Division of Medicaid

Office of the Governor

State of Mississippi

DUR Board Meeting

February 23, 2006

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

February 23, 2006

Welcome	**John Mitchell, MD**
Old Business	
Reading and Approval of November 17, 2005 DUR Board Meeting Minutes	**Lew Anne Snow, RN**
CNS Update	**Frankie Rutledge**
Updates	**Dennis Smith, RPh**
Cost Management Analysis	
DUR Activity Report	
Pharmacy Program Update	**Judith Clark, RPh**
IQH, Information and Quality Healthcare	**Bo Bowen**
New Business	**Dennis Smith, RPh**
DUR Intervention	
Childhood Onset of Type 2 Diabetes	
Topical Corticosteroid Utilization in Children	
First Quarter Criteria Recommendations	
Boxed Warning Update	
Next Meeting Information	**John Mitchell, MD**

Minutes of the November 17, 2005
Drug Utilization Review (DUR) Board Meeting

Members Attending: Harold Blakely, RPh, Montez Carter, RPh, Randy Calvert, RPh, John Mitchell, M.D., Lee Montgomery, M.D., Leigh Ann Ross, PharmD, Rudy Runnels, M.D., Wallace Strickland

Members Absent: Billy Brown, PharmD, Andrea Phillips, M.D., Troy Griffin

Also Present: Judith Clark, RPh, Terri Kirby, RPh, Don Thompson, Deputy Director for Medicaid, Carlos Faler, Bureau Director for Program Integrity, - DOM
Dennis Smith, RPh, Samuel Warman, RPh, Lew Anne Snow, R.N., Kathleen Burns, R.N.-HID

Dr. John Mitchell called the meeting to order at 2:07 p.m.

Approval of the minutes for the September 29, 2005 meeting:
Dr. Runnels made a motion to accept the minutes as submitted. Randy Calvert seconded the motion. All voted in favor of the approval.

CNS Update:
Presentation was made by Frankie Rutledge on the four projected quality goals:

1. Improve continuity of care
2. Eliminate redundant treatments
3. Coordinate care among providers
4. Decrease risks associated with inappropriate use

Ms. Rutledge continued with the prescriber feedback response rate being between 8% and 10%. The most common response being "this is not my patient". The clinical concerns were pointed out. Those are:

1. patients on high numbers of behavioral health drugs
2. long-term use of benzodiazepines
3. multiple prescribers of anticonvulsants/mood stabilizers
4. switching atypical antipsychotics without sufficient trial

With the implementation of MMA Part D as of Jan 1, 2005, BPM will redesign the 2006 enhancement. The focus will include up to 60 indicators being distributed among adults age 64 and younger and children. Indicators for opiates have also been added.

Updates

Cost management analysis:
Dennis Smith presented the Top 25 Drugs based on the number of claims dated 8/01/05 thru 8/31/05. The top drug was Hydrocodone w/acetaminophen with 19,428 paid claims. This was in response to a request from the DUR Board to do a month by month report on the Top 25 drug in paid claims. Ms. Clark included that Hurricane Katrina may have had

an impact on the increase in mental health Rxs. She continued that there are many outstanding claims due to Hurricane Katrina from other states.

Osteoporosis:
Dennis continued with in light of Medicare Part D, the patient mix will therefore change. He suggested tabling this intervention until after January 1, 2006.

Narcotic Utilization:
Dennis continued with an overview of a handout in response to the P & T Committees' request. In the first nine months of 2005, there were over 83,000 claims for hydrocodone-containing products billed to Medicaid. A pharmacy claims search was made to identify all beneficiaries who have received narcotic prescriptions from more than one prescriber within a 30 day time- frame. Beneficiaries with a cancer diagnosis were excluded from this search. The analysis yielded the following observations:

1. 4, 075 beneficiaries received more than one narcotic within 30 days from more than one prescriber
2. 1,864 beneficiaries received three or more narcotics from more than one prescriber during the 90 day search period
3. 884 beneficiaries received narcotics from three or more prescribers during the 90 day search.

Due to the national scope of this problem, many state Medicaid programs have responded in various ways .The most common policy is the imposition of monthly quantity limits on these products. Another common action is "lock-in" of high-utilizing beneficiaries to a specific prescriber and pharmacy.

Recommendations:

1. Evaluate and explore a prospective DUR edit in the POS system for any duplicate narcotic prescription from a second prescriber within a 31 day period, excluding beneficiaries with a cancer diagnosis.
2. Intensify the quantity limits.
3. Encourage a lock-in program which would limit high-utilizing beneficiaries to a specific primary care physician and/or pain management specialist and a specific pharmacy

After much discussion, a motion was made by Mr. Strickland to lock-in to (1) pharmacy with additional motions made by Randy Calvert to limit narcotics to (2) units per day. This was seconded by Montez Carter. This would include all long-acting Opoids. All voted in favor of these motions. Carlos Faler, Director of Program Integrity for the Division of Medicaid, informed the Board that his department has an ongoing process to deal with the above mentioned problems. He asked to give his department some time to implement certain restrictions they have researched for several months. This was unanimously agreed upon by the Board. The Board would still like to implement the quantity limits on narcotics as voted on earlier.

Synagis
Lew Anne Snow presented the requested overview of the Synagis program. The current prior authorization process has eased the access for appropriate Synagis therapy. The Synagis injections remain as one of the top drugs in total claims during the months of

October thru March. The post season analysis results provided a most impressive utilization to meet the needs of the premature infants of the Medicaid population in Mississippi. Dr Mitchell commented to the Board that Synagis appears to be maintained with the PA process. He concluded that unless the Board had further directions, HID would continue without changes. No further recommendations were made at this point.

Pharmacy Program Update:
Judy Clark introduced Don Thompson, Deputy Director of Health Services to the board. She also distributed to the board members a copy of the Product Quantity Limits included changes that became effective on November 1, 2005.

New Business

Marinol Utilization:
Dronabinol is indicated for the treatment of nausea and vomiting associated with cancer chemotherapy in patients who have failed to respond adequately to conventional treatments. It is also approved to treat appetite loss associated with weight loss in people with AIDS. In July, Megace was re-categorized in terms of its primary therapeutic class. Whereas its therapeutic class was previously steroid antineoplastics, the classification is now appetite stimulants. As a result of this change, megestrol acetate suspension is no longer covered by Medicaid. This has resulted in a search for a substitute agent for the treatment of cachexia. Dennis continued with the study on Marional pointing out dosing and administration with mention of adverse effects and abuse potential. The utilization during the year between 10/01/2004 and 09/30/2005 was 1545 claims for this agent at a cost of over $760,000. Among these claims, there was only one beneficiary with a diagnosis of HIV or AIDS. HID was unable to associate a cancer diagnosis with any of these beneficiaries. There has been no significant increase in the number of claims for this agent since the re-categorization of megestrol acetate suspension.
Conclusion:
Based on the above information, almost all of the patients receiving treatment with Marinol do not have a diagnosis related to the approved indications for this agent.
Recommendation:
An intervention which identifies patients who have received Marinol without a diagnosis of HIV, AIDS, or cancer is recommended. This letter would be sent to prescribers and would include information about the approved indications, appropriate use and abuse potential of this agent.
Motion: Dr Ross made a motion to accept HID's recommendation excluding the dual eligible to see if the numbers change. Dr. Montgomery seconded the motion. All voted in favor of this motion.

Oxandrin Utilization:
Oxandrin is indicated as adjunctive therapy to promote weight gain after weight loss following extensive surgery, chronic infections or severe trauma. It is also indicated to offset the protein catabolism associated with prolonged administration of corticosteroids. Lastly, it is indicated for the relief of the bone pain frequently accompanying osteoporosis. Dennis continued with an overview of dosing, administration, adverse

effects and abuse potential . Utilization between 10/22/2004 and10/21/2005 was 474 claims for this agent with a cost of over $205,000. The number of claims has not significantly increased since the recategorization of megestrol acetate suspension.

Conclusion:

There is no evidence to support inappropriate use of this agent.

Recommendation:

No intervention is recommended at this time but continued monitoring of Oxandrin is advised

Lyrica Utilization:

Pregabalin is indicated for the management of neuropathic pain associated with diabetic peripheral neuropathy and post herpetic neuralgia. It is also indicated as adjunctive therapy for adult patients with partial onset seizures. Dennis continued with dosing, administration and mechanism of action reviews.

Utilization:

Dennis presented a chart to the Board and continued with the conclusions of the study.

1. 10 beneficiaries or 32% have a diagnosis of diabetes
2. Of the 10 beneficiaries, only 4 have claims for anti-diabetic medications
3. 9 beneficiaries or 29% have at least one recent claim for another anticonvulsant medication
4. None of the recipients who have received Lyrica have a diagnosis of herpes zoster or post herpetic neuralgia.

Recommendation:

Although this new medication has seen limited utilization to this point, this analysis indicates that a significant number of patients who have received Lyrica do not have a diagnosis for which it is indicated. It is recommended that this agent be monitored over the coming months to evaluate utilization trends.

Motion: Dr. Montgomery made a motion to accept the recommendations as indicated by HID. Dr. Runnels seconded the motion. All voted in favor of the motion.

Black Box Warnings:

Avinza:

Audience: pain specialists, other healthcare professionals and consumers

Posted 11/03/2005 Ligand pharmaceuticals and FDA notified healthcare professionals of revisions to BOXED WARNING, WARNINGS, PRECAUTIONS, and CLINICAL PHARMACOLOGY and DOSAGE AND ADMINISTRATION sections of the prescribing information to highlight and strengthen the warning that patients should not consume alcohol while taking Avinza. Additionally, patients must not use prescription or non-prescription medications containing alcohol while on Avinza therapy.

Cylert and generic pemoline products:

Audience: Neuropsychiatric healthcare professionals, Pediatricians, Pharmacists and consumers.

Posted 10/24/2005 FDA has concluded that the overall risk or liver toxicity from Cylert and generic pemoline products outweighs the benefits of this drug.. In May 2005, Abbott chose to stop sales and marketing of Cylert in the U.S. All generic companies have also

agreed to stop sales and marketing of this product. Health care professionals who prescribe Cylert or any of its generics, should transition their patients to an alternative therapy. Cylert will remain available through pharmacies and wholesalers until supplies are exhausted. No additional product will be available.

Cymbalta:
Audience: Neuropsychiatric and other healthcare professionals
POSTED 10/17/2005 Eli Lilly and FDA notified healthcare professionals of revision to the PRECAUTIONS/Hepatotoxicity section of the prescribing information for Cymbalta. This medication is indicated for treatment of major depressive disorder and diabetic peripheral neuropathic pain. Post marketing reports of hepatic injury suggest that patients with preexisting liver disease who take duloxetine may have an increased risk for further liver damage. The new labeling extends the precaution against using Cymbalta in patients with substantial alcohol use to include those patients with chronic liver disease. It is recommended that Cymbalta not be administered to patients with any hepatic insufficiency.

Paxil:
Audience: Neuropsychiatric and other healthcare professionals
Posted 09/27/2005 GlaxoSmithKline Kline and FDA notified healthcare professionals of changed to the pregnancy/PRECAUTIONS sections of the prescribing Information for Paxil and Paxil CR to describe the results of a GSK retrospective epidemiologic study of major congenital malformations for paroxetine as compared to other antidepressants. Healthcare professionals are advised to carefully weigh the potential risks and benefits of using parosetine therapy in women during pregnancy and to discuss these findings as well as treatment alternatives with their patients.

Toprol XL
Topamax
Audience: All healthcare professionals
Posted 09/26/2005 AstraZeneca and FDA notified healthcare professionals with reports of medication dispensing or prescribing errors between Toprol XL indicated for the treatment of hypertension, long-term treatment of angina pectoris and heart failure NYHA Class 11 or 111 and Topamax, a product of Ortho-McNeil Neurologics, Inc, indicated for the treatments of epilepsy and migraine prophylaxis. These reports include instances where Toprol XL was incorrectly administered to patients instead of Topamax, Tegretol or Tegretol XL and vice versa, some of them leading to adverse events.

Election of officers:
With the conclusion of the meeting being near, Ms Clark reminded the Board that they needed to elect officers. The following were elected:

- Chairman: Dr. John Mitchell, Nominated by Harold Blakely and seconded by Lee Ann Ross
- Vice-Chairman: Randy Calvert, Nominated by Lee Anne Ross and seconded by Montez Carter

All voted in favor of this motion

Ms. Clark reminded the Board that the dates of the DUR Board for 2006 will be sent out in letter form. She also asked for them to submit topics that they would be interested in for the upcoming year and submit them to DOM.

Dr. Mitchell adjourned the meeting after asking for any other business at 4:00p.m.

Respectfully submitted:
Health Information Designs

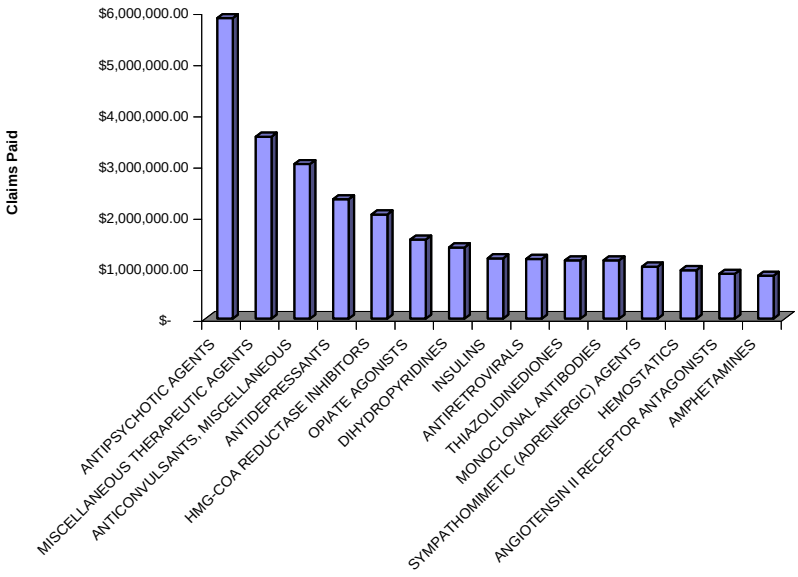
MISSISSIPPI MEDICAID
Cost Management Analysis
Nov-05

TOP 15 THERAPEUTIC CLASSES BY TOTAL COST OF CLAIMS FROM 11/01/05-11/30/05

AHFS Therapeutic Class	Rx	Paid	Paid/Rx	% Total Claims
ANTIPSYCHOTIC AGENTS	23,496	$ 5,868,424.74	$ 249.76	2.98%
MISCELLANEOUS THERAPEUTIC AGENTS	29,021	$ 3,554,409.77	$ 122.48	3.68%
ANTICONVULSANTS, MISCELLANEOUS	21,351	$ 3,020,215.28	$ 141.46	2.71%
ANTIDEPRESSANTS	38,874	$ 2,331,501.91	$ 59.98	4.93%
HMG-COA REDUCTASE INHIBITORS	20,281	$ 2,034,669.76	$ 100.32	2.57%
OPIATE AGONISTS	51,957	$ 1,542,073.07	$ 29.68	6.59%
DIHYDROPYRIDINES	21,722	$ 1,389,878.98	$ 63.98	2.75%
INSULINS	12,337	$ 1,178,520.02	$ 95.53	1.56%
ANTIRETROVIRALS	2,131	$ 1,166,404.48	$ 547.35	0.27%
THIAZOLIDINEDIONES	7,919	$ 1,136,874.96	$ 143.56	1.00%
MONOCLONAL ANTIBODIES	892	$ 1,136,409.13	$ 1,274.00	0.11%
SYMPATHOMIMETIC (ADRENERGIC) AGENTS	19,973	$ 1,014,850.35	$ 50.81	2.53%
HEMOSTATICS	42	$ 945,965.03	$22,522.98	0.01%
ANGIOTENSIN II RECEPTOR ANTAGONISTS	14,765	$ 875,183.58	$ 59.27	1.87%
AMPHETAMINES	8,556	$ 835,602.61	$ 97.66	1.08%
TOTAL TOP 15	273,317	$ 28,030,983.67	$ 102.56	34.64%

Total Rx Claims From 11/01/05-11/30/05	788,968

Top 15 Therapeutic Classes
Based on Total Cost of Claims



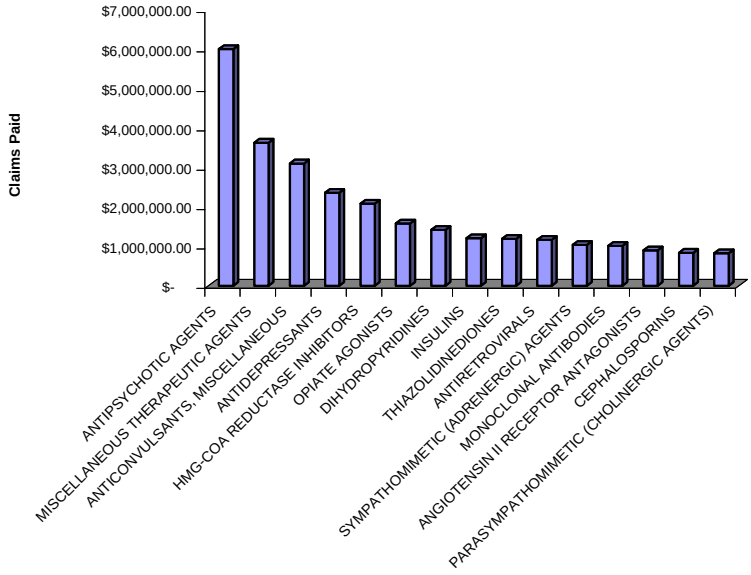
MISSISSIPPI MEDICAID
Cost Management Analysis
Dec-05

TOP 15 THERAPEUTIC CLASSES BY TOTAL COST OF CLAIMS FROM 12/01/05-12/31/05

AHFS Therapeutic Class	Rx	Paid	Paid/Rx	% Total Claims
ANTIPSYCHOTIC AGENTS	23,972	$ 6,003,338.90	$ 250.43	3.01%
MISCELLANEOUS THERAPEUTIC AGENTS	29,463	$ 3,631,423.88	$ 123.25	3.70%
ANTICONVULSANTS, MISCELLANEOUS	21,843	$ 3,100,634.36	$ 141.95	2.75%
ANTIDEPRESSANTS	39,223	$ 2,360,412.14	$ 60.18	4.93%
HMG-COA REDUCTASE INHIBITORS	20,889	$ 2,085,314.42	$ 99.83	2.63%
OPIATE AGONISTS	52,857	$ 1,579,243.89	$ 29.88	6.64%
DIHYDROPYRIDINES	22,098	$ 1,418,910.44	$ 64.21	2.78%
INSULINS	12,661	$ 1,208,408.76	$ 95.44	1.59%
THIAZOLIDINEDIONES	8,036	$ 1,190,011.32	$ 148.09	1.01%
ANTIRETROVIRALS	2,091	$ 1,165,092.15	$ 557.19	0.26%
SYMPATHOMIMETIC (ADRENERGIC) AGENTS	20,418	$ 1,034,747.98	$ 50.68	2.57%
MONOCLONAL ANTIBODIES	816	$ 1,012,935.33	$ 1,241.34	0.10%
ANGIOTENSIN II RECEPTOR ANTAGONISTS	15,179	$ 900,009.49	$ 59.29	1.91%
CEPHALOSPORINS	16,504	$ 839,457.78	$ 50.86	2.07%
PARASYMPATHOMIMETIC (CHOLINERGIC AGENTS	5,682	$ 823,114.10	$ 144.86	0.71%
TOTAL TOP 15	291,732	$ 28,353,054.94	$ 97.19	36.67%

Total Rx Claims From 12/01/05-12/31/05	795,456

Top 15 Therapeutic Classes
Based on Total Cost of Claims



Health Information
Designs, Inc.

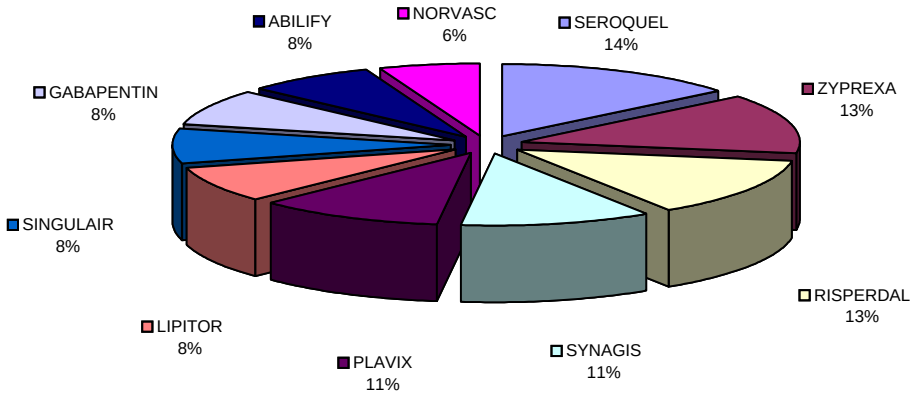
MISSISSIPPI MEDICAID
Cost Management Analysis
Nov-05

TOP 25 DRUGS BASED ON TOTAL CLAIMS COST FROM 11/01/05-11/30/05

Drug	AHFS Therapeutic Class	Rx	Paid	Paid/Rx
SEROQUEL	ANTIPSYCHOTIC AGENTS	6,004	$ 1,452,320.97	$ 241.89
ZYPREXA	ANTIPSYCHOTIC AGENTS	3,616	$ 1,355,722.35	$ 374.92
RISPERDAL	ANTIPSYCHOTIC AGENTS	5,486	$ 1,352,177.64	$ 246.48
SYNAGIS	MONOCLONAL ANTIBODIES	892	$ 1,136,409.13	$ 1,274.00
PLAVIX	MISCELLANEOUS THERAPEUTIC AGENTS	9,032	$ 1,114,472.70	$ 123.39
LIPITOR	HMG-COA REDUCTASE INHIBITORS	9,030	$ 811,139.15	$ 89.83
SINGULAIR	MISCELLANEOUS THERAPEUTIC AGENTS	8,798	$ 810,156.24	$ 92.08
GABAPENTIN	ANTICONVULSANTS, MISCELLANEOUS	7,212	$ 794,836.27	$ 110.21
ABILIFY	ANTIPSYCHOTIC AGENTS	2,108	$ 791,554.25	$ 375.50
NORVASC	DIHYDROPYRIDINES	10,145	$ 581,450.55	$ 57.31
ARICEPT	PARASYMPATHOMIMETIC (CHOLINERGIC AGENTS)	4,029	$ 574,294.00	$ 142.54
ZOLOFT	ANTIDEPRESSANTS	5,828	$ 573,207.99	$ 98.35
LOTREL	DIHYDROPYRIDINES	6,756	$ 564,892.85	$ 83.61
ADVAIR DISKUS	SYMPATHOMIMETIC (ADRENERGIC) AGENTS	3,429	$ 534,469.72	$ 155.87
ACTOS	THIAZOLIDINEDIONES	3,361	$ 531,466.91	$ 158.13
ZYRTEC	SECOND GENERATION ANTIHISTAMINES	10,292	$ 518,856.74	$ 50.41
TOPAMAX	ANTICONVULSANTS, MISCELLANEOUS	2,068	$ 517,450.13	$ 250.22
OMNICEF	CEPHALOSPORINS	6,072	$ 488,010.04	$ 80.37
ZOCOR	HMG-COA REDUCTASE INHIBITORS	3,309	$ 428,072.67	$ 129.37
PULMICORT	ADRENALS	2,051	$ 415,108.93	$ 202.39
FENTANYL	OPIATE AGONISTS	1,720	$ 406,256.69	$ 236.20
AVANDIA	THIAZOLIDINEDIONES	3,205	$ 405,051.75	$ 126.38
LEXAPRO	ANTIDEPRESSANTS	5,536	$ 404,814.26	$ 73.12
ZITHROMAX	MACROLIDES	9,098	$ 394,865.23	$ 43.40
COREG	BETA-ADRENERGIC BLOCKING AGENTS	3,916	$ 382,499.49	$ 97.68
TOTAL TOP 25		132,993	$ 17,339,556.65	$ 130.38

Total Rx Claims From 11/01/05-11/30/05	788,968

Top 10 Drugs
Based on Total Claims Cost



Health Information
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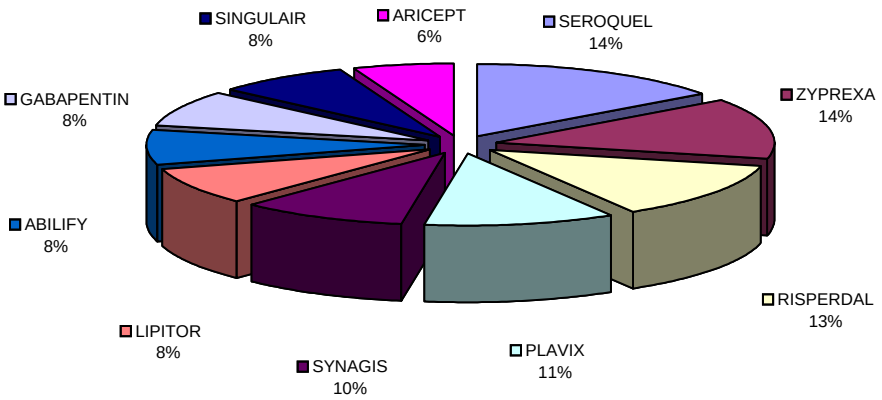
MISSISSIPPI MEDICAID
Cost Management Analysis
Dec-05

TOP 25 DRUGS BASED ON TOTAL CLAIMS COST FROM 12/01/05-12/31/05

Drug	AHFS Therapeutic Class	Rx	Paid	Paid/Rx
SEROQUEL	ANTIPSYCHOTIC AGENTS	6,217	$ 1,539,009.79	$ 247.55
ZYPREXA	ANTIPSYCHOTIC AGENTS	3,685	$ 1,399,610.72	$ 379.81
RISPERDAL	ANTIPSYCHOTIC AGENTS	5,382	$ 1,315,038.48	$ 244.34
PLAVIX	MISCELLANEOUS THERAPEUTIC AGENTS	9,313	$ 1,148,542.62	$ 123.33
SYNAGIS	MONOCLONAL ANTIBODIES	816	$ 1,012,935.33	$ 1,241.34
LIPITOR	HMG-COA REDUCTASE INHIBITORS	9,291	$ 837,145.00	$ 90.10
ABILIFY	ANTIPSYCHOTIC AGENTS	2,198	$ 821,131.54	$ 373.58
GABAPENTIN	ANTICONVULSANTS, MISCELLANEOUS	7,295	$ 811,663.20	$ 111.26
SINGULAIR	MISCELLANEOUS THERAPEUTIC AGENTS	8,735	$ 803,804.69	$ 92.02
ARICEPT	PARASYMPATHOMIMETIC (CHOLINERGIC AGENTS)	4,201	$ 604,269.11	$ 143.84
NORVASC	DIHYDROPYRIDINES	10,203	$ 585,609.59	$ 57.40
ZOLOFT	ANTIDEPRESSANTS	5,906	$ 582,162.18	$ 98.57
LOTREL	DIHYDROPYRIDINES	6,884	$ 574,527.36	$ 83.46
OMNICEF	CEPHALOSPORINS	6,883	$ 551,488.54	$ 80.12
ADVAIR DISKUS	SYMPATHOMIMETIC (ADRENERGIC) AGENTS	3,410	$ 549,556.73	$ 161.16
ACTOS	THIAZOLIDINEDIONES	3,414	$ 538,884.44	$ 157.85
TOPAMAX	ANTICONVULSANTS, MISCELLANEOUS	2,056	$ 519,338.17	$ 252.60
ZYRTEC	SECOND GENERATION ANTIHISTAMINES	9,919	$ 500,046.20	$ 50.41
AVANDIA	THIAZOLIDINEDIONES	3,483	$ 474,103.62	$ 136.12
ZOCOR	HMG-COA REDUCTASE INHIBITORS	3,419	$ 442,365.07	$ 129.38
PULMICORT	ADRENALS	2,131	$ 427,580.02	$ 200.65
FENTANYL	OPIATE AGONISTS	1,735	$ 424,626.94	$ 244.74
COREG	BETA-ADRENERGIC BLOCKING AGENTS	4,152	$ 420,338.88	$ 101.24
LEXAPRO	ANTIDEPRESSANTS	5,593	$ 409,947.37	$ 73.30
GEODON	ANTIPSYCHOTIC AGENTS	1,248	$ 370,671.27	$ 297.01
TOTAL TOP 25		127,569	$ 17,664,396.86	$ 138.47

Total Rx Claims From 12/01/05-12/31/05	795,456

Top 10 Drugs
Based on Total Claims Cost



Retrospective Drug Utilization Review Activities

October-December 2005

#541- Diabetes/Proteinuria/Negating ACEI & ARB

- 785 beneficiaries
- Waiting for responses and 120 days post intervention period

#1536- Diabetes/Hypertension/Cardiovascular Drugs (Negating)

- 1,780 beneficiaries identified by Initial Criteria Exception Report
- Waiting for responses and 120 days post intervention period

#1607-Certain Antihypertensive Agents/Post MI/Beta-blockers, ACEI and Aldosterone Antagonists

- 112 beneficiaries identified by Initial Criteria Exception Report
- Waiting for responses and 120 days post intervention period

#1608-Certain Antihypertensive Agents/Stroke/Thiazide diuretics & ACEI

- 325 beneficiaries identified by Initial Criteria Exception Report
- Waiting for responses and 120 days post intervention period

#1609-Certain Antihypertensive Agents/Chronic Kidney Disease/ACEI & ARB

- 3,285 beneficiaries identified by Initial Criteria Exception Report
- Waiting for responses and 120 days post intervention period

November 2005-January 2006

#2150-Narcotic (opioids)/Sickle cell anemia/absence of hydroxyurea use

- 220 beneficiaries identified by Initial Criteria Exception Report
- Waiting for responses and 120 days post intervention period

Childhood Onset of Type 2 Diabetes

The Problem

The United States is currently experiencing an epidemic of obesity among children and adolescents. Closely associated with this trend is a sharp increase in the number of children being diagnosed with type 2 diabetes. While types 2 diabetes was once termed "adult-onset" diabetes, this condition has become increasingly common among patients between the ages of 6 and 19 years. In fact, it is estimated that as many as 8 – 45% of new-onset childhood diabetes cases in the United States may be type 2.[i]

Children in the Mississippi Medicaid population are certainly not immune to this epidemic. The following chart shows the number of beneficiaries under the age of 21 with a diagnosis of diabetes. **Using the percentages above, it can be estimated that between 380 and 2,137 of children covered by Mississippi Medicaid have type 2 diabetes.**

Mississippi Medicaid Statistics	
Age Range (years)	**Diagnosis of DM**
0-10	1322
11-15	1234
16-20	2193
Total	**4749**

Two very important factors in the development of type 2 diabetes in children are puberty and obesity. The changes in hormone levels brought on by puberty can cause insulin resistance and decreased insulin action. Although type 2 cases in patients as young as 4 years have been reported, it most commonly occurs during mid-puberty.

Obesity plays a role because abundant adipose tissue contributes to insulin resistance. In addition, hyperinsulinemia is common in obese children and the pancreatic β-cells are unable to compensate for increased insulin resistance associated with puberty.

Treatment

While experience to date in dealing with the treatment of type 2 diabetes in children is limited, some general guidelines have been published to guide providers in the management of this disorder. The American Diabetes Association (ADA) issued a consensus statement on Type 2 Diabetes in Children and Adolescents.[ii] According to the ADA, at the time of diagnosis it can be very difficult to determine the correct classification of diabetes in children (type 1 versus type 2), due to the similarity of symptoms and findings.

As with adults, the general treatment goals for children with type 2 diabetes include blood glucose level control, A1C level control and prevention of complications. An appropriate treatment plan should include education, meal planning, physical activity and in most cases, medications.

Conclusions and recommendations

It is alarming to consider the possible ramifications of the rapid emergence of type 2 diabetes in childhood and adolescence in our state and country. This increase in incidence and earlier onset of the disease will create a significant long-term burden on the healthcare system and Mississippi Medicaid will likely bear a significant burden when this disease progresses to chronic complications.

The encouragement of appropriate, aggressive treatment of children with diabetes will benefit not only individual patients, but the healthcare system as a whole, specifically Mississippi Medicaid.

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[i] Copeland KC, Becker D, Gottschalk M, Hale D. Type 2 Diabetes in Children and Adolescents: Risk Factors, Diagnosis, and Treatment. *Clinical Diabetes*. 23:4, 181-185, 2005.

[ii] Consensus Statement: Type 2 Diabetes in Children and Adolescents. American Diabetes Association (ADA). *Diabetes Care*. March 2000.

Topical Corticosteroid Use in Children

Problem
The use of topical corticosteroid agents in children is a common and necessary mode of treatment for various dermatoses. Considering the risks and warnings associated with topical corticosteroid use and the resulting adverse effect potential, appropriate use of highly potent topical corticosteroids is very important.

As the labeling of the topical corticosteroids states, pediatric patients may demonstrate greater susceptibility to topical corticosteroid-induced hypothalamic-pituitary-adrenal (HPA) axis suppression and Cushing's syndrome than mature patients because of a larger skin surface area to body weight ratio. HPA axis suppression, Cushing's syndrome, and intracranial hypertension have been reported in pediatric patients receiving treatment with these agents. Manifestations of adrenal suppression in pediatric patients include linear growth retardation, delayed weight gain, low plasma cortisol levels, and absence of response to adrenocorticotrophic hormone (ACTH) stimulation. Manifestations of intracranial hypertension include bulging fontanelles, headaches, and bilateral papilledema.

Topical Immunomodulator agents (TIMs)
A discussion of topical corticosteroid agents would not be complete without mention of the TIMs, or topical calcineurin inhibitors. In the aftermath of recent labeling changes for Elidel® and Protopic®, prescribers may be choosing alternatives for some children who have been treated with these agents.

For reference, the black box warning for the TIMs is included here:

Warning

Long-term Safety of Topical Calcineurin Inhibitors Has Not Been Established

Although a causal relationship has not been established, rare cases of malignancy (e.g., skin and lymphoma) have been reported in patients treated with topical calcineurin inhibitors.

Therefore:

- Continuous long-term use of topical calcineurin inhibitors in any age group should be avoided, and application limited to areas of involvement with atopic dermatitis.
- Elidel®/Protopic® are not indicated for use in children less than two years of age.

In response to this labeling change, the American Academy of Dermatology released a statement of disagreement. The Academy states that the addition of a black box warning and medication guide was unwarranted and could limit access to these agents, or limit

treatment options if qualified patients decide not to use these medications based on fear of a malignancy risk.[i]

Scope

The intent of this review is to highlight the prescribing information associated with these agents and to explore possible approaches to encourage appropriate use of these agents in children.

Potency of topical corticosteroids has been classified by various organizations, resulting in several different rating systems. For purposes of this review, we have used the National Psoriasis Foundation Corticosteroid Potency Chart as a reference. This chart is included below for reference.[ii]

Method

In order to quantify the utilization of these agents in pediatric Medicaid recipients, pharmacy claims were analyzed to determine the frequency at which higher potency agents are prescribed in younger age groups.

Two age ranges were targeted for analysis: 1) under age two and 2) age two through 18.

Relative Potency of Corticosteroids

The following potency chart categorizes brand-name topical corticosteroid medications along with the name of the corresponding generic drug. The list positions these medications according to their potency. The list may not be comprehensive. [i]

BRAND NAME	GENERIC NAME
CLASS 1 - Superpotent	
Clobex Lotion, 0.05%	Clobetasol propionate
Cormax Cream/Solution, 0.05%	Clobetasol propionate
Diprolene Gel/Ointment, 0.05%	Betamethasone dipropionate
Olux Foam, 0.05%	Clobetasol propionate
Psorcon Ointment, 0.05%	Diflorasone diacetate
Temovate Cream/Ointment/Solution, 0.05%	Clobetasol propionate
Ultravate Cream/Ointment, 0.05%	Halobetasol propionate
CLASS 2 - Potent	
Cyclocort Ointment, 0.1%	Amcinonide
Diprolene Cream AF, 0.05%	Betamethasone dipropionate
Diprosone Ointment, 0.05%	Betamethasone dipropionate
Elocon Ointment, 0.1%	Mometasone furoate
Florone Ointment, 0.05%	Diflorasone diacetate
Halog Ointment/Cream, 0.1%	Halcinonide
Lidex Cream/Gel/Ointment, 0.05%	Fluocinonide
Maxiflor Ointment, 0.05%	Diflorasone diacetate
Maxivate Ointment, 0.05%	Betamethasone dipropionate

BRAND NAME	GENERIC NAME
Psorcon Cream 0.05%	Diflorasone diacetate
Topicort Cream/Ointment, 0.25%	Desoximetasone
Topicort Gel, 0.05%	Desoximetasone
CLASS 3 - Upper Mid-Strength	
Aristocort A Ointment, 0.1%	Triamcinolone acetonide
Cutivate Ointment, 0.005%	Fluticasone propionate
Cyclocort Cream/Lotion, 0.1%	Amcinonide
Diprosone Cream, 0.05%	Betamethasone dipropionate
Florone Cream, 0.05%	Diflorasone diacetate
Lidex-E Cream, 0.05%	Fluocinonide
Luxiq Foam, 0.12%	Betamethasone valerate
Maxiflor Cream, 0.05%	Diflorasone diacetate
Maxivate Cream/Lotion, 0.05%	Betamethasone dipropionate
Topicort Cream, 0.05%	Desoximetasone
Valisone Ointment, 0.1%	Betamethasone valerate
CLASS 4 - Mid-Strength	
Aristocort Cream, 0.1%	Triamcinolone acetonide
Cordran Ointment, 0.05%	Flurandrenolide
Derma-Smoothe/FS Oil, 0.01%	Fluocinolone acetonide
Elocon Cream, 0.1%	Mometasone furoate
Kenalog Cream/Ointment/Spray, 0.1%	Triamcinolone acetonide
Synalar Ointment, 0.025%	Fluocinolone acetonide
Uticort Gel, 0.025%	Betamethasone benzoate
Westcort Ointment, 0.2%	Hydrocortisone valerate
CLASS 5 - Lower Mid-Strength	
Cordran Cream/Lotion/Tape, 0.05%	Flurandrenolide
Cutivate Cream, 0.05%	Fluticasone propionate
DermAtop Cream, 0.1%	Prednicarbate
DesOwen Ointment, 0.05%	Desonide
Diprosone Lotion, 0.05%	Betamethasone dipropionate
Kenalog Lotion, 0.1%	Triamcinolone acetonide
Locoid Cream, 0.1%	Hydrocortisone butyrate
Pandel Cream 0.1%	Hydrocortisone probutate
Synalar Cream, 0.025%	Fluocinolone acetonide
Uticort Cream/Lotion, 0.025%	Betamethasone benzoate
Valisone Cream/Ointment, 0.1%	Betamethasone valerate
Westcort Cream, 0.2%	Hydrocortisone valerate

CLASS 6 - Mild	
Aclovate Cream/Ointment, 0.05%	Alclometasone dipropionate
DesOwen Cream, 0.05%	Desonide
Synalar Cream/Solution, 0.01%	Fluocinolone acetonide
Tridesilon Cream, 0.05%	Desonide
Valisone Lotion, 0.1%	Betamethasone valerate
CLASS 7 - Least Potent	
Topicals with hydrocortisone, dexamethasone, methylprednisolone and prednisolone	

This chart was developed as a general guide for patients and is not intended to be a source of medical information to be used by healthcare professionals.

Pediatric Prescribing Guidelines

Among the agents considered, there is some variability in terms of pediatric labeling. Generally, the superpotent agents are recommended in children over the age of two. Some of these agents are only recommended for use in children over age twelve and one agent, clobetasol propionate (Clobex® lotion, shampoo and spray) is recommended only for use in patients 18 and over. This labeling emphasizes the importance of appropriate use of these topical medications, especially in younger children.

Utilization Data

Pediatric utilization of potent and superpotent topical corticosteroids among Mississippi Medicaid recipients is presented in the following chart. This data reflects pharmacy claims for these agents among beneficiaries between the ages of 0 and 18 between July 1, 2005 and December 23, 2005.

		Age Range	
Generic Name	**Potency Category***	**<2 years**	**2-18 years**
Amcinonide	P	8	91
Betamethasone dipropionate	P/SP	27	258
Clobetasol propionate	SP	9	128
Clobetasol propionate/emollient	SP	1	3
Desoximetasone	P	100	575
Diflorasone diacetate	P/SP	3	48
Diflorasone diacetate/emollient	P/SP	0	7
Fluocinonide	P	32	311
Halcinonide	P	0	3
Halobetasol propionate	SP	2	28
TOTAL		182	1452

* P = Potent, SP = Superpotent

Results

The chart above indicates utilization of these agents in very young children. While this information does not include diagnosis or other patient-specific information, it does suggest an opportunity to encourage appropriate pediatric use of these agents.

Recommendation

Option 1: A broad retro-DUR criteria could be implemented based on an age limit determined by the DUR Board. With this approach, a criteria exception would occur for these products when prescribed for a child below this age limit, but would not be specific to the labeling of the specific agent. The following is an example of this approach.

Topical Corticosteroids/Potent and Superpotent

Alert Message: Higher potency topical corticosteroids are generally not recommended for use in children under the age of two. Some products have higher age limits, such as age 12 or 18 years. Because of higher ratio of skin surface area to body mass, pediatric patients are at a greater risk than adults of HPA axis suppression and Cushing syndrome when they are treated with topical corticosteroids. They are therefore also at greater risk of adrenal insufficiency during or after withdrawal of treatment. Adverse effects including striae have been reported with inappropriate use of topical corticosteroids in infants and children.

Option 2: A series of retro-DUR criteria focusing on age-appropriate use of specific agents could be developed. The prescriber would receive a letter highlighting the pediatric labeling for the particular product with the goal of positively impacting the prescriber's future use of the product. The following is an example of this approach.

Clobetasol propionate

Alert Message: Topical clobetasol propionate is not recommended for use in patients under the age of twelve. Safety and effectiveness in pediatric patients have not been established. Because of a higher ratio of skin surface area to body mass, pediatric patients are at a greater risk than adults of HPA axis suppression and Cushing syndrome when they are treated with topical corticosteroids. They are therefore also at greater risk of adrenal insufficiency during or after withdrawal of treatment. Adverse effects including striae have been reported with inappropriate use of topical corticosteroids in infants and children.

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[i] "American Academy of Dermatology Responds to FDA Decision on Eczema Medications". Press release dated January 19, 2006. American Academy of Dermatology. Schaumburg, IL. Accessed online.

[ii] Reprinted from Steroids. Portland, Ore.: National Psoriasis Foundation, 1998:6-7. Updated July 2004.

MISSISSIPPI MEDICAID
RETROSPECTIVE DRUG UTILIZATION REVIEW
CRITERIA RECOMMENDATIONS
FEBRUARY 2006

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

1. Tussionex / Overutilization _____ _____

Alert Message: Tussionex (hydrocodone/chlorpheniramine) may be over-utilized. Physical dependence and tolerance may develop upon repeated administration. In treating allergic rhinitis or common cold, it is vital to assess the patient regularly and systematically to ensure continued effectiveness of selected agent and the relative occurrence of side effects.
Conflict Code: ER – Overutilization (Duration)
Drugs/Disease:

Util A	Util B	Util C
Tussionex		

Day Supply: 15 days in 90 days

References:
Micromedex Healthcare Series, Drugdex Drug Evaluations, 2005.
Tussionex Prescribing Information, December 2002, Celltech Pharmaceuticals, Inc.

2. Long-Acting Beta Agonists / Therapeutic Appropriateness

_____ _____

Alert message: Even though long-acting beta-2 agonists (LABA) decrease the frequency of asthmatic episodes, these medications may make the episodes more severe when they do occur. LABAs should not be the first medicine used to treat asthma. They should be added to the asthma treatment plan only if other medications do not control asthma.
Conflict Code: TA - Therapeutic Appropriateness

Util A	Util B	Util C
Serevent Diskus		
Advair Diskus		
Foradil		

References:
MedWatch - The FDA Safety Information and Adverse Event Reporting Program, 2005.

3. Rosiglitazone / Therapeutic Appropriateness _____ _____

Alert Message: Post-marketing reports suggest that Avandia/Avandamet/Avandaryl (rosiglitazone-containing products) may cause new onset and worsening of diabetic macular edema. Concurrent peripheral edema may also occur in these patients. Macular edema resolved or improved, in some cases, following discontinuation of the drug or dose reduction.
Conflict Code: TA – Therapeutic Appropriateness
Drugs/Disease:

Util A	Util B	Util C
Rosiglitazone		

References:
MedWatch: The FDA Safety Information and Adverse Event Reporting Program, 2006.

Recommendations	*Approved*	*Rejected*

4. Avinza / Therapeutic Appropriateness _____ _____

Alert Message: Patients must not consume alcoholic beverages while on Avinza (morphine extended-release) therapy. Additionally, patients must not use prescription or non-prescription medications containing alcohol while on Avinza therapy. Consumption of alcohol while taking Avinza may result in the rapid release and absorption of a potentially fatal dose of morphine.
Conflict Code: TA – Therapeutic Appropriateness
Severity: Major (Black Box Warning)

Util A	Util B	Util C
Avinza	Alcoholism	
	Alcohol Abuse	
	Alcohol-containing Medications	

References:
MedWatch - The FDA Safety Information and Adverse Event Reporting Program, 2005.
Avinza Prescribing Information, Oct. 2005, Ligand Pharmaceuticals Inc.

5. Lindane / Therapeutic Appropriateness _____ _____

Alert Message: Lindane can be poisonous if not used properly. Seizures and death have been reported following use with repeat or prolonged application, but also in rare cases following a single application. The medication should only be used by patients who cannot tolerate or have failed first-line treatment with safer medications. Infants, children, the elderly, patients with other skin conditions and those who weigh less than 110 lbs (50 kg) may be at greater risk for serious neurotoxicity.
Conflict Code: TA - Therapeutic Appropriateness (Black Box Warning)
Drug/Disease:

Util A	Util B	Util C (Negating)
Lindane		Crotamiton
		Malathion
		Permethrin

References:
FDA Public Health Advisory: Safety of Topical Lindane Products for the Treatment of Scabies and Lice, FDA Center for Drug Evaluation and Research, March 28, 2003.
Lindane Shampoo Prescribing Information, April 2005, Alliant Pharmaceuticals.
Facts & Comparisons, 2005 Updates.

6. Beta Blockers / Therapeutic Appropriateness _____ _____

Alert Message: Non-selective beta-blockers should be used with caution in patients with diabetes. These agents may mask the signs and symptoms of hypoglycemia and delay recovery time. Beta blockade also reduces the release of insulin in response to hyperglycemia; it may be necessary to adjust the dose of antidiabetic drugs. Cardioselective beta-blockers are preferred due to the decreased risk of adverse effects on glucose regulation.
Conflict Code: TA - Therapeutic Appropriateness
Drug/Disease:

Util A	Util B	Util C
Propranolol	Diabetes (Drugs & ICD9s)	
Penbutolol		
Carteolol		
Pindolol		
Timolol		
Nadolol		

References:
Facts & Comparison, 2005 Updates.
Micromedex Healthcare Series, Drugdex Drug Evaluations, 2006.

Boxed Warning Update

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 or 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 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 use of the drug, shall be expressed as provided under the "Adverse Reactions" section of the labeling.

Ketek (telithromycin)

Audience: Infectious Disease, Hepatology and other healthcare professionals

[Posted 01/20/2006] Annals of Internal Medicine published an article reporting three patients who experienced serious liver toxicity following administration of Ketek (telithromycin). These cases were also reported to FDA MedWatch. Telithromycin is marketed and used extensively in many other countries, including countries in Europe and Japan. While it is difficult to determine the actual frequency of adverse events from voluntary reporting systems such as the MedWatch program, the FDA is continuing to evaluate the issue of liver problems in association with use of telithromycin in order to determine if labeling changes or other actions are warranted. As a part of this, FDA is continuing to work to understand better the frequency of liver-related adverse events reported for approved antibiotics, including telithromycin.

Elidel Cream (pimecrolimus)
Protopic Ointment (tacrolimus)

Audience: Dermatological and other healthcare professionals

[Posted 01/20/2006] The Food and Drug Administration announced the approval of updated labeling for two topical eczema drugs, Elidel Cream (pimecrolimus) and Protopic Ointment (tacrolimus). The labeling will be updated with a boxed warning about a possible risk of cancer and a Medication Guide (FDA-approved patient labeling) will be distributed to help ensure that patients using these

prescription medicines are aware of this concern. The new labeling also clarifies that these drugs are recommended for use as second-line treatments. This means that other prescription topical medicines should be tried first. Use of these drugs in children under 2 years of age is not recommended.

Clozaril (clozapine) tablets

Audience: Neuropsychiatric healthcare professionals and patients

[Posted 01/13/2006] Novartis and FDA notified healthcare professionals of revisions to the BOXED WARNING, WARNINGS, CONTRAINDICATIONS, PRECAUTIONS (Information for Patients and Pharmacokinetic-Related Interactions subsections), and ADVERSE REACTIONS (Postmarketing Clinical Experience subsection) sections of the prescribing information for Clozaril (clozapine) tablets. Recommendations from the FDA's Psychopharmacological Drugs Advisory Committee regarding the white blood cell monitoring schedule, required for all clozapine users, has resulted in modification in the monitoring schedule. Additional labeling changes address safety issues related to dementia-related psychosis, paralytic ileus, hypercholesterolemia and pharmacokinetic interaction with citalopram.

Avandia (rosiglitazone maleate)
Avandamet (rosiglitazone maleate/metformin HCl)

Audience: Endocrinologists, other healthcare professionals and patients

[Posted 01/05/2006] GlaxoSmithKline and FDA notified healthcare professionals about post-marketing reports of new onset and worsening diabetic macular edema for patients receiving rosiglitazone. In the majority of these cases, the patients also reported concurrent peripheral edema. In some cases, the macular edema resolved or improved following discontinuation of therapy and in one case, macular edema resolved after dose reduction.

Long-acting Beta2-Adrenergic Agonists:
Advair Diskus (fluticasone propionate & salmeterol inhalation powder)
Foradil Aerolizer (formoterol fumarate inhalation powder)
Serevent Diskus (salmeterol xinafoate inhalation powder)

Audience: Pulmonologists, other healthcare professionals and consumers

[Posted 11/18/2005] FDA notified manufacturers of Advair Diskus, Foradil Aerolizer, and Serevent Diskus to update their existing product labels with new warnings and a Medication Guide for patients to alert health care professionals and patients that these medicines may increase the chance of severe asthma episodes, and death when those episodes occur. All of these products contain long-acting beta2-adrenergic agonists (LABA). Even though LABAs decrease the frequency of asthma episodes, these medicines may make asthma episodes more severe when they occur. A Medication Guide with information about these risks will be given to patients when a prescription for a LABA is filled or refilled.

Paroxetine HCl - Paxil and generic paroxetine

Audience: Neuropsychiatric and other healthcare professionals
[Posted 12/08/2005] The FDA has determined that exposure to paroxetine in the first trimester of pregnancy may increase the risk for congenital malformations, particularly cardiac malformations. At the FDA's request, the manufacturer has changed paroxetine's pregnancy category from C to D and added new data and recommendations to the WARNINGS section of paroxetine's prescribing information. FDA is awaiting the final results of the recent studies and accruing additional data related to the use of paroxetine in pregnancy in order to better characterize the risk for congenital malformations associated with paroxetine.

Physicians who are caring for women receiving paroxetine should alert them to the potential risk to the fetus if they plan to become pregnant or are currently in their first trimester of pregnancy. Discontinuing paroxetine therapy should be considered for these patients. Women who are pregnant, or planning a pregnancy, and currently taking paroxetine should consult with their physician about whether to continue taking it. Women should not stop the drug without discussing the best way to do that with their physician.