen M, et.al. Ciprofloxacin greatly increases concentrations and hypotensive effect of tizanidine by inhibiting its cytochrome P450 1A2-mediated presystemic metabolism. Clin Pharmacol Ther. 2004 Dec;76(6):598-606.
Zanaflex Prescribing Information, April 2005, Athena Neurosciences.

3. SNRI's / Therapeutic Duplication _____ _____

Therapeutic duplication of serotonin norepinephrine reuptake inhibitors may be occurring. Concomitant use of these drugs may cause additive adverse effects.
Conflict Code: TD – Therapeutic Duplication
Drug/Disease:

Util A	Util B	Util C
Duloxetine		
Venlafaxine		

References:
Facts & Comparisons, 2005 Updates.
Micromedex Healthcare Series, Drugdex Drug Evaluations, 2005.

Recommendations ***Approved*** ***Rejected***

4. Overactive Bladder Medications / Therapeutic Duplication _____ _____

Therapeutic duplication of medications to treat overactive bladder may be occurring. Concomitant use of these drugs may cause additive adverse effects.
Conflict Code: TD – Therapeutic Duplication
Drug/Disease:

Util A	Util B	Util C
Darifenacin		
Solifenacin		
Oxybutynin		
Flavoxate		
Tolterodine		
Tropsium		

References:
Facts & Comparisons, 2005 Updates.
Micromedex Healthcare Series, Drugdex Drug Evaluations, 2005.

5. Darifenacin / High Dose _____ _____

Alert Message: Enablex (darifenacin) may be over-utilized. The recommended maximum dose is 15 mg per day.
Conflict Code: HD – High Dose
Drug/Disease:

Util A	Util B	Util C
Darifenacin		

Maximum Dose: 15mg/day
References:
Facts & Comparisons, 2005 Updates.
Micromedex Healthcare Series, Drugdex Drug Evaluations, 2005.
Enablex Prescribing Information, Dec. 2004, Novartis Pharmaceuticals, Inc.

6. Darifenacin / Potent 3A4 Inhibitors _____ _____

Alert Message: The daily dose of Enablex (darifenacin), a CYP 3A4 substrate, should not exceed 7.5 mg when coadministered with a potent CYP3A4 inhibitor (e.g., ketoconazole itraconazole, ritonavir, nelfinavir, clarithromycin, and nefazodone). Exceeding the recommended dose during concurrent therapy may increase the risk of adverse effects of darifenacin.
Conflict Code: DD – Drug/Drug Interaction (ER-overutilization)
Drug/Disease:

Util A	Util B	Util C	
Darifenacin		Ketoconazole	Erythromycin
		Itraconazole	Troleandomycin
		Ritonavir	Indinavir
		Nelfinavir	
		Clarithromycin	
		Nefazodone	

Max Dose: 7.5mg
References:
Micromedex Healthcare Series, Drugdex Drug Evaluations, 2005.
Facts & Comparisons, 2005.

Recommendations ***Approved*** ***Rejected***

7. Darifenacin / Hepatic Impairment _____ _____

Alert Message: The daily dose of Enablex (darifenacin) should not exceed 7.5 mg once daily for patients with moderate hepatic impairment. Darifenacin is not recommended for use in patients with severe hepatic impairment.
Conflict Code: ER - Overutilization
Drug/Disease:

Util A	Util B	Util C
Darifenacin		Hepatic Impairment

Max Dose: 7.5 mg
References:
Micromedex Healthcare Series, Drugdex Drug Evaluations, 2005.
Facts & Comparisons, 2005.

8. Darifenacin / CYP2D6 Substrates _____ _____

Alert Message: Caution should be exercised when Enablex (darifenacin), a moderate 2D6 inhibitor, is used concomitantly with medications that are predominantly metabolized by CYP2D6 and which have a narrow therapeutic window (e.g. flecainide and thioridazine). Concurrent use with darifenacin may result in elevated plasma concentrations of the substrates and increase risk of adverse effects.
Conflict Code: DD – Drug/Drug Interaction
Drug/Disease:

Util A	Util B	Util C
Darifenacin	Flecainide Thioridazine	

References:
Facts & Comparisons, 2005 Updates.
Enablex Prescribing Information, Dec. 2004, Novartis Pharmaceuticals, Inc.

9. Darifenacin / Digoxin _____ _____

Alert Message: Caution should be exercised when Enablex (darifenacin) is used concomitantly with digoxin. Concurrent use of darifenacin (30mg daily) with digoxin (0.25mg) at steady state resulted in a 16% increase in digoxin exposure. Routine monitoring of digoxin should continue.
Conflict Code: DD – Drug/Drug Interaction
Drug/Disease:

Util A	Util B	Util C
Darifenacin	Digoxin	

References:
Facts & Comparisons, 2004 Updates.
Enablex Prescribing Information, Dec. 2004, Novartis Pharmaceuticals, Inc.

10. Darifenacin / Narrow Angle Glaucoma _____ _____

Alert Message: Enablex (darifenacin), an anticholinergic agent, should be used with caution in patients being treated for narrow-angle glaucoma and only when the potential benefits outweigh the risks. Darifenacin is contraindicated in patients with uncontrolled narrow-angle glaucoma.
Conflict Code: MC – Drug Actual Disease Precaution
Drug/Disease:

Util A	Util B	Util C
Darifenacin	Narrow-angle Glaucoma	

References:
Facts & Comparisons, 2005 Updates.
Enablex Prescribing Information, Dec. 2004, Novartis Pharmaceuticals, Inc.

Recommendations ***Approved*** ***Rejected***

11. Darifenacin / Urinary Retention _____ _____

Alert Message: Enablex (darifenacin), an anticholinergic agent, is contraindicated in patients with urinary retention or gastric retention and in patients who are at risk for these conditions.
Conflict Code: MC – Drug Actual Disease Precaution
Drug/Disease:

Util A	Util B	Util C
Darifenacin	Urinary Retention	
	Gastric Retention	

References:
Facts & Comparisons, 2005 Updates.
Enablex Prescribing Information, Dec. 2004, Novartis Pharmaceuticals, Inc.

12. Darifenacin / GI Obstruction-Decreased GI Motility _____ _____

Alert Message: Enablex (darifenacin), an anticholinergic agent, should be administered with caution to patients with GI obstructive disorders because of the risk of gastric retention. Darifenacin, like other anticholinergic drugs, may decrease GI motility and should be used with caution in patients with severe constipation, ulcerative colitis, and myasthenia gravis.
Conflict Code: DB – Drug/Drug marker and/or Diagnosis
Drug/Disease:

Util A	Util B	Util C
Darifenacin	Ulcerative Colitis	
	Myasthenia Gravis	
	Intestinal Obstruction	
	Slow Transit Constipation	

References:
Facts & Comparisons, 2005 Updates.
Enablex Prescribing Information, Dec. 2004, Novartis Pharmaceuticals, Inc.

13. Anticholinergic Agents / Therapeutic Duplication _____ _____

Alert Message: The concomitant use of anticholinergic agents may increase the frequency and/or severity of dry mouth, constipation, blurred vision and other anticholinergic adverse effects.
Conflict Code: TD – Therapeutic Duplication
Drug/Disease:

Util A	Util B	Util C
Belladonna	Benzotropine	
Atropine	Biperiden	
Scopolamine	Procyclidine	
Homatropine	Trihexyphenidyl	
Tropicamide	Flavoxate	
Hyoscyamine	Oxybutynin	
Glycopyrrolate	Tolterodine	
Mepenzolate	Tropsium	
Propantheline	Solifenacin	
Dicyclomine	Orphenadrine	
Clidinium	Darifenacin	

References:
Facts & Comparisons, 2005 Updates.

Recommendations ***Approved*** ***Rejected***

14. Solifenacin / High Dose _____ _____

Alert Message: Vesicare (solifenacin) may be over-utilized. The recommended maximum dose is 10 mg per day. Higher doses have resulted in a higher incidence of adverse reactions.
Conflict Code: HD – High Dose
Drug/Disease:

Util A	Util B	Util C
Solifenacin		

Maximum Dose: 10mg/day
References:
Facts & Comparisons, 2005 Updates.
Micromedex Healthcare Series, Drugdex Drug Evaluations, 2005.

15. Solifenacin / Hepatic Impairment _____ _____

Alert Message: The daily dose of Vesicare (solifenacin) should not exceed 5.0 mg for patients with moderate hepatic impairment. Solifenacin is not recommended for use in patients with severe hepatic impairment.
Conflict Code: ER - Overutilization
Drug/Disease:

Util A	Util B	Util C
Solifenacin		Hepatic Impairment

Max Dose: 5.0 mg
References:
Facts & Comparisons, 2005.
Vesicare Prescribing Information, Nov. 2004 GlaxoSmithKline.

16. Solifenacin / Renal Impairment _____ _____

Alert Message: The daily dose of Vesicare (solifenacin) should not exceed 5.0 mg for patients with severe renal impairment (Ccr less than 30 mL/min). Significant increases in the AUC and elimination half-life have been noted with single oral doses of solifenacin 10 mg and have been correlated to the degree of renal impairment.
Conflict Code: ER - Overutilization
Drug/Disease:

Util A	Util B	Util C
Solifenacin		Chronic Renal Failure

Max Dose: 5.0 mg
References:
Facts & Comparisons, 2005.
Vesicare Prescribing Information, Nov. 2004 GlaxoSmithKline.

17. Solifenacin / Potent 3A4 Inhibitors _____ _____

Alert Message: The daily dose of Vesicare (solifenacin), a CYP 3A4 substrate, should not exceed 5.0 mg when coadministered with a potent CYP3A4 inhibitor (e.g., ketoconazole itraconazole, ritonavir, nelfinavir, clarithromycin, and nefazodone). Exceeding the recommended dose during concurrent therapy may increase the risk of adverse effects.
Conflict Code: DD – Drug/Drug Interaction
Drug/Disease:

Util A	Util B	Util C	
Darifenacin		Ketoconazole	Erythromycin
		Itraconazole	Troleandomycin
		Ritonavir	Indinavir
		Nelfinavir	
		Clarithromycin	
		Nefazodone	

Max Dose: 5.0mg
References:
Facts & Comparisons, 2005.
Vesicare Prescribing Information, Nov. 2004 GlaxoSmithKline.

Recommendations ***Approved*** ***Rejected***

18. Solifenacin / Narrow Angle Glaucoma _____ _____

Alert Message: Vesicare (solifenacin), an anticholinergic agent, should be used with caution in patients being treated for narrow-angle glaucoma and only when the potential benefits outweigh the risks. Solifenacin is contraindicated in patients with uncontrolled narrow-angle glaucoma.
Conflict Code: MC – Drug Actual Disease Precaution
Drug/Disease:

Util A	Util B	Util C
Solifenacin	Narrow-angle Glaucoma	

References:
Facts & Comparisons, 2005 Updates.
Vesicare Prescribing Information, Nov. 2004 GlaxoSmithKline.

19. Solifenacin / Urinary Retention & Gastric Retention _____ _____

Alert Message: Vesicare (solifenacin), an anticholinergic agent, is contraindicated in patients with urinary retention or gastric retention and in patients who are at risk for these conditions.
Conflict Code: MC – Drug Actual Disease Precaution
Drug/Disease:

Util A	Util B	Util C
Solifenacin	Urinary Retention	
	Gastric Retention	

References:
Facts & Comparisons, 2005 Updates.
Vesicare Prescribing Information, Nov. 2004 GlaxoSmithKline.

20. Solifenacin / GI Obstruction-Decreased GI Motility _____ _____

Alert Message: Vesicare (solifenacin), an anticholinergic agent, should be administered with caution to patients with GI obstructive disorders because of the risk of gastric retention. Solifenacin, like other anticholinergic drugs, may decrease GI motility and should be used with caution in patients with constipation, ulcerative colitis, and myasthenia gravis.
Conflict Code: DB – Drug/Drug marker and/or Diagnosis
Drug/Disease:

Util A	Util B	Util C
Solifenacin	Ulcerative Colitis	
	Myasthenia Gravis	
	Intestinal Obstruction	
	Slow Transit Constipation	

References:
Facts & Comparisons, 2005 Updates.

21. Solifenacin / QT Prolongation & QT Prolongation Drugs _____ _____

Alert Message: Vesicare (solifenacin) should be administered with caution to patients with a history of QT prolongation or on medications known to prolong the QT interval. A significant effect on QTc has been observed following the administration of solifenacin (10 or 30 mg) in healthy female volunteers. The QT prolonging effect was greater with the 30 mg dose as compared with the 10 mg dose and did not appear to be as great as that of the positive control moxifloxacin at its therapeutic dose.
Conflict Code: DB – Drug/Drug marker and/or Diagnosis
Drug/Disease:

Util A	Util B				Util C
Solifenacin	QT Prolongation ICD-9s				
	Quinidine	Thioridazine	Moxifloxacin	Chlorpromazine	
	Procainamide	Mesoridazine	Mefloquine	Levofloxacin	
	Disopyramide	Droperidol	Tacrolimus		
	Amiodarone	Pimozide	Gatifloxacin		
	Bretylium	Sotalol	Pentamidine		
	Dofetilide	Sparofloxacin	Ziprasidone		

References:
Facts & Comparisons, 2005 Updates.
Vesicare Prescribing Information, Nov. 2004, GlaxoSmithKline.

Recommendations ***Approved*** ***Rejected***

22. Tolterodine IR & XL/High Dose _____ _____

Alert Message: Detrol/Detrol XL (tolterodine) may be over-utilized. The manufacturer's recommended dose is 4.0 mg daily.
Conflict Code: HD – High Dose
Drug/Disease:

Util A	Util B	Util C
Tolterodine		

Max Dose: 4.0 mg
References:
Facts & Comparisons, 2005 Updates.
Detrol XL Prescribing Information, April 2004, Pfizer, Inc.

23. Tolterodine IR/Hepatic Impairment _____ _____

Alert Message: The daily dose of Detrol or Detrol XL (tolterodine) should not exceed 2.0 mg for patients with significantly reduced hepatic or renal function.
Conflict Code: HD – High Dose
Drug/Disease:

Util A	Util B	Util C (Inclusive)
Tolterodine		Hepatic Impairment
		Renal Impairment
		Lanthanum
		Sevelamer
		Doxercalciferol
		Paricalcitol
		Calcitriol

Max Dose: 2.0 mg
References:
Facts & Comparisons, 2005 Updates.
Detrol XL Prescribing Information, April 2004, Pfizer, Inc.

24. Tolterodine//Potent 3A4 Inhibitors _____ _____

Alert Message: The daily dose of Detrol/ Detrol XL (tolterodine), a CYP 3A4 substrate, should not exceed 2.0 mg when coadministered with a potent CYP3A4 inhibitor (e.g., ketoconazole itraconazole, erythromycin, clarithromycin, cyclosporine and vinblastine). Exceeding the recommended dose during concurrent therapy may increase the risk of adverse effects of tolterodine.
Conflict Code: HD - High Dose (drug/drug Interaction)
Drug/Disease:

Util A	Util B	Util C (Inclusive)	
Tolterodine		Ketoconazole	Erythromycin
		Itraconazole	Cyclosporine
		Ritonavir	Troleandomycin
		Nelfinavir	Indinavir
		Clarithromycin	Vinblastine
		Nefazodone	Cyclosporine

Max Dose: 2.0 mg
References:
Facts & Comparisons, 2005 Updates.
Detrol XL Prescribing Information, April 2004, Pfizer, Inc.
Detrol Prescribing Information, July 2003, Pfizer, Inc.

Recommendations ***Approved*** ***Rejected***

25. Oxybutynin/High Dose (Adults) _____ _____

Alert Message: Ditropan (oxybutynin immediate-release) may be over-utilized. The manufacturer's recommended maximum dose is 5 mg 4 times per day.
Conflict Code: HD – High Dose
Drug/Disease:

Util A	Util B	Util C
Oxybutynin IR		

Age Range: 18 years and older
Max Dose: 20 mg/day
References:
Facts & Comparisons, 2005 Updates.

26. Oxybutynin/High Dose-Pediatric _____ _____

Alert Message: Ditropan (oxybutynin immediate-release) may be over-utilized. The manufacturer's recommended maximum dose is 5 mg 3 times per day.
Conflict Code: HD – High Dose
Drug/Disease:

Util A	Util B	Util C
Oxybutynin IR		

Age Range: 5 – 18 years
Max Dose: 15 mg/day
References:
Facts & Comparisons, 2005 Updates.

27. Oxybutynin Extended Release/High Dose _____ _____

Alert Message: Ditropan XL (oxybutynin extended-release) may be over-utilized. The manufacturer's recommended maximum dose is 30 mg per day.
Conflict Code: HD – High Dose
Drug/Disease:

Util A	Util B	Util C
Oxybutynin XL		

Max Dose: 30 mg/day
References:
Facts & Comparisons, 2005 Updates.

28. Oxybutynin Extended Release/Hepatic & Renal Impairment _____ _____

Alert Message: Ditropan/Ditropan XL (oxybutynin) should be used with caution in patients with renal or hepatic impairment.
Conflict Code: DB – Drug-Drug Marker and/or Diagnosis
Drug/Disease:

Util A	Util B	Util C
Oxybutynin XL	Renal Impairment	
	Hepatic Impairment	

References:
Facts & Comparisons, 2005 Updates.

Recommendations ***Approved*** ***Rejected***

29. Oxybutynin Transdermal / High Dose _____ _____

Alert Message: Oxytrol (oxybutynin transdermal) may be over-utilized. The manufacturer's recommended dose is one 3.9 mg/day system applied twice weekly (every 3 to 4 days).
Conflict Code: HD – High Dose
Drug/Disease:

Util A	Util B	Util C
Oxybutynin XL		

Max Dose: 3.9 mg/day
References:
Facts & Comparisons, 2005 Updates.

30. Oxybutynin/Contraindications _____ _____

Alert Message: Ditropan (oxybutynin), an anticholinergic agent, is contraindicated in patients with urinary retention, gastric retention and other severe conditions of decreased gastrointestinal motility, uncontrolled narrow-angle glaucoma, paralytic ileus and in patients who are at risk for these conditions.
Conflict Code: MC - Drug (Actual) Disease Contraindication/Precaution
Drug/Disease:

Util A	Util B	Util C
Oxybutynin	Urinary Retention	
	Gastric Retention	
	Paralytic Ileus	

References:
Ditropan Prescribing Information, March 2003, OrthoMcNeil Pharmaceuticals Inc.
Micromedex Healthcare Series, Drugdex Drug Evaluations, 2005.

31. Oxybutynin / Disease State Precautions _____ _____

Alert Message: Ditropan (oxybutynin), an anticholinergic agent, should be used with caution in patients with hyperthyroidism, cardiac arrhythmias, congestive heart failure, coronary heart disease, hiatal hernias, hypertension, autonomic neuropathy, ulcerative colitis and prostatic hypertrophy. Oxybutynin may aggravate the symptoms of these conditions.
Conflict Code: MC - Drug (Actual) Disease Contraindication/Precaution
Drug/Disease:

Util A	Util B	Util C
Oxybutynin	Hyperthyroidism	
	Cardiac Arrhythmias	
	Congestive Heart Failure	
	Coronary Heart Disease	
	Hiatal Hernia	
	Hypertension	
	Ulcerative Colitis	
	Prostatic Hypertrophy	

References:
Ditropan Prescribing Information, Mar. 2003, OrthoMcNeil Pharmaceuticals Inc.
Micromedex Healthcare Series, Drugdex Drug Evaluations, 2005.

Recommendations ***Approved*** ***Rejected***

32. Oxybutynin / GI Obstruction-Decreased GI Motility _____ _____

Alert Message: Ditropan/Ditropan XL (oxybutynin), an anticholinergic agent, should be administered with caution to patients with GI obstructive disorders because of the risk of gastric retention. Oxybutynin, like other anticholinergic drugs, may decrease GI motility and should be used with caution in patients with severe constipation, ulcerative colitis, and myasthenia gravis.
Conflict Code: DB – Drug/Drug marker and/or Diagnosis
Drug/Disease:

Util A	Util B	Util C
Oxybutynin	Ulcerative Colitis	
	Myasthenia Gravis	
	Intestinal Obstruction	
	Slow Transit Constipation	

References:
Facts & Comparisons, 2005 Updates.

33. Oxybutynin/GERD _____ _____

Alert Message: Ditropan/Ditropan XL/Oxytrol (oxybutynin) should be used with caution in patients who have gastrointestinal reflux or who are concurrently taking drugs (such as bisphosphonates) that can cause or exacerbate esophagitis.
Conflict Code: DB – Drug/Drug marker and/or Diagnosis
Drug/Disease:

Util A	Util B	Util C
Oxybutynin	GERD	
	Bisphosponates	
	Potassium	
	NSAIDS	
	Iron	
	Quinidine	
	Doxycycline	
	Clindamycin	
	Tetracycline	
	Trimethoprim	

References:
Facts & Comparisons, 2005 Updates.
Ditropan Prescribing Information, March 2004, OrthoMcNeil Pharmaceuticals, Inc.
Oxytrol Prescribing Information, Feb. 2003, Watson Pharma, Inc.

34. Flavoxate/High Dose _____ _____

Alert Message: Flavoxate may be overutilized. The manufacturer's recommended maximum dose is 800 mg (200 mg 4 times a day).
Conflict Code: HD – High Dose
Drug/Disease:

Util A	Util B	Util C
Flavoxate		

Max Dose: 800mg/day
References:
Facts & Comparisons, 2005 Updates.

Recommendations ***Approved*** ***Rejected***

35. Flavoxate/Contraindications _____ _____

Alert Message: Flavoxate, an anticholinergic agent, is contraindicated in patients who have pyloric or duodenal obstruction, obstructive intestinal lesions or ileus, achalasia, GI hemorrhage, or obstructive uropathies of the lower urinary tract.
Conflict Code: MC – Drug (Actual Disease) Contraindication/Precaution
Drug/Disease:

Util A	Util B	Util C
Flavoxate	Pyloric Obstruction	
	Duodenal Obstruction	
	Obstructive Intestinal Lesions or Ileus	
	Achalasia	
	GI Hemorrhage	
	Urinary obstruction	

References:
Facts & Comparisons, 2005 Updates.

36. Flavoxate/Glaucoma _____ _____

Alert Message: Flavoxate should be used with caution in patients who have glaucoma. Flavoxate is an anticholinergic agent and use in these patients may aggravate the condition.
Conflict Code: DB – Drug/Drug Marker and/or Diagnosis
Drug/Disease:

Util A	Util B	Util C
Flavoxate	Glaucoma	
	Brimonidine	
	Apraclonidine	
	Dipivefrin	
	Levobunolol	
	Betaxolol	
	Metipranolol	
	Carteolol	
	Timolol	
	Pilocarpine	

References:
Micromedex Healthcare Series, Drugdex Drug Evaluations, 2005.
Facts & Comparisons, 2005 Updates.

37. Trospium / High Dose _____ _____

Alert Message: Sanctura (trospium) may be over-utilized. The manufacturer's recommended daily dose is 20 mg twice daily.
Conflict Code: HD – High Dose
Drug/Disease:

Util A	Util B	Util C
Trospium		

Max Dose: 40mg/day
References:
Sanctura Prescribing Information, July 2004, Odyssey Pharmaceuticals, Inc.
Facts & Comparisons, 2005 Updates.

Recommendations ***Approved*** ***Rejected***

38. Trospium / / Renal Impairment _____ _____

Alert Message: The daily dose of Sanctura (trospium) should not exceed 20 mg once daily at bedtime for patients with severe renal impairment (Ccr less than 30 mL/min). A 4.5-fold and 2-fold increase in mean AUC and Cmax respectively and the appearance of an additional elimination phase with a long half-life (33hr) was detected in patients with severe renal sufficiency.
Conflict Code: ER - Overutilization
Drug/Disease:

Util A	Util B	Util C
Trospium		Chronic Renal Failure

Max Dose: 20 mg/day
References:
Facts & Comparisons, 2005.
Sanctura Prescribing Information, July 2004, Odyssey Pharmaceuticals, Inc.

39. Trospium / Urinary & Gastric Retention _____ _____

Alert Message: Sanctura (trospium), an anticholinergic agent, is contraindicated in patients with urinary retention or gastric retention and patients at risk for these conditions
Conflict Code: MC – Drug Actual Disease Contraindication/Precaution
Drug/Disease:

Util A	Util B	Util C
Trospium	Urinary Retention	
	Gastric Retention	

References:
Facts & Comparisons, 2005 Updates.
Sanctura Prescribing Information, July 2004, Odyssey Pharmaceuticals, Inc.

40. Trospium / Narrow Angle Glaucoma _____ _____

Alert Message: Sanctura (trospium), an anticholinergic agent, should be used with caution in patients being treated for narrow-angle glaucoma and only when the potential benefits outweigh the risks. Trospium is contraindicated in patients with uncontrolled narrow-angle glaucoma.
Conflict Code: MC – Drug Actual Disease Contraindication/Precaution
Drug/Disease:

Util A	Util B	Util C
Solifenacin	Narrow-angle Glaucoma	

References:
Facts & Comparisons, 2005 Updates.
Sanctura Prescribing Information, July 2004, Odyssey Pharmaceuticals, Inc.

41. Trospium / GI Obstruction-Decreased GI Motility _____ _____

Alert Message: Sanctura (trospium) should be administered with caution to patients with GI obstructive disorders because of the risk of gastric retention. Trospium, like other anticholinergic drugs, may decrease GI motility and should be used with caution in patients with ulcerative colitis, intestinal atony and myasthenia gravis.
Conflict Code: MC – Drug Actual Disease Contraindication/Precaution
Drug/Disease:

Util A	Util B	Util C
Darifenacin	Ulcerative Colitis	
	Myasthenia Gravis	
	Intestinal Atony	

References:
Facts & Comparisons, 2005 Updates.

Recommendations ***Approved*** ***Rejected***

42. Trospium/Drugs Eliminated by ATS _____ _____

Alert Message: Sanctura (trospium) is eliminated via active tubular secretion and possesses the potential for pharmacokinetic interactions with other drugs that are eliminated by the same route (e.g., digoxin, procainamide, morphine, vancomycin, metformin, and tenofovir). Coadministration of trospium with drugs that are eliminated by active tubular secretion may increase the serum concentration of trospium and/or the coadministered drug because of competition for this elimination pathway. Careful patient monitoring is recommended
Conflict Code: DD – Drug/Drug Interaction
Drug/Disease:

Util A	Util B		Util C
Trospium	Digoxin	Vancomycin	
	Procainamide	Metformin	
	Morphine	Tenofovir	

References:
Facts & Comparisons, 2005.
Sanctura Prescribing Information, July 2004, Odyssey Pharmaceuticals, Inc.

43. Telithromycin / Pimozide _____ _____

Alert Message: The concurrent use of Ketek (telithromycin) and pimozide is contraindicated due to increased risk of cardiotoxicity (e.g., QT prolongation, torsades de pointes, cardiac arrest). Although no formal drug interaction studies have been conducted, telithromycin may inhibit pimozide CYP 3A4-mediated metabolism causing elevated plasma levels. Both agents are known to cause QTc prolongation.
Conflict Code: DD – Drug/Drug Interaction
Severity: 1 - Major
Drug/Disease:

Util A	Util B	Util C
Telithromycin	Pimozide	

References:
Ketek Prescribing Information, Oct. 2004, Aventis Pharmaceuticals, Inc.
Physicians' Desk Reference, Micromedex Healthcare Series, 2005.

44. Atypical Antipsychotics/ / FDA Approved Indications _____ _____

Alert Message: The atypical antipsychotics are not approved for the treatment of behavioral disorders in elderly patients with dementia. The FDA has determined that patients with dementia treated with atypical antipsychotics are at an increased risk of death compared to placebo. In analysis of seventeen placebo-controlled studies of four drugs in this class, the rate of death for those elderly patients with dementia was about 1.6 to 1.7 times that of placebo.
Conflict Code: TA - Therapeutic Appropriateness (Black Box Warning)
Drug/Disease:

Util A	Util B	Util C (Negating)
Clozapine		Schizophrenia
Risperidone		Bipolar
Olanzapine		
Quetiapine		
Ziprasidone		
Aripiprazole		

Age Range: 65 year of age or older
References:
MedWatch: FDA Safety Information and Adverse Event Reporting Program, 2005.
Micromedex Healthcare Series, Drugdex Drug Evaluations, 2005.
Physicians' Desk Reference, Micromedex Healthcare Series, 2005.

Boxed Warning Update

Trileptal (oxcarbazepine) Tablets and Oral Solution

Audience: *Neuropsychiatric healthcare professionals and consumers*
Novartis Pharmaceuticals and FDA notified healthcare professionals about revisions to the WARNINGS and PRECAUTIONS sections of the prescribing information for TRILEPTAL (oxcarbazepine) tablets and oral suspension, indicated for use as monotherapy or adjunctive therapy in the treatment of partial seizures in adults and children ages 4-16 years with epilepsy. The updated WARNINGS section describes serious dermatological reactions, including Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) that have been reported in both children and adults in association with Trileptal use. The PRECAUTIONS section has been updated to include language regarding multi-organ hypersensitivity reactions that have been reported in association with Trileptal use.

FDA Alert: 4/7/2005:

Celebrex has been associated with an increased risk of serious adverse cardiovascular (CV) events in a long-term placebo controlled trial. Based on the currently available data, FDA has concluded that an increased risk of serious adverse CV events appears to be a class effect of non-steroidal anti-inflammatory drugs (NSAIDs) (excluding aspirin). FDA has requested that the package insert for all NSAIDs, including Celebrex, be revised to include a boxed warning to highlight the potential increased risk of CV events and the well described risk of serious, and potentially life-threatening, gastrointestinal bleeding. FDA has also requested that the package insert for all NSAIDs be revised to include a contraindication for use in patients immediately post-operative from coronary artery bypass (CABG) surgery.

This information reflects FDA's current analysis of all available data concerning this drug. FDA intends to update this sheet when additional information or analyses become available.

Prescription Non-Selective NSAIDs

FDA will request that manufacturers of all prescription products containing non-selective NSAIDs revise their product labeling to include:

- A boxed warning regarding the potential serious adverse CV events and the serious, and potentially life-threatening GI adverse events associated with the use of this class of drugs.
- A contraindication for use in patients who have recently undergone coronary artery bypass surgery.
- A Medication Guide for patients regarding the potential for CV and GI adverse events associated with the use of this class of drugs. The Medication Guide will be required to be given to patients at the time each prescription is dispensed. The Medication Guide will also inform patients of the need to discuss with their doctor the risks and benefits of using NSAIDs and the importance of using the

lowest effective dose for the shortest duration possible if treatment with an NSAID is warranted for an individual patient.

Patients who are taking a prescription non-selective NSAID should discuss questions or concerns about this new information with their physician.

OTC Non-Selective NSAIDs

FDA will ask manufacturers of all OTC products containing ibuprofen (Motrin, Advil, Ibu-Tab 200, Medipren, Cap-Profen, Tab-Profen, Profen, Ibuprohm), naproxen (Aleve), and ketoprofen (Orudis, Actron) to revise their labeling to include:

- More specific information about the potential CV and GI risks,
- Instructions about which patients should seek the advice of a physician before using these drugs,
- Stronger reminders about limiting the dose and duration of treatment in accordance with package instructions, unless otherwise advised by a physician, and
- A warning about potential skin reactions.

Patients who are taking an OTC NSAID should carefully follow the labeled directions, particularly with regard to dose and duration of use, and should contact their physician regarding any questions or concerns they may have about this new information.

Note: Aspirin is a nonselective NSAID. However, aspirin is also a platelet inhibitor and has been shown in clinical trials to reduce the risk of CV events. Patients taking aspirin to prevent CV events should NOT stop taking it, unless specifically advised to do so by their physician.

Novantrone prescribing information revisions and risks of cardiotoxicity and secondary acute myelogenous leukemia (AML)

May 24, 2005: Serono and FDA notified healthcare professionals of revisions to the BOXED WARNING, WARNINGS, and DOSAGE AND ADMINISTRATION sections of the prescribing informations for Novantrone (mitoxantrone), indicated for treatment of multiple sclerosis (MS). The Dear Healthcare Professional letter provides additional informations concerning the risks of cardiotoxicity associated with Novantrone and also provides supplemental information regarding secondary acute myelogenous leukemia (AML) reported in MS patients with Novantrone.

Code of Federal Regulations definition for Black Box:

Citation: Title 21 CFR 201.57 Section E

(e) Warnings. Under this section heading, the labeling shall describe serious adverse reactions and potential safety hazards, limitations in use imposed by them, and steps that should be taken if they occur. The labeling shall be revised to include a warning as soon as there is reasonable evidence of an association of a serious hazard with a drug; a causal relationship need not have been proved. A specific warning relating to a use not provided for under the "Indications and

Usage: section of labeling may be required by the Food and Drug Administration if the drug is commonly prescribed for a disease of condition, and there is lack of substantial evidence of effectiveness for that disease or condition, and such usage is associated with serious risk or hazard. Special problems, particularly those that may lead to death or serious risk or hazard. Special problems, particularly those that may lead to death or serious injury, may be required by the Food and Drug Administration to be placed in a prominently displayed box. The boxed warning ordinarily shall be based on clinical data, but serious animal toxicity may also be the basis of a boxed warning in the absence of clinical data. If a boxed warning is required, its location will be specified by the Food and Drug Administration. The frequency of these adverse reactions and , if known, the approximate mortality and morbidity rates for patients sustaining the reaction, which are important to safe and effective used of the drug, shall be expressed as provided under the “Adverse Reactions” section of the labeling.