Division of Medicaid
Office of the Governor
State of Mississippi
Drug Utilization Review (DUR) Board Meeting

MISSISSIPPI DIVISION OF
MEDICAID

November 9, 2017 at 2:00pm

Woolfolk Building, Room 145

Jackson, MS

Prepared by:

MS | DUR Evidence-Based DUR Initiative
The University of Mississippi School of Pharmacy

Drug Utilization Review Board

Allison Bell, PharmD
University of MS School of Pharmacy
2500 North State St.
Jackson, MS 39216
Term Expires: June 30, 2018

Rhonda Dunaway, RPh
Coastal Family Health Center
9113 Hwy 49 Suite 200
Gulfport 39503
Term Expires: June 30, 2020

Craig L. Escudé, MD **(Chair)**
Mississippi State Hospital
PO Box 97
Whitfield, MS 39193
Term Expires: June 30, 2019

Juanice Glaze, RPh
Wal-Mart Pharmacy
5901 U.S. Highway 49
Hattiesburg, MS 39402
Term Expires: June 30, 2019

Alice F. Messer, FNP-BC
Newsouth Neurospine
2470 Flowood Drive
Flowood, MS 39232
Term Expires: June 30, 2019

Ray Montalvo, MD
KDMC Specialty Clinic
940 Brookway Boulevard
Brookhaven, MS 39601
Term Expires: June 30, 2020

Holly R. Moore, PharmD
Anderson Regional Medical Center
2124 14th Street
Meridian, MS 39301
Term Expires: June 30, 2020

Janet Ricks, DO
UMMC, Family Medicine
2500 North State Street
Jackson, MS 39216
Term Expires: June 30, 2018

Sue H. Simmons, MD
Maben Medical Clinic
49 Turner St.
Maben, MS 39750
Term Expires: June 30, 2018

Dennis Smith, RPh
Polk's Discount Drugs
1031 Star Rd
Brandon, MS 39042
Term Expires: June 30, 2020

James Taylor, PharmD
North MS Medical Center
830 S. Gloster Street
Tupelo, MS 38801
Term Expires: June 30, 2019

Pearl Wales, PharmD
Be Jay PE Pharmacy 1668
West Peace Street
Canton, MS 39047
Term Expires: June 30, 2018

2018 Proposed DUR Board Meeting Dates

March 1, 2018
May 31, 2018
September 13, 2018
December 6, 2018

As with any analysis, great efforts are made to ensure that the information reported in this document is accurate. The most recent administrative claims data available are being used at the time the reports are generated, which includes the most recent adjudication history. As a result, values may vary between reporting periods and between DUR Board meetings, reflecting updated reversals and claims adjustments.

Unless otherwise indicated, all MS-DUR analyses are conducted for the entire Mississippi Medicaid program including beneficiaries receiving services through the Medicaid fee-for-service (FFS) and the two Mississippi Medicaid Coordinated Care Organizations (CCOs). When dollar figures are reported, the reported dollar figures represent reimbursement amounts paid to providers and are not representative of final Medicaid costs after rebates. Any reported enrollment data presented are unofficial and are only for general information purposes for the DUR Board.

Please refer to the Mississippi Division of Medicaid website for the current official Universal Preferred Drug List (PDL).

http://www.medicaid.ms.gov/providers/pharmacy/preferred-drug-list/

MISSISSIPPI DIVISION OF MEDICAID
OFFICE OF THE GOVERNOR
DRUG UTILIZATION REVIEW BOARD
AGENDA
November 9, 2017

DUR Board Meeting Minutes

MISSISSIPPI DIVISION OF MEDICAID
DRUG UTILIZATION REVIEW (DUR) BOARD
MINUTES OF THE APRIL 27, 2017 MEETING

DUR Board Members:	Aug 2015	Nov 2015	Jan 2016	Apr 2016	Jul 2016	Sep 2016	Feb 2017	April 2017
Allison Bell, PharmD	✓	✓	✓	✓		✓	✓	✓
Craig Escudé, MD						✓	✓	✓
Juanice Glaze, RPh						✓	✓	✓
Antoinette M. Hubble, MD	✓	✓	✓	✓	✓	✓	✓	✓
Cherise McIntosh, PharmD		✓		✓			✓	
Alice Messer, FNP-BC						✓	✓	✓
Janet Ricks, DO		✓	✓			✓	✓	✓
Sue Simmons, MD	✓		✓	✓		✓	✓	
Dennis Smith, RPh	✓	✓	✓	✓		✓		✓
James Taylor, PharmD						✓	✓	
Cynthia Undesser, MD	✓		✓	✓	✓			✓
Pearl Wales, PharmD (Chair)		✓	✓	✓	✓	✓	✓	✓
TOTAL PRESENT	**9**	**10**	**10**	**11**	**3***	**10**	**10**	**9**

**Only eight members were active due to new appointments to DUR Board not being approved by Governor prior to meeting.*

Dr. Ricks arrived during the presentation on the CPC program and was not present for the votes on the prior minutes or the DUR Board by-laws.

Also Present:

Division of Medicaid (DOM) Staff:
Terri Kirby, RPh, CPM, Pharmacy Director; Cindy Noble, PharmD, MPH, DUR Coordinator; Gail McCorkle, RPh, Clinical Pharmacist; Chris Yount, MA, PMP, Staff Officer - Pharmacy; Sue Reno, DOM Program Integrity

MS-DUR Staff:
Ben Banahan, PhD, MS-DUR Project Director; Eric Pittman, PharmD, MS-DUR Clinical Director

Conduent Staff:
Lew Anne Snow, RN BSN, Pharmacy Services Sr. Analyst, Mississippi Medicaid Project; Leslie Leon, PharmD, Clinical Pharmacist, Mississippi Medicaid Project

Change Healthcare Staff:
Chad Bissell, PharmD, MS Account Manager; Laureen Biczak, DO, Medical Director; Shannon Hardwick, RPh, CPC Pharmacist; Paige Clayton, PharmD, On-Site Clinical Pharmacist

Coordinated Care Organization (CCO) Staff:
Heather Odem, PharmD, Director of Pharmacy-Mississippi, United Healthcare Community & State; Conor Smith, RPh, Director of Pharmacy, Magnolia Health; Mike Todaro, PharmD, Vice President, Pharmacy Operations, Magnolia Health

Visitors:
Judy Clark, Consultant; Phil Hecht, Abbvie; Jason Swartz, Otsuka; Kim Clark, ViiV; Steve Curry, ALK; Jason Schwier, Amgen

Call to Order:
Dr. Wales called the meeting to order at 2:01 pm.

Dr. Banahan introduced Dr. Eric Pittman, Clinical Director MS-DUR. Ms. Kirby introduced Chris Yount, DOM Staff Officer-Pharmacy, and other special attendees in the audience. Ms. Kirby thanked board members rotating off for their service.

Old Business:
Dr. Escude' moved that the minutes of the February 2, 2017 DUR Board Meeting be approved; seconded by Dr. Hubble. The motion was approved unanimously by the DUR Board.

Dr. Wales informed board members they were each provided a conflict of interest statement that needed to be signed and returned by the end of the meeting.

Dr. Noble provided background on the updated DUR by-laws which had been mailed to the Board Members prior to the meeting. Motion for approval of the updated by-laws was made by Dr. Hubble; seconded by Dr. Undesser. The revised by-laws were approved unanimously by the DUR Board.

Pharmacy Program Update:
Ms. Kirby informed the board that new reimbursement methodology has been submitted to CMS for approval. Once approved, CMS requires that DOM process FFS program reimbursement adjustments retroactively to April 1. The CCOs have the option to not make adjustments as long as their reimbursed amounts meet the contract requirement of being not less than the FFS amounts. The FFS adjustments will be completed over time retroactive to April 1, 2017 rather than all at once.

Overview of Complex Pharmaceutical Care Program:
Dr. Biczak presented a general overview of the Complex Pharmaceutical Care (CPC) program provided by Change Healthcare. Ms. Hardwick presented information related to the Mississippi program. She described how patients are identified for the program and provided examples of cases that have been addressed by the CPC program during the first few months. Dr. Wales asked if the CCOs had similar programs. Representatives from both UHC and Magnolia indicated they had similar programs utilizing nurses and pharmacists that do case management for selected disease states.

Resource Utilization Review:
Dr. Banahan informed the board that the CCO encounter data appears to be complete for this report. He noted that enrollment has remained fairly consistent during the last six months. It was noted that a slight increase in the average cost per prescription and beneficiary occurred across all programs due to utilization of some expensive new therapies. Dr. Banahan stated the top drug categories have been consistent with respect to claim volume and amount paid with the exception of the neuraminadase

inhibitors, such as Tamiflu, which have increased sharply due to influenza season. No other significant trends or changes were noted.

Feedback and Discussion from the Board
Dr. Escude' brought up the topic of individuals with intellectual and developmental disabilities (IDD) and the use of multiple antipsychotics. He would like MS-DUR to look into this trend and the appropriateness of antipsychotic use to the degree that it can be determined from claims data. Dr. Escude' particularly was interested in verifying that appropriate medical work up is being done before these medications are prescribed to rule out any underlying medical issues. A follow-up conference call with interested board members was recommended.

N**EW BUSINESS**

Research Reports:

Unique Hepatitis C Treatment Regimens Used Since 2015 in Mississippi Medicaid
MS-DUR presented an analysis showing the utilization of Hepatitis C treatment regimens in Mississippi Medicaid from January 1, 2015 through February 28, 2017. Trends identified were consistent across FFS and the CCOs. There was a sharp increase in the number of beneficiaries starting treatment in the first three quarters of 2015, when the new therapies were released. Since that time the numbers have leveled out to approximately 50 -60 new prescription starts per quarter. The number of individuals who initiated treatment but did not complete the therapy regimen was noted. This is an area where the CPC program should impact and improve therapy completion rates in the FFS individuals.

Celexa® (Citalopram) Utilization and Dosing Management
Dr. Banahan summarized a MS-DUR analysis of citalopram utilization and dosing management. Since 2007, the FDA has made several safety updates regarding antidepressants as a whole and citalopram individually. Currently the MS Medicaid Universal Preferred Drug List (UPDL) has a minimum age limit of 9 years for citalopram and no dosage limits. Based on current FDA labeling, the following changes were proposed by MS-DUR:

1. Limit total daily dose of citalopram to a maximum of 40 mg/day for beneficiaries < 60 years.
2. Limit total daily dose of citalopram to a maximum of 20 mg/day for beneficiaries $\geq$ 60 years.
3. Change citalopram minimum age limit from 9 years to 18 years to be consistent with FDA boxed warning on suicidality and antidepressant drugs found in citalopram's drug label information. (Class).
4. MS-DUR would conduct a one-time educational mailing outlining the proposed changes to include all prescribers writing citalopram prescriptions during the last year that were for (a) children and adolescents <18 years of age, (b) adults age $\geq$ 60 with daily doses > 20 mg, or (c) adults < 60 years of age with daily doses exceeding 40mg.

After discussion, a motion was made by Dr. Undesser and seconded by Mr. Smith to accept items 1 and 2 as proposed. The motion was approved unanimously by roll call vote with no abstentions.

A motion was made by Dr. Undesser and seconded by Mr. Smith to accept item 3 with the addition that ***current individuals would be grandfathered and this proposed clinical edit would apply to new starts only***. The motion was approved unanimously by roll call vote with no abstentions.

A motion was made by Dr. Escude' and seconded by Dr. Undesser to accept item 4 ***with the notification of the grandfathered clause included***. The motion was approved unanimously by roll call vote with no abstentions.

Type 2 Diabetes (T2DM) Treatment Patterns in Mississippi Medicaid

Dr. Banahan reviewed a MS-DUR analysis for DOM's beneficiaries with T2DM regarding diabetes treatment patterns. MS-DUR's analysis depicted T2DM medication regimens across the FFS and CCOs. The 2017 American Diabetes Association's (ADA's) "Standards of Medical Care in Diabetes" antihyperglycemic therapy in T2DM general recommendations was also reviewed and contrasted with the American Association of Clinical Endocrinologist/ American College of Endocrinology)AACE/ACE) 2017 glycemic control algorithm. The study examined prescribing patterns in Mississippi Medicaid for 2016. The goal was to analyze these patterns and determine if any changes should be made to the align Mississippi Medicaid with the 2017 ADA standards. The following recommendations were presented by MS-DUR based on the analysis:

1. DOM should implement an electronic edit to require manual prior authorization (PA) for concomitant use of GLP-1 and DPP-4.
2. DOM should implement an electronic edit to require manual PA for addition of fourth concurrent antihyperglycemic agents.
3. DOM should investigate regimens that do not include metformin.
4. DOM should investigate further T2DM treatment with only a sulfonylurea agent.
5. MS-DUR should conduct a one-time educational mailing highlighting the new ADA guidelines directed to prescribers who have had patients in the last year with regimens that were not consistent with the ADA Standards of Care recommendations.
6. MS-DUR should explore collaboration with the Mississippi Diabetes Coalition for educational initiatives.

After discussion, Dr. Escude' made a motion, seconded by Dr. Ricks, to accept item 1 as presented, accept item 2 with the amendment to read ***fourth concurrent noninsulin agent***, and accept items 4 – 6 as presented. The motion was approved unanimously by roll call vote with no abstentions. The Board noted that further investigation of item 3 was not needed and that any issues related to item 3 could be addressed by the educational mailing.

FDA Drug Safety Information Updates January – March 2017

Dr. Banahan presented a summary of FDA drug safety updates for the first quarter of 2017.

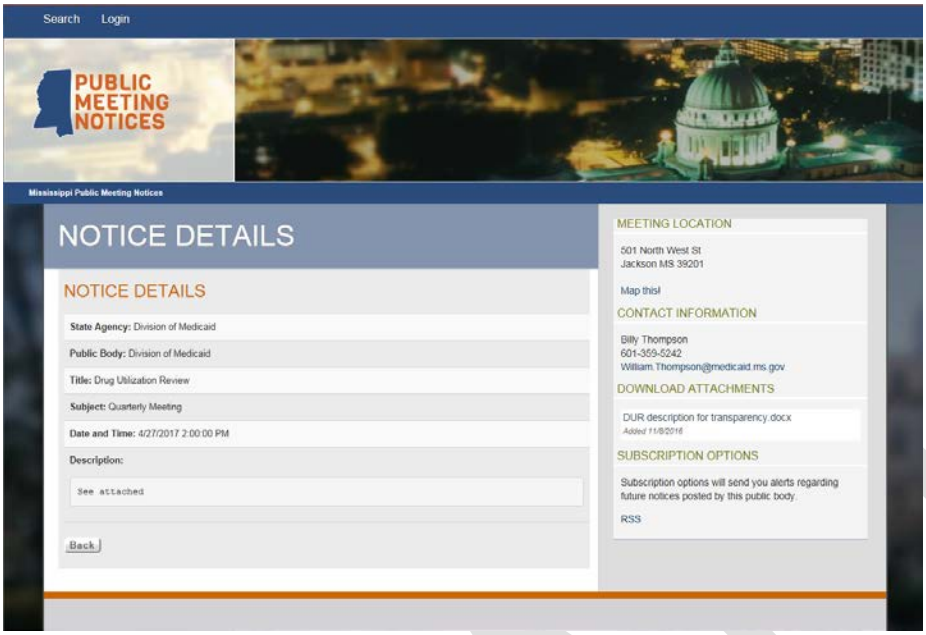
Next Meeting Information:

Dr. Wales announced that the next meeting of the DUR Board will take place on July 27, 2017 at 2:00 p.m. Dr. Wales thanked everyone for their attendance and participation at the April DUR Board meeting. The meeting adjourned at 4:19 pm.

Submitted,

Eric Pittman, PharmD
Evidence-Based DUR Initiative, MS-DUR

PUBLIC MEETING NOTICES



MISSISSIPPI DIVISION OF MEDICAID
DRUG UTILIZATION REVIEW (DUR) BOARD
MINUTES OF THE JULY 27, 2017 MEETING

DUR Board Members:	Nov 2015	Jan 2016	Apr 2016	Jul 2016	Sep 2016	Feb 2017	April 2017	July 2017
Allison Bell, PharmD	✓	✓	✓		✓	✓	✓	✓
Craig Escudé, MD					✓	✓	✓	✓
Juanice Glaze, RPh					✓	✓	✓	
Alice Messer, FNP-BC					✓	✓	✓	✓
Janet Ricks, DO	✓	✓			✓	✓	✓	
Sue Simmons, MD		✓	✓		✓	✓		
James Taylor, PharmD					✓	✓		
Pearl Wales, PharmD (Chair)	✓	✓	✓	✓	✓	✓	✓	✓
TOTAL PRESENT	**10**	**10**	**11**	**3***	**10**	**10**	**9**	**4***

**Only eight members were active due to new appointments to DUR Board not being approved by Governor prior to meeting.*

Also Present:

Division of Medicaid (DOM) Staff:
Terri Kirby, RPh, CPM, Pharmacy Director; Cindy Noble, PharmD, MPH, DUR Coordinator; Gail McCorkle, RPh, Clinical Pharmacist; Chris Yount, MA, PMP, Staff Officer - Pharmacy; Sue Reno, DOM Program Integrity; Andrea McNeal, DOM Program Integrity

MS-DUR Staff:
Ben Banahan, PhD, MS-DUR Project Director; Eric Pittman, PharmD, MS-DUR Clinical Director; Siddhi Korgaonkar, University of Mississippi graduate student, MS-DUR Analyst; Nilesh Gangan, University of Mississippi graduate student, MS-DUR Analyst

Conduent Staff:
Lew Anne Snow, RN BSN, Pharmacy Services Sr. Analyst, Mississippi Medicaid Project; Leslie Leon, PharmD, Clinical Pharmacist, Mississippi Medicaid Project

Change Healthcare Staff:
Shannon Hardwick, RPh, CPC Pharmacist; Paige Clayton, PharmD, On-Site Clinical Pharmacist

Coordinated Care Organization Staff:
Heather Odem, United Healthcare; Conor Smith, RPh, Director of Pharmacy, Magnolia Health; Mike Todaro, PharmD, Vice President, Pharmacy Operations, Magnolia Health

Visitors:
Ray Montalvo, MD; Phil Hecht, Abbvie; Jason Swartz, Otsuka; Steve Curry, ALK; John Kirby, Sanofi; Evelyn Johnson, Capital Resources; Bruce Wallace, Silvergate Pharmaceuticals; Bill Rampy, Silvergate Pharmaceuticals; Joey Sturgeon, Silvergate Pharmaceuticals; Quynhchan Doan, Abbvie

Call to Order:
Dr. Wales called the meeting to order at 2:05pm. Due to a delay in new appointments being made by the Governor's Office, there were only eight active DUR Board members for the meeting. With only four members present, there was not a quorum and no official business could be conducted.

Ms. Kirby introduced Chris Yount, DOM Staff Officer-Pharmacy, and other special attendees in the audience. Ms. Kirby thanked board members rotating off for their service.

Dr. Banahan introduced the University of Mississippi graduate students in attendance who work as analysts with MS-DUR.

Old Business:
Dr. Banahan asked if anyone had corrections for the draft minutes from the April 27, 2017 Board Meeting. Dr. Bell noted that the minutes refer to item 4 in the recommendations of the Celexa report and there is no item 4 listed. Dr. Pittman pointed out item 4 had been inadvertently combined with item 3 in the minutes and this issue will be corrected

Pharmacy Program Update:
Ms. Kirby informed the Board that new reimbursement methodology has been approved by CMS. Drug schedules will be broken into different categories with different reimbursement methodologies and dispensing fees associated with each. Ms. Kirby gave a brief explanation of each category to the Board. Implementation dates will be posted on Medicaid's website. Claims with a date of service of April 1, 2017 and forward will have to be reprocessed. Medicaid will collaborate with Magnolia Health and United Healthcare to make these adjustments. Adjustments will be processed over time to minimize financial impact on pharmacies. The 340B providers who use point of sale (POS) or pharmacy claims will also be impacted. This will not impact 340B claims on the medical side.

Dr. Noble informed the board that several DOM representatives attended the recent "Opioid and Heroin Mississippi Drug Summit." The actions the DUR Board recommended in the past year regarding opioids are in line with CDC recommendations and are being implemented by DOM. Medicaid will be purchasing necessary software required to integrate morphine milligram equivalent dosing into the POS system and is making significant progress toward implementation. Ms. Messer commented that she has noted a significant change in her practice regarding opioid use. Patients are much more open to discussions regarding reducing doses and titrating off opioids. Ms. Kirby noted that at a recent meeting she attended with other state Medicaid pharmacy directors that one state had changed their provider agreement to restrict pharmacy providers from splitting opioids between paid claims and cash. Board members discussed the complexity of defining and implementing opioid prescribing restrictions.

Resource Utilization Review:
Dr. Pittman informed the board that encounter data from the coordinated care plans appears to be complete for the report included in this DUR packet. He noted that cost per beneficiary and per prescription filled have remained consistent over the past six months. The top categories, by number of claims and dollars paid, has remained consistent as well.

Feedback and Discussion from the Board
Dr. Wales asked if there was any additional information about alternative sleep aids in reference to the clinical edit suggested for temazepam to be in alignment with that of the triazolam edits, that Dr. Noble

stated was in place. Dr. Wales asked for follow-up on alternatives. Dr. Pittman will research current alternatives and provide a report.

Ms. Messer inquired about gabapentin and its abuse potential. MS-DUR will undertake an analysis reviewing gabapentin use and dosages, and concomitant use with opioids and benzodiazepines.

Dr. Escude' mentioned a new gout medication and asked if this was something DOM should be watching.

Dr. Escude' suggested that an orientation booklet be developed to explain common acronyms and terms for new members. Committee members expressed agreement with his suggestion.

NEW BUSINESS

Research Reports:

Use of Antipsychotics in Beneficiaries with Intellectual and Developmental Disabilities

Dr. Escude' requested at the April DUR Board meeting that MS-DUR investigate the use of antipsychotics in individuals with intellectual and developmental disabilities (IDD). Studies have shown that antipsychotics may be inappropriately used in this population to treat behaviors that may be masking underlying physical issues that are undetected. The MS-DUR analysis showed approximately 23% of individuals with IDD in MS Medicaid received an antipsychotic from January 2016 through June 2017. Of those 23%, approximately one-third had a psychiatric diagnosis. Another one-third had an IDD diagnosis of pervasive developmental disorder (PDD) which encompasses autistic spectrum disorder. Several antipsychotics have indications for use in autistic spectrum disorder. The remaining one-third of IDD patients prescribed an antipsychotic did not have a primary indication for use that could be identified. These patterns were consistent across all the pharmacy programs. The provider types prescribing antipsychotics in the IDD population were broken down. It was noted that although the statistics found in Mississippi appear better than national trends, there is still area for education to be done.

MS-DUR recommended an educational intervention be developed for providers initiating antipsychotic therapy in IDD patients without a primary psychiatric diagnosis. Dr. Escude' will work with MS-DUR to develop these educational materials. Dr. Noble noted it will take some time to develop the educational materials, and MS-DUR may be able to share these materials with the Board at the November meeting.

Use of Codeine and Tramadol

Dr. Pittman summarized the FDA safety notice that came out in April 2017 regarding codeine and tramadol use in children. Based on this safety alert, MS-DUR examined the utilization of these products for the DOM 2016 calendar year. Dr. Pittman summarized the findings in reference to the recent FDA safety alerts. Dr. Pittman also noted that in 2013, the FDA sent out a safety alert contraindicating the use of codeine to treat pain after tonsillectomy or adenoidectomy in children less than 18 years of age. It was also noted that currently there are no age restrictions for codeine or tramadol products in the MS Medicaid Universal Preferred Drug List (UPDL).

MS-DUR made several recommendations based on the FDA alerts and results from the analysis conducted. Several board members questioned what alternative treatments could be recommended.

Dr. Pittman referenced a recent article in Pediatrics[1] discussing therapeutic alternatives to codeine use in children. Dr. Bell suggested that if use is restricted, providers should be given information about recommended alternatives. Dr. Escude' expressed concern about the FDA issuing a contraindication and DOM not taking action to restrict use. Discussion was held pertaining to DOM's responsibility to restrict access and potential liability with respect to FDA contraindications. Dr. Escude' suggested DOM explore legal counsel regarding this topic. Dr. Bell suggested MS-DUR look at all of the opioids with respect to use by age and need for age restrictions.

Cytokine and CAM Antagonist Utilization

Dr. Banahan reviewed a MS-DUR study on cytokine and CAM antagonist utilization in MS Medicaid. This group represents one of the top drug classes by dollars paid with that amount approximately doubling in MS Medicaid over the past year. Heather Odem with UHC reported that Louisiana Medicaid determined approximately 30% of UHC Community and State claims were being rejected because of not following recommended step care therapy, provider type or lack of an appropriate diagnosis. MS-DUR recommended implementing an electronic PA edit to add a diagnosis check for the utilization of all medications in the cytokine and CAM antagonist class. Dr. Escude' suggested MS-DUR look at provider types and whether patients had seen a specialist in situations when a primary care physician (PCP) was prescribing.

FDA Drug Safety Information Updates January – March 2017

Dr. Pittman presented a summary of FDA drug safety updates for the second quarter of 2017.

Next Meeting Information:

Dr. Wales announced that the next meeting of the DUR Board will take place on November 9, 2017 at 2:00 p.m. Dr. Wales thanked everyone for their attendance and participation at the April DUR Board meeting. The meeting adjourned at 3:16 pm.

Submitted,

Eric Pittman, PharmD
Evidence-Based DUR Initiative, MS-DUR

[1] Tobias JD, Green TP, Cote CJ; Section on Anesthesiology and Pain Medicine, Committee on Drugs. Codeine: Time to Say "No." Pediatrics 2016 Sept;

PUBLIC MEETING NOTICES

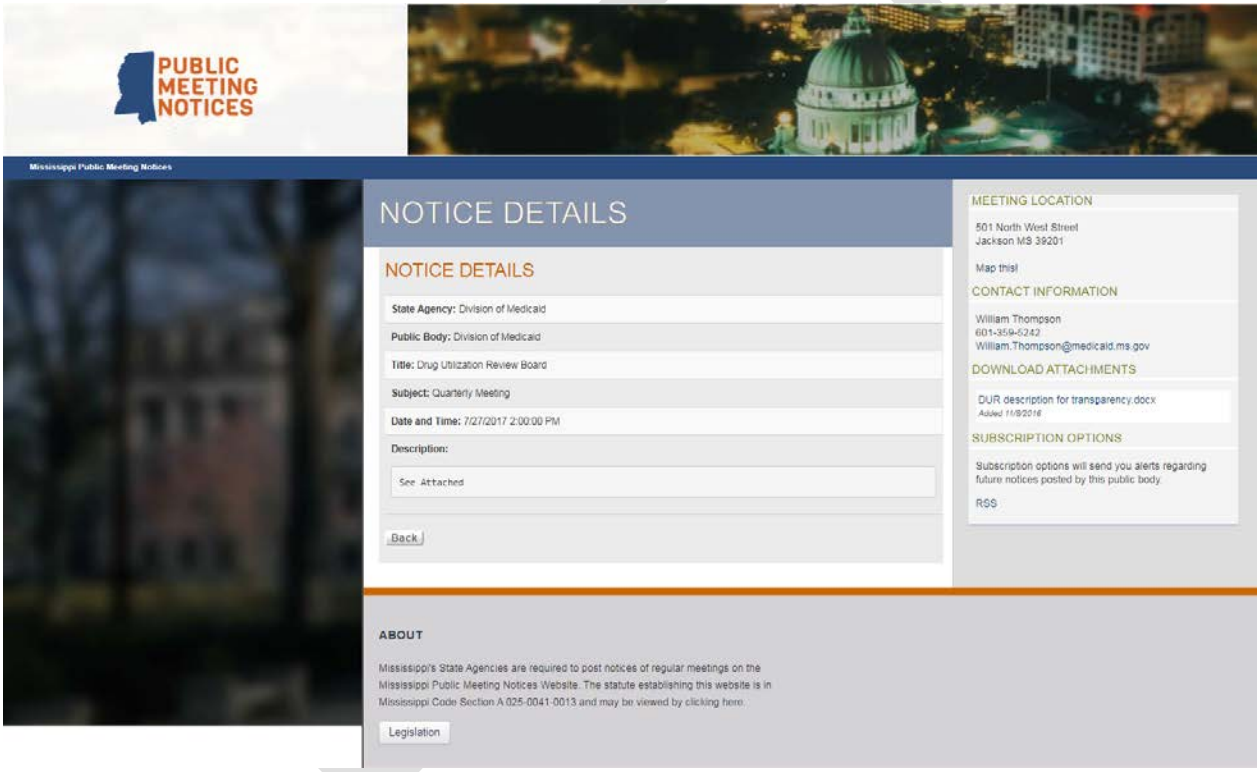
Drug Utilization Board (DUR) Meetings
Mississippi Division of Medicaid

Description: The Mississippi Division of Medicaid's Drug Utilization Review (DUR) Board is a quality assurance body which seeks to assure appropriate drug therapy to include optimal beneficiary outcomes and appropriate education for physicians, pharmacists, and the beneficiary. The Drug Utilization Review (DUR) Board is composed of twelve participating physicians and pharmacists who are active MS Medicaid providers and in good standing with their representative organizations.

The Board reviews utilization of drug therapy and evaluates the long-term success of the treatments.

The Drug Utilization Review (DUR) Board meets quarterly.

DUR website can be located at http://www.medicaid.ms.gov/DUR.aspx.



Resource Utilizaton Review

TABLE A: ENROLLMENT STATISTICS FOR LAST 6 MONTHS March 1, 2017 through August 31, 2017							
			Mar-17	Apr-17	May-17	Jun-17	Jul-17	Aug-17
Total enrollment			740,709	739,713	739,360	737,727	734,700	731,505
Dual-eligibles			156,234	155,894	155,802	155,608	155,271	154,896
Pharmacy benefits			632,252	630,307	629,522	627,796	625,029	621,644
	LTC		17,352	17,273	17,283	17,209	17,147	17,008
	PLAN %	FFS	22.8%	22.7%	22.6%	22.2%	22.2%	22.2%
		MSCAN-UHC	37.5%	37.5%	37.6%	37.7%	37.7%	37.7%
		MSCAN-Magnolia	39.7%	39.8%	39.8%	40.1%	40.1%	40.1%

TABLE B: PHARMACY UTILIZATION STATISTICS FOR LAST 6 MONTHS March 1, 2017 through August 31, 2017							
		Mar-17	Apr-17	May-17	Jun-17	Jul-17	Aug-17
# Rx Fills	FFS	113,893	102,083	104,464	97,507	93,209	105,300
	MSCAN-UHC	205,672	187,050	189,370	168,614	163,124	165,155
	MSCAN-Mag	249,942	228,775	229,239	210,217	202,977	239,460
# Rx Fills / Bene	FFS	0.8	0.7	0.7	0.7	0.7	0.8
	MSCAN-UHC	0.9	0.8	0.8	0.7	0.7	0.7
	MSCAN-Mag	1.0	0.9	0.9	0.8	0.8	1.0
$ Paid Rx	FFS	$14,049,415	$12,815,689	$13,403,184	$14,348,727	$12,585,608	$14,769,666
	MSCAN-UHC	$17,297,025	$15,485,619	$15,838,261	$14,730,747	$14,708,681	$12,627,288
	MSCAN-Mag	$20,152,346	$18,621,197	$18,895,088	$17,555,155	$16,592,438	$17,283,493
$ /Rx Fill	FFS	$123.36	$125.54	$128.30	$147.16	$135.03	$140.26
	MSCAN-UHC	$84.10	$82.79	$83.64	$87.36	$90.17	$76.46
	MSCAN-Mag	$80.63	$81.40	$82.43	$83.51	$81.75	$72.18
$ /Bene	FFS	$97.46	$89.57	$94.21	$102.95	$90.70	$107.02
	MSCAN-UHC	$72.95	$65.52	$66.91	$62.24	$62.42	$53.88
	MSCAN-Mag	$80.29	$74.23	$75.41	$69.73	$66.20	$69.33

NOTE: Paid amounts represent amount reported on claims as paid to the pharmacy. These amounts do not reflect final actual costs after rebates, etc.

TABLE C: TOP 10 DRUG CATEGORIES BY NUMBER OF CLAIMS IN AUG 2017 (FFS AND CCOs)

Category	Month Year	Rank Volume	# RXs	$ Paid	# Unique Benes
CNS stimulants	Aug 2017	1	26,012	$5,732,748	22,642
	Jul 2017	2	21,667	$5,024,703	18,856
	Jun 2017	2	21,967	$5,023,835	18,795
narcotic analgesic combinations	Aug 2017	2	21,635	$575,081	19,760
	Jul 2017	1	21,980	$570,797	20,247
	Jun 2017	1	23,535	$619,959	21,479
adrenergic bronchodilators	Aug 2017	3	17,322	$1,496,269	14,684
	Jul 2017	4	12,598	$1,141,156	10,950
	Jun 2017	5	12,826	$1,065,096	11,202
aminopenicillins	Aug 2017	4	16,056	$170,146	15,751
	Jul 2017	9	10,875	$105,032	10,660
	Jun 2017	7	12,048	$116,392	11,829
nonsteroidal anti-inflammatory agents	Aug 2017	5	15,668	$198,647	15,014
	Jul 2017	3	13,881	$168,724	13,303
	Jun 2017	3	14,040	$172,916	13,464
antihistamines	Aug 2017	6	15,240	$254,186	14,767
	Jul 2017	5	12,196	$268,113	11,819
	Jun 2017	4	13,187	$297,710	12,736
glucocorticoids	Aug 2017	7	12,159	$709,794	11,535
	Jul 2017	14	9,153	$609,888	8,715
	Jun 2017	12	9,974	$637,130	9,512
leukotriene modifiers	Aug 2017	8	12,034	$196,476	11,818
	Jul 2017	11	10,277	$145,583	10,079
	Jun 2017	11	10,518	$170,746	10,305
atypical antipsychotics	Aug 2017	9	11,832	$1,468,136	10,475
	Jul 2017	7	11,482	$1,849,838	10,279
	Jun 2017	9	11,845	$1,965,195	10,440
contraceptives	Aug 2017	10	11,830	$550,984	11,274
	Jul 2017	6	11,883	$551,089	11,207
	Jun 2017	6	12,369	$573,773	11,629

NOTE: Pharmacy encounter data for UHC is incomplete for August 2017. This should not affect ranks but does affect total amounts for paid, number of claims, and number of beneficiaries in August.

TABLE D: TOP 10 DRUG CATEGORIES BY DOLLARS PAID IN AUG 2017 (FFS AND CCOs)

Category	Month Year	Rank Paid Amt	# RXs	$ Paid	# Unique Benes
CNS stimulants	Aug 2017	1	26,012	$5,732,748	22,642
	Jul 2017	1	21,667	$5,024,703	18,856
	Jun 2017	1	21,967	$5,023,835	18,795
factor for bleeding disorders	Aug 2017	2	125	$3,472,487	88
	Jul 2017	4	107	$2,383,265	84
	Jun 2017	3	108	$2,984,191	82
antiviral combinations	Aug 2017	3	751	$2,663,303	713
	Jul 2017	2	773	$2,704,978	738
	Jun 2017	2	838	$3,526,852	770
insulin	Aug 2017	4	4,743	$2,438,542	3,571
	Jul 2017	3	4,835	$2,645,302	3,606
	Jun 2017	4	4,911	$2,708,491	3,667
adrenergic bronchodilators	Aug 2017	5	17,322	$1,496,269	14,684
	Jul 2017	6	12,598	$1,141,156	10,950
	Jun 2017	7	12,826	$1,065,096	11,202
atypical antipsychotics	Aug 2017	6	11,832	$1,468,136	10,475
	Jul 2017	5	11,482	$1,849,838	10,279
	Jun 2017	5	11,845	$1,965,195	10,440
bronchodilator combinations	Aug 2017	7	3,288	$985,076	3,042
	Jul 2017	7	3,206	$1,044,496	3,007
	Jun 2017	6	3,299	$1,067,327	3,061
antirheumatics	Aug 2017	8	619	$927,681	581
	Jul 2017	9	613	$973,203	583
	Jun 2017	9	598	$948,285	579
gamma-aminobutyric acid analogs	Aug 2017	9	8,796	$895,436	8,301
	Jul 2017	8	8,776	$991,535	8,222
	Jun 2017	8	8,995	$1,035,650	8,409
chelating agents	Aug 2017	10	90	$825,552	80
	Jul 2017	10	94	$835,977	84
	Jun 2017	10	89	$800,103	71

NOTE: Pharmacy encounter data for UHC is incomplete for August 2017. This should not affect ranks but does affect total amounts for paid, number of claims, and number of beneficiaries in August.

TABLE E: TOP 25 DRUG MOLECULES
BY NUMBER OF CLAIMS IN AUG 2017 (FFS and CCOs)

Drug Molecule Therapeutic Category	Jul 2017 # Claims	Aug 2017 # Claims	Aug 2017 $ Paid	Aug 2017 # Unique Benes
amoxicillin / aminopenicillins	10,783	15,945	$168,739	15,644
albuterol / adrenergic bronchodilators	11,656	15,832	$869,636	13,671
acetaminophen-hydrocodone / narcotic analgesic combinations	15,172	14,775	$169,361	13,784
montelukast / leukotriene modifiers	10,276	12,032	$196,002	11,816
cetirizine / antihistamines	7,696	10,221	$142,494	10,063
azithromycin / macrolides	5,649	10,098	$176,369	9,905
lisdexamfetamine / CNS stimulants	7,232	8,876	$2,409,739	8,615
gabapentin / gamma-aminobutyric acid analogs	7,337	7,362	$97,525	7,028
ibuprofen / nonsteroidal anti-inflammatory agents	5,912	6,928	$63,535	6,802
amlodipine / calcium channel blocking agents	6,850	6,870	$37,609	6,672
fluticasone nasal / nasal steroids	4,936	6,603	$123,983	6,563
omeprazole / proton pump inhibitors	6,309	6,442	$66,285	6,296
methylphenidate / CNS stimulants	4,926	6,030	$1,448,073	5,450
amphetamine-dextroamphetamine / CNS stimulants	5,123	5,954	$388,820	5,134
clonidine / antiadrenergic agents, centrally acting	5,593	5,936	$121,755	5,588
sulfamethoxazole-trimethoprim / sulfonamides	5,649	5,818	$120,040	5,703
mupirocin topical / topical antibiotics	5,520	5,454	$69,575	5,320
amoxicillin-clavulanate / penicillins/beta-lactamase inhibitors	3,866	5,414	$142,165	5,323
prednisolone / glucocorticoids	3,488	5,319	$110,445	5,187
ondansetron / 5HT3 receptor antagonists	3,732	4,637	$65,374	4,523
cefdinir / third generation cephalosporins	2,912	4,483	$146,011	4,434
triamcinolone topical / topical steroids	4,528	4,435	$69,227	4,284
lisinopril / angiotensin converting enzyme (ACE) inhibitors	4,545	4,420	$24,273	4,298
ranitidine / H2 antagonists	4,013	4,406	$91,558	4,284
guanfacine / antiadrenergic agents, centrally acting	3,986	4,322	$80,783	4,107

NOTE: Pharmacy encounter data for UHC is incomplete for August 2017. This should not affect ranks but does affect total amounts for paid, number of claims, and number of beneficiaries in August.

TABLE F: TOP 25 DRUG MOLECULES
BY DOLLARS PAID IN AUG 2017 (FFS and CCOs)

Drug Molecule Therapeutic Category	Jul 2017 $ Paid	Aug 2017 $ Paid	Aug 2017 # Claims	Aug 2017 # Unique Benes
lisdexamfetamine / CNS stimulants	$2,075,308	$2,409,739	8,876	8,615
antihemophilic factor / factor for bleeding disorders	$1,462,405	$1,959,505	48	31
methylphenidate / CNS stimulants	$1,205,186	$1,448,073	6,030	5,450
anti-inhibitor coagulant complex / factor for bleeding disorders	$671,954	$1,183,251	10	4
adalimumab / antirheumatics	$1,079,478	$1,012,983	191	181
ledipasvir-sofosbuvir / antiviral combinations	$864,891	$998,435	32	29
albuterol / adrenergic bronchodilators	$717,637	$869,636	15,832	13,671
deferasirox / chelating agents	$835,487	$825,239	88	79
dexmethylphenidate / CNS stimulants	$668,108	$796,391	3,145	2,646
insulin glargine / insulin	$860,970	$789,979	1,832	1,774
somatropin / growth hormones	$733,774	$750,539	180	170
insulin aspart / insulin	$810,214	$719,874	1,275	1,216
pregabalin / gamma-aminobutyric acid analogs	$681,942	$636,500	1,423	1,366
lurasidone / atypical antipsychotics	$650,340	$613,564	508	492
epinephrine / adrenergic bronchodilators	$387,688	$597,108	1,400	1,386
budesonide / glucocorticoids	$492,038	$531,129	1,182	1,161
cobicistat/elvitegravir/emtricitabine/tenofov / antiviral combinations	$529,930	$510,131	191	182
fluticasone-salmeterol / bronchodilator combinations	$469,037	$471,297	1,302	1,282
etanercept / TNF alpha inhibitors	$417,620	$402,264	98	91
amphetamine-dextroamphetamine / CNS stimulants	$424,809	$388,820	5,954	5,134
insulin detemir / insulin	$409,245	$374,639	760	727
ivacaftor-lumacaftor / CFTR combinations	$396,018	$368,352	21	19
atomoxetine / CNS stimulants	$358,697	$348,063	844	791
lacosamide / miscellaneous anticonvulsants	$359,125	$341,689	436	393
clobazam / benzodiazepine anticonvulsants	$349,909	$339,786	214	194

NOTE: Pharmacy encounter data for UHC is incomplete for August 2017. This should not affect ranks but does affect total amounts for paid, number of claims, and number of beneficiaries in August.

TABLE G: TOP 25 DRUG MOLECULES
BY CHANGE IN NUMBER OF CLAIMS FROM JUN 2017 TO AUG 2017 (FFS and CCOs)

Drug Molecule	Jun 2017 # Claims	Jul 2017 # Claims	Aug 2017 # Claims	Aug 2017 $ Paid	Aug 2017 # Unique Benes
amoxicillin / aminopenicillins	11,950	10,783	15,945	$168,739	15,644
albuterol / adrenergic bronchodilators	12,061	11,656	15,832	$869,636	13,671
azithromycin / macrolides	6,458	5,649	10,098	$176,369	9,905
cetirizine / antihistamines	8,385	7,696	10,221	$142,494	10,063
lisdexamfetamine / CNS stimulants	7,251	7,232	8,876	$2,409,739	8,615
montelukast / leukotriene modifiers	10,516	10,276	12,032	$196,002	11,816
prednisolone / glucocorticoids	3,950	3,488	5,319	$110,445	5,187
fluticasone nasal / nasal steroids	5,249	4,936	6,603	$123,983	6,563
amoxicillin-clavulanate / penicillins/beta-lactamase inhibitors	4,273	3,866	5,414	$142,165	5,323
cefdinir / third generation cephalosporins	3,425	2,912	4,483	$146,011	4,434
methylphenidate / CNS stimulants	4,994	4,926	6,030	$1,448,073	5,450
ibuprofen / nonsteroidal anti-inflammatory agents	5,980	5,912	6,928	$63,535	6,802
epinephrine / adrenergic bronchodilators	680	860	1,400	$597,108	1,386
ondansetron / 5HT3 receptor antagonists	3,953	3,732	4,637	$65,374	4,523
amphetamine-dextroamphetamine / CNS stimulants	5,314	5,123	5,954	$388,820	5,134
sulfamethoxazole-trimethoprim / sulfonamides	5,325	5,649	5,818	$120,040	5,703
cephalexin / first generation cephalosporins	3,018	3,157	3,499	$66,618	3,455
mupirocin topical / topical antibiotics	4,975	5,520	5,454	$69,575	5,320
prednisone / glucocorticoids	2,674	2,457	3,146	$25,697	3,047
dexmethylphenidate / CNS stimulants	2,689	2,658	3,145	$796,391	2,646
clonidine / antiadrenergic agents, centrally acting	5,626	5,593	5,936	$121,755	5,588
brompheniramine/dextromethorphan/pse / upper respiratory combinations	237	174	537	$11,059	530
ranitidine / H2 antagonists	4,121	4,013	4,406	$91,558	4,284
dextromethorphan-promethazine / upper respiratory combinations	172	122	450	$3,474	428
cefprozil / second generation cephalosporins	548	465	807	$34,532	800

NOTE: Pharmacy encounter data for UHC is incomplete for August 2017. This should not affect ranks but does affect total amounts for paid, number of claims, and number of beneficiaries in August.

TABLE H: TOP 25 DRUG MOLECULES
BY CHANGE IN AMOUNT PAID FROM JUN 2017 TO AUG 2017 (FFS and CCOs)

Drug Molecule	Jun 2017 $ Paid	Jul 2017 $ Paid	Aug 2017 $ Paid	Aug 2017 # Claims	Aug 2017 # Unique Benes
antihemophilic factor / factor for bleeding disorders	$1,201,124	$1,462,405	$1,959,505	48	31
lisdexamfetamine / CNS stimulants	$2,076,159	$2,075,308	$2,409,739	8,876	8,615
epinephrine / adrenergic bronchodilators	$306,260	$387,688	$597,108	1,400	1,386
methylphenidate / CNS stimulants	$1,231,957	$1,205,186	$1,448,073	6,030	5,450
dexmethylphenidate / CNS stimulants	$641,963	$668,108	$796,391	3,145	2,646
albuterol / adrenergic bronchodilators	$727,576	$717,637	$869,636	15,832	13,671
asfotase alfa / miscellaneous metabolic agents	$0	$62,851	$124,503	3	2
eltrombopag / platelet-stimulating agents	$18,153	$43,726	$81,765	7	6
azithromycin / macrolides	$120,932	$104,145	$176,369	10,098	9,905
hydroxyprogesterone / progestins	$278,516	$291,423	$332,600	105	97
amoxicillin / aminopenicillins	$115,201	$103,936	$168,739	15,945	15,644
elbasvir-grazoprevir / antiviral combinations	$38,440	$86,493	$88,835	5	5
immune globulin intravenous and subcutaneous / immune globulins	$106,125	$163,609	$154,213	13	9
eteplirsen / miscellaneous uncategorized agents	$11,835	$23,670	$59,175	10	1
glycerol phenylbutyrate / urea cycle disorder agents	$92,266	$43,936	$138,322	3	2
amphetamine / CNS stimulants	$124,779	$136,080	$166,694	554	534
rosuvastatin / HMG-CoA reductase inhibitors (statins)	$76,459	$84,965	$117,704	525	507
beclomethasone / inhaled corticosteroids	$266,614	$277,016	$301,630	1,641	1,624
sulfamethoxazole-trimethoprim / sulfonamides	$86,482	$96,042	$120,040	5,818	5,703
prednisolone / glucocorticoids	$78,173	$72,502	$110,445	5,319	5,187
liraglutide / GLP-1 receptor agonists	$155,741	$164,637	$185,601	258	250
sildenafil / impotence agents	$107,577	$153,935	$136,398	46	41
deferasirox / chelating agents	$799,517	$835,487	$825,239	88	79
montelukast / leukotriene modifiers	$170,411	$145,342	$196,002	12,032	11,816
glucagon / glucose elevating agents	$39,817	$40,760	$63,988	167	156

NOTE: Pharmacy encounter data for UHC is incomplete for August 2017. This should not affect ranks but does affect total amounts for paid, number of claims, and number of beneficiaries in August.

TABLE I: TOP 15 DRUG SOLID DOSAGE FORM HIGH VOLUME (100+ RX FILLS LAST MONTH) PRODUCTS WITH UNIT COST > $1
BY PERCENT CHANGE IN AMOUNT PAID PER UNIT JUN 2017 TO AUG 2017 (FFS and CCOs)

Drug Product Therapeutic Category	Aug 2017 # Claims	Aug 2017 $ Paid	Aug 2017 Avr. Paid Per Rx	Aug 2017 Avr. Units Per Rx	Jun 2017 Paid Per Unit	Jul 2017 Paid Per Unit	Aug 2017 Paid Per Unit	Percent Change
Crestor (rosuvastatin) 10 mg tablet / HMG-CoA reductase inhibitors (statins) (P)	158	$37,695	$238.58	30	$4.68	$5.53	$7.95	69.9%
Crestor (rosuvastatin) 20 mg tablet / HMG-CoA reductase inhibitors (statins) (P)	196	$46,144	$235.43	29	$4.79	$5.41	$8.03	67.7%
rizatriptan 10 mg tablet / antimigraine agents (P)	142	$3,067	$21.60	10	$1.26	$1.83	$1.65	30.8%
Focalin XR (dexmethylphenidate) 20 mg capsule, extended release / CNS stimulants (P)	454	$162,273	$357.43	31	$9.91	$10.55	$11.62	17.2%
cefprozil 500 mg tablet / second generation cephalosporins (P)	162	$5,218	$32.21	19	$1.27	$1.29	$1.47	15.7%
Focalin XR (dexmethylphenidate) 15 mg capsule, extended release / CNS stimulants (P)	378	$130,814	$346.07	30	$9.85	$10.99	$11.40	15.6%
ketorolac 10 mg tablet / nonsteroidal anti-inflammatory agents (P)	850	$21,518	$25.32	17	$1.07	$1.08	$1.22	13.7%
carbamazepine 100 mg tablet, extended release / dibenzazepine anticonvulsants (P)	117	$14,026	$119.88	13	$93.23	$85.08	$103.26	10.8%
Focalin XR (dexmethylphenidate) 10 mg capsule, extended release / CNS stimulants (P)	446	$146,758	$329.05	29	$10.13	$10.33	$11.09	9.5%
cefuroxime 500 mg tablet / second generation cephalosporins (P)	199	$5,481	$27.54	18	$1.13	$1.16	$1.24	9.2%
Focalin XR (dexmethylphenidate) 5 mg capsule, extended release / CNS stimulants (P)	161	$52,598	$326.69	29	$10.40	$11.12	$11.22	7.9%
TriCare (multivitamin, prenatal) Prenatal Multivitamins with Folic Acid 1 mg tablet / iron products (P)	175	$6,552	$37.44	31	$1.02	$1.02	$1.08	6.0%
Concept DHA (multivitamin, prenatal) Prenatal Multivitamins with Folic Acid 1 mg capsule / vitamin and mineral combinations (P)	943	$34,928	$37.04	30	$1.04	$1.04	$1.09	5.0%

TABLE I: TOP 15 DRUG SOLID DOSAGE FORM HIGH VOLUME (100+ RX FILLS LAST MONTH) PRODUCTS WITH UNIT COST > $1
BY PERCENT CHANGE IN AMOUNT PAID PER UNIT JUN 2017 TO AUG 2017 (FFS and CCOs)

Drug Product Therapeutic Category	Aug 2017 # Claims	Aug 2017 $ Paid	Aug 2017 Avr. Paid Per Rx	Aug 2017 Avr. Units Per Rx	Jun 2017 Paid Per Unit	Jul 2017 Paid Per Unit	Aug 2017 Paid Per Unit	Percent Change
NexIUM (esomeprazole) 40 mg delayed release capsule / proton pump inhibitors (P)	101	$24,518	$242.75	31	$7.52	$6.22	$7.80	3.7%
methylphenidate 27 mg/24 hr tablet, extended release / CNS stimulants (P)	558	$127,124	$227.82	30	$7.24	$7.20	$7.46	3.1%

New Business

Special Analysis Projects

ANTIPSYCHOTIC USE IN INDIVIDUALS WITH INTELLECTUAL AND DEVELOPMENTAL DISABILITIES IN MISSISSIPPI MEDICAID

CARRIED OVER FROM JULY 2017 DUR BOARD MEETING WITH APPENDIX ADDED

BACKGROUND

At the April 27, 2017, DUR Board Meeting Dr. Escude', the Board Co-chair, asked MS-DUR to research antipsychotic use among beneficiaries diagnosed with intellectual and development disabilities (IDD). He indicated that in this population antipsychotics are sometimes prescribed to treat behaviors that actually may be attempts by the patient to communicate about other underlying health problems. Some underlying health issues of the IDD population could be misinterpreted as behavioral issues; therefore, the patient could be treated with antipsychotics instead medications for the physical or neurological health problem.

The use of antipsychotic medications in individuals with IDD is common due to the significantly higher rate of psychosis among adults with IDD when compared with the general population[1]. These medications are used to not only treat functional psychiatric illnesses such as schizophrenia but also may be used to treat problem behaviors in the IDD population. However, not all problem behaviors have a psychopathology origin. Some problem behaviors, such as aggression and self-injury, could be a symptom of a health-related disorder or other circumstance where certain needs of the individual are not being met. Since beneficiaries with IDD often cannot verbally express their health problem, they sometimes exhibit behaviors that may signal underlying health problems. Thus, it is important to carefully assess the possible cause(s) of problem behaviors before prescribing antipsychotics. Adults with IDD have a higher rate of physical conditions such as sensory impairments, cerebral palsy, epilepsy, and cardiovascular or gastrointestinal problems that can influence the choice of medication. The lack of careful assessment may lead to unnecessary prescribing of antipsychotic medications and the failure to correctly identify and address the underlying health issue causing the problem behavior.

Antipsychotic medications are effective for individuals with a functional psychiatric diagnosis but their use can be problematic in the IDD population and should be used judiciously. Some adults with IDD may have atypical responses or side effects at low doses to antipsychotic medications. Some patients may be taking multiple medications and be at increased risk of adverse medication events[2]. The goal of treatment should not only be symptom control but improvement in the quality of life of the individual with IDD.

[1] Deb S, Thomas M & Bright C. Mental Disorder in Adults with Intellectual Disability. Journal of Intellectual Disability Research 2001; 45 (6): 506-514.

[2] Vanderbilt Kennedy Center for Excellence in Developmental Disabilities. Health Care for Adults with Intellectual and Developmental Disabilities. Psychotropic Medication Issues. http://vkc.mc.vanderbilt.edu/etoolkit/mental-and-behavioral-health/psychotropic-medication-therapy/. Accessed 6/27/2017.

METHODS

A retrospective study was conducted using Mississippi Medicaid medical and pharmacy claims for the period January 2016 – June 2017. The analysis included data from the fee-for-service (FFS) and coordinated care organizations (CCOs). Beneficiaries with any outpatient or inpatient medical claim having an IDD diagnosis were identified as the target population. The ICD-10 codes used to identify beneficiaries with IDD are listed in Table 1. Beneficiaries were identified using both a "limited" set of codes and a broader set of codes, referred to as "any" diagnosis in the results.

TABLE 1: ICD-10 Codes Used to Identify ANY IDD Diagnosis and LIMITED IDD Diagnosis

ICD-10 Code	Description	Any	Limited
F84.0	Autistic disorder	X	X
F84.2	Rett's syndrome	X	X
F84.3	Other childhood disintegrative disorder	X	X
F84.5	Asperger's syndrome	X	X
F84.8	Other pervasive developmental disorders	X	X
F84.9	Pervasive developmental disorder, unspecified	X	X
F70	Mild intellectual disabilities	X	X
F71	Moderate intellectual disabilities	X	X
F72	Severe intellectual disabilities	X	X
F73	Profound intellectual disabilities	X	X
F78	Other intellectual disabilities	X	X
F79	Unspecified intellectual disabilities	X	X
Q86.0	Fetal alcohol syndrome	X	
Q87.1	Congenital malformation syndromes predominantly associated with short stature (Prader-Willie syndrome)	X	
Q90	Down syndrome	X	
Q91.3	Trisomy 18, unspecified (Edward's syndrome)	X	
Q93.4	Deletion of short arm of chromosome 5 (Cri-Due-Chat syndrom)	X	
Q91.7	Trisomy 13, unspecified (Patau's syndrome)	X	
Q98.4	Klinefelter syndrome, unspecified	X	
Q99.2	Fragile X chromosome	X	

TABLE 2: Codes to Identify Primary Indications for Antipsychotic Medication Use

ICD-10 Code	Description
F20	Schizophrenia
F22	Delusional disorders
F23	Brief psychotic disorder
F28	Other psychotic disorder not due to a substance or known physiological condition
F29	Unspecified psychosis not due to a substance or know physiological condition
F30	Manic episode
F31	Bipolar disorder
F32.3	Major depressive disorder, single episode, severe with psychotic features
F33.3	Major depressive disorder, recurrent, severe with psychotic symptoms
F44.89	Other dissociative and conversion disorders
F84	Pervasive developmental disorders
F95	Tic disorder

Draft Document for NCINQ 2013 Public Comment.
http://www.chcs.org/media/NCINQ_2013_Public_Comment_4-30-13.pdf

All prescriptions for antipsychotic medications filled during the observation period were extracted for the beneficiaries identified as potential IDD patients. Medical claims were extracted for beneficiaries with IDD and taking antipsychotics to determine whether the beneficiaries had diagnoses that were identified as being primary indications for antipsychotic medication use (Table 2). Codes to identify primary indications for antipsychotic medication use were determined based on the technical specifications for the "Use of Antipsychotics in Children without a Primary Indication" quality measure proposed in 2013 by the National Collaborative for Innovation in Quality Measurement.[3]

[3] AHRQ-CMS CHIPRA National Collaborative for Innovation in Quality Measurement. Antipsychotic Medication Use Measures for Children and Adolescents – Draft Document for NCINQ 2013 Public Comment. http://www.chcs.org/media/NCINQ_2013_Public_Comment_4-30-13.pdf. Accessed 5/7/2013.

RESULTS

Prevalence of IDD and Treatment with Antipsychotics

Using the broader any IDD related diagnosis, 17,183 beneficiaries were classified as having IDD. The number decreased to 16,031 when the more limited IDD diagnosis classification was used (Table 3). Overall, 22-23% of beneficiaries with IDD were treated with an antipsychotic. The percentage using antipsychotics was highest among beneficiaries 12-20 years of age and dropped significantly for beneficiaries ≥ 46 years of age.

TABLE 3: Characteristics of Beneficiaires With IDD Diagnosis* and Treatment With Antipsychotic Medication
(January 2016 - June 2017)

		Any IDD Related Diagnosis*		Limited IDD Diagnosis*	
		Number With IDD Diagnosis	Treated With Antipsychotic	Number With IDD Diagnosis	Treated With Antipsychotic
TOTAL		17,183	3,794 (22.1%)	16,031	3,739 (23.3%)
Age	< 12 years	4,716	1,005 (21.3%)	4,069	983 (24.2%)
	12-20 years	3,474	1,213 (34.9%)	3,231	1,192 (36.9%)
	21-45 years	5,332	1,172 (22.0%)	5,146	1,161 (22.6%)
	46-64 years	2,870	399 (13.9%)	2,804	398 (14.2%)
	65+ years	791	5 (0.6%)	781	5 (0.6%)
Pharmacy Program	FFS	9,763	1,666 (17.1%)	9,272	1,644 (17.7%)
	UHC	3,797	1,099 (28.9%)	3,488	1,087 (31.2%)
	MAG	3,623	1,029 (28.4%)	3,271	1,008 (30.8%)

** See Table 1 for list of diagnosis codes classified as any and limited IDD diagnosis.*

Beneficiaries with IDD were disproportionately enrolled in the FFS program. Despite each CCO having almost twice as many enrollees as the FFS program, there were ~2.5 times as many beneficiaries with IDD in the FFS program as in either CCO. The percentage of beneficiaries with IDD being treated with antipsychotics was lower in FFS (17%) than in the CCOs (28-31%). A detailed analysis within each pharmacy program found that the percentage of beneficiaries with IDD receiving antipsychotics was similar across programs for beneficiaries less than 21 years of age. Use of antipsychotics among adults in the FFS program decreased with age but increased in the CCOs.

Prevalence of Primary Indications for Antipsychotics Use

Approximately two-thirds of beneficiaries that were treated with antipsychotics had diagnoses in their medical claims that were primary indications for the use of antipsychotics (Table 4). ICD-10 code F84 – pervasive developmental disorders- is one of the primary diagnoses for which antipsychotics are indicated. This ICD-10 code was included in the primary diagnosis set for identifying IDD patients. The use of an antipsychotic with primary indications was examined using the full list of primary indication codes (referred to as "Any Primary Diagnosis") and the primary diagnosis list excluding F84. The results of the beneficiaries with IDD can be summarized as follows:

- Approximately 37% appear to be treated with antipsychotics to manage behaviors that are related to pervasive developmental disorder,
- Approximately 31% are being treated with antipsychotics to manage conditions that are primary indications for use excluding pervasive developmental disorder,
- Approximately 32% are being treated with antipsychotics without a diagnosis that is a primary indication for use.

These treatment patterns were consistent across the three pharmacy programs.

FIGURE 1: Use of Antipsychotics Among Beneficiaries With IDD

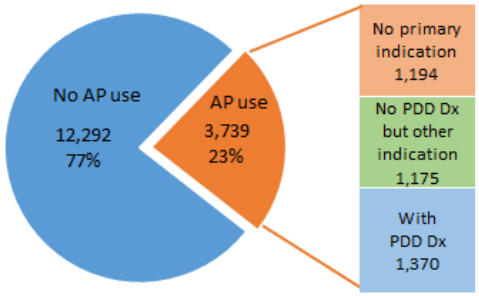


TABLE 4: Prevalence of Primary Indication for Antipsychotic Use Among Beneficiaires With IDD Diagnosis* Being Treated With Antipsychotic Medication
(January 2016 - June 2017)

		Any IDD Related Diagnosis*			Limited IDD Diagnosis*		
			Having Primary Indication for Antipsychotic Use**			Having Primary Indication for Antipsychotic Use**	
		Treated With Antipsychotic	Any Primary Diagnosis	Primary Diagnosis Other Than F84	Treated With Antipsychotic	Any Primary Diagnosis	Primary Diagnosis Other Than F84
TOTAL		3,794	2,554 (67.3%)	1,184 (31.2%)	3,739	2,545 (68.1%)	1,175 (31.4%)
Age	< 12 years	1,005	721 (71.7%)	67 (6.7%)	983	717 (72.9%)	64 (6.5%)
	12-20 years	1,213	835 (68.8%)	312 (25.7%)	1,192	833 (69.9%)	309 (25.9%)
	21-45 years	1,172	731 (62.4%)	543 (46.3%)	1,161	728 (62.7%)	540 (46.5%)
	46-64 years	399	263 (65.9%)	258 (64.7%)	398	263 (66.1%)	258 (64.8%)
	65+ years	5	4 (80.0%)	4 (80.0%)	5	4 (80.0%)	4 (80.0%)
Pharmacy Program	FFS	1,666	1,095 (65.7%)	452 (27.1%)	1,644	1,092 (66.4%)	449 (27.3%)
	UHC	1,099	769 (70.0%)	371 (33.8%)	1,087	767 (70.6%)	369 (34.0%)
	MAG	1,029	690 (67.1%)	361 (35.1%)	1,008	686 (68.0%)	357 (35.4%)
Provider Type for Initial Antipsychotic Prescription	Psych	1,284	917 (71.4%)	493 (38.4%)	1,271	913 (71.8%)	489 (38.5%)
	NP-Mental	733	525 (71.6%)	309 (42.2%)	726	524 (72.2%)	308 (42.4%)
	MD-Other	1,443	901 (62.4%)	279 (19.3%)	1,420	898 (63.2%)	276 (19.4%)
	NP-Other	285	177 (62.1%)	87 (30.5%)	276	176 (63.8%)	86 (31.2%)

** See Table 1 for list of diagnosis codes classified as any and limited IDD diagnosis.*
*** See Table 3 for list of diagnosis codes considered to be primary indications for antipsychotic medication use.*

Table 4 also shows the prevalence of a primary indication for antipsychotic use by the type of provider writing the initial antipsychotic prescription filled during the observation period. Approximately half of the beneficiaries had their initial antipsychotic prescription written by a provider other than a mental health specialist. There were significant differences in the prevalence of primary indications for antipsychotics by type of provider.

When mental health providers wrote the initial antipsychotic prescription, ~32% of the time IDD was the primary indication, ~40% of the time other mental health conditions were the primary indication, and ~38% of the time no primary indication was found. When other providers wrote the initial antipsychotic prescription, ~63% of the time IDD was the primary indication, ~17% of the time other mental health conditions were the primary indication, and ~20% of the time no primary indication was found.

Analysis of Providers Writing Initial Antipsychotic Prescriptions for IDD Patients

Although the number of initial prescriptions for antipsychotics were similar between mental health providers and other providers, there were more than twice as many non-mental health providers writing these prescriptions (Table 5).

TABLE 5: Provider Types Writing Initial Antipsychotic Prescriptions for IDD Patients

Provider Type for Initial Antipsychotic Prescription	Number of Providers	Number of Beneficiaries With Any IDD Diagnosis* Prescribed Antipsychotic	
		Average for Provider Type	Total for Provider Type
Psych	152	8.4	1,284
NP-Mental	77	9.5	733
MD-Other	402	3.6	1,443
NP-Other	112	2.5	285

** See Table 1 for list of diagnosis codes classified as any and limited IDD diagnosis.*

CONCLUSIONS AND RECOMMENDATIONS

The major findings from this analysis include:

- There are a large number of Medicaid beneficiaries with diagnoses of IDD.
- Almost one-fourth of these beneficiaries are being treated with antipsychotics.
- More than one-third of the beneficiaries with IDD being treated with antipsychotics have pervasive developmental disorder as the primary indication for their use of antipsychotics.
- Almost one-third of the beneficiaries taking antipsychotics have no primary indication for the use of an antipsychotic.
- More than half of these beneficiaries are being prescribed antipsychotics by non-mental health providers.

The IDD population is difficult to treat appropriately due to communication issues that frequently exist. The frequent use of antipsychotics in this population without mental health diagnoses and without primary indicators for the use of antipsychotics could signal inappropriate use of antipsychotics.

MS-DUR recommends that an educational intervention be initiated to provide education to providers initiating therapy with antipsychotics for IDD patients who do not have other mental health diagnoses that are primary indicators for use. MS-DUR would work with Dr. Escude' to develop the educational materials for this intervention.

APPENDIX

DRAFT EDUCATION MAILING

MISSISSIPPI DIVISION OF MEDICAID

Provider Summary: Psychotropic Medication Usage and Underlying Medical Issues in People With IDD

Diagnosing psychiatric problems in people with Intellectual and Developmental Disabilities (IDD) can be a challenge. People with IDD are often treated with psychotropic medications for behavioral issues which actually may be a form of communication of a medical issue rather than a behavioral health issue.[1,2] This can lead to overuse of psychotropic medications and misdiagnosis of underlying medical conditions. Because of this, it is important to rule out potential causes of adverse behaviors in people with IDD before starting or increasing psychotropic medication in this population.[3]

Below is a list of behaviors that may be pointing to an underlying medical condition in people with IDD:

1. **GI distress/reflux** - Hand mouthing, pica, food refusal, coughing when lying down, physical or verbal aggression particularly around meal times.

2. **Earache, headache, sinusitis or other head issue** – Head banging, head butting, hitting or slapping self, inserting objects into ear or nose, crying, withdrawal from areas with light or noise, sitting with head in lap, “refusals” to listen or respond (loss or reduction in hearing), hands over ears or face, head tilting.

3. **Dental issues** – Hitting self, hands in mouth, refusal to eat, spitting out food, physical or verbal aggression particularly around meal times.

4. **Constipation** – Guarding abdomen, rocking, not able to sit still (up and down), hitting self in abdomen, fetal position when lying, knees drawn up to when chest sitting, physical or verbal aggression without definite antecedent, refusal to eat.

5. **Seizure disorder** – Disrobing, increased agitation, failure to “pay attention” in children or “daydreaming”, sexually acting out, physical or verbal aggression with no antecedent, repetitive or ritualistic type behaviors that are short lived, rapid eye blinking, tantrums, falls, sudden “sleep”, random talking, hard to “reach”.

6. **UTI** – New onset urinary incontinence, agitation, not able to sit still (up and down), repetitive trips to toilet, screaming when approaching toilet or with incontinence, grabbing genitals or rubbing with objects, hands in pants, physical or verbal aggression with no antecedent, abdominal guarding, rocking, change in cognitive status, fatigue.

7. **Pneumonia** – Fatigue, withdrawal, refusal to eat, falls, increased irritability, change in cognitive status, refusal to lie down to sleep.

8. **Sexual abuse** – New onset urinary or fecal incontinence, withdrawal, excessive masturbation, refusal to allow bathing or aggression during bathing, self restraint (wrapping self inside shirt, wrapping blanket or throw tightly around themselves, knees to chest and hugging), sexual aggression toward others, agitation, verbal or physical aggression when approached by caregiver or others - especially if the person shares characteristics with abuser (male, female, tall, short hair, Caucasian, African American), suicidal behavior/attempts, night terrors.

[1] Deb, Shoumitro, et al. "International guide to prescribing psychotropic medication for the management of problem behaviours in adults with intellectual disabilities." *World Psychiatry* 8.3 (2009): 181-186.
[2] Santosh, Paramala Janardhanan, and Gillian Baird. "Psychopharmacotherapy in children and adults with intellectual disability." *The Lancet* 354.9174 (1999): 233-242.
[3] Aggarwal R, Guanci N, Appareddy V. ”Issues in Treating Patients with Intellectual Disabilities.” Psychiatric Times. 2013, August.

9. **Medication side effects** – Blinking, medication refusal, refusal to eat, urinary or fecal incontinence, constipation, urinary retention, aggression, fatigue, weight gain or loss, agitation, scratching self, falls, change in cognitive status, tics, dystonia symptoms, muscle twitching.

10. **Chest pain** – Scratching, hitting or rubbing chest, crying, yelling out, agitation, anxiety, shortness of breath, weakness.

It is recommended that consideration of an underlying medical condition be considered whenever these behaviors are noted, especially if it is a change from any usual pattern of behaviors or when the person has not responded as expected to psychotropic medication. Diligence in this area may prevent unnecessary side effect and suffering in people with IDD.

For more information visit:
http://vkc.mc.vanderbilt.edu/etoolkit/mental-and-behavioral-health/psychotropic-medication-therapy/
http://detectMS.com

Prepared for Mississippi Division of Medicaid by
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Serious Mental Illness Among Individuals with IDD

Definition & Diagnosis

Diagnosis of serious mental illness (SMI) requires adult patients to meet the following criteria:

- A mental, behavioral, or emotional disorder (excluding intellectual or developmental disabilities & substance use disorders)
- Currently diagnosable or diagnosable within the past year
- Illness meets diagnostic criteria specified in the 5th edition of the *Diagnostic & Statistical Manual of Mental Disorders*
- Results in serious functional impairment & substantially limits or interferes with daily activities (e.g., employment, social involvement, relationship maintenance, etc.)

Commonly diagnosed SMIs include:

- Major depression
- Schizophrenia
- Bipolar disorder
- Other mental disorders causing serious impairment

The cause of mental illness is not reducible to any lone factor, but rather is influenced by a constellation of biological & social factors, including genetic predisposition, intellectual or developmental abilities, physical health, environmental factors, traumatic events, social connections, family history, economic situation, & individual personality characteristics.

Sources: APA 2015; NADD 2015; NAMI 2015; NIMH 2015; SAMHSA 2015

Facts & Figures

People with cognitive disorders, known as intellectual & developmental disabilities (IDD), have significantly higher rates of mental illness & related problem behaviors when compared to the general population.

- Roughly 1.5-3.0% of people are diagnosed with an IDD, & of those, up to 35% have a co-occurring mental illness
- In 2012, approximately 9.6 million U.S. adults aged 18+ were living with a SMI, representing just over 4% of the general U.S. population
- Down Syndrome is associated with lower rates of mental illness & related problem behaviors than other IDD-related conditions, such as autism spectrum disorders (ASD)
- Early identification & intervention is key to preventing the development of SMI, as 50% of mental illnesses emerge by age 14, & 75% of mental illnesses manifest by age 24
- Overall, women are more likely than men to be diagnosed with SMI (4.9% & 3.2%, respectively)
- Asians, Hawaiian Natives, & Pacific Islanders are the least likely ethnicities to report SMI (2.0% & 1.8%, respectively)
- A 2008 analysis of 31 studies reveals that while people with SMI are somewhat more likely than the general population to perpetrate violence, they are far more likely to become victims of violence

Sources: Choe et al. 2008; Mantry et al. 2007; NADD 2015; NIMH 2015; Webb et al. 2010

Risk Factors

Some subpopulations, such as people diagnosed with IDD, face a greater risk of developing SMI. At-risk people generally have less access to care, disrupted service use, & poorer health outcomes, as documented among patients with IDD. Specialized medical & behavioral providers are especially important for patients with SMI who have co-occurring conditions, such as ASD or other forms of IDD, yet community-based heath care specialized for patients with IDD is rarely available. Health disparities among vulnerable populations may be caused by limited health clinics, a dearth of information about mental health care, the absence of culturally and/or linguistically diverse health providers, & the scarcity of specialized health care providers.

Groups at high risk for SMI include:

- People with ASD and/or IDD
- People with physical disabilities
- LGBTQ populations
- Transition-age youth
- Adults aged 26-49
- Native Americans/Alaskans & Latinos

Sources: Arc 2015; Bradford 2008; Burkett et al. 2015; Grinker et al. 2015; Melville et al. 2008; NIMH 2015; Robertson et al. 2015; Ryan et al. 2015; SAMHSA 2015;

Social Stigma

Research reveals that people with IDD are one of the most stigmatized groups, & that patients with SMI experience even greater social stigma than those with IDD. Social stigma often leads to negative stereotypes that devalue people with distinguishing characteristics, such as obvious developmental disorders or mental illnesses. Negative stereotypes frequently result in social isolation & discrimination in social institutions such as education, employment, & health care. Not only is social stigma a risk factor for mental illness, it is also a barrier faced by patients with when they contemplate seeking mental health care. Because of the lack of sensitivity toward people who are mentally ill, patients with IDD, who are already harshly stigmatized for their cognitive disabilities, may feel discouraged from procuring treatment until their mental illness has dangerously escalated. Patients with IDD & co-occurring SMI experience multiple layers of stigma, yet have less access than the general public to specialized resources that address their confounding ailments.

To prevent the escalation of SMI, particularly among at-risk populations, public awareness about the following items is vital:

- Prevalence of mental illness in the general population, & common warning signs or risk factors
- Holistic, community-based treatment options available to patients who are suffering from mental illness
- Support services available to families & caregivers of patients with SMI, especially for those of patients with co-occurring conditions, such as IDD
- Intervention/de-escalation tactics for employers & law enforcement who may be first-responders to behavioral or emotional SMI-related emergencies

Sources: AAID 2009; Arc 2015; Burkett et al. 2015; Grinker et al. 2015; NADD 2015; Oullette-Kuntz et al. 2010; Ryan et al. 2015; Scior et al. 2013; Starke 2011

Co-occurring Conditions

Co-occurring conditions are two or more illnesses experienced simultaneously. Common co-occurring conditions with SMI include IDD, substance abuse, cardiovascular issues, & diabetes. Symptoms of IDD-related conditions sometimes mask or are prioritized over mental health red flags, which can reduce the overall efficacy of treatment plans. Patients diagnosed with SMI & co-occurring conditions, such as IDD, should receive treatments that comprehensively address all components of their mental & physical health conditions. If left untreated, patients with SMI are more likely to experience early death or develop degenerative co-occurring chronic conditions.

Prompt medical attention to SMI & co-occurring conditions is important for the following reasons:

- 50% to 90% of people with SMI have one or more co-occurring chronic medical conditions
- A diagnosis of SMI is associated with death from 7 to 25 years earlier than for those without a SMI
- 90% of all people who die by suicide have a SMI
- 20-25% of homeless people report having a SMI
- Health costs for patients with both mental illness & chronic health issues are about 75% higher than patients without a mental illness

Sources: Dixon 1999; MHPA 2015; NADD 2015; SAMHSA 2015; Sterling et al. 2010; Viron 2012

Treatment: Medical, Psychological, Social

Patients with SMI & co-occurring IDD often need specialized treatment plans & additional support to regain their mental health. SMI is characterized by patients' difficulty managing daily responsibilities, such as strained relationships, job loss, & reduced ability to perform self care. Though SMI can be successfully combated via a three pronged approach (medical, psychological, social), SMI often involves episodes of illness & relapse, which requires patience & persistence from all parties involved in a treatment plan.

- Patients can become eligible for Medicaid because they are disabled by SMI, or they may be eligible because of other health issues, such as ASD or IDD, & simultaneously have a mental health condition
- While antipsychotic & mood stabilizing medications are useful components of SMI treatment, they may be associated with an elevated risk of sudden cardiac death, & other adverse reactions that make it difficult to socially engage, such as sedation, weight gain, & sexual dysfunction
- Successful treatment approaches to SMI involve both medical care & community based approaches that address psychosocial issues including relationships, housing, employment, & transportation
- Integration of mental & emotional health development into community health outreach can support the prevention of other public health issues, such as unplanned pregnancy, violence, tobacco use, & homelessness
- Due to a lack of robust research & provider training, medical & behavioral health interventions for people with ASD or IDD are generally not evidence-based & can produce unrealistic or discriminatory treatment plans

Sources: APA 2015; Arc 2015; Bellack et al. 2006; Burkett et al. 2015; Grinker et al. 2015; MHPA 2015; Melville et al. 2008; Muench et al. 2010; Ray et al. 2001; Robertson et al. 2015; Ryan et al. 2015; SAMHSA 2015

Overlap & Links Between SMI & IDD

Research on SMI demonstrates that at-risk populations, such as those with IDD or other disabilities, are more likely to have co-occurring conditions & barriers to specialized health care. While much of the recent research on SMI has focused on racial & economic disparities in mental health care, it is important to note that patients with IDD often face physical & social challenges (i.e., chronic illness, social exclusion, difficult developmental transitions) that are known contributors to the onset of SMI. Due to a lack of specialized IDD knowledge among health care providers, some patients with IDD may manifest SMI symptoms & related problem behaviors that are misattributed to common IDD symptoms.

A recent review of the top fifteen medical journals reveals that fewer than ten articles have been published about IDD among adults in the past fifteen years. This dearth of medical attention to IDD indicates that currently practicing health providers are largely unprepared to manage patients with IDD who may have several serious co-occurring conditions (IDD, SMI, & chronic/frequent physical illness). Because many patients with IDD are now living in independent or semi-independent settings, it is imperative that community health professionals be provided more extensive information about how to properly address the special health care needs of patients with IDD, especially mental wellness.

With focused training & support from medical specialists of IDD, community health care providers will be more prepared to identify patients with IDD who experience mental health crises. Patients with IDD require an SMI treatment plan that provides solutions on multiple levels (medical, psychological, social), coupled with family & caregiver support.

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Web Resources

- **American Association on Intellectual & Developmental Disabilities: www.aaidd.org**
- **American Psychological Association: www.apa.org**
- **DETECT Mississippi: www.detectms.com**
- **Medicaid Health Plans of America: www.mhpa.org**
- **National Alliance on Mental Illness: www.nami.org**
- **National Institute of Mental Health: www.nimh.nih.gov**
- **Substance Abuse & Mental Health Services Administration: www.samhsa.gov**
- **The National Association for the Dually Diagnosed: www.thenadd.org**
- **The Arc. For people with intellectual & developmental disabilities: www.thearc.org**

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USE OF CODEINE AND TRAMADOL IN MISSISSIPPI MEDICAID

CARRIED OVER FROM JULY 2017 DUR BOARD MEETING WITH UPDATES AND APPENDIX ADDED

BACKGROUND

In April 2017, the FDA issued a notice restricting the use of codeine and tramadol medications in children.[1] Both medications are classified as opioid narcotics. Codeine is approved to treat pain and cough. It is often used in combination with other medications in both prescription and OTC cough and pain medications. Tramadol is a prescription medication approved to treat moderate to moderately severe pain. Single ingredient codeine medications and all tramadol containing medications are FDA-approved only for use in adults.

Codeine and tramadol medications have been shown to carry serious risks such as slowed or difficult breathing and death, especially in children under 12 years of age. Since 2013, the FDA has made multiple safety updates to the labeling of both codeine and tramadol containing medications in regards to their use in children and adolescents. The new FDA drug safety communication stated the following information for the labeling of these products:

- FDA's strongest warning, called a *Contraindication*, to the drug labels of codeine and tramadol alerting that codeine should not be used to treat pain or cough and tramadol should not be used to treat pain in children younger than 12 years.
- A new *Contraindication* to the tramadol label warning against its use in children younger than 18 years to treat pain after surgery to remove the tonsils and/or adenoids.
- A new *Warning* to the drug labels of codeine and tramadol to recommend against their use in adolescents between 12 and 18 years who are obese or have conditions such as obstructive sleep apnea or severe lung disease, which may increase the risk of serious breathing problems.
- A strengthened *Warning* to mothers that breastfeeding is not recommended when taking codeine or tramadol medicines due to the risk of serious adverse reactions in breastfed infants. These can include excess sleepiness, difficulty breastfeeding, or serious breathing problems that could result in death.

The Mississippi Division of Medicaid (DOM) Universal Preferred Drug List (UPDL) currently does not include any age limits for short-acting narcotics and has a minimum age limit of 18 for selected long-acting narcotics (Xartemis® XR and Zohydro® ER). The following Universal Preferred Drug List (UPDL) excerpt illustrates no current age restrictions for codeine and tramadol medications.

[1] U.S. Food and Drug Administration. FDA MedWatch Codeine and Tramadol Medicines: Drug Safety Communication Restricting Use in Children, Recommending Against Use in Breastfeeding Women. April 20, 2017.

Figure 1: Mississippi Medicaid UPDL Narcotic Analgesics[2]

PREFERRED AGENTS	NON-PREFERRED AGENTS		PA CRITERIA
ANALGESICS, NARCOTIC - SHORT ACTING			
Acetaminophen/codeine codeine dihydrocodeine/ APAP/caffeine hydrocodone/APAP hydromorphone IBUDONE (hydrocodone/ibuprofen) meperidine morphine oxycodone capsules oxycodone/APAP oxycodone/aspirin oxycodone/ibuprofen pentazocine/APAP tramadol tramadol/APAP	ABSTRAL (fentanyl) ACTIQ (fentanyl) butalbital/APAP/caffeine/codeine butalbital/ASA/caffeine/codeine butorphanol tartrate (nasal) DEMEROL (meperidine) DILAUDID (hydromorphone) fentanyl FENTORA (fentanyl) FIORICET W/ CODEINE (butalbital/APAP/caffeine/codeine) FIORINAL W/ CODEINE (butalbital/ASA/caffeine/codeine) hydrocodone/ibuprofen LAZANDA NASAL SPRAY (fentanyl) levorphanol LORCET (hydrocodone/APAP) LORTAB (hydrocodone/APAP) MAGNACET (oxycodone/APAP) NORCO (hydrocodone/APAP) NUCYNTA (tapentadol)	ONSOLIS (fentanyl) OPANA (oxymorphone) OXECTA (oxycodone) oxycodone tablets pentazocine/naloxone PERCOCET (oxycodone/APAP) PERCODAN (oxycodone/ASA) REPREXAINE (hydrocodone/ibuprofen) ROXICET (oxycodone/acetaminophen) RYBIX (tramadol) SUBSYS (fentanyl) SYNALGOS-DC (dihydrocodeine/ aspirin/caffeine) TYLENOL W/CODEINE (APAP/codeine) TYLOX (oxycodone/APAP) ULTRACET (tramadol/APAP) ULTRAM (tramadol) VICODIN (hydrocodone/APAP) VICOPROFEN (hydrocodone/ibuprofen) XODOL (hydrocodone/acetaminophen) ZAMICET (hydrocodone/APAP) ZOLVIT (hydrocodone/APAP) ZYDONE (hydrocodone/acetaminophen)	Quantity Limits Applicable quantity limit in 31 rolling days. • **62 tablets** - codeine, oxycodone/ibuprofen, meperidine, hydromorphone, fentanyl, butalbital/codeine combinations, morphine, tapentadol, dihydrocodeine combinations, tramadol, pentazocine • **62 tablets CUMULATIVE** - hydrocodone combinations, oxycodone combinations • **124 tablets** - butalbital/APAP 750 • **145 tablets** - butalbital/APAP 650 • **186 tablets** - butalbital/APAP 325, butalbital/ASA 325 • **5mL (2 x 2.5 bottles)** - butorphanol nasal • **180 mL CUMULATIVE** - oxycodone liquids • **480 mL CUMULATIVE** - hydrocodone liquids

PREFERRED AGENTS	NON-PREFERRED AGENTS		PA CRITERIA
ANALGESICS, NARCOTIC - LONG ACTING			
BUTRANS (buprenorphine) EMBEDA (morphine/naltrexone) fentanyl patches morphine ER tablets	ARYMO ER (morphine) NR BELBUCA (buprenorphine) CONZIP ER (tramadol) DOLOPHINE (methadone) DURAGESIC (fentanyl) EXALGO (hydromorphone) hydromorphone ER HYSINGLA ER (hydrocodone) KADIAN (morphine) methadone MORPHABOND (morphine) NR morphine ER capsules MS CONTIN (morphine) NUCYNTA ER (tapentadol) OPANA ER (oxymorphone) oxycodone ER OXYCONTIN (oxycodone) oxymorphone ER RYZOLT (tramadol)	tramadol ER ULTRAM ER (tramadol) XARTEMIS XR (oxycodone/APAP) XTAMPZA (oxycodone myristate) ZOHYDRO ER (hydrocodone bitartrate)	Minimum Age Limit • 18 years - Xartemis XR, Zohydro ER Quantity Limits Applicable quantity limit per rolling days • 31 tablets/31 days - Conzip ER, Exalgo ER, Hysingla ER, Ryzolt , Ultram ER • 62 tablets/31 days - Arymo ER, Embeda, Kadian, Methadone, Morphine ER, Opana ER, oxycodone ER, Oxycontin, Xtampza ER, Zohydro ER • 10 patches/31 days – Duragesic • 4 patches/31 days – Butrans • 40 tablets/10 days - Xartemis XR Xartemis XR MANUAL PA • Have tried 2 different preferred agents in the past 30 days • Maximum duration of therapy = 20 days per calendar year

MS-DUR examined the use of prescription medications containing codeine and tramadol during 2016 to determine their prevalence of use in the Mississippi Medicaid population.

2 Mississippi Division of Medicaid. Universal Preferred Drug List. Short/Long Acting Narcotic Analgesics. Effective July 1, 2017.

METHODS

A retrospective analysis was conducted using DOM's medical and pharmacy claims for the period January 2016 – December 2016. The analysis included data from the fee-for-service (FFS) program and the coordinated care organizations (CCOs). National drug codes (NDCs) for the drugs containing codeine or tramadol listed in the FDA safety alert were identified. All claims for these drugs were extracted. Beneficiary age was calculated at the end of the observation period (December 31, 2016). Medical claims were used to identify beneficiaries with a diagnosis of sleep apnea (ICD codes 327.2, 780.57, 780.53, 786.03, R06.81, G47.3) or having a tonsillectomy/adenoidectomy (CPT codes 42820, 42821, 42825, 42826, 42830, 42831, 42835, 42836, 42960, 42961, 42962, 42970, 42971, 42972). All beneficiaries who were enrolled for at least one month during the study period were included in the analysis. Beneficiaries were classified as receiving codeine or tramadol for pain after a tonsillectomy/adenoidectomy if there was a prescription claim for these medications within 3 days of the procedure. The list of prescription codeine and tramadol medicines published by the FDA was utilized for the analysis (Figure 2)

Figure 2: FDA List of Prescription Codeine and Tramadol Medicines[1]

Medicines Containing Codeine	Medicines Containing Tramadol
Codeine Sulfate	Conzip
Butalbital, Acetaminopen, Caffeine, and Codeine phosphate	Ultracet
Fiorinal with codeine	Ultram
Soma Compound with codeine	Ultram ER
Tylenol with codeine	Generic products containing tramadol
Promethazine with codeine (cough)	
Prometh VC with codeine (cough)	
Triacin-C (cough)	
Tuxarin ER (cough)	
Tuzistra-XR (cough)	
Generic products containing codeine	
Medicines Containing Dihydrocodeine	
Synalgos-DC	

RESULTS

Codeine and Tramadol Use in Children Under 12

Across all age groups, 4.9% of beneficiaries had claims for at least one prescription for codeine and 2.2% had claims for at least one prescription for tramadol (Table 1). Use of both medications was highest in adults 18 to 44 years of age (6.8% for codeine and 5.4% for tramadol) and adolescents 12 to 17 years of age (5.9% for codeine and 1.0% for tramadol). Only 58 children under age 12 had prescriptions for tramadol. However, 16,007 children under the age of 12 had prescription claims for codeine products.

TABLE 1: Use of Codeine and Tramadol by Age Group and Selected Conditions
(FFS and CCOs for Calendar Year 2016)

		Beneficiaries				
			Filling Codeine Prescription		Filling Tramadol Prescription	
	Age Group	Total				
Overall	TOTAL	863,709	42,663	4.9%	19,254	2.2%
	0 to 5	159,809	5,997	3.8%	4	0.0%
	6 to 11	158,281	10,010	6.3%	54	0.0%
	12 to 17	132,171	7,848	5.9%	1,288	1.0%
	18 to 44	207,754	14,182	6.8%	11,206	5.4%
	45 and above	205,694	4,626	2.3%	6,702	3.3%
Beneficiaries Having Tonsillectomy or Adenoidectomy*	TOTAL	5,507	371	6.7%	1	0.0%
	0 to 5	2,593	127	4.9%	0	0.0%
	6 to 11	1,989	203	10.2%	0	0.0%
	12 to 17	641	37	5.8%	0	0.0%
	18 to 44	270	4	1.5%	1	0.4%
	45 and above	14	0	0.0%	0	0.0%
Beneficiaries With Sleep Apnea Diagnois	TOTAL	11,542	1,037	9.0%	1,069	9.3%
	0 to 5	1,673	99	5.9%	0	0.0%
	6 to 11	1,169	116	9.9%	3	0.3%
	12 to 17	622	57	9.2%	11	1.8%
	18 to 44	2,789	368	13.2%	462	16.6%
	45 and above	5,289	397	7.5%	595	11.3%

** Prescription was filled within 3 days after the procedure was completed.*

Codeine and Tramadol Use Following Tonsillectomy/Adenoidectomy

A total of 5,223 beneficiaries under the age of 18 had a tonsillectomy or adenoidectomy during 2016. Of these beneficiaries, 367 (7.0%) had prescription claims for codeine within three days of the procedure. None of these beneficiaries had claims for a tramadol prescription.

Codeine and Tramadol Use in Children/Adolescents with Sleep Apnea

Based on medical claims, 3,464 beneficiaries under age 18 were identified as having a diagnosis of sleep apnea. Of these beneficiaries, 272 (7.9%) had prescriptions for codeine products and 11 (0.3%) had prescriptions for tramadol. Other conditions listed in the FDA warning for

codeine and tramadol such as obesity and severe lung disease, or cough were not included in this analysis due to difficulties identifying these conditions using administrative claims.

(update)

Analysis was conducted of claims between May 1 and August 31, 2017 – after the FDA warning was issued. During the four months following the FDA warning, we have observed a significant decrease in the percentage of children under age 12 being prescribed codeine overall, following tonsillectomy/adenoidectomy and when patients had sleep apneia.

TABLE 2: Use of Codeine and Tramadol by Age Group and Selected Conditions
(FFS and CCOs for May - August 2017)

		Beneficiaries				
	Age Group	Total	Filling Codeine		Filling Tramadol	
Overall	TOTAL	759,600	10,448	1.4%	7,769	1.0%
	0 to 5	156,633	1,081	0.7%	2	0.0%
	6 to 11	141,095	1,839	1.3%	33	0.0%
	12 to 17	118,125	1,867	1.6%	528	0.4%
	18 to 44	156,076	4,134	2.6%	4,081	2.6%
	45 and above	187,671	1,527	0.8%	3,125	1.7%
Beneficiaries Having Tonsillectomy or Adenoidectomy*	TOTAL	1,636	99	6.1%	8	0.5%
	0 to 5	920	24	2.6%	0	0.0%
	6 to 11	553	49	8.9%	1	0.2%
	12 to 17	195	16	8.2%	2	1.0%
	18 to 44	62	10	16.1%	3	4.8%
	45 and above	5	0	0.0%	2	40.0%
Beneficiaries With Sleep Apnea Diagnois	TOTAL	5,672	212	3.7%	310	5.5%
	0 to 5	591	5	0.8%	0	0.0%
	6 to 11	370	6	1.6%	2	0.5%
	12 to 17	278	7	2.5%	0	0.0%
	18 to 44	1,531	94	6.1%	116	7.6%
	45 and above	2,902	100	3.4%	192	6.6%

** Prescription was filled within 3 days after the procedure was completed.*

CONCLUSIONS AND RECOMMENDATIONS

(update)

During the observation period prior to the updated FDA safety notice, prescribing behaviors indicated changes needed to be made in order to be compliant with the new safety warning. Tramadol use in children and adolescents was not very common, but some cases did occur that were in conflict with the FDA recommended contraindications and warnings. Codeine use in children under age 12 years and in children/adolescents with sleep apnea was fairly high. Analysis of the four months following the safety warning indicate significant improvement has been made, but further actions are needed to more fully address this safety issue.

Recommendations:

1. DOM should set a minimum age limit of 12 years for tramadol and codeine products.

2. DOM should modify the short and long-acting narcotic electronic PA rules to require the following: *(added since July meeting)*

    a. A manual PA for beneficiaries under age 18 years with diagnosis of sleep apnea prescribed codeine or tramadol.
    b. A manual PA for beneficiaries under age 18 years prescribed codeine or tramadol within 3 days of tonsillectomy or adenoidectomy.

3. MS-DUR should implement an educational initiative to notify providers of the recent (April 20, 2017) FDA recommendations and the new clinical edits being implemented.

APPENDIX

PROVIDER EDUCATIONAL SUMMARY TO BE INCLUDED IN MAILINGS

Tramadol and Codeine Use In Pediatrics: A Review of Recent FDA Safety Alerts.

Megan Herink, Pharm.D, Drug Use Research and Management, Oregon State University College of Pharmacy

FDA Safety Update

The Food and Drug Administration (FDA) announced in April 2017 that children younger than 12 years should not take tramadol or codeine due to the risk of respiratory depression and death.[1] This announcement expands on FDA labeling updates from 2013 that codeine use is contraindicated in children younger than 18 to treat pain after tonsillectomy or adenoidectomy[2] and drug safety communications in 2015 warning about the risk of respiratory depression in some children who are rapid metabolizers of codeine or tramadol due to the cytochrome P450 2D6 (CYP2D6) variant.[3] A warning was also added to tramadol and codeine drug labeling to recommend against their use in adolescents age 12 to 18 who are obese or who have conditions such as obstructive sleep apnea or severe lung disease which could increase the risk for respiratory suppression with codeine or tramadol (Table 1).[1] Furthermore, the FDA recommends restriction of these drugs for children older than 12 years of age and strengthened its labeling recommendation that breastfeeding mothers not take either drug because breastfed children could also experience potentially fatal respiratory depression. This review will evaluate the evidence behind the recent FDA safety alerts and discuss the place in therapy of these opioids in children.

Table1: Summary of Recent FDA Label Changes for Codeine and Tramadol[1]

Contraindications:

- Codeine and tramadol should not be used to treat pain in children younger than 12 years
- Codeine and tramadol should not be used to treat pain after tonsillectomy or adenoidectomy in children younger than 18 years

Warnings

- Avoid use in adolescents between 12 to 18 years who are obese or have conditions such as obstructive sleep apnea or severe lung disease, which may increase the risk of breathing problems
- Breastfeeding is not recommend when taking codeine or tramadol due to the risks of serious adverse reactions in breastfed infants

Tramadol

Tramadol is an opioid medication that is pharmacologically similar to other opioids but has a lower affinity for μ-opioid receptors and also acts as a weak inhibitor of the neuronal reuptake of norepinephrine and serotonin.[4] It has been suggested that tramadol has a lower potential of abuse and dependence due to its relatively low affinity for μ-opioid receptor. The affinity for the μ-opioid receptor is 4000-fold less than that of morphine; however, tramadol has still been shown to cause significant withdrawal syndrome which can include both opioid and serotonin-norepinephrine reuptake inhibitor (SNRI) - associated withdrawal symptoms.[5] Tramadol is a prodrug metabolized via CYP2D6 to O-desmethyltramadol, which has a 200-fold greater affinity for the μ-opioid receptor compared to the parent drug.[6] Therefore, poor metabolizers often fail to have successful analgesia in response to tramadol and ultra-rapid metabolizers are at a higher risk for side effects due to higher concentrations (Table 2).[6]

Table 2: CYP2D6 Polymorphisms[6]

Phenotype	Prevalence	Clinical Effect
Poor Metabolizer	5-10%	Insufficient Pain Relief
Intermediate Metabolizer	2-11%	Expected analgesia
Extensive Metabolizer	77-92%	Expected analgesia
Ultra-rapid metabolizer	1-2%	Potential for toxicities

In 2014, the U.S. Drug Enforcement Agency (DEA) scheduled tramadol as a Schedule IV substance.[7] The DEA reviewed available data and concluded that tramadol produces similar pharmacological effects as other opioids, including analgesia and respiratory depression. Since tramadol also inhibits reuptake of serotonin and norepinephrine, additional safety concerns include the risk of serotonin syndrome and an increased risk of seizures.[5,8] However, the most common adverse reactions with tramadol include nausea, dizziness, and vomiting.

Although tramadol is not approved by the FDA for use in children under 18 years of age, it is commonly used off-label because it is assumed to be safer and less potent than other opioids.[9] In 2014, nearly 167,000 children in the U.S. received a prescription for a tramadol-containing product from outpatient retail pharmacies.[1] However, there is a lack of evidence for efficacy and safety in this population. A Cochrane systematic review evaluated the effectiveness and side effect profile of tramadol for postoperative pain relief in children and adolescents undergoing surgical procedures.[10] Evidence from 5 trials found that the need for rescue analgesia in the postoperative care unit was reduced in children receiving tramadol compared to placebo (RR 0.40; 95% CI 0.20 to 0.78).[10] However, overall strength of the evidence was low or very low due to small sample sizes, methodological problems, and an inability to perform an accurate risk-benefit analysis since adverse events were poorly reported.[10]

Tramadol FDA Warning:

The FDA reviewed data from January 1969 to March 2016 which identified 9 cases worldwide of respiratory depression in children younger than 18 years of age, including 3 deaths.[1] With the exception of a 15-year-old treated for multiple days with tramadol, respiratory depression occurred within the first 24 hours of drug administration.

The 3 fatalities occurred in children younger than 6 years of age. Elevated serum tramadol concentrations were noted in all 3 cases. The indications for tramadol in these 3 children were to treat pain after tonsillectomy, pain after clubfoot surgery, and to manage fever.

In one fatal case where the CYP2D6 genotype was identified, a 5-year-old child was prescribed a single tramadol dose in the evening post-tonsillectomy. A urine sample showed increased metabolite concentrations. Genotyping of CYP2D6 was conducted, and 3 functional alleles were found that were consistent with ultra-rapid metabolism.[1]

One non-fatal case involved a 6-year-old who was prescribed tramadol for neuropathy of the hands and feet. After the third dose, the patient experienced respiratory depression and was unresponsive. The patient fully recovered after receiving two doses of naloxone.

Four other non-fatal cases reported in teenagers using tramadol for musculoskeletal pain or sciatica described unresponsiveness or somnolence after one or a few doses of tramadol; all required medical intervention.

A review of the available medical literature for data regarding tramadol use during breastfeeding did not reveal any cases of adverse events. However, tramadol and its active metabolite are present in breast milk and caution is advised in breastfeeding mothers.

Codeine

Codeine is another opioid analgesic often combined with acetaminophen for moderate pain relief in adults. Its analgesic effect comes from the demethylation of codeine into morphine. It offers unpredictable analgesia and requires conversion to morphine by CYP2D6. Like tramadol, its conversion is subject to wide genetic variation leading to either poor pain control in slow metabolizers or high risk of overdose in ultra-rapid metabolizers. Codeine is also used to manage cough and is typically combined with promethazine or other cold medications found in over-the-counter products. Codeine depresses the cough reflex by direct effect on the cough center in the medulla. However, there are no well-controlled scientific studies in children, and therefore, the evidence to support efficacy in reducing cough is limited. In 2014, 1.9 million pediatric patients received a prescription for a codeine product from U.S. outpatient retail pharmacies. [1] Of the total pediatric patients, nearly 1.4 million patients received codeine-containing analgesic products, and 483,000 patients received codeine containing cough-and-cold products. [1] Interestingly, prescriptions for codeine-containing products only slightly decreased in frequency between 2001 and 2010, despite convincing studies documenting their lack of benefit and serious adverse effects.[3]

Codeine FDA Warning:

The FDA reviewed adverse event reports submitted to the FDA from January 1969 to May 2015 and identified 64 cases of serious breathing problems and 24 deaths with codeine or codeine-containing medicines in children younger than 18 years of age. Fifty of these cases were in children under the age of 12 years. Respiratory depression occurred after a median of 5 doses in these cases (range of one to 18). [1]

The most commonly reported products used in reported cases of breathing problems were acetaminophen with codeine used for pain and promethazine with codeine used for cough and cold. Of the 24 deaths, the majority (21) occurred in children under 12 who received codeine for pain post tonsillectomy or adenoidectomy, other post-operative pain, general pain, sore or strep throat pain and cough and cold.[1] There were also numerous cases of excess sleepiness and serious breathing problems in breastfed infants from women taking codeine, including one death. The first case report of a death in a nursing infant from codeine was published in 2006.[11]

Only 10 cases included information regarding CYP2D6 genotype. However, 7 of the 10 identified cases were ultra-rapid metabolizers, of whom 5 died. The other 3 identified patients were considered extensive metabolizers, which including one death. There were limited data to evaluate an association between codeine or morphine blood levels and respiratory depression. Only 15 of the 64 cases reported drug levels, but 13 were above the therapeutic range.

Summary

Codeine and tramadol are problematic since they are metabolized by the CYP2D6 hepatic enzymes. The prevalence of the ultra-rapid CYP2D6 phenotype varies widely and has been estimated at 0.5 to 1% in Chinese and Japanese, 0.5 to 1% in Hispanics, 1 to 10% in Caucasians, 3% in African Americans, and 16 to 28% in North Africans, Ethiopians, and Arabs. Data are not currently available for other ethnic groups.[1]

Although the strongest risk of respiratory depression and death are in the ultra-rapid metabolizers of CYP2D6, routine genotyping prior to therapy is not recommended at this time. According to the FDA, this is for several reasons. First, extensive metabolizers may convert codeine to morphine at levels similar to ultra-rapid metabolizers. Also, the positive predictive value of the test is likely low, and the number needed to screen to prevent one event is very high. Lastly, genotyping is difficult to implement routinely.

All tramadol and single-ingredient codeine products are only FDA-approved for use in adults. These therapies should be avoided in children, particularly those under 12 years of age and adolescents less than 18 years with risk factors for respiratory depression, obesity, obstructive sleep apnea or severe lung disease.

There are several alternative analgesics, including non-opioids that are not affected by CYP2D6 metabolism. Tramadol, codeine, and to a lesser extent hydrocodone and oxycodone all require CYP2D6 for metabolism and could accumulate in ultrarapid metabolizers. Any opioid should be used cautiously in pediatric patients with obstructive sleep apnea. If an opioid is needed, the lowest effective weight-based dose should be used for acute pain on an as-needed basis. Acetaminophen or ibuprofen should be recommended for mild or moderate pain.

For the treatment of cough, patients should be educated that cough is usually self-limiting in children, related to an underlying infection and does not require treatment is important. Additional treatment options include fluids, humidity, and honey for children one year or older. All cough and cold medicines should be avoided in children < 6 years of age since the risk of side effects outweighs benefit.

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CYTOKINE AND CAM ANTAGONIST UTILIZATION IN MISSISSIPPI MEDICAID

CARRIED OVER FROM JULY 2017 DUR BOARD MEETING WITH UPDATES

BACKGROUND

Cytokine and cell-adhesion molecule (CAM) antagonists have a major role in the treatment of chronic inflammatory diseases such as rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, plaque psoriasis and inflammatory bowel disease. Utilization of this class of medications continues to increase. Pharmacy payers across the United States are tasked with the responsibility of ensuring these medications are appropriately prescribed.

Mississippi Division of Medicaid's (DOM) current Universal Preferred Drug List (UPDL) for this class of medications is shown below. Presently, Cosentyx®, Enbrel®, Humira® and generic methotrexate are preferred products.

DOM Universal Preferred Drug List – Effective 7-1-2017

CYTOKINE & CAM ANTAGONISTS			
	COSENTYX (secukinumab) SmartPA ENBREL (etanercept) HUMIRA (adalimumab) methotrexate	ACTEMRA (tocilizumab) CIMZIA (certolizumab) ENTYVIO (vedolizumab) ILARIS (canakinumab) INFLECTRA (infliximab) KINERET (anakinra) ORENCIA (abatacept) OTEZLA (apremilast) OTREXUP (methotrexate) RASUVO (methotrexate) REMICADE (infliximab) RHEUMATREX (methotrexate) SILIQ (brodalumab) NR SIMPONI (golimumab) STELARA (ustekinumab) TALTZ (ixekizumab) TREXALL (methotrexate) XELJANZ (tofacitinib) XELJANZ XR (tofacitinib)	Orencia IV Infusion, Remicade IV Infusion and Stelara (first dose) are for administration in hospital or clinic setting. PA will not be issued at Point of Sale without justification. **Cosentyx** • ≥ **18 years** = Minimum Age • Documented diagnosis of plaque psoriasis, psoriatic arthritis or ankylosing spondylitis in the past 2 years **AND** • 90 consecutive days of Humira in the past year

MS-DUR reviewed prior authorization (PA) criteria for cytokine and CAM antagonists across Medicaid programs and health plans in several states. Many of these programs require a prior authorization process for these medications. All PA forms examined included requirements for approved diagnoses according to the FDA labeling and for other conditions, required prior failure with other products (step-therapy). Step therapy examples included the following: 1) for Crohn's and ulcerative colitis- failure on corticosteroids, aminosalicylates, or immunomodulators; 2) for rheumatoid arthritis- failure on methotrexate and/or disease-modifying antirheumatic drugs (DMARDs).

Due to increasing utilization for this category, MS-DUR examined cytokine and CAM antagonist utilization to determine if additional criteria might be needed to appropriately manage this class of medications.

METHODS

A retrospective analysis was conducted using Mississippi Medicaid medical and pharmacy claims for the period January 2016 – May 2017. The analysis included data from the fee-for-service (FFS) program and the coordinated care organizations (CCOs). Pharmacy and office-administered medical claims for all drugs listed in the Cytokine & CAM Antagonists class in the UPDL were extracted. Utilization and program payments were examined monthly. Since there is not a current diagnosis check, beneficiaries with paid claims for Enbrel® and Humira® were evaluated for the presence of an approved diagnosis in the medical claims during the time period examined.

RESULTS

Type of Claims

Table 1 provides the number of claims from this class with the majority accounted for in the pharmacy point-of-sale (POS) system. Remicade® was almost exclusively office-administered. Simponi®, Orencia® and methotrexate had both medical and pharmacy claims. Enbrel® and Humira® are almost always paid through the POS system and can be easily managed through an electronic or manual PA.

TABLE 1: Number of Claims by Type and Drug
(January 2016 - May 2017)

	FFS		UHC		MAG	
	Type of Claim		Type of Claim		Type of Claim	
Drug	Medical	Pharmacy	Medical	Pharmacy	Medical	Pharmacy
TOTAL for class	263	2,441	124	3,668	523	4,725
Actemra (tocilizumab)	9	3	22	26	50	4
Cimzia (certolizumab)	0	6	0	15	16	30
Cosentyx (secukinumab)	0	5	0	22	0	79
Enbrel (etanercept)	0	308	0	494	0	682
Entyvio (cwsoliumV)	3	2	8	0	13	0
Humira (adalimumab)	1	504	0	1,086	0	1,081
Ilaris (canakinumab)	0	7	0	6	0	0
Kineret (anakinra)	0	19	0	4	0	4
Orencia (abatacept)	23	28	17	18	24	34
Otezla (apremilast)	0	35	0	59	0	75
Otrexup/Rrasuvo/Trexall/ Rheumatrex (methotrexate)	0	2	0	26	0	15
Remicade (infliximab)	90	0	53	3	245	0
Simponi (golimumab)	20	12	0	21	4	23
Stelara (ustekinumab)	5	3	0	4	3	23
Taltz (ixekizumab)	0	0	0	1	0	8
Xeljanz/Xeljanz XR (tofacitinib)	0	50	0	97	0	70
methotrexate	112	1,457	24	1,796	169	2,597

Utilization and Payment Trends

Table 2 shows the total number of claims for each drug in this class by month. From January 2016 to May 2017 there has been a 37% increase in total claims for this class. This has been primarily driven by a 54% increase in claims for Humira® and a 43% increase in claims for Enbrel®.

TABLE 2: Number of Prescriptons and Office-Administered Claims by Drug and Month
(Includes FFS and CCOs)

	Month Filled / Administered																
Drug	**Jan-16**	**Feb-16**	**Mar-16**	**Apr-16**	**May-16**	**Jun-16**	**Jul-16**	**Aug-16**	**Sep-16**	**Oct-16**	**Nov-16**	**Dec-16**	**Jan-17**	**Feb-17**	**Mar-17**	**Apr-17**	**May-17**
TOTAL for class	571	633	644	589	649	682	668	735	702	769	697	699	728	702	791	742	742
methotrexate	315	362	357	324	370	384	371	388	359	404	360	339	365	354	382	361	360
Humira (adalimumab)	123	136	137	129	141	143	136	158	156	183	157	176	176	172	193	173	183
Enbrel (etanercept)	72	65	81	82	75	78	85	94	94	93	93	82	89	81	117	98	105
Remicade (infliximab)	19	24	26	17	15	24	17	23	26	25	22	24	30	27	25	27	20
Orencia (abatacept)	8	8	7	5	2	7	7	12	6	4	6	11	8	7	9	14	13
Xeljanz/Xeljanz XR (tofacitinib)	11	6	10	8	13	11	15	15	14	16	15	17	9	15	16	15	11
Otezla (apremilast)	3	7	6	6	10	8	9	11	15	13	14	12	11	10	10	12	12
Cosentyx (secukinumab)	2	2	2	5	8	8	10	9	8	5	7	4	5	5	6	11	9
Stelara (ustekinumab)	0	2	0	0	1	2	2	1	3	2	1	5	2	4	5	2	6
Simponi (golimumab)	6	7	4	4	6	4	2	4	4	4	5	5	4	6	4	4	7
Actemra (tocilizumab)	4	5	8	3	1	5	4	9	5	10	7	12	10	9	9	10	6
Cimzia (certolizumab)	4	6	3	4	2	3	4	5	6	3	3	4	4	4	3	2	3
Otrexup/Rrasuvo/Trexall/ Rheumatrex (methotrexate)	0	0	0	0	1	2	2	4	2	5	3	4	5	3	4	5	3
Kineret (anakinra)	2	2	1	1	2	2	2	1	1	1	2	1	2	1	1	3	2
Entyvio (vedolizumab)	0	0	0	1	0	0	0	0	2	0	2	2	5	3	6	4	1
Taltz (ixekizumab)	0	0	0	0	0	0	0	1	1	1	0	1	2	0	1	1	1
Ilaris (canakinumab)	2	1	2	0	2	1	2	0	0	0	0	0	1	1	0	0	0

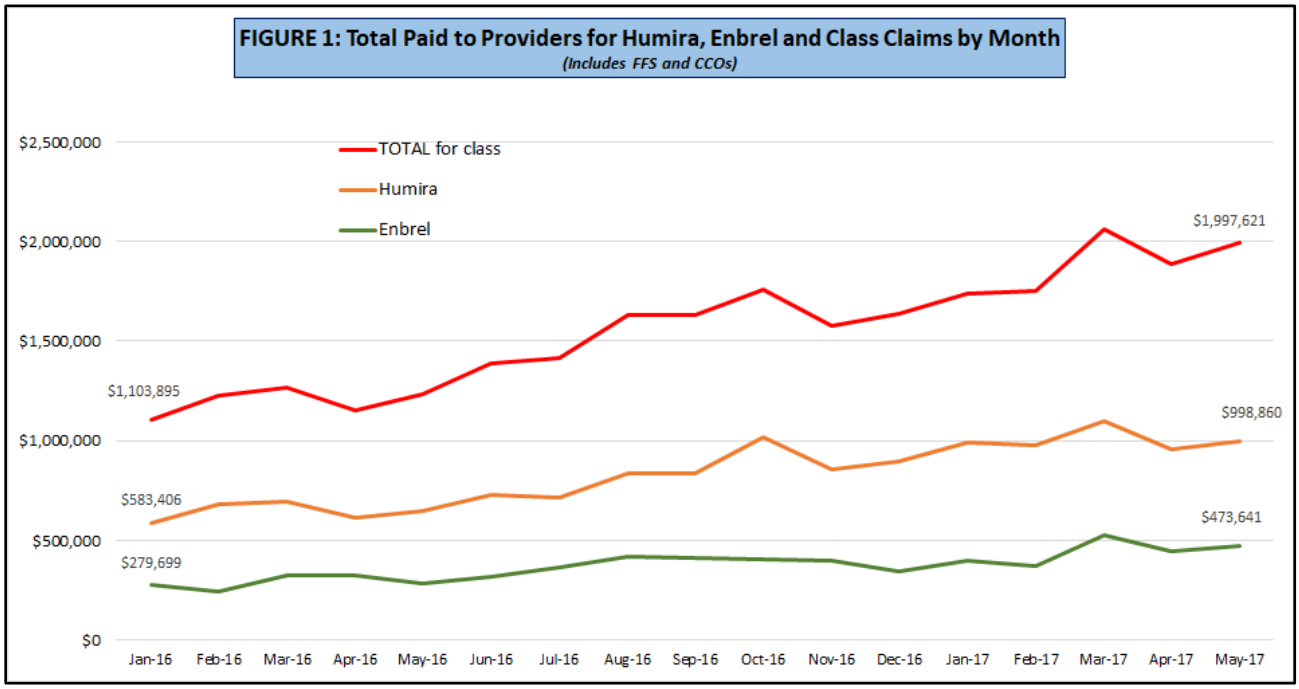
Table 3 provides details regarding the total monthly payment for each drug in this class. From January 2016 to May 2017 there has been a 97% increase in the total amount paid for drugs in this class. Increased utilization shown in Table 2 accounts for some of the increase. However, increases in the average cost per prescription and the introduction of newer more costly medications have been responsible for most of the increase in the total paid. The cost per prescription for Humira® increased 16.6% from $4,743 to $5,528 and Enbrel had a 16.1% increase from $3,885 to $4,512 per prescription. Although Stelara® is currently used by only a few beneficiaries, at an average prescription cost of $15,000 to $18,000, its use has contributed significantly to the total amount paid in this category.

TABLE 3: Total Paid to Providers for Prescriptions and Office-Administered Claims by Drug and Month
(Includes FFS and CCOs)

	Month Filled / Administered																
Drug	**Jan-16**	**Feb-16**	**Mar-16**	**Apr-16**	**May-16**	**Jun-16**	**Jul-16**	**Aug-16**	**Sep-16**	**Oct-16**	**Nov-16**	**Dec-16**	**Jan-17**	**Feb-17**	**Mar-17**	**Apr-17**	**May-17**
TOTAL for class	$1,103,895	$1,225,921	$1,270,043	$1,154,342	$1,231,575	$1,386,378	$1,417,200	$1,631,434	$1,633,154	$1,758,197	$1,574,970	$1,636,473	$1,738,241	$1,749,602	$2,064,574	$1,890,590	$1,997,621
methotrexate	$9,926	$11,059	$11,465	$10,578	$13,562	$13,624	$11,646	$12,284	$11,028	$11,998	$10,399	$9,773	$10,716	$10,391	$11,205	$10,203	$10,367
Humira (adalimumab)	$583,406	$680,532	$693,888	$612,169	$649,784	$725,964	$713,295	$839,060	$834,714	$1,020,817	$855,316	$899,491	$990,264	$980,189	$1,099,057	$956,773	$998,860
Enbrel (etanercept)	$279,699	$244,931	$322,765	$324,299	$285,225	$316,942	$366,097	$417,458	$411,134	$404,676	$398,082	$346,133	$401,116	$370,515	$527,315	$446,367	$473,641
Remicade (infliximab)	$68,903	$92,466	$89,509	$59,559	$54,931	$78,179	$64,855	$85,231	$109,045	$92,689	$100,149	$91,291	$109,167	$101,771	$106,977	$174,583	$149,280
Orencia (abatacept)	$27,515	$27,513	$22,466	$17,349	$3,356	$19,632	$21,252	$41,436	$22,308	$13,039	$20,959	$36,156	$27,408	$24,781	$31,778	$43,922	$49,437
Xeljanz/Xeljanz XR (tofacitinib)	$33,636	$20,085	$33,476	$26,781	$43,519	$40,299	$54,953	$54,953	$51,289	$58,616	$54,953	$62,280	$36,083	$60,139	$64,148	$60,139	$44,102
Otezla (apremilast)	$7,600	$17,732	$15,199	$15,597	$27,320	$21,856	$24,588	$30,051	$40,979	$35,515	$38,247	$32,783	$30,811	$29,218	$29,218	$37,091	$37,497
Cosentyx (secukinumab)	$7,723	$8,256	$8,256	$45,403	$70,168	$61,914	$54,487	$51,514	$34,345	$34,342	$30,052	$17,172	$21,465	$38,634	$31,081	$49,375	$53,922
Stelara (ustekinumab)	$0	$26,699	$0	$0	$9,336	$25,657	$28,008	$15,241	$43,248	$16,572	$9,336	$71,256	$10,616	$63,395	$77,275	$30,220	$105,900
Simponi (golimumab)	$22,695	$29,539	$12,513	$16,166	$24,968	$16,917	$8,051	$25,312	$19,088	$17,743	$19,137	$21,661	$19,383	$18,339	$20,118	$15,582	$30,508
Actemra (tocilizumab)	$7,170	$4,301	$11,946	$3,611	$119	$12,301	$12,442	$22,815	$12,237	$26,154	$13,463	$18,582	$15,250	$16,390	$13,380	$14,811	$9,695
Cimzia (certolizumab)	$13,813	$21,197	$10,598	$14,131	$7,066	$10,598	$14,831	$16,771	$20,479	$10,239	$10,239	$13,947	$14,613	$14,613	$10,726	$6,823	$10,710
Otrexup/Rrasuvo/Trexall/ Rheumatrex (methotrexate)	$0	$0	$0	$0	$412	$886	$886	$2,456	$1,035	$3,079	$1,982	$2,132	$2,992	$1,721	$2,447	$3,188	$1,500
Kineret (anakinra)	$7,699	$7,699	$3,849	$3,849	$7,699	$7,699	$7,699	$3,849	$3,849	$3,849	$7,699	$3,849	$7,814	$3,907	$3,907	$15,625	$11,717
Entyvio (vedolizumab)	$0	$0	$0	$4,851	$0	$0	$0	$0	$9,707	$0	$4,957	$5,246	$26,184	$15,402	$31,224	$21,171	$5,439
Taltz (ixekizumab)	$0	$0	$0	$0	$0	$0	$0	$13,001	$8,668	$8,668	$0	$4,720	$14,160	$0	$4,720	$4,720	$5,046
Ilaris (canakinumab)	$34,112	$33,912	$34,112	$0	$34,112	$33,912	$34,112	$0	$0	$200	$0	$0	$200	$200	$0	$0	$0

NOTE: Total paid are reimbursement amounts paid to providers and are not representative of final Medicaid costs after rebates.

Figure 1 provides a graphical presentation of the increases in the total amount paid for this category of drugs from Jan 2016 through May 2017.



Presence of Diagnoses to Support Use of Enbrel® and Humira®

Table 4 summarizes the various FDA approved indications for Enbrel® and Humira®. Medical claims for beneficiaries taking these two products were examined to determine whether diagnoses were present that supported use for an approved indication. Of note, medical diagnoses searches can only be reviewed for the previous two years within the current electronic PA system. Consequently, only diagnoses that appeared in the last two years and occurred during the observation period were examined for the utilization of these products.

TABLE 4: Approved Indications for Enbrel and Humira

Indication	Enbrel	Humira
Rheumatoid arthritis	X	X
Juvenile idiopathic arthritis	X	X
Psoriatic arthritis	X	X
Plaque psoriasis	X	X
Alkylosing spondylitis	X	X
Adult Crohn's disease		X
Pediatric Crohn's disease		X
Ulcerative colitis		X
Hidradenitis suppurativa		X
Uveitis		X

(Updated) As shown in Table 5, both Humira® and Enbrel® claims were broken down by the number of vials and diagnosis associated with each claim. A typical Humira maintenance dose should be 2 vials which corresponds to the majority of its use. With Humira®, loading doses of 4 or 6 vials is standard in the initiation of therapy in Crohn's disease, plaque psoriasis, hidradenitis suppurativa, ulcerative colitis, and uveitis. Maintenance doses can go up to 4 vials monthly in

rheumatoid arthritis and hidradenitis suppurativa and up to 8 vials for Crohn's disease exacerbations. Enbrel® dosing is typically 4 vials monthly. There are no approved loading doses for Enbrel®. The only approved dose above 4 vials monthly is for severe plaque psoriasis where the dose can go up to 8 vials monthly for 3 months. Highlighted in the table are the only instances noted where dosing may have been outside of accepted quantities.

(Updated table)

Table 5. Number of Vials Per Claim by Drug and Diagnosis*
(January 2016 - July 2017 -- FFS and CCOs)

Drug	Diagnosis	Number of Vials Per Claim				
		1 vial	2 vials	4 vials	6 vials	8 vials
Humira (adalimumab)	Crohn's Disease	0	596	62	47	0
	Plaque Psoriasis	0	368	116	5	0
	Rheumatoid Arthritis	0	962	80	3	0
	Hidradenitis Suppurativa	0	31	163	26	1
	uvenile Idiopathic Arthriti	0	72	35	0	0
	Psoriatic Arthritis	0	35	2	0	0
	Ankylosing Spondylitis	0	41	0	0	0
	Ulcerative Colitis	0	128	10	11	0
	Uveitis	0	6	1	0	0
	Unknown	0	187	27	7	0
Enbrel (etanercept)	Crohn's Disease*	0	0	9	0	0
	Plaque Psoriasis	11	0	268	0	95
	Rheumatoid Arthritis	19	24	1048	0	0
	Hidradenitis Suppurativa*	2	0	17	0	0
	uvenile Idiopathic Arthriti	15	0	97	0	0
	Psoriatic Arthritis	0	0	2	0	0
	Ankylosing Spondylitis	0	0	1	0	0
	Unknown	14	0	49	0	4

** Diagnosis was found in medical claims prior to prescription fill.*
*** Diagnoses for which Enbrel does not have FDA approval.*

CONCLUSIONS AND RECOMMENDATIONS *(Updated)*

The Cytokine & CAM class experienced a 37% increase in utilization and a 97% increase in total amount paid for claims for the observation period. The increase in total paid can be attributed to an increase in utilization, price increases for the leading products, and the introduction of newer and more expensive medications. With the introduction of new medications and a focused effort from pharmaceutical manufacturers on product marketing, this trend will continue. As an initial focus for management of these products, MS-DUR suggests the following recommendations to the DUR Board.

Recommendations: *(Updated)*

1. MS-DUR should continue to monitor this category of drugs to ensure providers continue following recommended prescribing in regards to diagnosis and dose.

GABAPENTIN AND PREGABALIN USE IN MISSISSIPPI MEDICAID

Prepared by University of Mississippi MS-DUR
Version 10/11/2017

BACKGROUND

The prescribing of gabapentin and pregabalin, collectively referred to as gabapentinoids, has risen sharply in recent years. In 2016, gabapentin was the 10th most commonly prescribed medication in the United States with 64 million prescriptions dispensed, up from 39 million in 2012. Additionally, pregabalin (Lyrica) sales in dollars more than doubled from 2012 to 2016 to $4.4 billion nationally.[1] These medications consistently rank in the top 10 drug categories by dollars paid monthly by Mississippi's Division of Medicaid (DOM).

Gabapentin is FDA approved for the treatment of partial onset seizures, with and without secondary generalization, in adults and pediatric patients ≥ 3 years of age and in the management of postherpetic neuralgia in adults.[2] Pregabalin is FDA approved for the management of neuropathic pain associated with diabetic peripheral neuropathy or spinal cord injury, postherpetic neuralgia, partial onset seizures in adults, and fibromyalgia.[3] Both medications are increasingly being prescribed for non-FDA approved indications, particularly for the management of various pain syndromes.

Increased prescribing of gabapentin and pregabalin may be due in part to clinicians seeking alternatives to opioids in the treatment of pain. Prescription drug misuse or abuse is a growing problem in the United States. According to the National Institute on Drug Abuse, results from a 2014 survey report estimate that 52 million Americans (approximately 20% of the U.S. population age ≥ 12 years) have used a prescription medication for nonmedical purposes.[4] Opioid abuse is largely implicated in this trend. With recent attention focused on the opioid crisis, many clinicians are looking to gabapentinoids as additional options to treat pain. These medications can be used to decrease or eliminate opioid use in certain patients. However, there is evidence of increasing abuse of gabapentin and pregabalin. Literature reviews referencing gabapentinoid abuse cite a 1.6% prevalence of gabapentinoid abuse in the general population. Within populations of people who abuse opioids, the prevalence of gabapentinoid abuse increased to 15-22%.[5,6]

[1] Goodman,C and Brett, Allan. "Gabapentin and pregabalin for pain – Is increased prescribing a cause for concern?" N Engl J Med 2017; 377:411-414.
[2] Neurontin® [package insert]. New York: Pfizer, Inc. 2015.
[3] Lyrica® [package insert]. New York: Pfizer, Inc. 2016.
[4] Volkow ND. National Institute of Health National Institute on Drug Abuse. https://www.drugabuse.gov/publications/research-reports/prescription-drugs/director. (last updated Aug 2016)
[5] Evoy, Kirk E., Megan D. Morrison, and Stephen R. Saklad. "Abuse and misuse of pregabalin and gabapentin." *Drugs* (2017): 1-24.
[6] Smith, Rachel V., Jennifer R. Havens, and Sharon L. Walsh. "Gabapentin misuse, abuse and diversion: a systematic review." *Addiction* 111.7 (2016): 1160-1174.

The mechanism of action of gabapentinoids and the association with abuse is not fully understood. Gabapentin and pregabalin are both analogues of gamma-aminobutyric acid (GABA), a neurotransmitter that slows down the activity of nerve cells in the brain. While these medications do not directly bind to GABA receptors, they are thought to exert GABA-mimetic properties. They share many similarities with other medications associated with abuse potential in that they produce withdrawal syndrome and certain psychoactive effects.[7]

Due to the potential for abuse, MS-DUR examined use of gabapentinoids in DOM beneficiaries. The analysis included reviewing the daily dosage ranges prescribed, diagnoses and concomitant opioid use.

METHODS

A retrospective analysis was conducted for the period of January 1, 2017 through June 30, 2017 using DOM prescription claims data from the Fee For Service (FFS) and the two coordinated care organizations, United Healthcare (UHC) and Magnolia (MAG). Claims were identified using national drug codes (NDC) for gabapentin and pregabalin. For beneficiaries with claims for these gabapentinoids during the study period, any concurrent claims for opioids were also identified. For gabapentinoid claims that had a concomitant opioid claim, days of overlap were calculated. Each beneficiary's gabapentinoid claim was assessed to determine if it can be classified as an early refill, based on the previous prescription fill date and the days of medication supplied for that previous claim. For each gabapentinoid claim, the daily dosage level was calculated based on the strength of the medication filled, quantity supplied, and days of supply. Daily dosage levels were also categorized.

RESULTS

Table 1 provides an overview of claims for gabapentin and pregabalin as well as concomitant opioid use. During the 6 month observation period, 177 claims were processed for a daily dosage > 3600mg, the maximum FDA approved daily dose. For pregabalin, the maximum FDA approved daily dose is 600mg. A total of 65 pregabalin claims were processed for a daily dosage >600mg during the 6 month observation period. More than 50% of gabapentinoid claims in this timeframe are associated with concomitant opioid use.

[7] Schifano F. Misuse and abuse of pregabalin and gabapentin: cause for concern? CNS Drugs. 2014;28:491–6.

Table 1: Prescription Claims for Gabapentinoids and Concomitant Opioid Use (January 1, 2017 thru June 30, 2017 - FFS and CCOs)						
Drug	**Daily Dosage levels**	**Total # Claims**	**Claims With Concomitant Opioid Use**	**% of Claims With Concomitant Opioid Use**	**Mean Days of Overlap**	**# Claims with Early Refills (%)**
Gabapentin	< 1200 mg	21,809	11,427	52%	24.6	11,445 (26.3)
	1200 mg - 2400 mg	19,380	11,606	60%	24.8	
	2400 mg - 3600 mg	2,185	1,327	61%	23.6	
	> 3600 mg	177	126	71%	27.3	
Pregabalin	0 - 600 mg	8,420	5,696	68%	24.8	2,360 (27.8)
	601 mg - 1200 mg	63	34	54%	21.9	
	1200 mg - 2400 mg	2	2	100%	4.0	

Table 2 illustrates the daily dosing for total gabapentinoid prescriptions by DOM's three pharmacy programs. There was a noticeable difference in the number of claims for daily dosage > 3600mg of gabapentin in FFS as compared to UHC and MAG. In regards to pregabalin, both UHC and MAG had substantially more claims for a daily dosage > 600mg compared to FFS.

Table 2: Number of Prescriptions By Dose Level and Pharmacy Program (January 1, 2017 thru June 30, 2017)				
		Pharmacy Program		
Drug	**Daily Dosage Level**	**FFS**	**UHC**	**MAG**
Gabapentin	< 1200 mg	4,495	7,400	9,914
	1200 mg - 2400 mg	3,354	6,840	9,186
	2401 mg - 3600 mg	73	1,014	1,098
	> 3600 mg	114	45	18
Pregabalin	0 - 600 mg	1,670	3,110	3,648
	601 mg - 1200 mg	4	21	38
	1201 mg - 2400 mg	0	1	1

Table 3 displays the prevalence of appropriate diagnoses present in medical claims. Appropriate diagnoses were determined by both FDA-approved diagnoses for each agent or an acceptable diagnoses supported by CMS approved pharmacy compendia. Approximately two-thirds of gabapentinoid prescriptions did not have an appropriate diagnosis found in the medical claims. Through MS-DUR's literature review, follow-up discussions with providers support that gabapentinoids are often used in various pain syndromes to reduce or eliminate the use of opioids.

Table 3: Prevalence of Appropriate Diagnoses for Gabpentinoid Claims by Pharmacy Program (January 1, 2017 thru June 30, 2017)		
Plan	Number of gabapentinoid claims	Percent of claims associated with appropriate diagnoses*
FFS	9,758	31.3%
UHC	18,454	33.2%
MAG	23,911	33.4%

** Appropriate diagnosis found in medical claims.*

CONCLUSIONS AND RECOMMENDATIONS:

There is substantial evidence supporting the increased utilization of the gabapentinoid class of medications in recent years. Although providers may use these medications to limit opioid prescribing, these agents are not void of potential side effects. Data shows that although there is not significant use of these products above FDA recommended dosing for DOM beneficiaries, it does occur on a limited basis. Based on current utilization patterns for these products, MS-DUR proposes the following recommendations to the DUR Board for consideration.

Recommendations:

1. DOM should set a maximum daily dosage of 3600mg for gabapentin products.

2. DOM should set a maximum daily dosage of 600mg for pregabalin products.

3. DOM should conduct a one-time educational mailing outlining the proposed changes to include all prescribers writing gabapentin and pregabalin prescriptions during the last six months that exceeded the recommended maximum daily dosage limits.

4. DOM should monitor concomitant opioid use with pregabalin /gabapentin claims to determine impact of pregabalin/gabapentin on reducing or eliminating opioids.

HIGH DOSE OPIOID PRESCRIBING TREND
JANUARY 2016 – AUGUST 2017
(FFS and CCOs)

BACKGROUND

In March of 2016, the Centers for Disease Control (CDC) released the final version of their Guidelines for Prescribing Opioids for Chronic Pain.[1] During the April 2016 DUR Board meeting, a summary of these recommendations and the claims data regarding how opioid prescribing for Mississippi Division of Medicaid (DOM) beneficiaries aligned with applicable CDC recommendations was presented. The following CDC recommendation addressed the prescribing of opioids with high morphine equivalent daily (MEDD) doses.

> *When opioids are started, clinicians should prescribe the lowest effective dosage. Clinicians should use caution when prescribing opioids at any dosage, should carefully reassess evidence of individual benefits and risks when increasing dosage to ≥50 morphine milligram equivalents (MME)/day, and should avoid increasing dosage to ≥90 MME/day or carefully justify a decision to titrate dosage to ≥90 MME/day.*

In response to the data presented and the above CDC recommendation, the DUR Board made the following recommendation related to MEDD doses for opioid prescriptions:

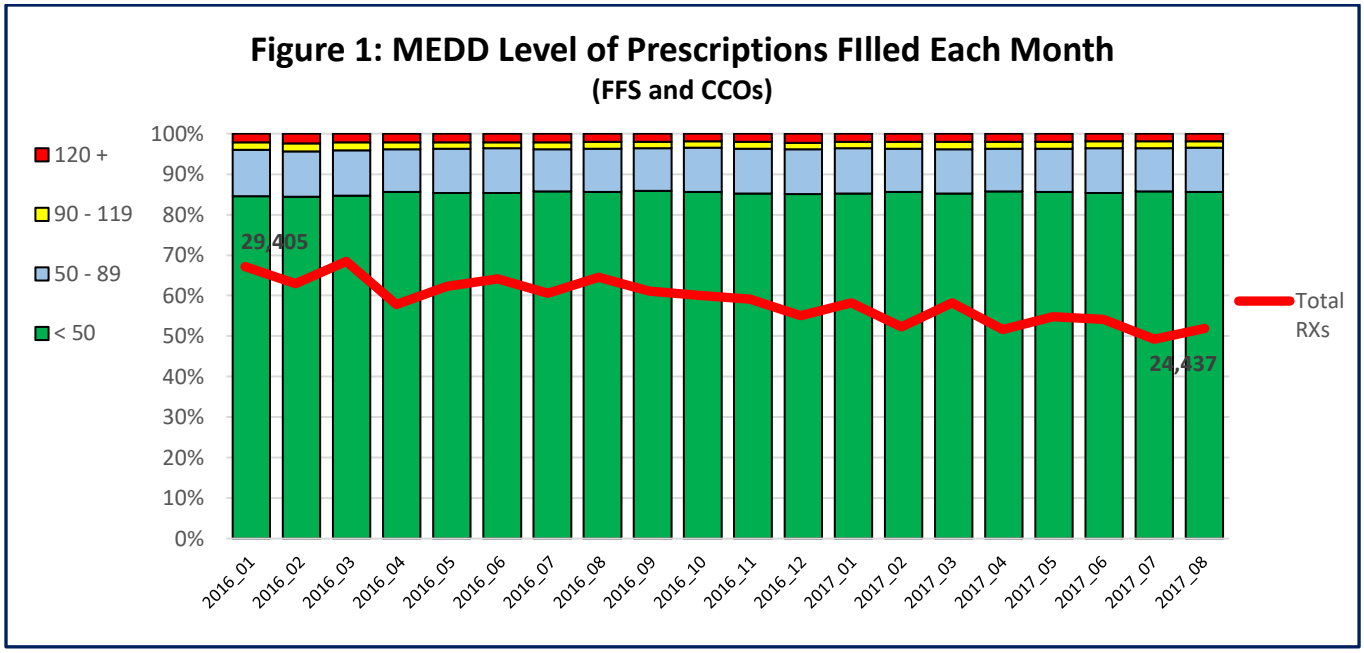
> *Individual prescriptions for opioids with an MEDD of ≥ 90 must require a manual PA with documentation that the benefits outweigh the risks and that the patient has been counseled about the risks of overdose and death.*

In September of 2016 MS-DUR began monthly educational mailings directed at prescribers who had beneficiaries filling opioid prescriptions for ≥90 MEDD during the prior month. This educational initiative mailing was done in advance to allow awareness and time to address this issue prior to implementation.

METHODOLOGY AND RESULTS

In order to evaluate the impact of this educational initiative on the prescribing of opioids with high MEDD levels, MS-DUR conducted a retrospective analysis of all opioid prescriptions filled by beneficiaries between January 2016 and August 2017. Beneficiaries with diagnoses of malignant cancer were excluded from the analysis. Table 1 shows the percentage of opioid prescriptions filled each month with MEDD < 50; 50 – 89; 90 – 119; and ≥120.

[1] CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016. http://www.cdc.gov/media/modules/dpk/2016/dpk-pod/rr6501e1er-ebook.pdf.



In January 2016, only 4 % of beneficiaries had prescriptions for ≥90 MEDD (1.8% of prescriptions had MEDD levels of 90 – 119 and 2.2% had MEDD levels of ≥120). This compares to 1.6% and 1.9%, respectively, (3% overall) reduction in total opioids prescriptions ≥90 MEDD in August 2017. Although there has been a slight reduction in the percentage of opioid prescriptions with high MEDD levels, the implementation of an electronic PA procedure can further reduce these numbers. It may be beneficial in the future for the DUR Board to review the data for opioid prescriptions between 50 and <90 MEED as the CDC guidelines recommended "*caution when prescribing opioids at any dosage, should carefully reassess evidence of individual benefits and risks when increasing dosage to ≥50 morphine milligram equivalents (MME)/day.*"

Although the percentage of high dose opioid prescriptions has remained fairly stable, the overall number of opioid prescriptions has dropped from 29,405 in January 2016 to 24,437prescriptions (16.89%) in August 2017. This may indicate that the national and state focus on the opioid crisis may have impacted providers prescribing practices of opioids.

MISSISSIPPI DIVISION OF MEDICAID

IMPORTANT INFORMATION ABOUT OPIOID PRESCRIPTIONS AND RISK OF OVERDOSE

DATE

Dear Dr. MD_NAME,

The Mississippi Division of Medicaid (DOM) Office of Pharmacy is committed to improving the quality of care provided to Mississippi Medicaid beneficiaries. DOM's Drug Utilization Review (DUR) Board, comprised of twelve Medicaid providers including physicians, nurse practitioners and pharmacists statewide, has recommended several quality improvement initiatives addressing the use of opioids for the treatment of pain. This letter is being sent as part of our initiative regarding high doses of opioid prescriptions.

WHY YOU ARE RECEVING THIS LETTER?
Our analysis of Medicaid prescription data for MONTH identified the following prescription filled by a beneficiary under your care.

Beneficiary Name			DOB		
BENFICIARY NAME			DOB		
Pharmacy	Date Filled	Medication Prescribed	Quantity	Days Supply	MEDD
PHARMACY	FILL_DATE	DRUG	QUANTITY	DS	MEDD

The enclosed Provider Summary describes the increased risks of overdose and death associated with high doses of opioids. Recent studies demonstrate that a patient's cumulative morphine equivalent daily dose (MEDD) is an indicator of potential dose-related risk for adverse drug reactions to opioids, including overdose. The Centers for Disease Control recently released guidelines for prescribing opioids which recommended that prescribers should carefully reassess evidence of individual benefits and risks when prescribing dosages ≥50 MEDD, and should avoid prescribing dosages ≥90 MEDD unless there is significant clinical justification. DOM's goal is to reduce beneficiaries' risks of adverse events associated with opioid use, such as overdose and addiction.

WHAT WE ASK OF YOU?
Several non-opioid pharmacologic therapies (including acetaminophen, NSAIDs, and selected antidepressants and anticonvulsants) are effective for chronic pain and we encourage you to consider these options first. For patients being prescribed opioids, please prescribe or titrate to lowest effective doses whenever possible. Given the documented increased risks associated with high dose opioid prescriptions, it is important that patients and/or caregivers be counseled about the risks of overdose and appropriate action steps, including considering offering naloxone when factors that increase risk for opioid overdose, such as history of overdose, history of substance use disorder, or higher opioid dosage (≥50 MME) are present. The following web address provides a MEDD calculator/conversion table for opioid products - http://www.pdmpassist.org/pdf/bja_performance_measure_aid_mme_conversion_tool.pdf.

Sincerely,

Benjamin F. Banahan, III, Ph.D.
Project Director
MS-DUR

Terri R. Kirby, RPh, CPM
Director, Office of Pharmacy
Division of Medicaid

MISSISSIPPI DIVISION OF MEDICAID

Provider Summary: Using Morphine Equivalent Daily Dosing To Prevent Opioid Abuse and Overdose

An estimated 20% of patients presenting to physician offices with non-cancer pain symptoms or pain-related diagnoses (including acute and chronic pain) receive an opioid prescription.[1] Over the past two decades, a marked increase in the use of opioid pain relievers has resulted in an explosion of opioid dependency and overdose deaths, and has fueled an epidemic of heroin addiction. Since 1999, opioid prescriptions have increased fourfold, and from 1999 to 2014, 165,000 Americans have died from overdoses of prescription pain-killers. Opioid prescribing practices have driven resurgence in heroin use, with four of five heroin users starting with prescription opioids. ***Mississippi is one of the nation's leaders in opioid prescriptions, with 1.2 opioid prescriptions for every citizen in 2012***.[2] Given the serious consequences of long-term opioid use, in March 2016 the Centers for Diseases Control and Prevention (CDC) released their final version of their "Guideline for Prescribing Opioids for the Management of Chronic Pain."[3]

Morphine Equivalent Daily Dose (MEDD)

Daily morphine milligram equivalents are used to assess comparative potency of opioid products, but not to convert a particular opioid dosage from one product to another. The terminology for daily morphine equivalency may vary depending on the resource used, and may be described as morphine equivalent daily dose (MEDD), morphine equivalent dose (MED), or morphine milligram equivalents (MME). By converting the dose of an opioid to a morphine equivalent dose, a clinician can determine whether a cumulative daily dose of opioids approaches an amount associated with increased risk.

Recent studies demonstrate that a patient's cumulative morphine equivalent daily dose (MEDD) is an indicator of potential dose-related risk for adverse drug reactions to opioids, including overdose.[4,5] Patients with a MEDD of 1 – 20 mg had a 0.2% annual overdose rate. Patients receiving a MEDD ≥ of 100 mg had almost nine times as much risk of overdose and a 1.8% annual overdose rate.[4]

Table 1. Increased Risk With Higher MEDD[4, 5]

MEDD Level	HR* for Any Overdose Event	OR** for Overdose Death
20 - 49	1.44	1.32
50 - 99	3.73	1.92
≥ 100	8.87	2.04

** Adjusted hazard ratio compared to MEDD of 1 - 19*
*** Adjusted odds ratio compared to MEDD of 1 - 19*

The 2016 CDC chronic pain management guidelines recommend that prescribers should carefully evaluate/ reassess evidence of individual benefits and risks when increasing dosage to ≥50 morphine milligram equivalents (MME)/day, and should avoid increasing dosage to ≥90 MME/day or carefully evaluate and justify a decision to titrate dosage to ≥90 MME/day.

Continued on back

[1] Daubresse M, Chang HY, Yu Y, et al. Ambulatory diagnosis and treatment of nonmalignant pain in the United States, 2000–2010. Med Care 2013;51:870–8.
[2] Mississippi State Dept of Health Mississippi Morbidity Report Vol 32, Number 2. Aug 2016.
[3] CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016 Recommendations and Reports / MMWR March 18, 2016 / 65(1);1–49 https://www.cdc.gov/mmwr/volumes/65/rr/rr6501e1.htm
[4] Dunn KM, Saunders KW, Rutter CM, et al. Opioid prescriptions for chronic pain and overdose: a cohort study. *Ann Intern Med*. 2010;152(2):85-92. Available at: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3000551/pdf/ukmss-32216.pdf. Accessed: August 13, 2015.
[5] Washington State Agency Medical Directors' Group. Interagency guideline on prescribing opioids for pain. June 2015. Available at: http://www.agencymeddirectors.wa.gov/Files/2015AMDGOpioidGuideline.pdf. Accessed: August 13, 2015.

Opioid Prescribing in the Mississippi Medicaid Population

A retrospective cohort study was conducted to calculate the MEDD levels for all Mississippi Medicaid beneficiaries having narcotic prescriptions paid by Medicaid during January - December 2015. MEDD levels were computed using the National Drug Code (NDC), days supply, and drug quantity fields and conversion factors in the Pharmacy Quality Alliance (PQA) technical specifications for opioid use quality measures

During 2015, a total of 352,622 paid pharmacy claims for prescription opioid medications were filled for 120,158 individual Medicaid beneficiaries. As shown in Table 2, 27.4% of beneficiaries were treated with opioid doses exceeding 50 MEDD, and 6.2% were treated with doses exceeding 90 MEDD. These beneficiaries had a significantly higher risk of opioid overdose.

Table 2: Beneficiaries Taking Opioid Prescriptions by Maximum Morphine Equivalent Daily Dose (MEDD)
(2015 - Excludes benericiaries with cancer diagnoses)

	Maximum MEDD	TOTAL	
For Individual Opioid Prescription	<50	92,573	77.0%
	50 - 89	22,059	18.4%
	90 - 119	3,609	3.0%
	120 +	1,917	1.6%
For ALL Concomitant Opioid Prescriptions	<50	87,204	72.6%
	50 - 89	25,515	21.2%
	90 - 119	4,458	3.7%
	120 +	2,981	2.5%

NOTE: Concomitant use was assumed to occur when beneficiaries filled opioid prescriptions with overlapping days of supply.

What You Can Do To Help Prevent Opioid Prescription Overdose

The CDC recommends opioids be prescribed at the lowest effective dose and for as short a period of time as possible.

- **You should monitor MEDD when writing opioid prescriptions.** Online calculators are available to estimate MEDD. One commonly used websites that offers an MEDD calculator is:

  http://www.pdmpassist.org/pdf/bja_performance_measure_aid_mme_conversion_tool.pdf

  A conversion table for the opioid products most frequently prescribed in the Mississippi Medicaid program can be downloaded from the MS-DUR website:

  http://pharmacy.olemiss.edu/cpmm/evidence-based-dur-initiative/ms-dur-resources-for-providers/

- **Before prescribing opioids, you should check your patient's information in the Mississippi Prescription Monitoring Program** to be sure the patient is not "doctor shopping", not already taking opioids prescribed by another provider and/or currently being treated for opioid dependence.

  http://www.mbp.state.ms.us/mbop/pharmacy.nsf/webpages/PMDB_PMDB?OpenDocument

- **When an MEDD above 50 is needed,** implement additional precautions, including increased frequency of follow-up and consider offering naloxone and overdose prevention education to both patients and the patients' household members.

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