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

MISSISSIPPI DIVISION OF
MEDICAID

December 5, 2019 at 1:00pm

Woolfolk Building, Room 117

Jackson, MS

Prepared by:

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

Drug Utilization Review Board

Lauren Bloodworth, PharmD (Co-Chair)
University of MS School of Pharmacy
201D Faser Hall
University, MS 38677
Term Expires: June 30, 2021

Beverly Bryant, MD
UMMC, School of Medicine
2500 North State Street
Jackson, MS 39216
Term Expires: June 30, 2021

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

Tanya Fitts, MD
Lafayette Pediatric Clinic
1300 Access Road, Suite 400
Oxford, MS 38655
Term Expires: June 30, 2021

Ray Montalvo, MD (Chair)
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, 2021

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

Cheryl Sudduth, RPh
Funderburk's Pharmacy
134 West Commerce Street
Hernando, MS 38632
Term Expires: June 30, 2022

James Taylor, PharmD
North MS Medical Center
830 S. Gloster Street
Tupelo, MS 38801
Term Expires: June 30, 2022

Alan Torrey, MD
Merit Health Medical Group
Pain Management
2080 South Frontage Road
Vicksburg, MS 39180
Term Expires: June 30, 2022

Veda Vedanarayanan, MD
Mississippi Center for Advanced Medicine
7731 Old Canton Road, Suite B
Madison, MS 39110
Term Expires: June 30, 2021

2020 DUR Board Meeting Dates

March 19, 2020
June 11, 2020
September 17, 2020
December 3, 2020

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
December 5, 2019

DUR Board Meeting Minutes

MISSISSIPPI DIVISION OF MEDICAID
DRUG UTILIZATION REVIEW (DUR) BOARD
MINUTES OF THE SEPTEMBER 19, 2019 MEETING

DUR Board Members:	Dec 2018	Mar 2019	May 2019	Sep 2019
Lauren Bloodworth, PharmD	✓		✓	✓
Beverly Bryant, MD	✓	✓		✓
Rhonda Dunaway, RPh	✓	✓	✓	✓
Tanya Fitts, MD	✓	✓	✓	
Ray Montalvo, MD (Chair)	✓	✓		✓
Holly Moore, PharmD	✓		✓	✓
Janet Ricks, DO	✓	✓	✓	
Dennis Smith, RPh	✓	✓	✓	✓
Cheryl Sudduth, RPh	NA	NA	NA	✓
James Taylor, PharmD	✓	✓	✓	✓
Alan Torrey, MD	NA	NA	NA	✓
Veda Vedanarayanan, MD	✓	✓	✓	✓
TOTAL PRESENT	**11***	**10***	**8***	**10**

** Total Present may not be reflected by individual members marked as present above due to members whose terms expired being removed from the list.*

Also Present:

Division of Medicaid (DOM) Staff:
Terri Kirby, RPh, CPM, Pharmacy Director; Cindy Noble, PharmD, MPH, DUR Coordinator; Carlos Latorre, MD, Medical Director; Chris Yount, MA, PMP, Staff Officer – Pharmacy; Sue Reno, RN, Program Integrity; Vanessa Banks, RN, Program Integrity; Christy Lyle, RN, Nurse Office Director of Clinical Support Services

University of Mississippi School of Pharmacy - MS-DUR Staff:
Eric Pittman, PharmD, MS-DUR Project Director; Kaustuv Bhattachaya, MS-DUR Analyst; Sushmitha Inguva, MS-DUR Analyst

Conduent Staff:
Lew Anne Snow, RN, BSN, Pharmacy Services Sr. Analyst, Mississippi Medicaid Project

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

IBM Watson Health:
Mary Sawardecker, MHA, RHIA, Analytic Consultant Sr., Mississippi Medicaid Project

Alliant Health:
Catherine Brett, MD, MPH, Alliant Health Solutions' Quality Director, MS UM/QIO

Coordinated Care Organization (CCO) Staff:
Heather Odem, PharmD, Director of Pharmacy - Mississippi, UnitedHealthcare Community & State; Jenni Grantham, PharmD, Director of Pharmacy, Magnolia Health; Mike Todaro; PharmD, Vice President Pharmacy Operations, Magnolia Health; Trina Stewart, PharmD, Pharmacy Manager, Molina Healthcare; Joseph Vazhappilly, PharmD, MBA, Associate Vice President, Pharmacy Services, Molina Healthcare

Visitors:
Brynna Clark, MPhA; Judy Clark, Consultant; Evelyn Johnson, Capital Resources; Alice Kelly Morgan, Pfizer; Beau Pender, Otsuka; Patrick Moty, Horizon Therapeutics; Melissa Sanders, UMMC FM; Peter Magargee, Sobi; Jeff Knappen, Spark; Gene Wingo, Biogen; Brooke Long , University of Mississippi (UM) Pharmacy Student; Andrea Washington, UM Pharmacy Student

Call to Order:
Dr. Ray Montalvo, Chair, called the meeting to order at 1:03pm and welcomed our new board members, Alan Torre, MD and Cheryl Sudduth, RPh.

OLD BUSINESS:
Mr. Smith moved to approve the minutes from the May 2019 DUR Board Meeting, seconded by Dr. Bloodworth and unanimously approved by the DUR Board.

Resource Utilization Review:
Dr. Pittman presented the resource utilization report for April 2019 – June 2019. No significant trends or shifts were noted for this period.

NEW BUSINESS

Update on MS-DUR Educational Interventions:
Dr. Pittman provided an overview of all DUR mailings that occurred May 2019 - August 2019. The mailings included on-going mailings addressing concomitant prescribing of opioids and benzodiazepines, prescribing of opioids at high morphine equivalent daily doses (MEDD), and provider shopping. A one-time mailing addressing the implementation of opioid prior authorization edits was also distributed.

CCO Update on Case Management Services for Beneficiaries at High Risk of Preterm Births:
Each CCO pharmacy director/manager presented information on their respective case management services their organizations have in place for beneficiaries at risk of experiencing a preterm birth.

UnitedHealthcare (UHC) Community and State: Heather Odem, Director of Pharmacy, described UHC's Maternal Child Health Program Healthy First Steps. A maternal child health coordinator who is a MS licensed RN receives pregnant member referrals. Members are given a clinical assessment and an individualized care plan is developed. Members are followed through their pregnancies and for 2 months after delivery. A variety of assistance approaches are provided for members enrolled in this service. For 2019 to date, the average preterm delivery rate for members enrolled in Healthy First Steps is 11%, compared to the Mississippi state average of 17%.

Molina Healthcare: Trina Stewart, Pharmacy Manager, detailed Molina's Motherhood Matters Pregnancy Program. She discussed triggers that are used to identify potential beneficiaries for enrollment in the program. The program provides individualized care specific for each beneficiary's

needs including smoking cessation and substance abuse treatment. They also have a dedicated Makena Care Management Team focused on educating beneficiaries on proper administration and monitoring adherence/compliance related issues.

Magnolia Health: Jenni Grantham, Director of Pharmacy, described the process Magnolia uses to identify and contact beneficiaries who are pregnant. Case management categorizes beneficiaries and reaches out to those beneficiaries who may be candidates for Makena. Case managers open a Makena Journal for each beneficiary receiving Makena which serves to document all information related to that pregnancy. Case management works closely with beneficiaries to meet their individual needs.

Special Analysis Projects:

Utilization of the CADD List

Dr. Pittman presented the DUR Board with a report on the drugs included in the Clinician Administered Drugs and Implantable Drug Devices (CADD) List. Dr. Pittman reviewed prescribing trends related to each drug category on the CADD List. With the introduction of the CADD List effective July 1, 2018, medications across all categories of the CADD List have seen shifts in claims from medical to point of sale (POS) pharmacy claims. Atypical long-acting injectable antipsychotics have also seen a significant increase in utilization since addition to the CADD List, indicating improved access. No formal recommendations were made regarding the CADD List.

Type 2 Diabetes Management and Utilization of Metformin

Dr. Noble presented background on the impact of diabetes and changes that are currently taking place in the diabetes treatment market. Dr. Pittman presented current treatment guideline recommendations and an overview of the utilization of noninsulin diabetes treatments in MS Medicaid. Some areas highlighted in the data analysis included the number of beneficiaries without a history of a documented trial of metformin prior to initiating another diabetes agent, the formulation of metformin used in those who had a documented trial of metformin, and those patients prescribed diabetes agents without documentation of a diabetes diagnosis. The DUR Board held a robust discussion around issues related to diabetes treatment.

At the conclusion of the discussion, the DUR Board did not make a formal recommendation regarding clinical edits related to diabetes treatment at this time. The Board felt it would be appropriate to wait until updated diabetes guidelines are released at the beginning of 2020 before making any formal recommendations. Dr. Bryant, with a second from Dr. Torrey, made a motion for DOM to develop a short educational bulletin promoting the use of metformin, describing benefits of extended release formulations over the immediate release formulations, and listing formulations of metformin that are preferred under the Universal Preferred Drug List (UPDL). The DUR Board unanimously approved the motion. Dr. Latorre volunteered to work with Dr. Pittman to develop this bulletin and distribute it to state medical societies for physicians, nurse practitioners, and physician assistants. Mr. Smith also encouraged DOM to explore opportunities for pharmacists to be able to intervene at POS to change metformin from immediate release to extended release formulations.

Synagis Update

Dr. Noble presented a background for the discussion on Synagis. Dr. Pittman provided the Board with an overview of 2018-2019 RSV season and utilization of Synagis.

Influenza Update
Dr. Pittman presented the Board with an overview of the 2018-2019 influenza season and influenza treatment patterns during this 2018-2019 season in Mississippi Medicaid. CDC's vaccination recommendations for the 2019-2020 season were provided. Following discussion from the Board, Dr. Taylor made a motion, seconded by Mr. Smith, supporting the removal of the influenza vaccine from counting toward the prescription drug limit of a beneficiary. The DUR Board unanimously approved the motion.

CMS Child Core Set Update
Dr. Pittman presented a brief description of a CMS Child Core Set report DOM submitted regarding the use of multiple concurrent antipsychotics in children and adolescents.

Opioid Initiative Update:
Ms. Kirby gave a brief update to the DUR Board on the implementation of DOM's opioid initiatives.

FDA Drug Safety Updates:
Dr. Pittman presented FDA drug safety communications for May 2019 – August 2019.

Pharmacy Program Update:
Ms. Kirby informed the Board of pharmacy stakeholder meetings that are currently being held. DOM has been hosting pharmacy stakeholder meetings throughout 2019 for the purpose of collaborating with pharmacists regarding cognitive services they can provide. The third meeting will be held on September 25, 2019. Ms. Kirby, along with Drew Snyder, recently visited Tyson's Drugs in Holly Springs, MS. She discussed ongoing efforts to involve pharmacists in the patient care process and reimburse pharmacists for patient care management (cognitive) services they provide.

Miscellaneous:
2020 Proposed Meeting Dates/Times
March 19, 2020
June 11, 2020
September 17, 2020
December 3, 2020
**Meeting times will remain at 1 pm for the next year.*

New Co-Chair:
Dr. Bloodworth volunteered to serve as Co-Chair for 2020. She was unanimously approved.

Next Meeting Information:
Dr. Taylor announced that the next meeting of the DUR Board will take place on December 5, 2019 at 1pm.

The meeting adjourned at 3:20 pm.

Submitted,

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

Meeting Location: Woolfolk Building, 501 North West Street, Conference Room 145, Jackson, MS 39201

Contact Information: Pharmacy Bureau:
Chris Yount, 601-359-5253: Christopher.yount@medicaid.ms.gov, or
Jessica Tyson, 601-359-5253; Jessica.Tyson@medicaid.ms.gov

Notice details:

State Agency: MS Division of Medicaid

Public Body: Drug Utilization Board (DUR) Meeting

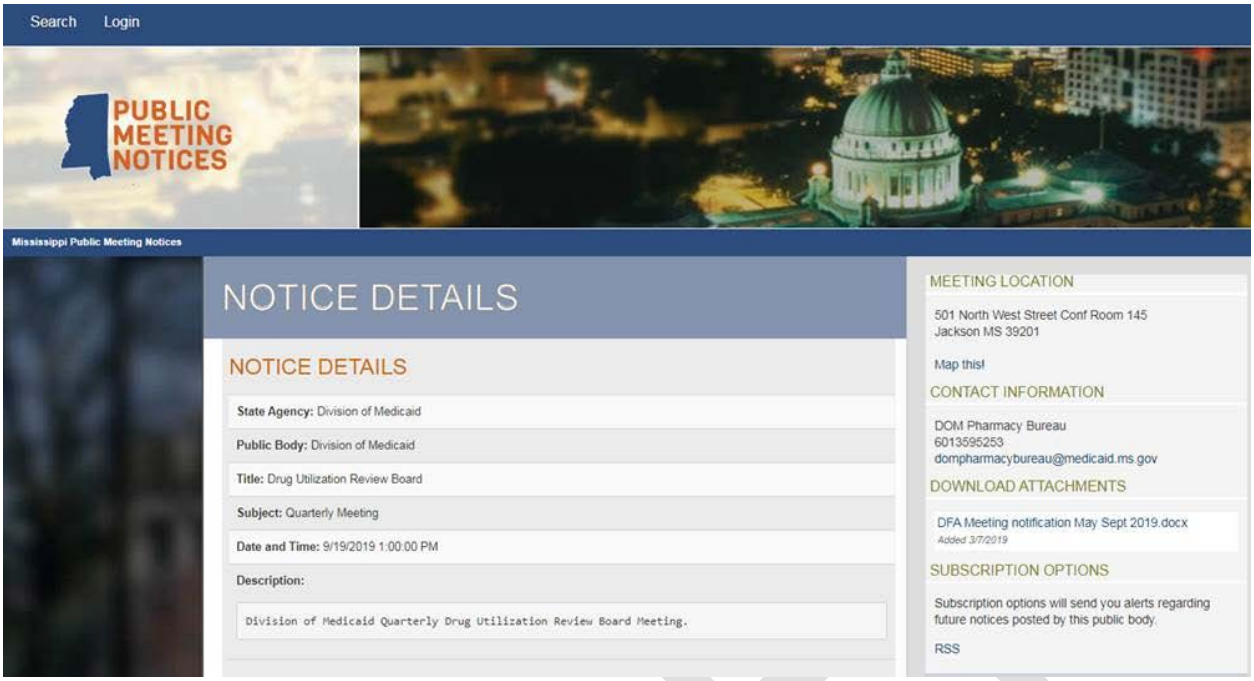
Subject: Quarterly Meeting

Date and Time: September 19, 2019 at 1PM

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.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PUBLIC MEETING NOTICES
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NOTICE DETAILS
NOTICE DETAILS
State Agency: Division of Medicaid
Public Body: Division of Medicaid
Title: Drug Utilization Review Board
Subject: Quarterly Meeting
Date and Time: 9/19/2019 1:00:00 PM
Description:
Division of Medicaid Quarterly Drug Utilization Review Board Meeting.
MEETING LOCATION
501 North West Street Conf Room 145
Jackson MS 39201
Map this!
CONTACT INFORMATION
DOM Pharmacy Bureau
6013595253
dompharmacybureau@medicaid.ms.gov
DOWNLOAD ATTACHMENTS
DFA Meeting notification May Sept 2019.docx
Added 3/7/2019
SUBSCRIPTION OPTIONS
Subscription options will send you alerts regarding future notices posted by this public body.
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Resource Utilizaton Review

TABLE 04A: ENROLLMENT STATISTICS FOR LAST 6 MONTHS
April 1, 2019 through September 30, 2019

			Apr-19	May-19	Jun-19	Jul-19	Aug-19	Sep-19
Total enrollment			694,976	694,525	694,276	693,715	691,238	687,336
Dual-eligibles			157,190	156,869	156,713	156,524	156,083	155,812
Pharmacy benefits			585,794	585,697	585,137	584,781	582,102	577,727
	LTC		17,154	17,179	17,044	17,129	17,064	16,879
	PLAN %	FFS	25.6%	25.4%	25.2%	25.4%	25.5%	25.1%
		MSCAN-UHC	30.3%	30.0%	29.7%	29.3%	28.9%	28.9%
		MSCAN-Magnolia	35.2%	34.9%	34.6%	34.2%	34.0%	34.0%
		MSCAN-Molina	8.9%	9.7%	10.5%	11.1%	11.6%	12.0%

TABLE 04B: PHARMACY UTILIZATION STATISTICS FOR LAST 6 MONTHS
April 1, 2019 through September 30, 2019

		Apr-19	May-19	Jun-19	Jul-19	Aug-19	Sep-19
# Rx Fills	FFS	109,016	102,316	90,836	98,457	108,168	102,376
	MSCAN-UHC	162,500	148,997	128,555	139,665	155,140	150,591
	MSCAN-Mag	214,564	198,973	175,314	186,430	204,002	200,930
	MSCAN-Mol	30,909	30,436	29,327	33,520	40,177	41,128
# Rx Fills / Bene	FFS	0.7	0.7	0.6	0.7	0.7	0.7
	MSCAN-UHC	0.9	0.8	0.7	0.8	0.9	0.9
	MSCAN-Mag	1.0	1.0	0.9	0.9	1.0	1.0
	MSCAN-Mol	0.6	0.5	0.5	0.5	0.6	0.6
$ Paid Rx	FFS	$12,721,801	$11,682,860	$10,803,982	$12,585,900	$12,468,970	$12,032,583
	MSCAN-UHC	$14,588,096	$14,059,702	$12,846,239	$14,206,990	$14,544,449	$14,146,651
	MSCAN-Mag	$20,067,923	$18,911,641	$17,247,824	$18,797,610	$19,650,976	$18,741,516
	MSCAN-Mol	$2,036,967	$2,101,121	$2,160,174	$2,557,322	$2,860,646	$2,889,472
$ /Rx Fill	FFS	$116.70	$114.18	$118.94	$127.83	$115.27	$117.53
	MSCAN-UHC	$89.77	$94.36	$99.93	$101.72	$93.75	$93.94
	MSCAN-Mag	$93.53	$95.05	$98.38	$100.83	$96.33	$93.27
	MSCAN-Mol	$65.90	$69.03	$73.66	$76.29	$71.20	$70.26
$ /Bene	FFS	$84.83	$78.53	$73.27	$84.73	$84.00	$82.98
	MSCAN-UHC	$82.19	$80.02	$73.92	$82.92	$86.46	$84.73
	MSCAN-Mag	$97.32	$92.52	$85.19	$93.99	$99.29	$95.41
	MSCAN-Mol	$39.07	$36.98	$35.16	$39.40	$42.36	$41.68

TABLE C: TOP 10 DRUG CATEGORIES BY NUMBER OF CLAIMS IN SEP 2019 (FFS AND CCOs)

Category	Month Year	Rank Volume	# RXs	$ Paid	# Unique Benes
CNS stimulants	Sep 2019	1	26,951	$5,461,341	23,524
	Aug 2019	1	26,775	$5,452,890	23,097
	Jul 2019	1	22,264	$4,533,121	19,124
aminopenicillins	Sep 2019	2	16,410	$212,868	16,114
	Aug 2019	4	15,751	$203,878	15,486
	Jul 2019	11	10,163	$127,862	9,956
nonsteroidal anti-inflammatory agents	Sep 2019	3	16,012	$225,294	15,314
	Aug 2019	3	16,327	$232,021	15,503
	Jul 2019	3	14,934	$213,310	14,151
adrenergic bronchodilators	Sep 2019	4	15,241	$859,715	13,316
	Aug 2019	2	17,194	$1,161,101	14,553
	Jul 2019	5	12,687	$861,122	10,814
antihistamines	Sep 2019	5	14,594	$211,663	14,118
	Aug 2019	5	14,789	$218,177	14,269
	Jul 2019	7	11,699	$177,239	11,205
narcotic analgesic combinations	Sep 2019	6	13,599	$630,545	12,490
	Aug 2019	6	14,390	$675,960	12,983
	Jul 2019	2	15,936	$707,555	14,355
atypical antipsychotics	Sep 2019	7	13,097	$3,297,127	11,321
	Aug 2019	7	13,511	$3,370,386	11,559
	Jul 2019	4	13,498	$3,436,121	11,410
glucocorticoids	Sep 2019	8	12,398	$205,546	11,951
	Aug 2019	10	11,284	$180,181	10,875
	Jul 2019	14	8,033	$153,914	7,713
leukotriene modifiers	Sep 2019	9	12,171	$202,593	11,947
	Aug 2019	8	12,839	$210,907	12,537
	Jul 2019	9	10,730	$177,085	10,403
SSRI antidepressants	Sep 2019	10	11,591	$139,523	10,905
	Aug 2019	9	12,182	$149,103	11,300
	Jul 2019	6	11,937	$143,567	10,998

TABLE D: TOP 10 DRUG CATEGORIES BY DOLLARS PAID IN SEP 2019 (FFS AND CCOs)

Category	Month Year	Rank Paid Amt	# RXs	$ Paid	# Unique Benes
CNS stimulants	Sep 2019	1	26,951	$5,461,341	23,524
	Aug 2019	1	26,775	$5,452,890	23,097
	Jul 2019	1	22,264	$4,533,121	19,124
atypical antipsychotics	Sep 2019	2	13,097	$3,297,127	11,321
	Aug 2019	2	13,511	$3,370,386	11,559
	Jul 2019	2	13,498	$3,436,121	11,410
insulin	Sep 2019	3	4,999	$2,769,792	3,698
	Aug 2019	3	5,219	$2,950,056	3,842
	Jul 2019	3	5,248	$2,904,615	3,900
antiviral combinations	Sep 2019	4	816	$2,640,501	754
	Aug 2019	4	865	$2,927,566	792
	Jul 2019	4	893	$2,846,415	790
antirheumatics	Sep 2019	5	966	$2,411,849	867
	Aug 2019	5	1,022	$2,631,807	910
	Jul 2019	5	1,010	$2,576,969	902
factor for bleeding disorders	Sep 2019	6	95	$1,602,197	69
	Aug 2019	6	110	$1,399,207	84
	Jul 2019	6	101	$1,932,681	81
gamma-aminobutyric acid analogs	Sep 2019	7	8,896	$1,093,959	8,340
	Aug 2019	9	9,397	$1,124,582	8,635
	Jul 2019	7	9,585	$1,181,951	8,779
bronchodilator combinations	Sep 2019	8	3,669	$1,088,530	3,410
	Aug 2019	7	3,920	$1,174,817	3,577
	Jul 2019	8	3,790	$1,159,470	3,445
adrenergic bronchodilators	Sep 2019	9	15,241	$859,715	13,316
	Aug 2019	8	17,194	$1,161,101	14,553
	Jul 2019	9	12,687	$861,122	10,814
chelating agents	Sep 2019	10	67	$757,895	60
	Aug 2019	10	83	$849,645	69
	Jul 2019	10	78	$823,779	61

TABLE E: TOP 25 DRUG MOLECULES
BY NUMBER OF CLAIMS IN SEP 2019 (FFS and CCOs)

Drug Molecule Therapeutic Category	Aug 2019 # Claims	Sep 2019 # Claims	Sep 2019 $ Paid	Sep 2019 # Unique Benes
amoxicillin / aminopenicillins	15,715	16,360	$211,904	16,065
albuterol / adrenergic bronchodilators	15,801	14,507	$639,197	12,777
montelukast / leukotriene modifiers	12,838	12,171	$202,593	11,947
azithromycin / macrolides	9,646	10,260	$188,314	10,051
cetirizine / antihistamines	9,661	9,636	$126,623	9,474
acetaminophen-hydrocodone / narcotic analgesic combinations	9,361	8,901	$111,187	8,363
lisdexamfetamine / CNS stimulants	8,673	8,672	$2,584,043	8,496
ibuprofen / nonsteroidal anti-inflammatory agents	7,945	7,991	$102,242	7,799
gabapentin / gamma-aminobutyric acid analogs	7,958	7,563	$117,159	7,125
fluticasone nasal / nasal steroids	8,023	7,415	$118,403	7,363
ondansetron / 5HT3 receptor antagonists	5,894	6,858	$123,118	6,646
methylphenidate / CNS stimulants	6,602	6,711	$1,339,518	6,046
amphetamine-dextroamphetamine / CNS stimulants	6,232	6,204	$295,755	5,406
prednisolone / glucocorticoids	5,310	6,190	$98,717	6,020
clonidine / antiadrenergic agents, centrally acting	6,497	6,179	$119,666	5,860
amoxicillin-clavulanate / penicillins/beta-lactamase inhibitors	5,050	5,750	$135,393	5,648
cefdinir / third generation cephalosporins	5,109	5,579	$123,992	5,500
amlodipine / calcium channel blocking agents	5,814	5,543	$48,541	5,304
omeprazole / proton pump inhibitors	5,628	5,335	$58,770	5,215
mupirocin topical / topical antibiotics	5,026	4,773	$85,773	4,666
sulfamethoxazole-trimethoprim / sulfonamides	4,747	4,712	$95,141	4,619
triamcinolone topical / topical steroids	4,695	4,434	$80,037	4,310
ranitidine / H2 antagonists	4,651	4,316	$69,471	4,173
guanfacine / antiadrenergic agents, centrally acting	4,447	4,286	$141,188	4,080
sertraline / SSRI antidepressants	4,359	4,166	$49,042	3,905

TABLE F: TOP 25 DRUG MOLECULES
BY DOLLARS PAID IN SEP 2019 (FFS and CCOs)

Drug Molecule Therapeutic Category	Aug 2019 $ Paid	Sep 2019 $ Paid	Sep 2019 # Claims	Sep 2019 # Unique Benes
lisdexamfetamine / CNS stimulants	$2,595,573	$2,584,043	8,672	8,496
adalimumab / antirheumatics	$1,802,756	$1,568,414	250	230
methylphenidate / CNS stimulants	$1,307,395	$1,339,518	6,711	6,046
paliperidone / atypical antipsychotics	$1,270,545	$1,182,117	555	502
insulin aspart / insulin	$927,063	$888,987	1,442	1,356
dexmethylphenidate / CNS stimulants	$865,501	$845,240	3,537	2,990
insulin glargine / insulin	$853,870	$809,690	1,777	1,687
aripiprazole / atypical antipsychotics	$751,108	$797,361	3,336	3,115
bictegravir/emtricitabine/tenofovir / antiviral combinations	$797,726	$781,566	253	243
deferasirox / chelating agents	$847,897	$756,497	63	59
albuterol / adrenergic bronchodilators	$748,800	$639,197	14,507	12,777
pregabalin / gamma-aminobutyric acid analogs	$696,910	$631,659	1,298	1,259
anti-inhibitor coagulant complex / factor for bleeding disorders	$357,403	$617,073	8	2
cobicistat/elvitegravir/emtricitabine/tenofov / antiviral combinations	$590,689	$547,073	178	173
etanercept / antirheumatics	$520,712	$540,340	108	100
lurasidone / atypical antipsychotics	$525,767	$530,170	399	383
hydroxyprogesterone / progestins	$578,202	$506,041	156	147
sofosbuvir-velpatasvir / antiviral combinations	$621,414	$492,151	35	32
somatropin / growth hormones	$537,130	$477,670	113	107
budesonide-formoterol / bronchodilator combinations	$470,256	$457,391	1,368	1,344
lacosamide / miscellaneous anticonvulsants	$435,583	$454,814	516	473
insulin detemir / insulin	$479,138	$444,067	802	771
fluticasone-salmeterol / bronchodilator combinations	$470,419	$423,208	1,253	1,219
buprenorphine-naloxone / narcotic analgesic combinations	$450,337	$420,542	1,113	955
ivacaftor-lumacaftor / CFTR combinations	$379,212	$399,326	21	19

TABLE G: TOP 25 DRUG MOLECULES
BY CHANGE IN NUMBER OF CLAIMS FROM JUL 2019 TO SEP 2019 (FFS and CCOs)

Drug Molecule	Jul 2019 # Claims	Aug 2019 # Claims	Sep 2019 # Claims	Sep 2019 $ Paid	Sep 2019 # Unique Benes
amoxicillin / aminopenicillins	10,112	15,715	16,360	$211,904	16,065
azithromycin / macrolides	5,035	9,646	10,260	$188,314	10,051
prednisolone / glucocorticoids	3,277	5,310	6,190	$98,717	6,020
albuterol / adrenergic bronchodilators	11,701	15,801	14,507	$639,197	12,777
cetirizine / antihistamines	6,916	9,661	9,636	$126,623	9,474
cefdinir / third generation cephalosporins	3,267	5,109	5,579	$123,992	5,500
ondansetron / 5HT3 receptor antagonists	4,581	5,894	6,858	$123,118	6,646
amoxicillin-clavulanate / penicillins/beta-lactamase inhibitors	3,545	5,050	5,750	$135,393	5,648
fluticasone nasal / nasal steroids	5,556	8,023	7,415	$118,403	7,363
lisdexamfetamine / CNS stimulants	7,137	8,673	8,672	$2,584,043	8,496
montelukast / leukotriene modifiers	10,730	12,838	12,171	$202,593	11,947
methylphenidate / CNS stimulants	5,401	6,602	6,711	$1,339,518	6,046
influenza virus vaccine, inactivated / viral vaccines	0	164	1,120	$33,588	1,119
prednisone / glucocorticoids	2,651	3,424	3,638	$39,513	3,517
ibuprofen / nonsteroidal anti-inflammatory agents	7,051	7,945	7,991	$102,242	7,799
amphetamine-dextroamphetamine / CNS stimulants	5,386	6,232	6,204	$295,755	5,406
oseltamivir / neuraminidase inhibitors	207	557	961	$73,427	957
dexmethylphenidate / CNS stimulants	2,823	3,507	3,537	$845,240	2,990
methylprednisolone / glucocorticoids	1,585	2,025	2,081	$30,508	2,061
benzonatate / antitussives	563	895	978	$13,006	953
cefprozil / second generation cephalosporins	418	716	752	$25,995	739
budesonide / inhaled corticosteroids	1,484	1,841	1,814	$239,319	1,760
dextromethorphan-promethazine / upper respiratory combinations	302	560	631	$7,307	600
brompheniramine/dextromethorphan/pse / upper respiratory combinations	167	396	459	$10,150	448
sulfamethoxazole-trimethoprim / sulfonamides	4,459	4,747	4,712	$95,141	4,619

TABLE H: TOP 25 DRUG MOLECULES
BY CHANGE IN AMOUNT PAID FROM JUL 2019 TO SEP 2019 (FFS and CCOs)

Drug Molecule	Jul 2019 $ Paid	Aug 2019 $ Paid	Sep 2019 $ Paid	Sep 2019 # Claims	Sep 2019 # Unique Benes
lisdexamfetamine / CNS stimulants	$2,130,457	$2,595,573	$2,584,043	8,672	8,496
methylphenidate / CNS stimulants	$1,126,681	$1,307,395	$1,339,518	6,711	6,046
dexmethylphenidate / CNS stimulants	$692,718	$865,501	$845,240	3,537	2,990
coagulation factor ix / factor for bleeding disorders	$69,625	$107,349	$219,679	8	3
corticotropin / corticotropin	$155,742	$432,264	$272,602	6	4
azithromycin / macrolides	$89,984	$177,599	$188,314	10,260	10,051
amoxicillin / aminopenicillins	$126,869	$203,185	$211,904	16,360	16,065
eteplirsen / miscellaneous uncategorized agents	$19,261	$102,522	$102,522	2	1
albuterol / adrenergic bronchodilators	$570,259	$748,800	$639,197	14,507	12,777
c1 esterase inhibitor, human / factor for bleeding disorders	$0	$130,282	$67,310	2	2
dextroamphetamine / CNS stimulants	$148,340	$188,526	$211,376	569	555
everolimus / mTOR inhibitors	$227,550	$252,630	$285,173	17	15
oseltamivir / neuraminidase inhibitors	$16,933	$42,807	$73,427	961	957
sildenafil / erectile dysfunction agents	$123,877	$167,499	$179,801	56	53
ustekinumab / interleukin inhibitors	$117,577	$106,565	$170,859	11	11
amoxicillin-clavulanate / penicillins/beta-lactamase inhibitors	$82,659	$117,358	$135,393	5,750	5,648
ondansetron / 5HT3 receptor antagonists	$72,201	$103,410	$123,118	6,858	6,646
cefdinir / third generation cephalosporins	$73,603	$115,075	$123,992	5,579	5,500
ibrutinib / multikinase inhibitors	$32,943	$66,691	$83,133	6	6
cladribine / antimetabolites	$0	$0	$49,758	1	1
gilteritinib / multikinase inhibitors	$0	$0	$45,116	2	2
prednisolone / glucocorticoids	$55,644	$86,260	$98,717	6,190	6,020
vigabatrin / gamma-aminobutyric acid analogs	$302,444	$305,997	$345,142	35	33
dasatinib / BCR-ABL tyrosine kinase inhibitors	$40,316	$57,324	$81,806	7	6
cetirizine / antihistamines	$90,656	$126,679	$126,623	9,636	9,474

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 JUL 2019 TO SEP 2019 (FFS and CCOs)

Drug Product Therapeutic Category	Sep 2019 # Claims	Sep 2019 $ Paid	Sep 2019 Avr. Paid Per Rx	Sep 2019 Avr. Units Per Rx	Jul 2019 Paid Per Unit	Aug 2019 Paid Per Unit	Sep 2019 Paid Per Unit	Percent Change
amphetamine-dextroamphetamine 10 mg capsule, extended release / CNS stimulants (P)	476	$32,369	$68.00	30	$1.72	$1.95	$1.90	10.4%
dexmethylphenidate 20 mg capsule, extended release / CNS stimulants (N)	171	$24,551	$143.57	30	$4.05	$4.15	$4.41	8.9%
colchicine 0.6 mg capsule / antigout agents (P)	147	$23,917	$162.70	36	$3.94	$3.96	$4.10	4.2%
cefprozil 500 mg tablet / second generation cephalosporins (P)	128	$4,532	$35.41	19	$1.23	$1.23	$1.28	3.4%
Saphris Black Cherry (asenapine) 10 mg tablet / atypical antipsychotics (P)	133	$106,568	$801.26	43	$18.72	$18.98	$19.07	1.8%
Vimpat (lacosamide) 200 mg tablet / miscellaneous anticonvulsants (P)	171	$155,163	$907.39	61	$14.11	$14.27	$14.36	1.8%
amphetamine-dextroamphetamine 25 mg capsule, extended release / CNS stimulants (P)	322	$17,805	$55.29	30	$1.44	$1.48	$1.47	1.5%
Latuda (lurasidone) 40 mg tablet / atypical antipsychotics (N)	107	$133,833	$1,250.78	32	$37.88	$37.83	$38.41	1.4%
Genvoya (cobicistat/elvitegravir/emtricitabine/tenofov) 150 mg-150 mg-200 mg-10 mg tablet / antiviral combinations (P)	178	$547,073	$3,073.44	32	$94.96	$95.37	$96.28	1.4%
Lyrica (pregabalin) 300 mg capsule / gamma-aminobutyric acid analogs (P)	103	$47,504	$461.20	60	$7.36	$7.37	$7.46	1.3%
Vyvanse (lisdexamfetamine) 20 mg tablet, chewable / CNS stimulants (P)	313	$93,728	$299.45	30	$9.49	$9.65	$9.61	1.3%
Biktarvy (bictegravir/emtricitabine/tenofovir) 50 mg-200 mg-25 mg tablet / antiviral combinations (P)	253	$781,566	$3,089.20	33	$91.77	$91.19	$92.84	1.2%
Eliquis (apixaban) 5 mg tablet / factor Xa inhibitors (P)	553	$219,933	$397.71	57	$6.91	$6.94	$6.97	0.9%

Products are only included if 100 or more fills in last month and average cost per unit in reference month was >= $1.

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 JUL 2019 TO SEP 2019 (FFS and CCOs)

Drug Product Therapeutic Category	Sep 2019 # Claims	Sep 2019 $ Paid	Sep 2019 Avr. Paid Per Rx	Sep 2019 Avr. Units Per Rx	Jul 2019 Paid Per Unit	Aug 2019 Paid Per Unit	Sep 2019 Paid Per Unit	Percent Change
Jardiance (empagliflozin) 25 mg tablet / SGLT-2 inhibitors (P)	239	$141,913	$593.78	38	$15.30	$15.49	$15.43	0.8%
QuilliChew ER (methylphenidate) 30 mg/24 hr tablet, chewable, extended release / CNS stimulants (P)	540	$181,704	$336.49	31	$10.51	$10.55	$10.58	0.7%

Products are only included if 100 or more fills in last month and average cost per unit in reference month was >= $1.

New Business

Special Analysis Projects

MISSISSIPPI DIVISION OF MEDICAID

MS-DUR INTERVENTION / EDUCATIONAL MAILING UPDATE

SEPTEMBER 2019 – NOVEMBER 2019

Ongoing Mailings:

HIGH MEDD (≥90 MEDD) MAILING Initiated Sept 2016 Completed July 2019			CONCOMITANT BENZODIAZEPINE / OPIOID USE Initiated Feb 2017 Completed July 2019		PROVIDER SHOPPING FOR OPIOIDS (≥4 Prescribers AND ≥4 Pharmacies) Initiated Nov 2017		
Month	**Prescribers Mailed**	**Benes Addressed**	**Prescribers Mailed**	**Benes Addressed**	**Prescribers Mailed**	**Pharms Mailed**	**Benes Addressed**
18-Dec	-	-	150	338	*21	*17	38
19-Jan	37	48	150	276	28	22	50
19-Feb	21	29	150	267	29	25	56
19-Mar	**68	**89	150	249	27	22	49
19-Apr	45	72	150	252	20	16	36
19-May	41	54	150	229	24	21	47
19-Jun	***30	***46	ǂ388	ǂ645	27	20	47
19-Jul	23	31	ǂ234	ǂ373	17	13	30
19-Aug					16	13	30
19-Sep					18	14	32
19-Oct					18	14	32
19-Nov					13	12	27

Notes

* Data for CCOs was incomplete at the time the mailing was run.

** Revised and updated MEDD calculation method incorporated into analysis.

*** Criteria for high MEDD threshold value changed from value of 50 or more to 90 or more.

ǂ Letter changed to incorporate information about opioid PA edits. Did not limit to 150 providers.

AN OVERVIEW OF ANTIDEPRESSANT USE IN CHILDREN AND ADOLESCENTS WITH A FOCUS ON TRICYCLIC ANTIDEPRESSANTS

BACKGROUND

Antidepressant use in children and adolescents are a safety concern. Antidepressant agents have a FDA boxed warning for increased risk of suicidal thoughts and behaviors in pediatric and young adult patients[1] with many not approved for use in children. Albeit seemingly low, there is a risk of suicidality when initiating antidepressants; there is also risk in not treating depressed patients with antidepressants in whom they are indicated. Clinicians must be cognizant of this risk and monitor high-risk patients per the Food and Drug Administration (FDA) recommended guidelines.[2] Below is the updated FDA Boxed Warning language for antidepressants:[3]

Suicidality and Antidepressant Drugs

Antidepressants increased the risk compared to placebo of suicidal thinking and behavior (suicidality) in children, adolescents, and young adults in short-term studies of major depressive disorder (MDD) and other psychiatric disorders. Anyone considering the use of [Insert established name] or any other antidepressant in a child, adolescent, or young adult must balance this risk with the clinical need. Short-term studies did not show an increase in the risk of suicidality with antidepressants compared to placebo in adults beyond age 24; there was a reduction in risk with antidepressants compared to placebo in adults aged 65 and older. Depression and certain other psychiatric disorders are themselves associated with increases in the risk of suicide. Patients of all ages who are started on antidepressant therapy should be monitored appropriately and observed closely for clinical worsening, suicidality, or unusual changes in behavior. Families and caregivers should be advised of the need for close observation and communication with the prescriber. [Insert Drug Name] is not approved for use in pediatric patients. [The previous sentence would be replaced with the sentence, below, for the following drugs: Prozac: Prozac is approved for use in pediatric patients with MDD and obsessive compulsive disorder (OCD). Zoloft: Zoloft is not approved for use in pediatric patients except for patients with obsessive compulsive disorder (OCD). Fluvoxamine: Fluvoxamine is not approved for use in pediatric patients except for patients with obsessive compulsive disorder (OCD).] (See Warnings: Clinical Worsening and Suicide Risk, Precautions: Information for Patients, and Precautions: Pediatric Use)

A summary of antidepressants available in the US is provided in Attachment A. Mississippi Medicaid includes many antidepressants on its Universal Preferred Drug List (UPDL) along with

[1] US Food and Drug Administration. Suicidality in Children and Adolescents Being Treated With Antidepressant Medications. https://www.fda.gov/drugs/postmarket-drug-safety-information-patients-and-providers/suicidality-children-and-adolescents-being-treated-antidepressant-medications. Accessed November 12, 2019.

[2] Christopher Noel (2015) Antidepressants and suicidality: History, the black-box warning, consequences, and current evidence. Mental Health Clinician: September 2015, Vol. 5, No. 5, pp. 202-211 https://mhc.cpnp.org/doi/full/10.9740/mhc.2015.09.202

[3] FDA. Revisions to Product Labeling. https://www.fda.gov/media/77404/download. Accessed November 19, 2019

associated FDA age restrictions (Attachment B). However, tricyclic antidepressants (TCAs) are not listed on the UPDL and FDA age restrictions have not been previously implemented. TCAs are rarely recommended for use in children due to safety concerns, potential for adverse events, and limited efficacy data.

MS-DUR conducted an evaluation of antidepressant prescribing patterns in children, adolescents, and young adults in the Mississippi Medicaid population with particular focus on the utilization of TCAs.

METHODS

A retrospective database analysis of Mississippi Medicaid beneficiaries was conducted related to the use of antidepressants in beneficiaries less than 21 years of age. Pharmacy point-of-sale (POS) and medical claims for fee-for-service (FFS) and coordinated care organizations [CCOs: UnitedHealthcare (UHC), Magnolia Health (Mag) and Molina Healthcare (MOL)] from January 1, 2018 to June 30, 2019 were reviewed. The index event was defined as the first paid claim in the study period. Beneficiaries with prior use of antidepressants were included in this analysis. A six month lookback period for prior antidepressant use and diagnoses was used in the study. Details regarding the beneficiaries' demographic characteristics (Table 1), antidepressant use by pharmacologic class and by beneficiary age (Table 2), and the type of provider prescribing the antidepressant (Table 3) are provided.

Additionally, a subgroup analysis was conducted for beneficiaries initially prescribed TCAs. New starts on TCAs were identified using a 6 month washout period prior to the first TCA claim. Demographic characteristics, provider type, diagnosis information, and prior antidepressant use were all assessed for TCA new starts. A six month lookback for determining diagnoses was also used in the subgroup analysis.

RESULTS

Table 1 depicts demographic characteristics of beneficiaries age less than 21 years prescribed antidepressants (ADs) between January 2018 and June 2019. Medication class for each beneficiary was determined by the medication class of the first AD claim during the study period.

- A total of 17,350 beneficiaries were prescribed ADs.
- Most beneficiaries receiving ADs were age >12 years (71.5%).
- Females and Caucasians were more likely to receive ADs.
- SSRIs were the most commonly prescribed pharmacologic class.
- Nearly 63% of all initial AD prescriptions during the study period were new starts with no recent history of other AD therapy.

* *Medication class was determined by the class of medication for the first AD fill for a beneficiary during the study period. Although not shown in Table 1, MS-DUR conducted additional analyses and determined 89.3% of beneficiaries were prescribed ADs from only 1 medication class during the study period.*

TABLE 1. Demographic Characteristics of Beneficiaries Age < 21 Years Prescribed Antidepressants between Janaury 2018 - June 2019

Characteristic	Number of beneficiaries (N= 17,350)
Age Category (yrs)	
0-12	4,940 (28.5%)
13-18	11,020 (63.5%)
19-20	1,390 (8.0%)
Sex	
Female	10,478 (60.4%)
Male	6,872 (39.6%)
Race	
Caucasian	10,491 (60.5%)
African American	5,989 (34.5%)
Hispanic	266 (1.5%)
Other	604 (3.5%)
Plan	
Fee-for-service	4,204 (24.2%)
United Healthcare	6,356 (36.6%)
Magnolia	6,461 (37.2%)
Molina	329 (1.9%)
Medication Class	
SSRI	13,252 (76.4%)
TCA	2,469 (14.2%)
SNRI	207 (1.2%)
Other *	1,422 (8.2%)
History of antidepressant use	
Prior Use**	6,432 (37.1%)
New Start	10,918 (62.9%)

* 'Other' category included tetracyclic antidepressants, monoamine oxidase inhibitors, phenylpiperazine antidepressants, and miscellaneous antidepressants.
** Prior use of antidepressants was evaluated in 6-month period prior to index antidepressant prescription in the study period.

Table 2 further describes the AD use by pharmacologic classes and ages of beneficiaries.

- SSRIs are the most prescribed class of AD across all age categories.
- TCAs are the second most prescribed class of AD in beneficiaries age ≤ 18 years.

TABLE 2. Antidepressant Use by Class and Beneficiary Age

Class	Age Category, N(%)			
	0-12 yrs	13-18 yrs	19-20 yrs	Total
SSRI	3,648 (73.8)	8,631 (78.3)	973 (70.0)	**13,252**
TCA	1,067 (21.6)	1,341 (12.2)	61 (4.4)	**2,469**
SNRI	14 (0.3)	149 (1.3)	44 (3.2)	**207**
Other	211 (4.3)	899 (8.2)	312 (22.4)	**1,422**
Total	**4,940**	**11,020**	**1,390**	**17,350**

SSRI - selective serotonin reuptake inhibitor; TCA - tricyclic antidepressant; SNRI - serotonin-norepinephrine reuptake inhibitor.

Table 3 identifies provider types by numbers of beneficiaries and pharmacy claims when prescribing antidepressants for beneficiaries age < 21 years during the analysis timeframe.

- Providers identified as practicing in a psychiatric or pediatric setting were the most frequent prescribers of ADs to beneficiaries age < 21 years.

TABLE 3. Provider Types for Antidepressants in Beneficiaries < 21 Years between January 2018 - June 2019

Provider Type	Number of Beneficiaries*	Number of Claims
MD-Psychiatry	4,000	16,953
MD-Pediatrics	3,288	15,721
NP-Psychiatry	3,541	15,600
NP-Other	4,206	15,039
MD-Family Physician	1,762	6,567
Physician Assistant	802	3,997
MD-Other	1,045	2,722
MD-Neurology	475	2,317
Provider-Other	736	2,121
MD-Internal Medicine	301	1,095
MD-Gastroenterology	135	493
MD-Urology	14	46
Mental Health	5	13
MD-Nephrology	3	3
Specialty N/A	3,304	11,469

*Number of beneficiaries is not mutually exclusive. Same beneficiary may have been seen by multiple provider types.

Table 4 examines AD use by FDA-approved diagnosis. A beneficiary was considered as having a FDA-approved diagnosis if any of the diagnoses included in Table 4 were present in claims data in a 6-month period prior to the first antidepressant fill during the study period.

- Of the 17,350 beneficiaries prescribed antidepressants during the study period, diagnosis information was present for 15,945 (91.9%) beneficiaries.
    - Among beneficiaries with diagnosis information available, 69.5% (n=9528) of beneficiaries prescribed antidepressants in the SSRI, SNRI, and other categories had FDA-approved indications present in claims data.
    - For beneficiaries prescribed TCAs, only **27.7%** (n=619) had FDA-approved indications present in claims data.

TABLE 4. Antidepressant Use by FDA-approved Diagnosis (N = 15,945)ǂ

Indication	Class							
	SSRI (N=12,177)		TCA (N=2,234)		SNRI (N=190)		Other (N=1,344)	
	Beneficiaries*	%	Beneficiaries*	%	Beneficiaries*	%	Beneficiaries*	%
Any of the FDA-approved indications listed below	**8,591**	**70.6**	**619**	**27.7**	**150**	**78.9**	**787**	**58.6**
Depression	4,867	40.0	191	8.6	92	48.4	444	33.0
Anxiety and Panic disorder	4,010	32.9	289	12.9	94	49.5	286	21.3
Bipolar Disorder	762	6.3	34	1.5	18	9.5	156	11.6
Adjustment Reactions	2,636	21.7	192	8.6	28	14.7	222	16.5
Other FDA-approved indication**	762	6.3	133	6.0	36	19.0	140	10.4
Non FDA-approved indication	**3,586**	**29.4**	**1,615**	**72.3**	**40**	**21.1**	**557**	**41.4**

Note: Diagnoses were evaluated in a 6-month period prior to the first antidepressant precription fill in study period.
ǂOf the 17,350 beneficiaries, corresponding diagnosis information was not available for 1,405 beneficiaries within a 6-month period prior to first antidepressant prescription fill in study period.
*Beneficiaries with multiple diagnoses may be counted more than once.
** Includes bulimia nervosa and eating disorders, premenstrual dysphoric disorder/tension syndromes, OCD, diabetic neuropathy, fibromyalgia, chronic pain (SNRIs), and nocturnal enuresis (TCAs).

TRICYCLIC ANTIDEPRESSANT SUB-GROUP ANALYSIS

Due to the lack of demonstrated clinical efficacy of TCAs in children and adolescents and safety concerns associated with these medications, a review of this specific pharmacologic category was conducted.[4,5] For a subgroup analysis, MS-DUR examined the use of TCAs in beneficiaries < 21 years of age. A small proportion of beneficiaries (n=2469, 14.2%) received TCAs between January 2018 – June 2019.

[4] Leonte K, Puliafico A, Na P, Rynn M. Pharmacotherapy for anxiety disorders in children and adolescents. UpToDate. https://www.uptodate.com/contents/pharmacotherapy-for-anxiety-disorders-in-children-and-adolescents. Accessed November 20, 2019
[5] National Institute for Health and Care Excellence. Depression in children and young people: identification and management. Clinical Guideline. September 2017. Available at: www.NICE.org.uk. Accessed: November 20, 2019.

- A total of 2,045 beneficiaries age < 21 years were initiated on TCAs during the study period.

  The demographic information (Table 5) regarding beneficiaries initiated on TCAs is similar, by percentage breakdown, to the demographics presented in Table 1 for beneficiaries prescribed any AD.

TABLE 5. Demographic Characteristics of Beneficiaries Age <21 Years Initiated on Tricyclic Antidepressants (TCA) between

Characteristic	Number of beneficiaries (N=2,045)
Age Category	
0-12	816 (39.9%)
13-18	1,160 (56.7%)
19-20	69 (3.4%)
Sex	
Female	1,219 (58.9%)
Male	826 (39.9%)
Race	
Caucasian	1,115 (53.9%)
African American	845 (40.8%)
Hispanic	47 (2.3%)
Other	38 (1.9%)
Plan	
Fee-for-service	469 (22.7%)
United Healthcare	789 (38.1%)
Magnolia	745 (36.0%)
Molina	42 (2.0%)

Similar to the provider types who prescribed any antidepressant to beneficiaries < age 21 years, pediatricians and psychiatrists were the most common provider types to initiate TCAs. (Table 6)

TABLE 6. Provider Types for the Initiation of TCAs in Beneficiaries Age < 21 Years between January 2018 - June 2019.

Provider Type	Number of beneficiaries*	Number of claims
MD-Pediatrics	583	1,594
NP-Other	418	1,028
MD-Psychiatry	149	565
MD-Neurology	219	544
MD-Family Physician	243	528
MD-Other	139	332
MD-Gastroenterology	92	263
NP-Psychiatry	62	174
Provider-Other	85	158
Physician Assistant	51	129
MD-Internal Medicine	36	93
MD-Urology	9	26
MD-Nephrology	1	1
Specialty N/A	212	470

*Number of beneficiaries is not mutually exclusive. Same beneficiary may have been seen by multiple provider types

As with other antidepressants, TCAs are used in the treatment of a variety of medical conditions. The different TCAs along with FDA-approved and compendia supported indications are provided in Figure 1.

FIGURE 1 – TCA FDA-approved and compendia supported indications

MICROMEDEX Recommendations for TCA Medications		
Generic (Brand) Products	**FDA Indications (Age)**	**Compendia Approved Indications***
Amitriptyline (Elavil, Vanatrip)	Depression (≥12 yrs)	Fibromyalgia (A)
		Headache (A)
		Irritable bowel syndrome (A)
		Pain (A)
		Postherpetic neuralgia (A)
		Subjective tinnitus (A)
Amoxapine (Amoxapine)	Depression (A)	None
	Endogenous depression (A)	
	Major depression with psychotic features (A)	
Clomipramine (Anafranil)	Obsessive-compulsive disorder (≥10 yrs)	Autism spectrum disorder (A)
		Depression (A,P)
		Disorder of ejaculation (A)
		Panic disorder (A)
Desipramine (Norpramin)	Depression (A)	Attention deficit hyperactivity disorder (P)
		Diabetic neuropathy (A)
		Postherpetic neuralgia (A)
Doxepin (Silenor, Sinequan)	Alcoholism (≥12 yrs)	Urticaria (A)
	Anxiety (≥12 yrs)	
	Depression (≥12 yrs)	
	Depression - psychotic disorder (≥12 yrs)	
	Insomnia - sleep maintenance (A)	
	Pruritus (A)	
Imipramine (Tofranil)	Depression (A)	Binging (A)
	Nocturnal enuresis (≥6 yrs)	Diabetic neuropathy (A)
		Panic disorder (A)
		Urinary incontinence (A)
Imipramine pamoate (Tofranil PM)	Depression (A)	Diabetic neuropathy (A)
		Panic disorder (A)
Nortriptyline (Pamelor, Aventyl)	Depression(≥12 yrs)	Attention deficit hyperactivity disorder (P)
		Diabetic neuropathy (A)
		Neurogenic bladder (A)
		Nocturnal enuresis (P)
		Postherpectic neuralgia (A)
		Smoking cessation assistance (A)
Protriptyline (Vivactil)	Depression(≥12 yrs)	Cataplexy (A)
Trimipramine (Surmontil)	Depression(≥12 yrs)	None

*"Strength of Recommendation" rating of at least IIB and "Efficacy" rating of at least IIA are considered a "medically-accepted indication."
(A) - Adult; (P) - Pediatrics

As a note of reference, under the current electronic prior authorization process (SmartPA®), the primary compendia resource for the DOM for establishing medically accepted indications is Thompson Micromedex DrugDex® (Micromedex). This is one of the official compendia approved by the Centers for Medicare and Medicaid Services. The criteria used for determining medically accepted indications are:

- *"Strength of Recommendation" rating of at least IIB (Recommended, In Some Cases)* ***and***
- *"Efficacy" rating of at least IIA (Evidence Favors Efficacy).*

TABLE 7. Diagnoses Associated with TCA Prescriptions in Beneficiaries < 21 Years by Age Category between January 2018 - June 2019

Diagnoses	Age Category						Total* (N = 1,853)	
	0-12 (N = 745)		13-18 (N = 1,041)		19-20 (N = 67)			
	6 month lookback** n (%)	1 week lookback n (%)	6 month lookback** n (%)	1 week lookback n (%)	6 month lookback** n (%)	1 week lookback n (%)	6 month lookback** n (%)	1 week lookback n (%)
Headache	229 (30.7)	190 (25.5)	462 (44.3)	381 (36.5)	23 (34.3)	15 (22.4)	714 (38.5)	586 (31.6)
Migraine	199 (26.7)	173 (23.2)	366 (35.2)	315 (30.3)	22 (32.8)	14 (20.9)	587 (31.7)	502 (27.1)
Attention-deficit hyperactivity disorder (ADHD)	304 (40.8)	242 (32.5)	200 (19.2)	134 (12.9)	7 (10.5)	6 (9.0)	511 (27.6)	382 (20.6)
Anxiety	77 (10.3)	53 (7.1)	213 (20.5)	151 (14.5)	21 (31.3)	18 (26.9)	311 (16.8)	222 (12.0)
Depression	32 (4.3)	26 (3.5)	194 (18.6)	140 (13.5)	20 (29.9)	13 (19.4)	246 (13.3)	179 (9.7)
Nocturnal enuresis	48 (6.3)	38 (5.0)	19 (1.8)	15 (1.4)	0 (0.0)	0 (0.0)	67 (3.6)	53 (2.8)
Irritable bowel syndrome	13 (1.7)	12 (1.6)	32 (3.1)	23 (2.2)	2 (3.0)	2 (3.0)	47 (2.5)	37 (2.0)
Obsessive compulsive disorder	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Alcohol related disorders	0 (0.0)	0 (0.0)	5 (0.5)	1 (0.1)	1 (1.5)	0 (0.0)	6 (0.3)	1 (0.1)

*Numbers of beneficiaries with diagnoses are not mutually exclusive. Diagnostic information was available for only 1,853 beneficiaries during the study period. Corresponding medical information was not available for 192 beneficiaries.
**Proportion of beneficiaries with diagnoses in a 6 month lookback prior to TCA prescription is inclusive of beneficiaries with diagnoses at 1 week prior to TCA prescription.

Upon analysis of diagnoses information available for beneficiaries < 21 years initiated on TCAs, the following was noted: (Table 7)

- Diagnoses information was present in medical claims for 1,853 out of 2,045 beneficiaries (90.6%) in the 6-month lookback period prior to the initial TCA prescription fill.
- Headache and migraine were the most common diagnoses present, followed by ADHD. Note that **none** of the TCAs have a FDA approved indication for any of these three diagnoses.
- Prescription fills are not routinely associated with a diagnosis code making it difficult to determine the exact diagnosis intended for a medication. However, a high proportion of beneficiaries had a diagnosis present within 1 week prior to the initial TCA fill. This increases the likelihood that a diagnosis is associated with a particular medication.
- Headache, migraine, and irritable bowel syndrome were the only three diagnoses associated with TCA use in children and adolescents that did not have a FDA approved or compendia supported indication to support their use.

CONCLUSIONS

A total of 17,350 beneficiaries age < 21 years were identified as receiving antidepressants between January 2018 – June 2019. While many antidepressant therapies lack FDA-approved indications for use in children, most beneficiaries prescribed antidepressants in categories other than TCAs had a FDA-approved indication associated with their use (69.5%). Beneficiaries prescribed TCAs did have a FDA-approved indication associated with their use 27.7% of the time. Most of the TCA use was for non FDA-approved indications. The primary diagnoses associated with the use of TCAs were headache and migraine.

RECOMMENDATIONS

1. DOM should implement an electronic edit for the initiation of TCA therapy with age limits corresponding to FDA-approved and compendia supported age limits for each agent. Beneficiaries with ongoing TCA therapy will be automatically grandfathered.

ATTACHMENT A

ANTIDEPRESSANT MEDICATION PHARMACOLOGIC CLASSIFICATION			
Generic Name	**Brand Name**	**Generic Name**	**Brand Name**
SSRI		**Other**	
Citalopram	Celexa	Tetracyclic	
Escitalopram	Lexapro	Maprotiline	Ludiomil
Fluoxetine	Prozac, Rapiflux, Sarafem, Selfemra	Mirtazapine	Remeron
Fluvoxamine	Luvox	Phenylpiperazine	
Paroxetine	Paxil, Brisdelle, Pexeva	Nefazodone	Serzone
Sertraline	Zoloft	Trazodone	Desyrel, Oleptro
SSNRI		Miscellaneous	
Desvenlafaxine	Pristiq, Khedezla	5-HTP	5-HTP
Duloxetine	Cymbalta, Irenka	Brexanolone	Zulresso
Levomilnacipran	Fetzima	Bupropion	Wellbutrin, Forfivo, Zyban
Milnacipran	Savella	Esketamine	Spravato
Venlafaxine	Effexor	St. John's Wort	St. John's Wort
TCA		Vilazodone	Viibryd
Amitriptyline	Elavil, Vanatrip	Vortioxetine	Brintellix, Trintellix
Amoxapine	Amoxapine	MAOI	
Clomipramine	Anafranil	Isocarboxazid	Marplan
Desipramine	Norpramin	Phenelzine	Nardil
Doxepin	Silenor, Sinequan	Selegiline	Eldepryl, Emsam, Zelapar
Imipramine	Tofranil	Tranylcypromine	Parnate
Nortriptyline	Pamelor, Aventyl		
Protriptyline	Vivactil		
Trimipramine	Surmontil		

ATTACHMENT B

MISSISSIPPI DIVISION OF MEDICAID

MISSISSIPPI DIVISION OF MEDICAID UNIVERSAL PREFERRED DRUG LIST

(For All Medicaid, MSCAN and CHIP Beneficiaries)

EFFECTIVE 11/01/2019
Version 2019.1
Updated: 10-31-2019

Conduent's SmartPA Pharmacy Application (SmartPA) is a proprietary electronic prior authorization system used for Medicaid fee for service claims. MSCAN plans may/may not -have electronic PA functionality. However, they must adhere to Medicaid's PA criteria.

THERAPEUTIC DRUG CLASS	PREFERRED AGENTS	NON-PREFERRED AGENTS	PA CRITERIA
ANTIDEPRESSANTS, OTHER SmartPA			
	bupropion bupropion SR bupropion XL TRINTELLIX (vortioxetine) mirtazapine trazodone venlafaxine venlafaxine ER capsules VIIBRYD (vilazodone)	APLENZIN (bupropion HBr) desvenlafaxine ER desvenlafaxine fumarate ER DESYREL (trazodone) EFFEXOR (venlafaxine) EFFEXOR XR (venlafaxine) EMSAM (selegiline transdermal) FETZIMA ER (levomilnacipran) FORFIVO XL (bupropion) KHEDEZLA ER (desvenlafaxine) MARPLAN (isocarboxazid) NARDIL (phenelzine) nefazodone OLEPTRO ER (trazodone) PARNATE (tranylcypromine) phenelzine PRISTIQ (desvenlafaxine) REMERON (mirtazapine) tranylcypromine venlafaxine XR	**Minimum Age Limit** • **18 years** - all drugs • **Cymbalta** – automatic approval for ages 7-17 with a diagnosis of GAD (Generalized Anxiety Disorder) **Non-Preferred Criteria** • Have tried 2 different preferred '*Antidepressants, Other' Class* in the past 6 months **OR** • Have tried BOTH a preferred '*Antidepressant, SSRI' and 'Antidepressants, Other'* in the past 6 months **OR** • 90 consecutive days on the requested agent in the past 105 days **Cymbalta (see Fibromyalgia Agents)**
		venlafaxine ER tablets WELLBUTRIN (bupropion) WELLBUTRIN SR (bupropion) WELLBUTRIN XL (bupropion HCl)	

MISSISSIPPI DIVISION OF MEDICAID

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THERAPEUTIC DRUG CLASS	PREFERRED AGENTS	NON-PREFERRED AGENTS	PA CRITERIA
ANTIDEPRESSANTS, SSRIs SmartPA			
	citalopram escitalopram fluoxetine fluvoxamine paroxetine CR paroxetine IR sertraline	CELEXA (citalopram) fluoxetine DR fluvoxamine ER LEXAPRO (escitalopram) LUVOX (fluvoxamine) LUVOX CR (fluvoxamine) paroxetine suspension PAXIL CR (paroxetine) PAXIL SUPENSION (paroxetine) PAXIL Tablets (paroxetine) PEXEVA (paroxetine) PROZAC (fluoxetine) SARAFEM (fluoxetine) ZOLOFT (sertraline)	**Minimum Age Limits** • **6 years** - Zoloft • **7 years** – Prozac • **8 years** - Luvox • **12 years** - Lexapro • **18 years –** Celexa, Luvox CR, Paxil, Pexeva, Prozac 90 mg **Citalopram Criteria** • <18 years and 90 consecutive days on citalopram in the past 105 days **OR** • < 60 years **AND** max daily dose ≤ 40 mg/day **OR** • ≥ 60 years **AND** max daily dose ≤ 20 mg/day **Non-Preferred Criteria** • Have tried 2 different preferred agents in the past 6 months **OR** • 90 consecutive days on the requested agent in the past 105 days

HPV VACCINE SERIES COMPLETION RATES AMONG MISSISSIPPI MEDICAID BENEFICIARIES WHO INITIATED VACCINATION SERIES JAN 1, 2017 – DEC 31, 2017

BACKGROUND

Human Papillomaviruses (HPV) is the most common sexually-transmitted infection in the United States affecting over 79 million Americans. HPVs are a group of more than 150 viruses, most commonly affecting adults and those in their late teens. HPV causes genital warts and certain cancers (cervical, vulvar, vaginal, penile, anal, and oropharyngeal).[1] It is estimated that 79% of HPV-associated cancers can be attributed to the virus.[2] The incidence rate of HPV-associated cancers in Mississippi was estimated as 14.3 per 100,000 persons, which is higher than the United States national average of 11.7 per 100,000 persons.[3]

Three vaccines, Gardasil® (4vHPV), Cervarix® (2vHPV) and Gardasil®9 (9vHPV) were licensed by the Food and Drug Administration (FDA) for immunization against HPV. As of 2017, Gardasil®9 is the only vaccine available in the United States.[4] The American Council on Immunization Practices (ACIP) recommends initiation of the HPV vaccination series in both males and females at ages 11 to 12 years. Vaccine initiation can occur, though, as early as 9 years of age. Multiple updates to the recommended HPV vaccination schedule have occurred over time. A timeline summary of substantial changes recommended by ACIP for HPV vaccination schedule is provided below:

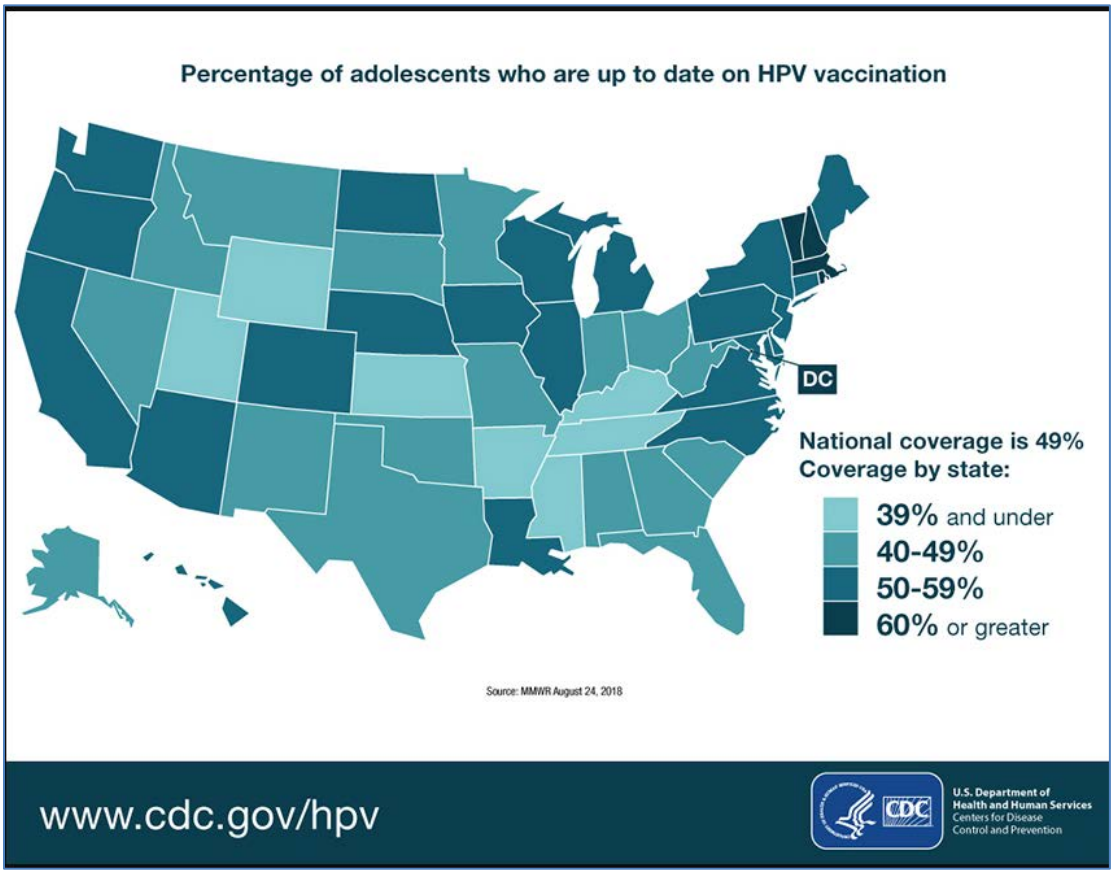
- **Prior to 2016** - a 3-dose vaccination schedule within a period of 12 months was recommended irrespective of age at initiation.[5,6]
- **December 2016** - two doses are recommended for children who initiate vaccination before age 15 years and three doses are recommended if initiated 15 years or later for completion of the HPV vaccine series.[7]
- **June 2019** – To further expand recommendations, catch-up vaccinations are recommended for all persons through age 26 years. For adults aged 27 through 45 years, ACIP did not recommend catch-up vaccination for all, although they did recognize that some persons

[1] Centers for Disease Control and Prevention (CDC). CDC – Human Papillomavirus Fact Sheet. https://www.cdc.gov/std/hpv/stdfact-hpv.htm Accessed November 13, 2019.
[2] Centers for Disease Control and Prevention (CDC). CDC - How Many Cancers Are Linked with HPV Each Year? https://www.cdc.gov/cancer/hpv/statistics/cases.htm. Published 2018. Accessed August 8, 2019.
[3] Viens LJ, Henley SJ, Watson M, et al. Human Papillomavirus-Associated Cancers - United States, 2008-2012. MMWR Morb Mortal Wkly Rep. 2016;65(26):661-666. Accessed August 8, 2019.
[4] American Cancer Society. HPV Vaccines. https://www.cancer.org/cancer/cancer-causes/infectious-agents/hpv/hpv-vaccines.html. Accessed November 10, 2019.
[5] Centers for Disease Control and Prevention (CDC). Quadrivalent Human Papillomavirus Vaccine Recommendations of the Advisory Committee on Immunization Practices (ACIP). Morb Mortal Wkly Rep. 2007;56. https://www.cdc.gov/mmwr/pdf/rr/rr56e312.pdf. Accessed August 8, 2019.
[6] Centers for Disease Control and Prevention (CDC). FDA licensure of bivalent Human papillomavirus vaccine (HPV2, Cervarix) for use in females and updated HPV vaccination recommendations from the Advisory Committee on Immunization Practices (ACIP). 2010;59(20). https://www.cdc.gov/mmwr/PDF/wk/mm5920.pdf. Accessed August 8, 2019.
[7] Meites E, Kempe A, Markowitz LE. Use of a 2-Dose Schedule for Human Papillomavirus Vaccination — Updated Recommendations of the Advisory Committee on Immunization Practices. MMWR Morb Mortal Wkly Rep. 2016;65(49):1405-1408. doi:10.15585/mmwr.mm6549a5.

who are inadequately vaccinated may benefit from vaccination due to at risk status for new HPV infection. For these persons, ACIP recommends shared clinical decision-making for HPV vaccination.[8]

According to the CDC's TeenVaxView, HPV vaccination rates are increasing as more children are up to date on HPV vaccination. Approximately 49% of adolescents ages 13-17 years were up to date on HPV vaccination series in the United States in 2017.[9] (Figure 1) In Mississippi, the percent of adolescents up to date on HPV vaccine was only 28.8%.[10]

Figure 1: HPV Vaccination Coverage Rates[9]



[8] Meites E, Szilagyi PG, Chesson HW, Unger ER, Romero JR, Markowitz LE. Human Papillomavirus Vaccination for Adults: Updated Recommendations of the Advisory Committee on Immunization Practices. MMWR Morb Mortal Wkly Rep 2019;68:698–702. DOI: http://dx.doi.org/10.15585/mmwr.mm6832a3

[9] Centers for Disease Control and Prevention (CDC). Human Papillomavirus Coverage Data. https://www.cdc.gov/hpv/hcp/vacc-coverage/index.html Accessed November 8, 2019.

[10] Centers for Disease Control and Prevention. TeenVaxView. 2017 Adolescent Human Papillomavirus (HPV) Vaccination Coverage Dashboard. https://www.cdc.gov/vaccines/imz-managers/coverage/teenvaxview/data-reports/hpv/dashboard/2017.html Accessed November 8, 2019.

Recent literature suggests that various factors such as age at initiation, gender, race, insurance coverage, provider specialty and geographic location are associated with HPV vaccination rates.[11, 12,13]

This report will assess HPV vaccine series completion rates in a sample of Mississippi Medicaid beneficiaries for the 2017 calendar year.

METHODS

A retrospective analysis was conducted using Mississippi Medicaid fee-for-service (FFS) and coordinated care organizations [CCOs: UnitedHealthcare (UHC) and Magnolia Health (Mag)] medical and pharmacy claims for the period of January 1, 2017 to December 31, 2017. Molina Healthcare was not included in the analysis due to the fact that the study period occurred prior to Molina's start date in Mississippi Medicaid. HPV related claims for beneficiaries aged 9 to 26 years during the study period were extracted for analysis. The first identified claim was recorded as the index event and the corresponding date as the index date. Beneficiaries who had a claim for an HPV vaccine in 2016 within a year of their index date in 2017 were excluded from the study to ensure that only true initiators in the study period were included. Beneficiaries were excluded if they did not have continuous enrollment during the study period or if they had been pregnant in the 12-month post-index period. This sample of beneficiaries was identified as "initiators". Beneficiaries were followed for 12 months in the post-index period to assess receipt of the remaining of the recommended doses of the vaccine.

[11] Franco, M., Mazzucca, S., Padek, M., & Brownson, R. C. (2019). Going beyond the individual: how state-level characteristics relate to HPV vaccine rates in the United States. *BMC Public Health*, *19*(1). doi: 10.1186/s12889-019-6566-y

[12] Widdice LE, Bernstein DI, Leonard AC, Marsolo KA, Kahn JA. Adherence to the HPV Vaccine Dosing Intervals and Factors Associated With Completion of 3 Doses. *Pediatrics*. 2011;127(1):77-84. doi:10.1542/peds.2010-0812

[13] Liu G, Kong L, Du P. HPV vaccine completion and dose adherence among commercially insured females aged 9 through 26 years in the US. *Papillomavirus Res*. 2016;2:1-8. doi:10.1016/j.pvr.2015.10.001

RESULTS

TABLE 1: HPV Vaccine-Eligible, Initiated and Completed Beneficiaries Aged 9-26 Years between January 1, 2017 – December 31, 2017 in Mississippi Medicaid

Characteristic	FFS [b]				UHC [b]				Mag [b]			
	Vaccine-eligible (N = 28813)	Initiated (N = 1046)	Completed (N = 244)	Completion rate (23.3%) [a]	Vaccine-eligible (N = 84748)	Initiated (N = 5943)	Completed (N = 1759)	Completion rate (29.6%) [a]	Vaccine-eligible (N = 87344)	Initiated (N = 6667)	Completed (N = 1925)	Completion rate (28.9%) [a]
Age group [b]												
9 to 10	3785	15	6	40.0%	18903	121	59	48.8%	19921	124	69	55.7%
11 to 12	3524	363	156	43.0%	16686	2552	1165	45.6%	17289	2881	1271	44.1%
13 to 14	3492	355	70	19.7%	15304	1996	455	22.8%	15643	2211	498	22.5%
15 to 18	6516	252	10	4.0%	26618	1249	74	5.9%	26589	1424	85	6.0%
19 to 26	11496	61	2	3.3%	7237	25	6	24.0%	7902	27	2	7.4%
Gender												
Female	16949	522	126	24.1%	44170	3026	907	30.0%	45988	3398	1020	30.2%
Male	11864	524	118	22.5%	40578	2917	852	29.2%	41356	3269	905	27.7%
Race												
Caucasian	10085	282	59	20.9%	27661	1553	482	31.0%	25019	1560	476	30.5%
African American	15512	672	156	23.2%	52855	4037	1146	28.4%	58339	4767	1323	27.8%
Hispanic	516	27	12	44.4%	2875	301	120	39.9%	2558	283	113	39.9%
Other	2700	65	17	26.2%	1357	52	11	21.2%	1428	57	13	22.8%

Note:

[a] Completion was defined as per ACIP guidelines, 2016. Completion rate was calculated as the proportion of completers among initiators within each category. Overall completion rate was 28.8% (3,928 of 13,656 beneficiaries).

[b] For beneficiaries who either initiated or completed, age and plan information was calculated as of their HPV vaccine initiation date. Since vaccine-eligible beneficiaries might not have an initiation date, age and plan information was calculated as of January 1, 2017. The 'Vaccine-eligible' numbers include benes who may have initiated and/or completed HPV vaccine series in the past.

Table 1 displays HPV completion rates among Medicaid beneficiaries:

- Total of 13,656 beneficiaries initiated therapy during this time period;
- Overall completion rate was 28.8% (3,928 of 13,656 beneficiaries);
- Completion rates were higher among beneficiaries age 12 years and younger;
- Beneficiaries in both UHC and Mag had higher completion rates compared to beneficiaries in FFS;
- Hispanic beneficiaries had higher completion rates compared to other races across all plans.

* Detailed analysis of provider type data (not included in Table 1) indicated completion rates were highest among pediatricians.

CONCLUSIONS

Despite HPV vaccination completion rates rising across the nation, Mississippi continues to rank among the bottom of all states with a reported “up to date” rate of 28.8% in 2017. Effective strategies need to be implemented to improve HPV vaccination rates among Medicaid beneficiaries. A coordinated effort among providers and pharmacists targeting beneficiaries initiating the HPV vaccination series to increase completion rates is optimal. As the most easily accessible healthcare professionals, pharmacists can play a vital role in increasing HPV completion rates. All vaccines administered to individuals < 19 years are required to be submitted to the Mississippi Immunization Information eXchange (MIIX). Pharmacists can register to have access to the MIIX system and report vaccines administered in the pharmacy setting.

RECOMMENDATIONS

1. MS-DUR, along with DOM, will develop provider education emphasizing the importance of timely follow-up for beneficiaries initiating HPV vaccination series.

2. DUR should work with DOM to develop an initiative to encourage pharmacists to become more involved in both initiating and completing HPV vaccinations.

3. DOM will collaborate with the Mississippi State Department of Health in developing strategies to increase HPV vaccination completion rates in Mississippi.

BUPRENORPHINE UTILIZATION TRENDS IN MISSISSIPPI MEDICAID

BACKGROUND

As a result of the opioid crisis, opioid use disorder (OUD) and opioid related overdoses have increased substantially. Literature has found that between 21% and 29% of patients prescribed opioids for chronic pain misuse them and addiction rates range from 8% to 12%.[1] According to data reported by the CDC, opioid overdoses increased 30 percent from July 2016 through September 2017 in 52 areas across 45 states.[2] It is estimated 26,000 Mississippians 12 years and older suffered from OUD from 2015-2017.[3] One of the focus areas for the U.S. Department of Health and Human Services (HHS) in combating the rise in misuse and abuse of opioids is improving access to treatment options for OUD.

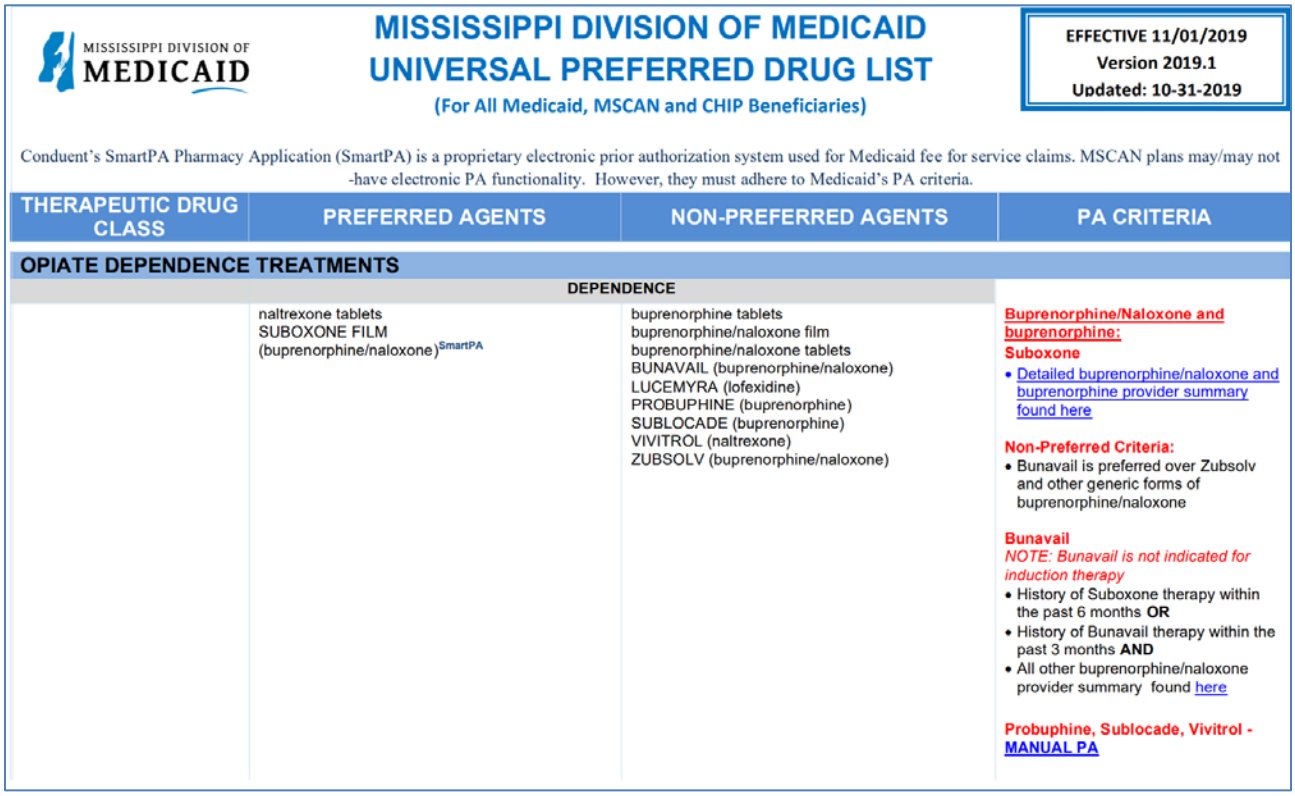
Medication-assisted treatment (MAT) is the use of medicine in combination with behavioral therapies for the effective treatment of opioid use disorders. Currently there are three FDA approved drugs for the treatment of opioid dependence: buprenorphine, methadone, and naltrexone. Each option has its own unique characteristics and requirements related to prescribing. Methadone is a long-acting opioid agonist that is only available through specialized opioid treatment programs (OTP) due to serious side effects and potential for abuse. Naltrexone is a pure opioid antagonist that is available in a once daily oral tablet or a long acting injectable agent. Buprenorphine is an opioid partial agonist available alone or in combination with naloxone.[4] Figure 1 displays Mississippi Medicaid's Universal Preferred Drug List (UPDL) for opiate dependence treatments. Also available on the Clinician Administered Drug and Device (CADD) list are injectable formulations of buprenorphine (Probuphine and Sublocade) and naltrexone (Vivitrol). Although Mississippi Medicaid will cover methadone for the treatment of OUD with the appropriate diagnosis, because of the shortage and stigma of methadone clinics, buprenorphine treatment is the primary alternative for many opiate-dependent patients. Methadone is listed on the PDL as non-preferred under the long-acting narcotic analgesic category.

Buprenorphine/naloxone (Suboxone) film and naltrexone tablets are preferred drugs under the opiate dependence treatments category on Medicaid's UPDL. For clinical reasons, single-agent buprenorphine is covered only for pregnant women. In 2016, the state removed a 24-month maximum length of coverage and limits on the number of times an individual could restart treatment. To further facilitate access to opioid use disorder treatment, requirements for prior authorization for buprenorphine and buprenorphine/naloxone were removed except for a

[1] Vowles KE, McEntee ML, Julnes PS, Frohe T, Ney JP, van der Goes DN. Rates of opioid misuse, abuse, and addiction in chronic pain: a systematic review and data synthesis. *Pain*. 2015;156(4):569-576. doi:10.1097/01.j.pain.0000460357.01998.f1.
[2] Vivolo-Kantor, AM, Seth, P, Gladden, RM, et al. *Vital Signs: Trends in Emergency Department Visits for Suspected Opioid Overdoses--United States, July 2016-September 2017*. Centers for Disease Control and Prevention
[3] Substance Abuse and Mental Health Services Administration. Behavioral Health Barometer: Region 1, Volume 5: Indicators as measured through the 2017 National Survey on Drug Use and Health and the National Survey of Substance Abuse Treatment Services. HHS Publication No. SMA-19-Baro-17-R1. Rockville, MD: Substance Abuse and Mental Health Services Administration, 2019.
[4] (FDA) Information about Medication-Assisted Treatment (MAT). https://tinyurl.com/yxrbece7. Accessed 11/5/2019.

diagnosis of opioid use disorder for individuals in fee-for-services plans as well as for those in managed care plans.

FIGURE 1- UPDL Opiate Dependence Treatments



MISSISSIPPI DIVISION OF MEDICAID

MISSISSIPPI DIVISION OF MEDICAID
UNIVERSAL PREFERRED DRUG LIST
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THERAPEUTIC DRUG CLASS	PREFERRED AGENTS	NON-PREFERRED AGENTS	PA CRITERIA
OPIATE DEPENDENCE TREATMENTS			
DEPENDENCE			
	naltrexone tablets SUBOXONE FILM (buprenorphine/naloxone) SmartPA	buprenorphine tablets buprenorphine/naloxone film buprenorphine/naloxone tablets BUNAVAIL (buprenorphine/naloxone) LUCEMYRA (lofexidine) PROBUPHINE (buprenorphine) SUBLOCADE (buprenorphine) VIVITROL (naltrexone) ZUBSOLV (buprenorphine/naloxone)	**Buprenorphine/Naloxone and buprenorphine:** **Suboxone** • Detailed buprenorphine/naloxone and buprenorphine provider summary found here **Non-Preferred Criteria:** • Bunavail is preferred over Zubsolv and other generic forms of buprenorphine/naloxone **Bunavail** *NOTE: Bunavail is not indicated for induction therapy* • History of Suboxone therapy within the past 6 months **OR** • History of Bunavail therapy within the past 3 months **AND** • All other buprenorphine/naloxone provider summary found here **Probuphine, Sublocade, Vivitrol - MANUAL PA**

DOM has available on its website the "Buprenorphine/Naloxone and Buprenorphine Therapy Coverage" provider summary sheet (Attachment A) available to facilitate providers in the prescribing of buprenorphine and buprenorphine/naloxone products.

In October of 2019, the Mississippi State Department of Health's Morbidity Report focused on buprenorphine prescription practices in Mississippi from 2012-2017 using data accessed through the Mississippi Prescription Drug Monitoring Program (PDMP) (Attachment B).[5] The report noted:

- In Mississippi, the number of buprenorphine prescriptions has increased by 58% from 2012 to 2017.
- Only one out of every five prescriptions were long-term buprenorphine prescriptions (30-day supply or more)

[5] Mississippi State Department of Health. Mississippi Morbidity Report. Bridging the Treatment Gap: Buprenorphine Prescription Practices in Mississippi, 2012-2017. Volume 35, Number 2; October 2019.

The findings from the Mississippi State Department of Health's (MSDH) report prompted MS-DUR to run similar analyses in the Medicaid population to assess buprenorphine prescribing trends in Medicaid specifically.

METHODS

A retrospective database analysis of Mississippi Medicaid beneficiaries was conducted using pharmacy claims for single agent buprenorphine and buprenorphine-naloxone combination products from January 1, 2012 to August 31, 2019. Claims for Butrans, Belbucca, and Buprenex products indicated for pain management were excluded from this analysis. The number of prescription fills, unique prescriptions, and long-term prescription fills each year were calculated for the entire study period. The number of unique prescriptions was assessed by calculating the number of prescriptions with unique prescription numbers each year. Long-term prescription fills were defined as prescription fills having a days supply of ≥30 days. Moreover, the number of unique prescriptions each year was stratified by gender (male or female), age group (≤24 years, 25-34 years, 35-44 years, 45-54 years, 55-64 years, and ≥65 years), and whether the prescription was issued by a Mississippi-based (MS-based) provider and are shown in Table 1.

Additionally, drug utilization since January 1, 2018 until August 31, 2019 was assessed to capture the current trends in buprenorphine use among beneficiaries enrolled in Mississippi Medicaid. Total number of prescription fills and beneficiaries utilizing buprenorphine were assessed, stratifying for gender and type of drug used (single agent buprenorphine or buprenorphine-naloxone combination). Number of prescription fills were further stratified by duration of each fill (≤3 days, 4-7 days, 8-29 days, 30 days, or >30 days) based on the days supply for each fill. See Table 2.

Moreover, buprenorphine prescription rates per 100 Medicaid eligible population was calculated at a county level (based on the beneficiary's county of residence), and is represented on Figure 2's map of Mississippi. Number of Medicaid eligible beneficiaries in each county was calculated as total number of beneficiaries with at least one month of Medicaid eligibility between January 2018 and August 2019. Furthermore, number of unique MS-based providers prescribing buprenorphine was also calculated and referenced at a county level in Figure 3.

RESULTS

TABLE 1. Buprenorphine Prescriptions in Mississippi Medicaid ** January 1, 2012 - August 31, 2019 (across all plans)									
Characteristics	**2012**	**2013**	**2014**	**2015**	**2016**	**2017**	**2018**	**2019 ł**	Change
Rx and Fills	No (%)	No (%)	No (%)	No (%)	No (%)	No (%)	No (%)	No (%)	**2012-2018***
Unique Rx[a]	4,444	5,910	5,607	6,706	7,256	9,251	11,293	8,872	154%
Total Rx Fills	4,984	6,750	6,349	7,448	7,936	9,977	12,056	9,467	142%
Rx fills for 30 or more days	3,522 (71%)	5,027 (74%)	4,274 (67%)	5,007 (67%)	5,545 (70%)	6,753 (68%)	7,865 (65%)	6,254 (66%)	123%
Total days of supply	135,952	182,428	163,367	190,784	207,980	259,126	310,121	237,336	128%
Gender									
Female	3,466 (78%)	4,515 (75%)	4,224 (75%)	5,047 (75%)	5,427 (75%)	7,026 (76%)	8,715 (77%)	6,822 (77%)	151%
Male	978 (22%)	1,395 (25%)	1,383 (25%)	1,659 (25%)	1,829 (25%)	2,225 (24%)	2,578 (23%)	2,050 (23%)	164%
Age Group									
≤ 24 years	400 (9%)	556 (10%)	425 (8%)	483 (7%)	366 (5%)	380 (4%)	412 (4%)	268 (3%)	3%
25 - 34 years	2,342 (53%)	3,098 (52%)	2,771 (49%)	3,129 (47%)	3,199 (44%)	3,877 (42%)	4,073 (36%)	3,247 (37%)	74%
35 - 44 years	997 (22%)	1,370 (23%)	1,568 (28%)	1,972 (29%)	2,478 (34%)	3,209 (35%)	4,024 (36%)	3,042 (34%)	304%
45 - 54 years	500 (11%)	592 (10%)	557 (10%)	743 (11%)	754 (11%)	1,158 (12%)	1,715 (15%)	1,254 (14%)	243%
55 - 64 years	205 (5%)	294 (5%)	286 (5%)	379 (6%)	459 (6%)	627 (7%)	1,068 (9%)	1,058 (12%)	421%
≥ 65 years	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0%)	3 (0%)	
Rx Issued by MS Providers									
	4,059 (91%)	5,162 (87%)	4,857 (87%)	5,588 (83%)	5,941 (82%)	7,739 (84%)	9,595 (85%)	7,372 (83%)	136%

ł Numbers for 2019 are through August 2019.

*Change has been calculated using 2012 and 2018 numbers, since we do not have complete data for 2019

**Rx fills for both buprenorphine and buprenorphine-naloxone were considered for the analysis; Claims for Butrans, Belbucca, and Buprenex were excluded from the analysis

[a]Unique Rx calculated based on prescription numbers for the claims

Over the seven year period between 2012 and 2018, prescription claims for buprenorphine products in Mississippi Medicaid have consistently increased. (Table 1)

- Unique Rx (prescriptions with different prescription numbers) increased 154% and Total Rx Fills increased 142% between 2012 and 2018 in Mississippi Medicaid.
- Comparing the same period reported in the MSDH report (2012-2017), Unique Rxs increased 108% and Total Rx Fills increased 100% in Mississippi Medicaid compared to a 58% and 59% increase, respectively, reported in the MSDH report.
    - Medicaid has made multiple updates to their criteria for prescribing buprenorphine products in efforts to increase beneficiary access to MAT. The increased proportion of buprenorphine claims in Mississippi Medicaid can partially be attributed to these changes in prescribing criteria for buprenorphine products and related provider education that has occurred over time. One of the significant changes occurred at the end of 2016 when the DUR Board recommended the removal of maximum length and restart limits. The impact of these changes can be seen in the 27.5% increase in number of Unique Rxs from 2016 to 2017 alone.
- The proportion of prescription fills for 30 or more days in Medicaid has consistently ranged between 65-70% annually. This proportion is much higher than the approximately 20% reported in the MSDH report. The financial situation of patients, cost of treatment and available insurance coverage can all present impediments to MAT therapy.
- Factors that may have contributed to the findings of Medicaid's days supply compared to the shorter duration (< 30 days) noted in the MSDH Mortality Report could include the following:
    - Lack of financial barriers for prescription coverage. Medicaid provided coverage for five medications per month until July 1, 2019 when coverage increased to six medications per month.
    - Medicaid has preferred as well as non-preferred buprenorphine products on its UPDL and does not have any restrictions on length of coverage. This could be a major factor contributing to a higher proportion of prescription fills in Medicaid for 30 or more days when compared to the numbers cited in the MSDH report.
- Other factors noted in the MSDH report influencing treatment duration include minimizing the risk of buprenorphine diversion or misuse and the availability of concomitant behavioral therapies and social support for patients. The potential for short-term buprenorphine prescription as cited in the MSDH report could also be attributed, in part, due to the diversion of this drug for self-medication of withdrawal symptoms or self-weaning from illicit opioid use. Provider comfort in prescribing buprenorphine products for extended period without monitoring patients for treatment compliance or addiction relapse was another potential reason noted in MSDH's report, though the proportion of beneficiaries with $\geq$ 30 days supply was greater in Medicaid.
- Females were approximately 3 times more likely than men to receive buprenorphine prescriptions in Medicaid. This stands to reason because second to children, women are the most likely recipients of Medicaid benefits.

- Buprenorphine prescriptions increased substantially for all age groups, except for beneficiaries age < 25 years. Beneficiaries between ages 35 and 64 years had the largest increase (300%).

To examine current prescribing trends more closely, buprenorphine product utilization was assessed between January 2018 and August 2019 in Mississippi Medicaid. Analysis was broken down by gender, drug type, and days supply per claim (Table 2).

TABLE 2. Prescription Claims and Beneficiaries by Gender and Drug Type between January 1, 2018 - Aug 31, 2019

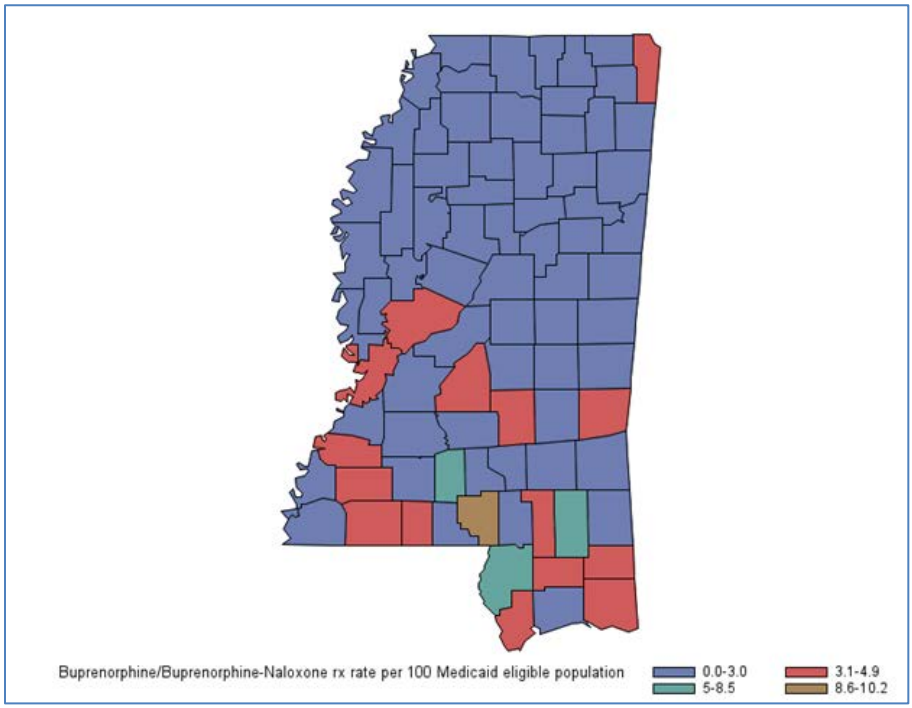
Gender	Drug Type	Days supply per claim					Total # of claims	# of unique beneficiaries
		≤ 3 days	4 - 7 days	8 - 29 days	30 days	> 30 days		
Female	Buprenorphine	52 (0.3%)	136 (0.8%)	712 (4.3%)	744 (4.5%)	14 (0.1%)	1,658 (10.0%)	339
	Buprenorphine-Naloxone	248 (1.5%)	1,360 (8.2%)	3,346 (20.2%)	9,889 (59.6%)	83 (0.5%)	14,926 (90.0%)	1,432
Male	Buprenorphine	3 (0.1%)	2 (0.0%)	78 (1.6%)	64 (1.3%)	1 (0.0%)	148 (3.0%)	31
	Buprenorphine-Naloxone	64 (1.3%)	382 (7.7%)	1,021 (20.7%)	3,304 (66.9%)	20 (0.4%)	4,791 (97.0%)	466

Note - Rx fills for both buprenorphine and buprenorphine-naloxone were considered for the analysis; Claims for Butrans, Belbucca, and Buprenex were excluded from the analysis

- Consistent with the trend reported in Table 1, 77.1% of claims were for females.
- Buprenorphine single agent products are only approved for use in pregnancy.
- 339 females received buprenorphine products during the analysis period.
- 65.6% of claims (n=14,119) during the analysis period were for ≥ 30 days supply.
- Overall 10.4% of claims (n=2247) were for 7 days or less.

MS-DUR conducted a geographical analysis of beneficiaries prescribed buprenorphine products based on the county of residence for each beneficiary. Buprenorphine prescription rates per 100 Medicaid eligible population were calculated at a county level and represented on a map of Mississippi (Figure 2). Denominator was the number of eligible beneficiaries in each county - calculated as the total number of beneficiaries in each county with at least one month of Medicaid eligibility between January 2018 and August 2019. Numerator was the number of buprenorphine prescriptions in each county during the study period. A map of Mississippi identifying each county can be found in Attachment C of this report.

FIGURE 2- Prescription Rates per 100 Medicaid Eligible Population by County

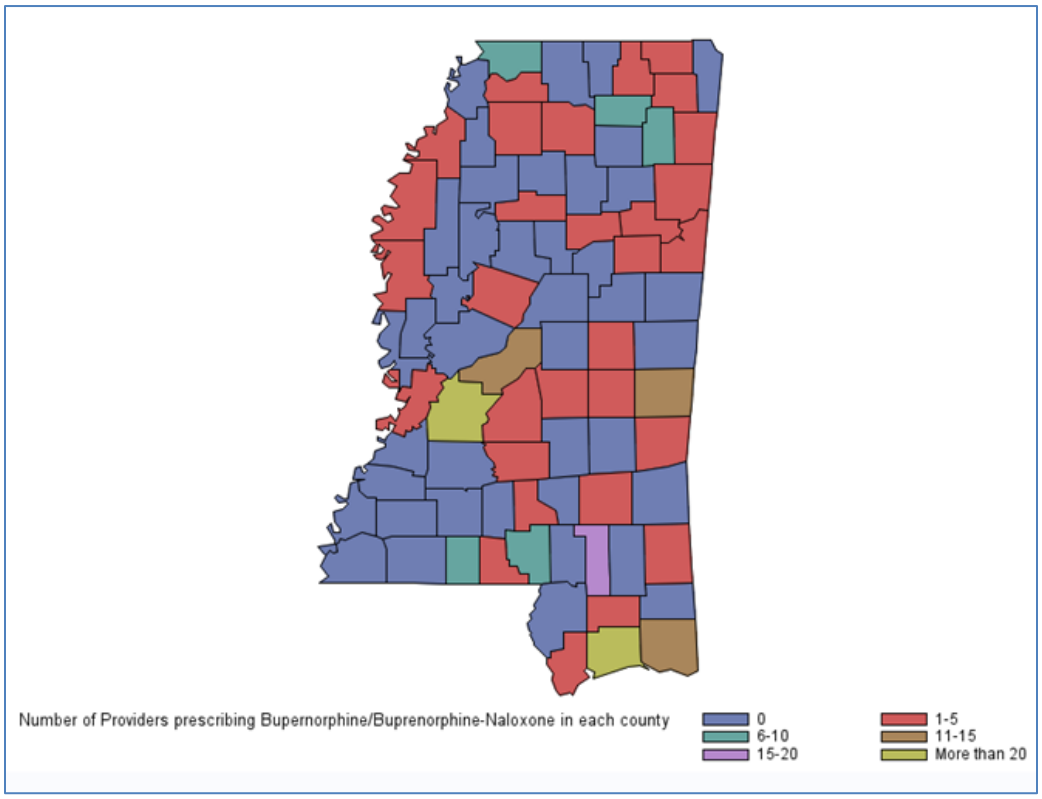


- Buprenorphine prescription rates appear higher along the southern and coastal counties.
- **Marion** County had the highest rate, followed **Lawrence, Pearl River,** and **Perry** counties.

Access to providers authorized to prescribe buprenorphine products and who are Medicaid providers has long been considered a limitation to utilization. In order to be able to prescribe buprenorphine products, a provider must obtain a waiver from the Drug Enforcement Agency (DEA).[6] According to data published on the Substance Abuse and Mental Health Services Administration (SAMHSA) website, there are 228 providers in Mississippi listed who are authorized to prescribe buprenorphine products as of November 2019. This number may be an underestimation of providers authorized to prescribe buprenorphine products because providers can opt to be excluded from SAMHSA's publicly available list of providers. Figure 3 displays a map of Mississippi of providers associated with buprenorphine claims for Medicaid beneficiaries between January 2018 and August 2019.

[6]Drug Enforcement Administration: DEA Requirements for DATA Waived Physicians (DWPs)
https://www.deadiversion.usdoj.gov/pubs/docs/dwp_buprenorphine.htm

FIGURE 3 – Number of Providers Prescribing Buprenorphine Products by County



- Approximately half of the counties in Mississippi did not have a provider who prescribed buprenorphine to a Medicaid beneficiary between January 2018 and August 2019.
- Hinds and Harrison counties had the most providers prescribe buprenorphine products followed by Forrest, Madison, Lauderdale, Jackson, Desoto, Lee, Union, Marion, and Pike counties.
- Based on data presented in Table 1, approximately 85% of prescriptions for buprenorphine products are written by providers in the state of Mississippi.

CONCLUSIONS

The prescribing of buprenorphine products has increased significantly among Medicaid beneficiaries since 2012. The increase among Medicaid beneficiaries is greater than the increase reported in the MSDH's recent Morbidity Report on buprenorphine use across the state. The 154% increase in prescribing of buprenorphine products can be attributed to many factors including efforts by DOM to reduce opioid use disorder and increase beneficiary access to MAT. Approximately 30-35% of buprenorphine claims are for < 30 days. Successful outcomes with MAT have been related to long-term maintenance treatment.[7] With buprenorphine products available on Medicaid's UPDL, short-term (< 30 days) therapy due to coverage or cost concerns should not be an issue. Another issue that may impact beneficiary access to buprenorphine products is the availability of authorized prescribers who are Medicaid providers.

RECOMMENDATIONS

1. MS-DUR should work with DOM to develop a provider education targeting providers currently prescribing buprenorphine products to:
    - inform providers of buprenorphine product utilization among Medicaid beneficiaries;
    - encourage long-term (30 days supply) prescribing for buprenorphine products.

2. MS-DUR should work with DOM to develop a provider bulletin to be distributed to provider member organizations to:
    - educate providers on the importance of MAT in combating opioid use disorder;
    - increase awareness in not only the need but how more Medicaid providers can obtain SAMHSA* certification as an Opioid Treatment Program and authorized to prescribe buprenorphine products.

**SAMHSA= Substance Abuse and Mental Health Services Administration. In the United States, the treatment of opioid dependence with medications is governed by the Certification of Opioid Treatment Programs, 42 Code of Federal Regulations (CFR) 8. This regulation created a system to accredit and certify opioid treatment programs (OTPs). OTPs provide medication-assisted treatment (MAT) for people diagnosed with an opioid-use disorder. MAT patients also must receive counseling, which can include different forms of behavioral therapy.*

3. Collaborate with MSDH to improve access to MAT across the state of Mississippi.

[7]Bart G. Maintenance medication for opiate addiction: the foundation of recovery. *J Addict Dis*. 2012;31(3):207–225. doi:10.1080/10550887.2012.694598

ATTACHMENT A

Buprenorphine/Naloxone and Buprenorphine THERAPY COVERAGE

Provider Summary Sheet

MISSISSIPPI DIVISION OF MEDICAID

START (first prescription fill in 90 days)

Induction and Stabilization Phase	Months 1 - 2	Maintenance Phase	Months 3 and after
	Up to 24mg/day**		Up to 16mg/day **

*** Maximum daily doses shown are for use of Suboxone®, the preferred product. If Zubsolv® or Bunavail® are approved for use, equivalent dosing limits will apply. Refer to the Uniform Preferred Drug List for criteria regarding use of non-preferred products.*
http://www.medicaid.ms.gov/providers/pharmacy/preferred-drug-list

- Buprenorphine/naloxone and buprenorphine are only approved for opioid dependence ICD-10 codes that must be found in medical claims or written on prescription and entered by pharmacist with prescription claim (F11.1xx, F11.2xx, F11.90, F19.20 or F19.21).
- Buprenorphine is only approved for use during pregnancy. Appropriate ICD-10 codes must be found in medical claims or written on prescription and entered by pharmacist with prescription claim. Appropriate codes can be found at: https://medicaid.ms.gov/wp-content/uploads/2018/09/ICD-10-codes-for-POS-claims-and-SMART-PAs-8.20.18.pdf
- All buprenorphine/naloxone and buprenorphine prescribers must have current XDEA number.

Opiate use restriction:

- Beneficiaries cannot fill a prescription for more than 5 day supply of opiate within last 30 days while on buprenorphine/naloxone therapy.
- Cumulative maximum of 10 days of opiate treatment within last 60 days while on buprenorphine/naloxone therapy.
- Medicaid claims are electronically reviewed for opiate use. Physicians and pharmacists are encouraged to use Prescription Monitoring Program (PMP) to monitor opiate use paid for by cash or other payers.

Trouble Shooting Rejections:

- ***Claim denied no diagnoses for opioid dependence or no diagnosis for pregnancy (buprenorphine use) found***
  Solution: *Physician should write diagnosis code on prescription and pharmacy should enter diagnosis code on pharmacy claim and call Medicaid PA unit if claim is still rejected for lack of diagnosis.*
- ***Beneficiary has claim for > 5 days of opiate use***
  Solution: *Manual PA required from physician for appeal with medical justification for continuing treatment while taking opioids.*
- ***Beneficiary has more than 10 days total opiate supply during last 60 days while on therapy***
  Solution: *Manual PA required from physician for appeal with medical justification for continuing treatment while taking opioids.*

Prepared by:

MS | DUR Evidence-Based DUR Initiative
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Revision: 12/11/2018

Medicaid PA Unit: Phone 877-537-0722
Fax 877-537-0720
Copies of this Summary Sheet are available at:
https://medicaid.ms.gov/providers/pharmacy/pharmacy-resources/

ATTACHMENT B

Mississippi State Department of Health

Mississippi Morbidity Report

Epidemiology Update

Volume 35, Number 2 October 2019

Bridging the Treatment Gap: Buprenorphine Prescription Practices in Mississippi, 2012-2017

Currently, the Food and Drug Administration (FDA) has approved three medications for the pharmacotherapy of opioid use disorder (OUD): methadone, buprenorphine, and naltrexone. Methadone and buprenorphine are widely-used, first-line treatment options for OUD, while naltrexone is rarely used. Medication-assisted treatment (MAT) with methadone and buprenorphine are highly effective for OUD detoxification and maintenance therapy.[1] Yet access to these medications is challenging for patients suffering from opioid addiction due to a shortage of treatment programs and prescribers. Because of its serious side effects and high potential for misuse/diversion, methadone is only disseminated within specialized Opioid Treatment Programs (OTP), known as methadone clinics. Unlike methadone, buprenorphine has a better drug-safety profile, lower risk for overdose, and could be used in office-based settings.[2]

Key Messages

- **In Mississippi, the number of buprenorphine prescriptions has increased by 58%, from 50,318 in 2012 to 79,657 in 2017. The total days of supply nearly doubled from 1.5 million to 2.7 million days; however, only one out of every five were long-term buprenorphine prescriptions (30-day supply).**
- **The uptrend in buprenorphine prescriptions may be due to a parallel increase in both the prevalence of patients with opioid use disorder and the number of buprenorphine prescribers.**
- **The low number of long-term buprenorphine prescriptions is a barrier to successful addiction treatment in our state; however, the exact reasons for this shortfall are unclear.**
- **To address this treatment barrier, the Mississippi medical community should invest in training programs and educational outreach designed to standardize the delivery of buprenorphine therapy.**

Regulations on Prescriptions

During the last two decades two legislative measures addressing the shortage of opioid-substitutional treatments have been introduced. In 2000, Congress passed the Drug Addiction Treatment Act (DATA) of 2000 allowing all physicians to treat opioid dependency with narcotics (except for methadone) in office-based settings.[3] In 2002, FDA approved buprenorphine for such use. The Comprehensive Addiction and Recovery Act (CARA) of 2016 extended the privilege of prescribing buprenorphine in office-based settings to nurse practitioners and physician assistants.[4] Buprenorphine practitioners are required, however, to obtain a waiver from the Drug Enforcement Agency (DEA), complete a course of training (8 hours for physicians and 24 hours for nurse practitioners/physician assistants), and keep records available for DEA inspections. It is important to note that such a buprenorphine waiver is not required in case of an emergency; any clinician may administer (but not prescribe) buprenorphine to patients with acute withdrawal symptoms for up to 72 hours (the 'three day" rule).

Barriers to Treatment

Although the goal of these legislative measures is to increase the availability of opioid-substitution treatments, few health care providers have taken advantage of the opportunity to treat patients in office-based settings. As of April 2019, only 65,207 clinicians had a buprenorphine waiver nationwide. In 2017, an estimated 42.3% of all counties across the nation had no practitioners licensed to prescribe buprenorphine.[5]

According to national-level research, the major concerns that keep physicians from pursuing office-based opioid-substitution treatments include insufficient training to diagnose and treat opioid use disorders,

intrusive DEA regulations, the stigma associated with treating drug-dependent patients, the potential for drug diversion or misuse, and lack of psychological and social support for patients.[6] Another serious constraint is the DEA regulation that caps the number of patients buprenorphine prescribers can see, limiting them to no more than 30 patients during the first year after receiving a waiver and no more than 100 patients after that.[7] Payment issues such as low reimbursement rates by Medicaid have further hindered efforts to expand office-based opioid-substitution treatments.[8]

Data and Objectives

The Mississippi Prescription Drug Monitoring Program (PDMP) collects data on prescriptions for all controlled substances in the state. This data source contains information on prescription dosage and days of supply, patient demographics and place of residence, and locations of prescribers and dispensing pharmacies. Because methadone clinics are excluded from reporting requirements, methadone prescriptions for opioid use disorders are not reported to the state PDMP. As a result, a comprehensive assessment of opioid-substitution treatments in Mississippi is not possible at this time. The scope of this report is limited, therefore, to the evaluation of buprenorphine prescription practices, an increasingly popular method of opioid-substitution treatment.

Methods

Included in this report are buprenorphine prescriptions dispensed to state residents by Mississippi and non-Mississippi providers between 2012 and 2017. For this study, we evaluated the number of unique prescriptions as well as the number of refills. The number of unique prescriptions was obtained using the unique prescription number generated by the dispensing pharmacy. Prescriptions for buprenorphine formulations used as an opioid analgesic (e.g., buprenorphine patches) were excluded from the analysis.

Buprenorphine Prescribing in Mississippi (Table)

The number of buprenorphine prescriptions issued in Mississippi increased by 58%, from 50,318 in 2012 to 79,657 in 2017. Following a rapid increase from 2012 to 2015, the number of buprenorphine prescriptions plateaued between 2016 and 2017. Moving in direct proportion with the number of prescriptions, the total days of supply nearly doubled, growing from 1,463,903 days in 2012 to 2,682,518 days in 2017. Unlike the number of prescriptions, the total days of buprenorphine supply continued to increase steadily throughout the study period due to an increasing number of buprenorphine prescription refills. The number of long-term prescription fills (30-day supply), however, was low. The proportion of such long-term prescriptions remained stable during the study period, accounting for only about one-fifth of all buprenorphine prescription fills each year.

Demographics

The demographic analysis revealed that men were more likely than women to be treated with buprenorphine. On average, 59% of all buprenorphine prescriptions each year were dispensed to men. Buprenorphine prescriptions increased for all age groups, except for patients younger than 25 years. The rate of increase, however, varied by age group. The proportion of patients between 25 and 34 years decreased; such patients accounted for 42% of all buprenorphine prescriptions in 2012 but only 32% in 2017. By comparison, the proportion of patients 35 years of age and older increased.

Prescribers of Buprenorphine in Mississippi

As of April 2019, the number of buprenorphine practitioners in Mississippi is 207 according to publicly available data from the Substance Abuse and Mental Health Services Administration (SAMHSA)

Table. Buprenorphine Prescriptions in Mississippi, 2012-2017

Characteristics	2012	2013	2014	2015	2016	2017	Change
Rx and Fills	No (%)	No (%)	No (%)	No (%)	No (%)	No (%)	2012-2017
Unique Rx	50,318	58,996	66,350	75,368	79,353	79,657	58%
Total Rx Fills	144,047	167,885	191,451	212,020	210,500	229,181	59%
Rx fills for 30 days*	28,359 (20%)	31,959 (19%)	34,478 (18%)	38,515 (18%)	40,165 (19%)	46,982 (21%)	66%
Total days of supply	1,463,903	1,729,806	1,961,184	2,214,407	2,353,675	2,682,518	83%
Gender							
Female	20,652 (41%)	24,445 (41%)	27,172 (41%)	30,994 (41%)	32,797 (41%)	34,241 (43%)	66%
Male	29,655 (59%)	34,512 (59%)	39,066 (59%)	44,196 (59%)	46,457 (59%)	45,314 (57%)	53%
unknown	11 (0%)	39 (0%)	112 (0%)	178 (0%)	99 (0%)	102 (0%)	
Age Group							
≤ 24 years	3,803 (8%)	4,069 (7%)	3,653 (6%)	3,599 (5%)	3,088 (4%)	2,366 (3%)	-38%
25-34 years	21,187 (42%)	24,395 (42%)	27,318 (41%)	29,238 (39%)	27,646 (35%)	25,658 (32%)	21%
35 - 44 years	14,035 (28%)	17,207 (29%)	19,903 (30%)	23,598 (31%)	26,382 (33%)	27,520 (35%)	96%
45 - 54 years	7,670 (15%)	8,985 (15%)	9,970 (14%)	11,786 (16%)	13,247 (17%)	13,580 (17%)	77%
55 - 64 years	3,025 (6%)	3,614 (6%)	4,502 (7%)	5,901 (8%)	7,347 (9%)	8,383 (10%)	177%
≥ 65 years	598 (1%)	726 (1%)	1,004 (2%)	1,246 (1%)	1,643 (2%)	2,150 (3%)	260%
Rx Issued by MS Providers							
	42,705 (85%)	39,848 (82%)	53,687 (81%)	58,648 (79%)	61,002 (78%)	61,829 (78%)	45%
MS DATA-Waived Newly Certified Practitioners							
With 30 Patients	14	10	8	17	23	48	
With 100 Patients	6	11	13	5	13	7	

*During the study period, the number of prescriptions for more than 30 days was negligible.
** Source: Substance Abuse and Mental Health Services Administration

(https://www.samhsa.gov/medication-assisted-treatment/practitioner-program-data/treatment-practitioner-locator). Between 2012 and 2017, the number of newly certified prescribers reached 120. As compared to 2012, there were more than three times more newly certified buprenorphine prescribers in 2017. These numbers could be underestimated, however, because buprenorphine practitioners could opt to be excluded from SAMHSA's publicly available list of buprenorphine providers.

Not all buprenorphine prescriptions during the study period were issued by Mississippi providers. On average during each year of the study, around one-fifth of all buprenorphine prescriptions were written by non-state health care practitioners. In fact, providers in Memphis, TN issued 7% of all buprenorphine prescriptions to Mississippi residents in 2017. During the same year, the highest percentage of prescriptions written by Mississippi providers were in Jackson (10%), followed by Hattiesburg (7%), Biloxi (6%), New Albany (5%), and Vicksburg (4%). These top five prescribers' locations accounted for one-third (33%) of all buprenorphine prescriptions dispensed in Mississippi during 2017.

Discussion

In six years, prescriptions for buprenorphine nearly doubled in Mississippi. Although the exact causality is difficult to establish, this may be due to an increasing prevalence of opioid use disorders. Findings from health care data support such a claim. Between 2014 and 2017 in Mississippi, the rate of opioid-related hospitalizations rose by 26% and the rate of opioid-related emergency department visits spiked by 45%.[9] It is also possible that health care providers treat patients with OUD more frequently as a result of the ongoing campaign aimed at opioid-harm reduction. Finally, another contributing factor for the uptrend in buprenorphine prescribing may be the increase in the number of buprenorphine prescribers in the state. Even though small, the increase in buprenorphine practitioners is encouraging because reducing opioid-related morbidity and mortality is not possible without available, accessible, and affordable treatments for patients with substance dependency.

Successful outcomes are also dependent on treatment duration and retention in therapy. Preventing relapse is best achieved with a long-term opioid-substitution treatment.[10] In contrast, short-term buprenorphine prescriptions (less than 30 days) are most likely indicated for emergency treatment of patients with acute opioid withdrawal symptoms. Our analysis revealed, however, that the majority (80%) of buprenorphine prescriptions fills were issued for less than 30 days. The information contained within PDMP data does not allow us to establish the causes for such short duration of treatment.

There could be several factors contributing to this high volume of short-term buprenorphine prescriptions. Currently, there is no consensus regarding the optimal duration of buprenorphine treatment or established guidelines governing the frequency of treatment monitoring.[11] Physicians may feel uncomfortable prescribing buprenorphine for an extended period without monitoring patients for treatment compliance or addiction relapse. Therefore, buprenorphine prescribers in Mississippi may prefer issuing prescriptions with short-duration to minimize the risk of buprenorphine diversion or misuse. Additional factors influencing treatment duration are the availability of concomitant behavioral therapies and social support for such patients. Likewise, the treatment duration may be influenced by the financial situation of each individual patient, cost of treatment, and available insurance coverage. The high cost of buprenorphine prescriptions may also be a barrier to sustained long-term treatment options. The National Institute on Drug Abuse, for instance, estimates that the average cost of buprenorphine treatment is about $115 per week or $5,980 per year.[12] Lastly, the high volume of short-term buprenorphine prescriptions may be due, in part, to the diversion of this drug for self-medication of withdrawal symptoms or self-weaning from illicit opioid use.[13,14]

There is no easy solution for providing comprehensive and sustained medical care for patients suffering from opioid addiction. Moreover, therapies, such as methadone replacement therapy, are controversial issues that face political and community suspicion and pushback. Mississippi experiences additional difficulties such as high unemployment rates, economically depressed communities, high levels of uninsured patients, a shortage of health care providers, and limited access to medical care. All these factors have led to an underdeveloped opioid treatment infrastructure in our state. According to SAMHSA, for example, there are only five methadone clinics in the state (https://dpt2.samhsa.gov/treatment/directory.aspx). Because of this shortage and stigmatization of methadone clinics, buprenorphine treatment is the only alternative for many opioid-dependent patients. In addition, treatment with buprenorphine is safer than methadone and the office-based treatment is more convenient for working patients. Therefore, augmenting the office-based buprenorphine prescribing practices, especially in rural and underserved areas, is crucial for our state.

To address treatment challenges within remote locations, several states have implemented nonconventional but promising models of care. Examples of such practices include establishing structures for connecting addiction-treatment specialists with distant locations (Vermont's Hub and Spoke model), engaging nurse practitioners and physician assistants to deliver MAT in community health centers, enhancing existing telemedicine services, and initiating buprenorphine treatment during emergency department visits for overdoses. With this report, we hope to stimulate the search for innovative solutions aimed at enhancing the state's addiction treatment capacity and encourage more clinicians to join the efforts of the few dedicated buprenorphine practitioners in Mississippi.

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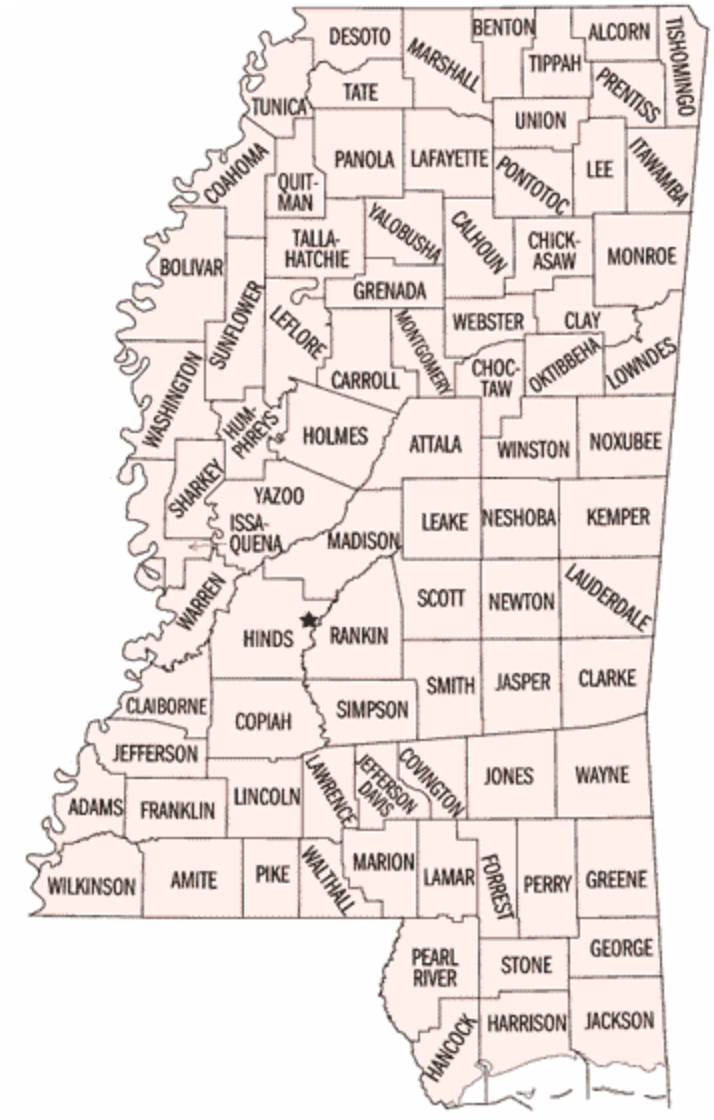
References

1. Kampman K, Jarvis M. American Society of Addiction Medicine (ASAM) National Practice Guideline for the Use of Medications in the Treatment of Addiction Involving Opioid Use. *J Addict Med*. 2015;9(5):358–367. doi:10.1097/ADM.0000000000000166.
2. Kahan M, Srivastava A, Ordean A, Cirone S. Buprenorphine: new treatment of opioid addiction in primary care. *Can Fam Physician*. 2011;57(3):281–289.
3. Drug Addiction Treatment Act of 2000. DATA-2000 - Public Law 106-310- 106th Congress - An Act.
4. Comprehensive Addiction and Recovery Act of 2016. Public Law 114–198. Page 130 Stat. 695. Available at: https://www.congress.gov/114/plaws/publ198/PLAW-114publ198.pdf.
5. Andrilla, C. H., Moore, T. E., Patterson, D. G. and Larson, E. H. (2019), Geographic Distribution of Providers With a DEA Waiver to Prescribe Buprenorphine for the Treatment of Opioid Use Disorder: A 5-Year Update. The Journal of Rural Health, 35: 108-112. doi:10.1111/jrh.12307.
6. Andrilla CHA, Coulthard C, Larson EH. Barriers Rural Physicians Face Prescribing Buprenorphine for Opioid Use Disorder. *Ann Fam Med*. 2017;15(4):359–362. doi:10.1370/afm.2099.
7. Fiscella K, Wakeman SE, Beletsky L. Buprenorphine Deregulation and Mainstreaming Treatment for Opioid Use Disorder: X the X Waiver. *JAMA Psychiatry*. 2019;76(3):229–230. doi:10.1001/jamapsychiatry.2018.
8. Haffajee RL, Bohnert ASB, Lagisetty PA. Policy Pathways to Address Provider Workforce Barriers to Buprenorphine Treatment. *Am J Prev Med*. 2018;54(6S3):S230–S242. doi:10.1016/j.amepre.2017.12.022.
9. Opioid-Related Hospitalizations and Emergency Department Visits in Mississippi, 2014-2015. Mississippi State Department of Health. 9/24/2018. Jackson. Mississippi.
10. Bart G. Maintenance medication for opiate addiction: the foundation of recovery. *J Addict Dis*. 2012;31(3):207–225. doi:10.1080/10550887.2012.694598.
11. Farmer CM, Lindsay D, Williams J, et al. Practice Guidance for Buprenorphine for the Treatment of Opioid Use Disorders: Results of an Expert Panel Process. Subst Abus. 2015;36(2):209–216. doi:10.1080/08897077.2015.1012613
12. National Institute on Drug Abuse. Medications to Treat Opioid Use Disorder. Accessed on 8/2/2019.
13. Richert T, Johnson B. Long-term self-treatment with methadone or buprenorphine as a response to barriers to opioid substitution treatment: the case of Sweden. *Harm Reduct J*. 2015;12:1. Published 2015 Feb 18. doi:10.1186/s12954-015-0037-2
14. Cicero TJ, Ellis MS, Chilcoat HD. Understanding the use of diverted buprenorphine. Drug Alcohol Depend. 2018;193:117–23.

ATTACHMENT C



FDA DRUG SAFETY COMMUNICATIONS

SEPTEMBER 2019 – NOVEMBER 2019

- 9/13/2019 FDA warns about rare but severe lung inflammation with Ibrance, Kisqali, and Verzenio for breast cancer

APPENDIX

MS-DUR BOARD
COMMON ABBREVIATIONS

AWP	Any Willing Provider, Average Wholesale Price
BENE	Beneficiary
CAH	Critical Access Hospital
CCO	Coordinated Care Organization
CDC	Centers for Disease Control
CHIP	Children's Health Insurance Program
CMS	Center for Medicare and Medicaid Services
COB	Coordination of Benefits
CPC	Complex Pharmaceutical Care
DME	Durable Medical Equipment
DOC	Department of Corrections
DOM	Division of Medicaid
DUR	Drug Utilization Review
EOB	Explanation of Benefits
EPSDT	Early and Periodic Screening, Diagnosis and Treatment
FA	Fiscal Agent
FFS	Fee For Service
FPW	Family Planning Waiver
FQHC	Federally Qualified Health Clinic
FY	Fiscal Year
HB	House Bill
HCPCS/ HEIDIS	Health Plan Employer Data and Information Set
HHS	Department of Health and Human Services
HIPAA	Health Insurance Portability and Accountability
IDD	Intellectual and Developmental Disabilities
LTC	Long Term Care
MAG	Magnolia Health
MEDD	Morphine Equivalent Daily Dose
MSCAN	Mississippi Coordinated Access Network
MSDH	Mississippi State Department of Health
NADAC	National Average Drug Acquisition Cost
NDC	National Drug Code
P&T	Pharmacy and Therapeutics
PA	Prior Authorization
PBM	Pharmacy Benefit Manager
PDL	Preferred Drug List
PI	Program Integrity
PIP	Performance Improvement Program
POS	Point of Sale, Place of Service, Point of Service
Pro-DUR	Prospective Drug Use Review
OTC	Over the Counter
QI	Quality Indicator
QIO	Quality Improvement Organization
QM	Quality Management
RA	Remittance Advise
REOMB	Recipient's Explanation of Medicaid Benefits
Retro-DUR	Retrospective Drug Utilization Review
RFI	Request for Information
RFP	Request for Proposal
RHC	Rural Health Clinic
SB	Senate Bill
SCHIP	State Child Health Insurance Program
SMART PA	Conduent's Pharmacy Application (SmartPA) is a proprietary electronic prior authorization system used for Medicaid fee for service claims
SPA	State Plan Amendment
UHC	United Healthcare
UM/QIO	Utilization Management and Quality Improvement Organization
UPDL	Universal Preferred Drug List
UR	Utilization Review
VFC	Vaccines for Children
WAC	Wholesale Acquisition Cost
WIC	Women, Infants, Children
340B	Federal Drug Discount Program