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

MISSISSIPPI DIVISION OF
MEDICAID

March 19, 2020 at 1:00pm

Woolfolk Building, Room 145

Jackson, MS

Prepared by:

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

Drug Utilization Review Board

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
March 19, 2020

Welcome — Ray Montalvo, MD (Chair)

Old Business — Ray Montalvo, MD
- Approval of December 2019 Meeting Minutes — page 5

Resource Utilization Review
- Enrollment Statistics — page 12
- Pharmacy Utilization Statistics — page 12
- Top 10 Drug Categories by Number of Claims — page 13
- Top 10 Drug Categories by Amount Paid — page 14
- Top 25 Drug Molecules by Number of Claims — page 15
- Top 25 Drug Molecules by Dollars Paid — page 16
- Top 25 Drug Molecules by Change in Number of Claims — page 17
- Top 25 Drug Molecules by Change in Dollars Paid — page 18
- Top 15 Solid Dosage Form High Volume Products By Percent Change In Amount Paid Per Unit — page 19

Follow-up and Discussion from the Board

New Business

MS-DUR Educational Interventions — page 22

Special Analysis Projects
- HIV Antiretroviral Adherence — page 29
- Atrial Fibrillation Gaps in Care — page 36
- PPI Deprescribing Update — page 46

FDA Drug Safety Updates — page 60

Pharmacy Program Update — Terri Kirby, RPh

Next Meeting Information — Ray Montalvo, MD
Remaining 2020 Dates: June 11, September 17, December 3

DUR Board Meeting Minutes

MISSISSIPPI DIVISION OF MEDICAID
DRUG UTILIZATION REVIEW (DUR) BOARD
MINUTES OF THE DECEMBER 5, 2019 MEETING

DUR Board Roster: State Fiscal Year 2020 (July 1, 2019- June 30, 2020)	Mar 2019	May 2019	Sep 2019	Dec 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	✓	✓
James Taylor, PharmD	✓	✓	✓	
Alan Torrey, MD	NA	NA	✓	
Veda Vedanarayanan, MD	✓	✓	✓	
TOTAL PRESENT	**10***	**8***	**10**	**8**

** 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; Gail McCorkle, RPh, Clinical Pharmacist; Carlos Latorre, MD, Medical Director; Sue Reno, RN, Program Integrity; Carmen Robinson, Performance Auditor, Program Integrity

University of Mississippi School of Pharmacy - MS-DUR Staff:
Eric Pittman, PharmD, MS-DUR Project Director

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

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

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

Visitors:
Brynna Clark, MPhA; Judy Clark, Consultant; Evelyn Johnson, Capital Resources; Lea Miller, Pfizer; Beau Pender, Otsuka; Brandy Sympreux, Sobi; Wendy Rockwell, Sobi; Brian Berhow, Sunovion; Doug Welch, Merck; Bruce Wallace, Azurity; Tracy Smalley, Amgen; Brent Young, GBT; Reed Branson, Capital Resources; David Large, Biohaven; Allison Balducci, BMS; Phil Hecht, Abbvie; Jon Hubanks, MSDH; Michael Peoples, Lilly

Call to Order:
Dr. Ray Montalvo, Chair, called the meeting to order at 1:05pm and welcomed everyone to the meeting.

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

Resource Utilization Review:
Dr. Pittman presented the resource utilization report for July 2019 – September 2019. Dr. Pittman pointed out trends in increased utilization of antibiotics, stimulants, influenza vaccine, and neuraminidase inhibitors; all of which are typical for this time period annually. He also pointed to a decrease in the utilization of narcotic analgesics corresponding with the implementation of opioid PA edits in August 2019.

Feedback and Discussion from Board:
Dr. Pittman updated the board on items related to topics from the September DUR Board meeting. He provided the Board with updated figures on reimbursements for influenza vaccine during the 2018-2019 flu season. Pharmacy point-of-sale (POS) reimbursements for influenza vaccine averaged $25.7 per vaccine, while medical reimbursement averaged $42.8 per vaccine. The Board was also presented a copy of the educational letter addressing the use of metformin as first-line therapy for diabetes drafted by Dr. Latorre. This letter will be distributed to provider member organizations.

NEW BUSINESS

Update on MS-DUR Educational Interventions:
Dr. Pittman provided an overview of all DUR mailings that occurred September 2019 – November 2019.

Special Analysis Projects:
An Overview of Antidepressant Use in Children and Adolescents with a Focus on Tricyclic Antidepressants
Dr. Pittman presented the DUR Board with a report on the use of antidepressants in children and adolescents, focusing on the use of tricyclic antidepressants (TCAs). Dr. Pittman highlighted the fact that the TCA medication class is currently not listed on the UPDL. Currently there are no age restrictions in the pharmacy claims processing system, via POS or SMART PA

programming. Following a robust discussion by the Board, the subsequent recommendations were presented:

1) DOM should implement an electronic edit for TCA therapy with minimum age limit of 25 years.

2) The P&T Committee should review the TCA class for addition to the UPDL as non-preferred.

3) Dr. Bryant, Dr. Fitts, and Dr. Vedanarayanan will work together to draft a provider education on the appropriateness of TCA therapy in children, adolescents, and young adults with MS DUR and DOM.

Dr. Bloodworth motioned to approve the recommendations, seconded by Mr. Smith, and unanimously approved by the Board.

HPV Vaccine Series Completion Rates

Dr. Pittman presented a report detailing HPV vaccine completion rates among Medicaid beneficiaries who initiated vaccination January 2017 - December 2017. Despite having higher HPV-associated cancers compared to national data, according to the Center for Disease Control and Prevention's HPV coverage data website for the percentage of adolescents ages 13-17 years who were up to date on HPV vaccination, Mississippi's adolescent up-to-date rate on HPV vaccine was only 28.8% compared to the 49% rate nationally. Following a robust discussion, the following recommendations were:

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 be more involved in both the initiation and completion of HPV vaccinations.

3) DOM will explore ways to collaborate with the Mississippi State Department of Health (MSDH) to develop strategies to increase HPV vaccination completion rates in Mississippi.

Dr. Bloodworth motioned to approve the recommendations, seconded by Dr. Fitts, and unanimously approved by the Board. Dr. Bloodworth and Dr. Fitts volunteered to work with DOM and MS-DUR to develop strategies and educational tools to increase HPV vaccine completion rates.

Buprenorpine Utilization Trends in Mississippi Medicaid

In October 2019, MSDH's Morbidity Report focused on buprenorphine prescribing practices in Mississippi. As a result of this MSDH report, MS-DUR conducted a similar analysis, specifically among Medicaid beneficiaries. Results showed that the proportional increase in buprenorphine prescribing among Medicaid beneficiaries was substantially greater than the data reported in

the MSDH Morbidity Report on buprenorphine prescribing across the entire state. Medicaid has taken multiple steps to increase beneficiary access to buprenorphine for medication assisted therapy (MAT). The Board commended DOM on initiatives implemented to increase access. Additional steps recommended to further increase beneficiary access to MAT were the following:

1) MS-DUR should work with DOM to develop education information 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

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

Dr. Bloodworth motioned to approve the recommendations, seconded by Dr. Bryant, and unanimously approved by the Board.

FDA Drug Safety Updates:
Dr. Pittman presented FDA drug safety communications for September 2019 – November 2019.

Pharmacy Program Update:
Ms. Kirby informed the DUR Board regarding the progress for the state plan amendment (SPA) for vaccination administration and reimbursement for pharmacists. Upon DOM executive director approval, the Vaccine SPA will need to be submitted to CMS for final approval. She informed the Board that pharmacy permits expire 12/31/2019 and renewals must be reported to Conduent, Medicaid's fiscal agent, in order for pharmacy claims to process on January 1, 2020 and thereafter. She stated that pharmacists Bob Lomenick and Wes Pitts' presentation of the pharmacy stakeholder group's proposal, to reimburse pharmacists for cognitive services, to Medicaid's Medical Care Advisory Committee meeting on November 1st was received favorably.

Miscellaneous:
2020 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.*

Next Meeting Information:
Dr. Montalvo announced that the next meeting of the DUR Board will take place on March 19, 2020 at 1pm.

The meeting adjourned at 3:10 pm.

Submitted,

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

Meeting Location: Woolfolk Building, 501 North West Street, Conference Room 117, Jackson, MS 39201

Contact Information: Office of Pharmacy:
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

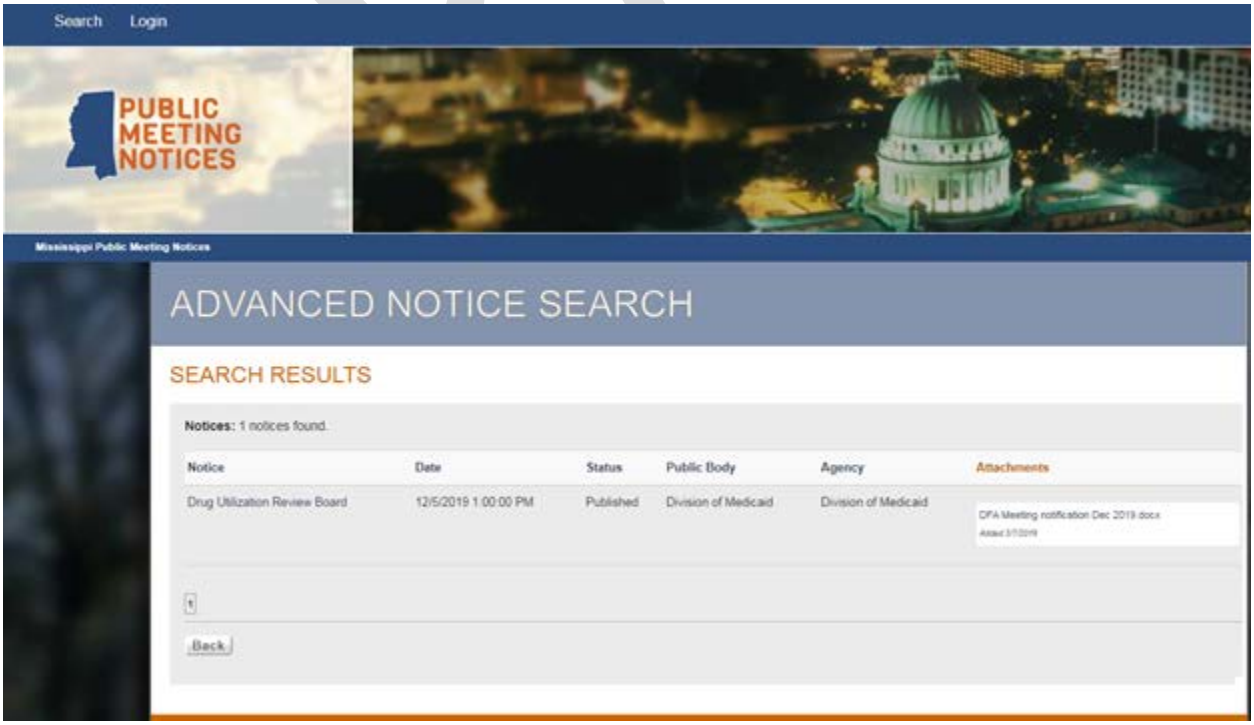
Subject: Quarterly Meeting

Date and Time: December 5, 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.



Resource Utilizaton Review

TABLE 04A: ENROLLMENT STATISTICS FOR LAST 6 MONTHS
July 1, 2019 through December 31, 2019

			Jul-19	Aug-19	Sep-19	Oct-19	Nov-19	Dec-19
Total enrollment			695,472	694,612	693,537	692,746	689,578	684,870
Dual-eligibles			157,199	156,915	156,877	156,841	156,568	154,555
Pharmacy benefits			586,555	585,491	583,921	582,234	578,858	574,916
	LTC		17,125	17,134	17,090	17,165	17,048	16,723
	PLAN %	FFS	25.6%	26.0%	25.9%	25.5%	24.9%	24.0%
		MSCAN-UHC	29.2%	28.7%	28.6%	28.9%	29.2%	29.6%
		MSCAN-Magnolia	34.1%	33.7%	33.6%	33.7%	33.9%	34.1%
		MSCAN-Molina	11.1%	11.6%	11.9%	11.9%	12.0%	12.3%

TABLE 04B: PHARMACY UTILIZATION STATISTICS FOR LAST 6 MONTHS
July 1, 2019 through December 31, 2019

		Jul-19	Aug-19	Sep-19	Oct-19	Nov-19	Dec-19
# Rx Fills	FFS	99,234	109,089	103,496	111,764	105,612	105,160
	MSCAN-UHC	139,651	155,098	150,535	161,619	160,429	160,737
	MSCAN-Mag	186,382	203,962	198,214	210,981	209,578	207,669
	MSCAN-Mol	33,475	40,121	41,073	43,916	44,942	45,835
# Rx Fills / Bene	FFS	0.7	0.7	0.7	0.8	0.7	0.8
	MSCAN-UHC	0.8	0.9	0.9	1.0	0.9	0.9
	MSCAN-Mag	0.9	1.0	1.0	1.1	1.1	1.1
	MSCAN-Mol	0.5	0.6	0.6	0.6	0.6	0.6
$ Paid Rx	FFS	$12,621,063	$12,514,100	$12,093,694	$12,481,497	$11,632,180	$11,872,252
	MSCAN-UHC	$14,206,113	$14,540,453	$14,146,282	$14,881,410	$13,833,051	$14,154,281
	MSCAN-Mag	$18,796,195	$19,648,595	$18,489,909	$19,377,026	$18,443,538	$18,484,652
	MSCAN-Mol	$2,358,749	$2,686,407	$2,740,103	$3,201,979	$3,252,331	$3,195,032
$ /Rx Fill	FFS	$127.18	$114.71	$116.85	$111.68	$110.14	$112.90
	MSCAN-UHC	$101.73	$93.75	$93.97	$92.08	$86.23	$88.06
	MSCAN-Mag	$100.85	$96.33	$93.28	$91.84	$88.00	$89.01
	MSCAN-Mol	$70.46	$66.96	$66.71	$72.91	$72.37	$69.71
$ /Bene	FFS	$84.05	$82.21	$79.97	$84.07	$80.70	$86.04
	MSCAN-UHC	$82.94	$86.53	$84.71	$88.44	$81.84	$83.17
	MSCAN-Mag	$93.97	$99.58	$94.24	$98.76	$93.99	$94.29
	MSCAN-Mol	$36.23	$39.55	$39.43	$46.21	$46.82	$45.18

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

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

Category	Month Year	Rank Volume	# RXs	$ Paid	# Unique Benes
CNS stimulants	Dec 2019	1	25,638	$5,045,000	22,045
	Nov 2019	1	25,543	$5,086,321	22,343
	Oct 2019	1	28,718	$5,817,925	24,607
aminopenicillins	Dec 2019	2	19,715	$260,473	19,322
	Nov 2019	2	21,280	$283,680	20,888
	Oct 2019	2	18,292	$238,309	17,896
adrenergic bronchodilators	Dec 2019	3	17,133	$817,909	15,032
	Nov 2019	3	18,609	$881,546	16,403
	Oct 2019	3	17,294	$895,950	14,941
neuraminidase inhibitors	Dec 2019	4	17,126	$1,346,092	16,999
	Nov 2019	21	7,202	$615,045	7,171
	Oct 2019	63	1,834	$146,890	1,826
nonsteroidal anti-inflammatory agents	Dec 2019	5	16,251	$232,920	15,550
	Nov 2019	4	16,389	$231,268	15,701
	Oct 2019	4	16,936	$242,906	16,065
antihistamines	Dec 2019	6	14,817	$214,071	14,202
	Nov 2019	6	15,533	$223,385	15,002
	Oct 2019	5	15,826	$232,283	15,136
glucocorticoids	Dec 2019	7	14,476	$235,857	13,872
	Nov 2019	5	16,030	$269,552	15,434
	Oct 2019	8	13,719	$229,951	13,159
macrolides	Dec 2019	8	13,456	$333,619	13,117
	Nov 2019	7	13,365	$332,458	13,058
	Oct 2019	13	10,895	$289,107	10,611
atypical antipsychotics	Dec 2019	9	13,411	$3,669,277	11,349
	Nov 2019	8	13,034	$3,309,733	11,197
	Oct 2019	7	13,871	$3,573,515	11,698
narcotic analgesic combinations	Dec 2019	10	12,698	$604,861	11,641
	Nov 2019	9	12,498	$599,552	11,551
	Oct 2019	6	13,915	$654,541	12,584

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

Category	Month Year	Rank Paid Amt	# RXs	$ Paid	# Unique Benes
CNS stimulants	Dec 2019	1	25,638	$5,045,000	22,045
	Nov 2019	1	25,543	$5,086,321	22,343
	Oct 2019	1	28,718	$5,817,925	24,607
atypical antipsychotics	Dec 2019	2	13,411	$3,669,277	11,349
	Nov 2019	2	13,034	$3,309,733	11,197
	Oct 2019	2	13,871	$3,573,515	11,698
insulin	Dec 2019	3	5,012	$2,724,634	3,687
	Nov 2019	3	4,833	$2,712,710	3,650
	Oct 2019	3	5,043	$2,792,742	3,722
antirheumatics	Dec 2019	4	1,057	$2,449,950	916
	Nov 2019	4	1,036	$2,495,464	925
	Oct 2019	4	1,136	$2,721,549	992
antiviral combinations	Dec 2019	5	830	$2,408,330	750
	Nov 2019	5	807	$2,383,685	751
	Oct 2019	5	874	$2,661,896	778
factor for bleeding disorders	Dec 2019	6	101	$1,449,963	68
	Nov 2019	6	104	$1,433,597	74
	Oct 2019	6	101	$1,594,612	75
neuraminidase inhibitors	Dec 2019	7	17,126	$1,346,092	16,999
	Nov 2019	14	7,202	$615,045	7,171
	Oct 2019	65	1,834	$146,890	1,826
bronchodilator combinations	Dec 2019	8	3,710	$1,066,973	3,385
	Nov 2019	7	3,779	$1,109,549	3,477
	Oct 2019	7	3,915	$1,163,334	3,588
interleukin inhibitors	Dec 2019	9	151	$927,088	135
	Nov 2019	10	142	$879,902	131
	Oct 2019	8	165	$962,237	141
adrenergic bronchodilators	Dec 2019	10	17,133	$817,909	15,032
	Nov 2019	9	18,609	$881,546	16,403
	Oct 2019	10	17,294	$895,950	14,941

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

Drug Molecule Therapeutic Category	Nov 2019 # Claims	Dec 2019 # Claims	Dec 2019 $ Paid	Dec 2019 # Unique Benes
amoxicillin / aminopenicillins	21,242	19,684	$259,634	19,291
oseltamivir / neuraminidase inhibitors	7,202	17,126	$1,346,092	16,999
albuterol / adrenergic bronchodilators	18,104	16,673	$681,427	14,717
azithromycin / macrolides	12,660	12,837	$239,784	12,553
montelukast / leukotriene modifiers	12,005	10,967	$180,137	10,635
cetirizine / antihistamines	10,539	9,576	$124,854	9,350
ibuprofen / nonsteroidal anti-inflammatory agents	8,679	8,952	$120,824	8,724
acetaminophen-hydrocodone / narcotic analgesic combinations	8,069	8,189	$105,705	7,699
lisdexamfetamine / CNS stimulants	8,195	8,074	$2,406,527	7,832
prednisolone / glucocorticoids	9,223	8,072	$126,998	7,760
ondansetron / 5HT3 receptor antagonists	7,751	7,725	$121,755	7,485
gabapentin / gamma-aminobutyric acid analogs	7,563	7,623	$119,496	7,083
cefdinir / third generation cephalosporins	7,808	7,360	$164,919	7,236
amoxicillin-clavulanate / penicillins/beta-lactamase inhibitors	7,269	6,706	$167,012	6,593
fluticasone nasal / nasal steroids	7,493	6,701	$105,103	6,615
methylphenidate / CNS stimulants	6,471	6,464	$1,228,383	5,751
clonidine / antiadrenergic agents, centrally acting	5,935	6,178	$112,135	5,732
amphetamine-dextroamphetamine / CNS stimulants	5,871	5,988	$269,026	5,114
amlodipine / calcium channel blocking agents	5,446	5,543	$58,292	5,241
omeprazole / proton pump inhibitors	5,385	5,402	$60,109	5,196
sertraline / SSRI antidepressants	4,249	4,332	$52,011	4,000
guanfacine / antiadrenergic agents, centrally acting	4,131	4,235	$137,124	3,991
atorvastatin / HMG-CoA reductase inhibitors (statins)	3,891	3,996	$48,391	3,743
prednisone / glucocorticoids	4,081	3,791	$40,166	3,645
risperidone / atypical antipsychotics	3,500	3,671	$186,207	3,287

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

Drug Molecule Therapeutic Category	Nov 2019 $ Paid	Dec 2019 $ Paid	Dec 2019 # Claims	Dec 2019 # Unique Benes
lisdexamfetamine / CNS stimulants	$2,444,137	$2,406,527	8,074	7,832
adalimumab / antirheumatics	$1,603,596	$1,588,070	256	230
paliperidone / atypical antipsychotics	$1,200,113	$1,395,663	619	528
oseltamivir / neuraminidase inhibitors	$615,045	$1,346,092	17,126	16,999
methylphenidate / CNS stimulants	$1,251,844	$1,228,383	6,464	5,751
aripiprazole / atypical antipsychotics	$795,971	$887,675	3,312	3,048
insulin aspart / insulin	$831,286	$871,061	1,428	1,345
bictegravir/emtricitabine/tenofovir / antiviral combinations	$846,702	$867,787	286	270
insulin glargine / insulin	$777,513	$799,901	1,822	1,713
dexmethylphenidate / CNS stimulants	$753,138	$753,813	3,330	2,782
albuterol / adrenergic bronchodilators	$734,028	$681,427	16,673	14,717
deferasirox / chelating agents	$865,451	$590,113	48	45
etanercept / antirheumatics	$537,854	$550,559	109	103
palivizumab / immune globulins	$610,427	$539,441	251	176
somatropin / growth hormones	$501,245	$535,886	128	118
cobicistat/elvitegravir/emtricitabine/tenofov / antiviral combinations	$525,200	$513,265	164	156
lurasidone / atypical antipsychotics	$485,821	$500,821	375	359
lacosamide / miscellaneous anticonvulsants	$419,738	$472,896	539	473
antihemophilic factor / factor for bleeding disorders	$350,118	$468,310	32	16
budesonide-formoterol / bronchodilator combinations	$466,927	$458,059	1,393	1,354
buprenorphine-naloxone / narcotic analgesic combinations	$421,848	$433,927	1,188	989
insulin detemir / insulin	$452,951	$422,392	799	756
emicizumab / factor for bleeding disorders	$352,418	$418,063	20	17
fluticasone-salmeterol / bronchodilator combinations	$422,701	$392,291	1,186	1,142
hydroxyprogesterone / progestins	$411,886	$383,414	120	104

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

Drug Molecule	Oct 2019 # Claims	Nov 2019 # Claims	Dec 2019 # Claims	Dec 2019 $ Paid	Dec 2019 # Unique Benes
oseltamivir / neuraminidase inhibitors	1,834	7,202	17,126	$1,346,092	16,999
azithromycin / macrolides	10,283	12,660	12,837	$239,784	12,553
amoxicillin / aminopenicillins	18,252	21,242	19,684	$259,634	19,291
cefdinir / third generation cephalosporins	6,210	7,808	7,360	$164,919	7,236
prednisolone / glucocorticoids	7,418	9,223	8,072	$126,998	7,760
amoxicillin-clavulanate / penicillins/beta-lactamase inhibitors	6,127	7,269	6,706	$167,012	6,593
benzonatate / antitussives	1,022	1,500	1,583	$20,233	1,538
ibuprofen / nonsteroidal anti-inflammatory agents	8,512	8,679	8,952	$120,824	8,724
famotidine / H2 antagonists	1,150	1,358	1,588	$24,945	1,478
ondansetron / 5HT3 receptor antagonists	7,519	7,751	7,725	$121,755	7,485
codeine-guaifenesin / upper respiratory combinations	223	316	397	$5,006	395
brompheniramine/dextromethorphan/pse / upper respiratory combinations	558	688	702	$15,358	686
losartan / angiotensin II inhibitors	2,157	2,210	2,295	$26,849	2,213
prednisone / glucocorticoids	3,664	4,081	3,791	$40,166	3,645
esomeprazole / proton pump inhibitors	2,039	2,062	2,152	$241,298	2,053
hydrochlorothiazide / thiazide and thiazide-like diuretics	2,493	2,516	2,595	$20,137	2,467
cefprozil / second generation cephalosporins	789	990	890	$29,762	871
doxycycline / tetracyclines	1,636	1,698	1,719	$24,696	1,689
cimetidine / H2 antagonists	41	100	115	$2,957	113
codeine-promethazine / upper respiratory combinations	99	109	160	$1,913	155
ofloxacin otic / otic anti-infectives	410	420	464	$15,168	454
chlorpheniramine/dextromethorp/phenylephrine / upper respiratory combinations	202	239	256	$4,207	254
palivizumab / immune globulins	202	257	251	$539,441	176
ciprofloxacin-dexamethasone otic / otic steroids with anti-infectives	1,192	1,263	1,239	$290,970	1,221
tiotropium / anticholinergic bronchodilators	431	441	472	$197,335	459

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

Drug Molecule	Oct 2019 $ Paid	Nov 2019 $ Paid	Dec 2019 $ Paid	Dec 2019 # Claims	Dec 2019 # Unique Benes
oseltamivir / neuraminidase inhibitors	$146,890	$615,045	$1,346,092	17,126	16,999
elexacaftor/ivacaftor/tezacaftor / CFTR combinations	$0	$167,334	$337,101	16	16
interferon gamma-1b / interferons	$55,144	$55,144	$165,037	4	4
paliperidone / atypical antipsychotics	$1,288,637	$1,200,113	$1,395,663	619	528
eteplirsen / miscellaneous uncategorized agents	$6,461	$6,461	$102,522	2	1
antihemophilic factor / factor for bleeding disorders	$385,533	$350,118	$468,310	32	16
ustekinumab / interleukin inhibitors	$181,462	$161,082	$242,377	13	12
antihemophilic factor-von willebrand factor / factor for bleeding disorders	$12,501	$55,678	$69,536	9	6
palivizumab / immune globulins	$489,590	$610,427	$539,441	251	176
esomeprazole / proton pump inhibitors	$193,709	$226,800	$241,298	2,152	2,053
azithromycin / macrolides	$194,258	$242,707	$239,784	12,837	12,553
emicizumab / factor for bleeding disorders	$382,301	$352,418	$418,063	20	17
teriflunomide / selective immunosuppressants	$153,053	$181,324	$188,636	26	23
pomalidomide / other immunosuppressants	$17,265	$51,794	$51,794	3	3
ledipasvir-sofosbuvir / antiviral combinations	$0	$12,011	$31,511	1	1
nintedanib / multikinase inhibitors	$29,848	$29,848	$59,695	6	6
ibrutinib / BTK inhibitors	$77,959	$131,657	$107,395	8	7
burosumab / miscellaneous metabolic agents	$0	$0	$27,316	2	1
cefdinir / third generation cephalosporins	$137,698	$178,479	$164,919	7,360	7,236
alpha 1-proteinase inhibitor / miscellaneous respiratory agents	$60,596	$42,765	$84,734	7	6
aminocaproic acid / factor for bleeding disorders	$7,449	$6,807	$29,972	9	7
amoxicillin / aminopenicillins	$237,473	$281,598	$259,634	19,684	19,291
clobazam / benzodiazepine anticonvulsants	$282,385	$273,970	$304,246	260	230
ruxolitinib / multikinase inhibitors	$27,124	$47,046	$47,947	4	3
venetoclax / miscellaneous antineoplastics	$11,824	$0	$32,430	4	4

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 OCT 2019 TO DEC 2019 (FFS and CCOs)

Drug Product Therapeutic Category	Dec 2019 # Claims	Dec 2019 $ Paid	Dec 2019 Avr. Paid Per Rx	Dec 2019 Avr. Units Per Rx	Oct 2019 Paid Per Unit	Nov 2019 Paid Per Unit	Dec 2019 Paid Per Unit	Percent Change
dexmethylphenidate 15 mg capsule, extended release / CNS stimulants (N)	175	$18,137	$103.64	30	$2.94	$2.93	$3.09	5.2%
dexmethylphenidate 30 mg capsule, extended release / CNS stimulants (N)	102	$11,946	$117.12	30	$3.39	$3.66	$3.52	4.0%
atomoxetine 40 mg capsule / CNS stimulants (P)	274	$23,566	$86.01	30	$2.38	$2.41	$2.48	3.9%
Farxiga (dapagliflozin) 10 mg tablet / SGLT-2 inhibitors (P)	121	$66,012	$545.55	35	$15.03	$15.32	$15.50	3.1%
atomoxetine 25 mg capsule / CNS stimulants (P)	220	$17,880	$81.27	31	$2.19	$2.22	$2.25	2.8%
Entresto (sacubitril-valsartan) 97 mg-103 mg tablet / angiotensin receptor blockers and neprilysin inhibitors (P)	126	$61,824	$490.66	62	$7.84	$7.97	$8.03	2.4%
Linzess (linaclotide) 145 mcg capsule / guanylate cyclase-C agonists (P)	109	$52,330	$480.09	34	$13.07	$13.18	$13.23	1.2%
Tradjenta (linagliptin) 5 mg tablet / dipeptidyl peptidase 4 inhibitors (P)	234	$122,681	$524.28	38	$13.16	$13.20	$13.32	1.2%
Xulane (ethinyl estradiol-norelgestromin) 35 mcg-150 mcg/24 hr film, extended release / contraceptives (P)	1,218	$165,839	$136.16	4	$37.70	$37.76	$38.03	0.9%
Saphris Black Cherry (asenapine) 10 mg tablet / atypical antipsychotics (P)	147	$123,112	$837.50	43	$18.72	$18.84	$18.86	0.8%
Vyvanse (lisdexamfetamine) 10 mg tablet, chewable / CNS stimulants (P)	111	$33,456	$301.40	30	$9.63	$9.71	$9.70	0.8%
Janumet (metformin-sitagliptin) 1000 mg-50 mg tablet / antidiabetic combinations (P)	118	$58,040	$491.87	74	$7.01	$7.06	$7.05	0.7%
QuilliChew ER (methylphenidate) 40 mg/24 hr tablet, chewable, extended release / CNS stimulants (P)	308	$96,598	$313.63	29	$10.49	$10.54	$10.55	0.6%

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 OCT 2019 TO DEC 2019 (FFS and CCOs)

Drug Product Therapeutic Category	Dec 2019 # Claims	Dec 2019 $ Paid	Dec 2019 Avr. Paid Per Rx	Dec 2019 Avr. Units Per Rx	Oct 2019 Paid Per Unit	Nov 2019 Paid Per Unit	Dec 2019 Paid Per Unit	Percent Change
colchicine 0.6 mg capsule / antigout agents (P)	144	$24,472	$169.94	36	$4.11	$4.03	$4.13	0.6%
Tivicay (dolutegravir) 50 mg tablet / integrase strand transfer inhibitor (P)	112	$195,301	$1,743.76	34	$51.04	$51.94	$51.32	0.5%

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 INITIATIVE UPDATE

DECEMBER 2019 – FEBRUARY 2020

Ongoing Intervention(s):

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
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
19-Dec					14	9	23
20-Jan					15	12	27
20-Feb					8	6	14

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.

One-Time Intervention(s):

- Metformin Recommendation – December 2019 (attached)
- HPV Vaccination Recommendation – March 2020 Provider Bulletin (attached)

Upcoming Intervention(s):

- TCA Age Edit – Draft attached

MISSISSIPPI DIVISION OF MEDICAID

Medicaid's MS-DUR Board recommends metformin as first-line therapy for diabetes

Every year an estimated 26,000 people in Mississippi are diagnosed with diabetes. In 2018, approximately 413,000 people in Mississippi – or 17.1% of the adult population – had diabetes, and Mississippi ranked 49 out of 50 states.[3,4] Appropriate treatment is crucial.

The Mississippi Division of Medicaid (DOM) and its Drug Utilization Review Board (MS-DUR) are formally recommending a trial of metformin as first-line therapy for the treatment of diabetes. Metformin is considered first-line due to its glycemic efficacy, lack of hypoglycemia, absence of weight gain, favorable cost, and general tolerability.

DOM and MS-DUR representatives encourage prescribers to consider starting every new diabetic patient on metformin provided there are no contraindications for its use. In addition, they offer the following metformin related recommendations:

- A counseling point to help avoid any gastrointestinal (GI) intolerance adverse effects (AE) is to take metformin with the largest meal(s).
- Titrating the metformin Immediate Release (IR) formulation by weekly increments of 500-850 mg for at least 1-2 weeks up to 2,550 mg daily can help minimize GI intolerance.
- For patients experiencing GI intolerance that continues, metformin Extended Release (ER) should be utilized, as this formulation has better gastrointestinal tolerability.
- Titrating the metformin ER formulation by weekly increments of 500 mg up to the maximum dose of 2,000 mg can help maximize metformin's benefit in these patients.
- Get to goal as soon as possible – adjust at ≤3 months until at goal.

However, for patients who fail metformin monotherapy, a broad variety of agents can be used in combination with metformin, or as monotherapy, in those who cannot use metformin. The choice of second-line and third-line agents varies based on patient characteristics, patient preferences, and properties of the medications, such as the risk of hypoglycemia or weight gain. Certain GLP1-RAs and SGLT2 inhibitor medications have shown benefits for chronic kidney disease and cardiovascular disease, including heart failure , which may be preferred in patients with those complications.*

Glucose control is the mainstay of therapy in patients with diabetes. In recent years, a variety of new agents with novel mechanisms of action have been approved for the treatment of Type 2 diabetes. While these provide more options for the treatment of these patients, the wide array of medications can lead to confusion as to which agents should be used. In general, both the American Diabetes Association (ADA) and the American Association of Clinical Endocrinologists (AACE) recommend that in addition to lifestyle modification, metformin is first-line for the treatment of Type 2 diabetes in most patients.[1,2] In general, the target A1C concentrations are 7% (ADA) or 6.5% (AACE), or as close to normal as is safe and achievable. The goal may be individualized in patients with other illnesses and in those at risk for hypoglycemia. Therapy can be started with more than one agent in patients with an A1C > 9% (ADA) or > 7.5% (AACE).

For further information or assistance, please see the contact information below.

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References:

1. ADA standards of care: https://clinical.diabetesjournals.org/content/37/1/1
2. AACE standards of care: https://www.aace.com/disease-state-resources/diabetes/clinical-practice-guidelines-treatment-algorithms/comprehensive
3. American Diabetes Foundation: https://www.diabetes.org/take-closer-look-statistics-state
4. American Health Rankings: https://www.americashealthrankings.org/learn/reports/2018-annual-report

- * GLP1-RA= Glucagon Like Peptide-1 Receptor Agonists, SGLT2 = Sodium Glucose Co-Transporter 2 inhibitors

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12/9/2019

Please forward this message to colleagues who might be interested. If you wish to be removed from this list or know of a colleague to add, send an email message to: matt.westerfield@medicaid.ms.gov.

About Mississippi Division of Medicaid

Medicaid is a state and federal program created by the Social Security Amendments of 1965, authorized by Title XIX of the Social Security Act, to provide health coverage for eligible, low income populations. In 1969, Medicaid was enacted by the Mississippi Legislature. All 50 states, five territories of the United States and District of Columbia participate in this voluntary matching program. The mission of the Mississippi Division of Medicaid is to responsibly provide access to quality health coverage for vulnerable Mississippians, by conducting operations with accountability, consistency and respect.

HPV VACCINATION SERIES COMPLETION FINDINGS and KEY RECOMMENDATIONS FOR IMPROVEMENT- ***YOU are the KEY to HPV cancer prevention.***

In the United States, approximately 19,000 new Human papillomavirus (HPV) infections occur in teens and young adults every day. Every year, there are approximately 14 million new HPV infections nationwide. About 50% of them occur in 15 to 24-year-olds. For most people, HPV clears on its own. But, for others who don't clear the virus, it could cause certain cancers and other diseases.

Mississippi's incidence rate of HPV related cancers reported for the 2008-2012 timeframe was estimated at 14.3 per 100,000 persons, higher than the U.S. national average of 11.7 per 100,000 persons.

According to the CDC's TeenVaxView, HPV vaccination rates are increasing as more children are up to date on HPV vaccination. Nationally, 51.1% vs. *only* 32.6% of Mississippi adolescents ages 13-17 years of age were up to date on HPV vaccination series.

Despite HPV vaccination completion rates rising across the nation, Mississippi continues to rank at the bottom of all states. A review of Medicaid's 2017 claims shared with the Drug Utilization Review Board (DUR) reported a completion rate of 28.8%, with 3928 of 13,656 beneficiaries having completed the vaccination series in 2017, which was a rate similar for all Mississippians in 2017.

As a result, the DUR Board recommended a need to promote effective strategies to improve HPV vaccination rates to prevent this sexually transmitted pathogen from causing anogenital and oropharyngeal disease in males and females.

Gardasil 9, the only HPV vaccine available in the US since 2016, is designed to protect against acquisition of HPV infection and development of subsequent HPV-associated disease. The CPT code for HPV 9 vaccine (Gardasil 9) is 90651.

Indications and age range: In accordance with the Advisory Committee on Immunization Practices (ACIP) in the US, HPV vaccination for all **females and males** is recommended in the following age ranges:

Age at initiation	Recommended number of HPV vaccine doses	Recommended interval between doses	Recommendation for interrupted schedule
9 - 14 Years *, except immunocompromised persons	2	0, 6–12 months§	If the vaccination schedule is interrupted, vaccine doses do not need to be repeated (no maximum interval).
15 - 26 Years and immunocompromised persons	3	0, 1–2, 6 months**	

**ACIP recommends routine HPV vaccination for adolescents at age 11 or 12 years; vaccination may be given starting at age 9 years.*
§ In a 2-dose schedule of HPV vaccine, the minimum interval between the first and second doses is 5 months.
*** In a 3-dose schedule of HPV vaccine, the minimum intervals are 4 weeks between the first and second doses, 12 weeks between the second and third doses, and 5 months between the first and third doses.*

ACIP recommends catch-up for persons through age 26 years who are not adequately vaccinated. ACIP recommends vaccination based on shared clinical decision making for individuals ages 27 through 45 years who are not adequately vaccinated.

Effective communication, parent education and avoiding missed opportunities are keys to improving HPV vaccination rates. A physician's recommendation is the single best predicator of vaccination success.

ADDITIONAL RESOURCES - *Successful strategies and communication techniques for use with parents about HPV vaccination can be found at the following links.*

Boosting Your HPV Vaccination Rates- Bundle all adolescent vaccinations and other suggestions. https://www.cdc.gov/hpv/hcp/boosting-vacc-rates.html

- For example: You can say, "Now that your son is 11, he is due for vaccinations today to help protect him from meningitis, HPV cancers, and whooping cough. Do you have any questions?"
- Remind parents of the follow-up shots their child will need and ask them to make appointments before they leave.

Answering Parents' Questions about HPV Vaccine - Most parents will accept HPV vaccination when you effectively recommend the vaccine and address their questions. https://www.cdc.gov/hpv/hcp/answering-questions.html

Top 10 Tips for HPV Vaccination Success—Attain and Maintain High HPV Vaccination Rates – https://www.cdc.gov/hpv/hcp/educational-materials.html

4 Key Phrases That Can Help to Shape a Clear Vaccination Recommendation

1. **"I've seen people with this disease."**
    - Ask your patient (or their parent) if they've ever know someone who's suffered from this disease. Sharing a personal or professional experience can help them understand the real impact the disease can have.
2. **"The CDC recommends you get this vaccine."**
    - Make sure your patients are aware of the CDC recommendation for each vaccine you are recommending they receive.
3. **"This vaccine may help prevent this disease."**
    - Help patients understand that the vaccine you are recommending may help protect them against a potentially serious disease (cancer).
4. **"I believe you (or your child) should get this vaccine."**
    - Your patients trust you as a health care provider. They want more than just the facts about vaccination; they want to know why you recommend it for them specifically.

About 80% of people will get an HPV infection in their lifetime. Recommending HPV vaccination for all 11–12 year-olds can protect them long before they are ever exposed. CDC recommends two doses of HPV vaccine for all adolescents at age 11 or 12 years.

Remember, YOU are the key to HPV cancer prevention.

Ref: https://www.cdc.gov/hpv/

[Insert Date]

IMPORTANT NOTICE REGARDING PRESCRIBING CHANGES FOR TRICYCLIC ANTIDEPRESSANTS

Dear Medicaid Prescriber:

In accordance with the Drug Utilization Review (DUR) Board's December 5, 2019 recommendations for changes related to the prescribing of tricyclic antidepressants (TCAs), the Division of Medicaid is planning to implement a prior authorization (PA) requirement for patients age less than 25 years who are prescribed TCAs. This recommendation is based on safety risks associated with tricyclic antidepressant use in children, adolescents and young adults. The FDA has issued and revised a black box warning related to antidepressant use in this age group. Current clinical practice guidelines support SSRI use as first-line therapy in treatment of child and adolescent depression and anxiety. (See FDA Boxed Warning below)

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)*

You have been identified as a prescriber of a TCA during the past year for a Medicaid beneficiary below the age of 25 years. Once the minimum age edit requirement is implemented, any TCA prescription for beneficiaries below age 25 years will require processing through Medicaid's Universal Prior Authorization form request. Prescribers of TCA's for patients less than 25 years of age will also need to attest on this form that the medical necessity outweighs the risk for this/these medication(s). The Universal Prior Authorization form can be found at https://medicaid.ms.gov/providers/pharmacy/pharmacy-prior-authorization/.

Additionally, prescribers are encouraged to note the diagnosis on the prescription and pharmacists are encouraged to submit the diagnosis as part of the prescription claim for the purpose of DUR/CMS quality measure reporting.

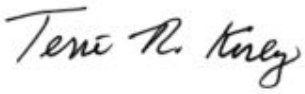
Evidence-Based DUR Initiative

A list of your patients that have been identified that will be impacted by this age requirement is included. The Division of Medicaid is informing prescribers of this change in advance. Advance knowledge of this change for the projected

July 2020 implementation date should allow adequate time to plan appropriately for uninterrupted care of your patients. You may submit prior authorization requests before the age requirement is implemented.

If we can be of any assistance, please do not hesitate to contact us.

Sincerely,



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MS-DUR

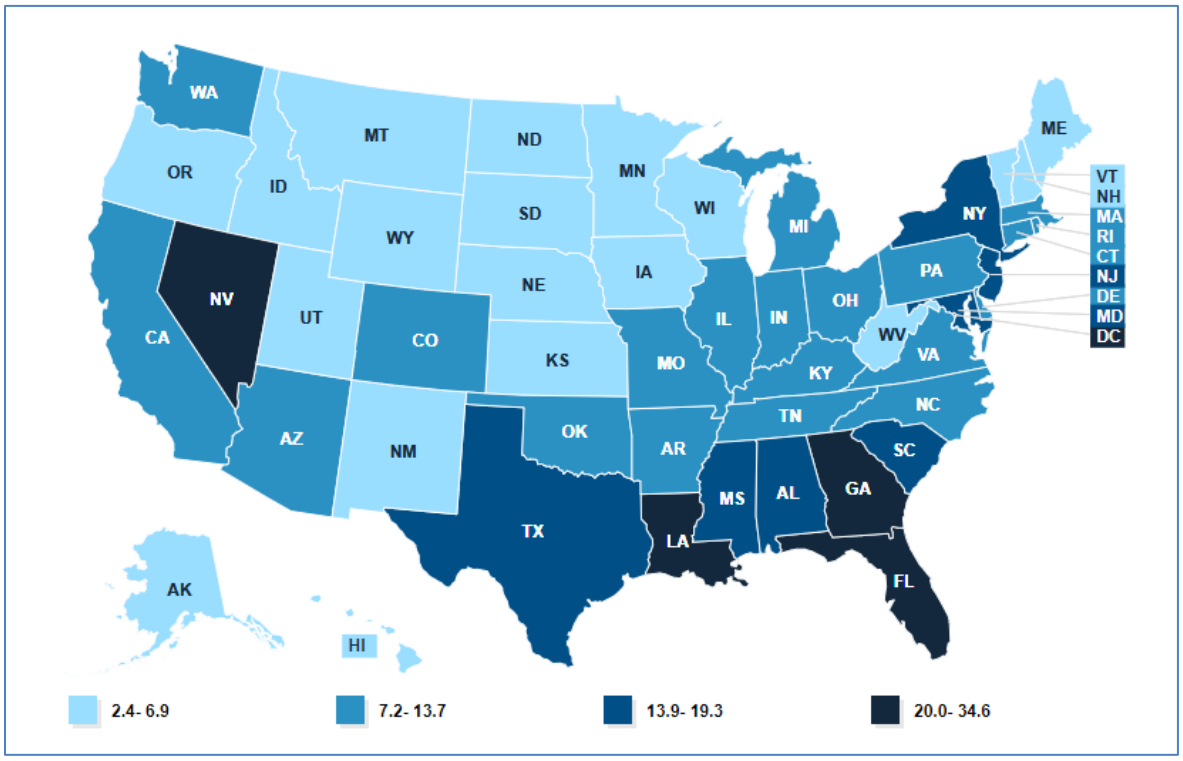
Beneficiary Name	Beneficiary Plan
BENEFICIARY 1	BENE 1 PLAN
BENEFICIARY 2	BENE 2 PLAN
BENEFICIARY 3	BENE 3 PLAN
BENEFICIARY 4	BENE 4 PLAN
BENEFICIARY 5	BENE 5 PLAN

ANTIRETROVIRAL ADHERENCE IN THE TREATMENT OF HIV

BACKGROUND

In 2018, an estimated 37.9 million individuals worldwide were living with human immunodeficiency virus (HIV).[1] Over 1.1 million individuals in the United States (US) currently live with the disease, with an estimated 38,000 new infections annually.[2] In 2018, HIV/AIDS and related infections were responsible for over 770,000 deaths worldwide with over 17,000 deaths in the United States alone.[3] Populations at greatest risk of contracting HIV include men who have sex with men, injection drug users, African Americans, and Hispanics.[4] Within the US, new HIV diagnoses are not distributed evenly across the country. Southern states experience the greatest disease burden and account for 52% of new US HIV/AIDS diagnoses.[2,5] The Centers for Disease Control and Prevention stated in 2019 that there was an "HIV epidemic" affecting Southern states, including Mississippi.[5] According to the 2018 HIV Surveillance Report, there are over 9,000 people living with HIV in Mississippi.[6] In 2018, Mississippi was tied with Maryland as having the 6th highest incidence of HIV infection in the US with a diagnosis rate of approximately 19.3 per 100,000 population.[7] (Figure 1) The US average diagnosis rate was 13.6 per 100,000 population. More specifically, Jackson, Mississippi had the 7th highest diagnosis rate of HIV infections (23.6) for all metropolitan statistical areas measured in the US.[6]

Figure 1: HIV Diagnosis Rates per 100,000 population for the US in 2018.[7]



To prevent disease progression, the National Institutes of Health (NIH) recommends immediate initiation of antiretroviral therapy (ART) in all patients diagnosed with HIV.[8] ART works to suppress viral replication, prevent disease progression and complications, and to prevent disease transmission.[8] In treatment-naïve patients, initial treatment generally consists of two nucleoside reverse transcriptase inhibitors (NRTIs) paired with one of the following: a non-nucleoside reverse transcriptase inhibitor (NNRTI); integrase strand transfer inhibitor (INSTI); or a protease inhibitor (PI) combination with a pharmacokinetic enhancing agent.[8]

Adherence to ART has been found to be critical to achieving viral load suppression. For appropriate suppression of HIV and prevention of progression to AIDS, a 90% adherence rate is recommended.

- The World Health Organization (WHO) recommends a goal of 90% adherence to ART therapy.[9] Studies have shown additional benefits when individuals taking ART attain adherence rates of 95% or greater.[10–12]
- The NIH guidelines do not recommend a specific threshold for adherence, but state that patients should maintain high adherence to achieve suppressed HIV replication, which is defined as plasma HIV-RNA less than 20-50 copies/mL blood.[4]
- WHO and NIH both emphasize the importance of adherence in attaining viral suppression and optimal outcomes and caution against nonadherence within this population. [8,9]

Lack of appropriate adherence to ART therapy may result in treatment failure, increased HIV transmission rates, and the emergence of viral drug resistance.[8] Despite severe consequences associated with nonadherence, the proportion of patients achieving WHO-defined 90% adherence threshold has been reported to be roughly half of all adults on ART.[9]

Factors associated with poor ART adherence include the following:

- psychiatric disorders,
- cognitive impairment,
- substance use disorder,
- unstable housing environment,
- concerns with adverse effects,
- low socioeconomic status,
- poor adherence to clinic visits.[8,13]

Not only is nonadherence a threat to population health, but it places an additional burden on payers with an estimated cost of non-adherence exceeding $30,000 per patient annually.[14]

The purpose of this report is to examine adherence to ART among Mississippi Medicaid beneficiaries. Understanding the scope of nonadherence within the Medicaid beneficiaries receiving ART for HIV/AIDS assists the Division of Medicaid (DOM) to develop interventions for improving ART adherence.

METHODS

A retrospective analysis of Medicaid point of sale (POS) pharmacy claims data from fee-for-service (FFS) and the three coordinated care organizations (CCOs) was conducted for the measurement period, calendar year 2019 (January 1, 2019 – December 31, 2019). Pharmacy Quality Alliance's (PQA) Proportion of Days Covered: Antiretroviral Medications Measure (PDC-ARV-2019) was utilized to assess adherence to antiretroviral therapy.

- PDC-ARV-2019 measures the percentage of individuals 18 years and older who meet the proportion of days covered (PDC) of 90% for ≥ 3 antiretroviral medications during the measurement year.
- The eligible population included all individuals 18 years and older on the first day of the measurement period with continuous enrollment who filled a prescription for ≥ 3 distinct antiretrovirals (as a single agent or as a combination) on 2 different dates of service during the measurement year. From this population, PDC was calculated.
- The earliest date of service with an overlap of ≥ 3 distinct antiretrovirals during the measurement period was designated as the index prescription start date (IPSD).

Figure 2 displays antiretroviral medications included in the measure.

Figure 2: PQA PDC-ARV-2019 Medication List

PDC-ARV-A: Antiretroviral Medications[a,b]

Single Agents		
• abacavir • atazanavir • darunavir • delavirdine • didanosine • dolutegravir • doravirine • efavirenz • emtricitabine	• enfuvirtide • etravirine • fosamprenavir • indinavir • lamivudine • maraviroc • nelfinavir • nevirapine	• raltegravir • rilpivirine • ritonavir • saquinavir • stavudine • tenofovir • tipranavir • zidovudine
Combination Agents:		
• abacavir &dolutegravir & lamivudine • abacavir & lamivudine • abacavir & lamivudine & zidovudine • atazanavir & cobicistat • bictegravir & emtricitabine & tenofovir • darunavir & cobicistat	• darunavir & cobicistat & emtricitabine & tenofovir • dolutegravir & rilpivirine • doravirine & lamivudine & tenofovir • efavirenz & emtricitabine & tenofovir • elvitegravir & cobicistat & emtricitabine & tenofovir	• emtricitabine & rilpivirine & tenofovir • emtricitabine & tenofovir • lamivudine & tenofivir • lamivudine & zidovudine • lopinavir & ritonavir

[a] Active ingredients are limited to oral and subcutaneous formulations only.
[b] Excludes zidovudine IV and products indicated for chronic hepatitis B (e.g., lamivudine 100mg [Epivir HBV 100mg]).

RESULTS

Table 1 describes the demographic characteristics of Medicaid beneficiaries included in the analysis and Tables 2, 2a, and 2b address ART adherence.

- 78.7% of beneficiaries were between ages 36 and 65 years.
- African Americans accounted for 75.8% of beneficiaries taking antiretroviral therapy.
    - *African Americans comprise a disproportionate amount of individuals diagnosed with HIV in the US. According to the CDC, in 2018 African Americans composed approximately 13% of the US population but account for 42% of new HIV diagnoses in the US and dependent areas.*

TABLE 1. Demographic Characteristics of Mississippi Medicaid Beneficiaries on Antiretroviral Therapy (Jan 2019 - Dec 2019)

Characteristic	FFS n = 209	UHC n = 296	Mag n = 444	Mol n = 53	Total n = 1002
Age					
18 to 35	54 (25.8%)	62 (21.0%)	77 (17.3%)	19 (35.9%)	212 (21.2%)
36 to 65	154 (73.7%)	234 (79.1%)	367 (82.7%)	34 (64.2%)	789 (78.7%)
66+	1 (0.5%)	0	0	0	1 (0.1%)
Sex					
Female	100 (47.9%)	143 (48.3%)	260 (58.6%)	26 (49.1%)	529 (52.8%)
Male	109 (52.2%)	153 (51.7%)	184 (41.4%)	27 (50.9%)	473 (47.2%)
Race					
African American	154 (73.7%)	224 (75.7%)	343 (77.3%)	38 (71.7%)	759 (75.8%)
Caucasian	35 (16.8%)	22 (7.4%)	40 (9.0%)	5 (9.4%)	102 (10.2%)
Other	20 (9.6%)	50 (16.9%)	61 (13.7%)	10 (18.9%)	141 (14.1%)

Note: FFS = Fee-for-service, UHC = UnitedHealthcare, Mag = Magnolia, Mol = Molina

TABLE 2. Medication Adherence by Days Supply for Antiretroviral Therapy Among Mississippi Medicaid Beneficiaries (Jan 2019 - Dec 2019)								
Proportion of Days Covered (PDC)	Days supply*							
	FFS		UHC		Mag		Mol	
	Less than 90-days n=185	90-days n=24	Less than 90-days n=261	90-days n=35	Less than 90-days n=386	90-days n=58	Less than 90-days n=51	90-days n=2
50 and lower	43 (23.2%)	0	56 (21.5%)	3 (8.6%)	57 (14.8%)	3 (5.2%)	9 (17.7%)	1 (50.0%)
50 to 79	56 (30.3%)	3 (12.5%)	72 (27.6%)	9 (25.7%)	78 (20.2%)	13 (22.4%)	20 (39.2%)	1 (50.0%)
80 to 89	23 (12.4%)	6 (25.0%)	37 (14.2%)	6 (17.1%)	60 (15.5%)	15 (25.9%)	9 (17.7%)	0
90 to 94	18 (9.7%)	2 (8.3%)	22 (8.4%)	6 (17.1%)	47 (12.2%)	4 (6.9%)	6 (11.8%)	0
95+	45 (24.3%)	13 (54.2%)	74 (28.4%)	11 (31.4%)	144 (37.3%)	23 (39.7%)	7 (13.7%)	0

Note: FFS = Fee-for-service, UHC = UnitedHealthcare, Mag = Magnolia, Mol = Molina

Medication adherence was calculated according to Pharmacy Quality Alliance's measure specification for Proportion of days covered: Antiretroviral medications (2019 update).

* Benefiaciaries who filled at least one prescription for a 90-day supply during the measurement period were classified into the 90-day group.

TABLE 2a: PDC ≥ 90			
Program	Overall PDC	PDC by Days Supply	
FFS	37.3%	< 90 days	34.1%
		90 days	62.5%
UHC	38.2%	< 90 days	36.8%
		90 days	48.6%
MAG	49.1%	< 90 days	49.5%
		90 days	46.6%
MOL	24.5%	< 90 days	25.5%
		90 days	0.0%

TABLE 2b: PDC ≥ 95			
Program	Overall PDC	PDC by Days Supply	
FFS	27.8%	< 90 days	24.3%
		90 days	54.2%
UHC	28.7%	< 90 days	28.4%
		90 days	31.4%
MAG	37.6%	< 90 days	37.3%
		90 days	39.7%
MOL	13.2%	< 90 days	13.7%
		90 days	0.0%

- Across all pharmacy programs, 42.1% (422/1002) of beneficiaries had a PDC > 90%.
- Magnolia had the highest proportion of beneficiaries with 49.1% having a PDC > 90%.
- Beneficiaries receiving antiretrovirals for 90 days supply did not appear to negatively impact PDC overall.
    - *The number of beneficiaries receiving 90 days supply was limited and the study period limited the number of subsequent claims observed. Antiretrovirals were added to DOM's 90 day list effective April 1, 2019.*

CONCLUSIONS

Adherence to antiretroviral therapy is crucial in attaining viral suppression and optimal outcomes in individuals treated for HIV. A 90% adherence is the minimum threshold established for achieving viral suppression, with many experts emphasizing the benefits of attaining 95% adherence or better. Among Medicaid beneficiaries, only 42.1% of beneficiaries achieved PDC $\geq$ 90%. Opportunities exist to improve adherence to antiretroviral therapy.

RECOMMENDATIONS -

1. DOM to collaborate with MSDH, UMMC Infectious Disease Department, and state medical/pharmacy/nursing associations on ART adherence issues.

2. DOM to conduct targeted outreach to providers:
    a. Commend providers having patients with PDCs $\geq$ 90 and seek guidance on best practices;
    b. Educate providers with patients having PDCs < 90.

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ATRIAL FIBRILLATION AND POTENTIAL GAPS IN CARE

BACKGROUND

Atrial fibrillation (Afib) is the most common sustained cardiac arrhythmia worldwide.[1,2] In 2019, an estimated 2.7 million to 6.1 million individuals living in the United States (US) alone have Afib, with approximately 12 million US cases projected by year 2030.[1,2] Common risk factors for incidence of Afib include advancing age, hypertension, smoking, diabetes and ischemic heart disease.[2] Afib-affected individuals have a four-to-fivefold increased risk of lifetime stroke as compared to individuals not affected by Afib.[3] Afib-associated strokes have consistently been classified as more debilitating, more deadly, and more likely to recur than strokes of other etiologies.[1–3] Given this information, it is not surprising that Afib-associated strokes are also linked to higher hospital, physician, and nursing home-related costs.[1,4] Despite increased risk and severity of Afib-associated stroke, appropriate pharmacological anticoagulation serves as a major modifiable protective factor against stroke in patients living with Afib.[1,3,5]

Figure 1. CHA_2DS_2VASc criteria and scoring system for stroke risk in atrial fibrillation.

Stroke risk factors	Score
Congestive heart failure/LV dysfunction	1
Hypertension	1
Aged ≥75 years	2
Diabetes mellitus	1
Stroke/TIA/TE	2
Vascular disease [prior MI, PAD, or aortic plaque]	1
Aged 65–74 years	1
Sex category [i.e. female gender]	1

Pharmacological stroke prophylaxis within the Afib population is achieved through oral anticoagulant therapy.[1,3,5] The chronic use of oral anticoagulants within the Afib population reduces the ability of blood to clot within the atria during fibrillation and decreases stroke risk. In 2019 the American Heart Association (AHA)/ American College of Cardiology (ACC)/ Heart Rhythm Society (HRS) Focused Update of the 2014 Guideline for Management of Patients with Atrial Fibrillation was published. In the selection of appropriate candidates for thromboembolism prophylaxis, emphasis is placed on balancing risks and benefits.[5] The guideline identified the CHA_2DS_2VASc risk assessment criteria (Figure 1) as an appropriate tool to guide pharmacological decision-making within the Afib population.[3,5] CHA_2DS_2 stands for (**C**ongestive heart failure, **H**ypertension, **A**ge (> 65 = 1 point, > 75 = 2 points), **D**iabetes, previous **S**troke/transient ischemic attack (2 points). **VASc** stands for vascular disease (peripheral arterial disease, previous myocardial infarction, aortic atheroma), and sex category (female gender) is also included in this scoring system. For patients with AFib and an elevated CHA_2DS_2-VASc score of 2 or greater in men or 3 or greater in women, oral anticoagulants are recommended.[3,5] Common therapeutic choices for stroke prevention in atrial fibrillation include non-vitamin K oral anticoagulants, or NOACs, [apixaban (Eliquis), edoxaban (Savaysa), dabigatran (Pradaxa), and rivaroxaban (Xarelto)], and vitamin K antagonists [warfarin (Coumadin)].[3] While the guideline recommends NOAC therapy over warfarin therapy in indicated

populations, the American College of Chest Physicians (CHEST) emphasizes the importance of patient preference and cost in this decision.[3] Detailed tables of the recommendations for selecting an anticoagulant regimen can be found in Appendix A.[5]

MS-DUR conducted an analysis of Medicaid beneficiaries with a diagnosis of Afib to assess potential gaps in care. Beneficiaries with a diagnosis of Afib and indication for chronic antithrombotic therapy based on CHA_2DS_2VASc criteria but not on oral anticoagulant therapy were identified.

METHODS

A retrospective analysis was conducted using Mississippi Medicaid fee-for-service (FFS) and coordinated care organization [CCOs: UnitedHealthcare (UHC), Magnolia (MAG), and Molina (MOL)] claims for the period of December 1, 2018 to November 30, 2019. Medicaid beneficiaries with atrial fibrillation were identified using the CMS Chronic Conditions Warehouse (CCW) algorithm of at least 1 inpatient claim or 2 outpatient claims at least 30 days apart using the first two diagnosis codes. Beneficiaries that were dual-eligible in Medicaid and Medicare at any time during the study period were excluded from the analysis. Information on the beneficiaries' race, gender, age, and health plan (FFS/UHC/MAG/MOL) was summarized in the analysis. Age and health plan were assessed as of the date for the first Afib claim in the analysis period, hereafter referred to as the index Afib diagnosis date.

CHA_2DS_2-VASc *stroke risk score*

For each beneficiary with Afib, CHA_2DS_2-VASc stroke risk score was determined to assess stroke risk. CHA_2DS_2-VASc risk score was calculated in the 12 month period prior to the index Afib diagnosis date based on diagnoses for congestive heart failure, hypertension, diabetes, vascular disease, prior stroke or thromboembolism or transient ischemic attack, age (65-74 years, ≥75 years), and gender. The CHA_2DS_2-VASc risk score was dichotomized into two categories: high and low. For females, the threshold for high CHA_2DS_2-VASc risk score was 3 or more, while it was 2 or more for males.

Prior bleeding events

History of bleeding events was assessed for each beneficiary with Afib in the 12 months prior to the index Afib diagnosis date. A history of major bleeding events as defined by medical claims of gastrointestinal bleeding (MGB), intracranial hemorrhage (ICH), and major bleeding from other sites was assessed for the analyses.

Anticoagulant drug utilization

Finally, for beneficiaries with Afib having high CHA_2DS_2-VASc risk scores and no history of bleeding events, anticoagulant drug utilization was assessed in the study period. Anticoagulant drugs included in the assessment were warfarin, apixaban, dabigatran, rivaroxaban, betrixaban, and edoxaban. (*Although betrixaban does not have an indication for stroke prophylaxis, utilization was assessed. There were no claims found for betrixaban during the study period.)* As a follow-up to our primary analysis, any hospitalization event experienced by beneficiaries with Afib who had a high CHA_2DS_2-VASc risk score, no history of bleeding events, and no anticoagulant drug use during the analysis period was flagged.

RESULTS

Table 1 provides a descriptive summary of Medicaid beneficiaries with a diagnosis of atrial fibrillation during the study period.

TABLE 1: Descriptive Summary of Beneficiaries with Atrial Fibrillation (AFib) Diagnosis Enrolled in Medicaid (FFS and CCOs) Who Are Not Dual Eligible in Medicare (Dec 2018 - Nov 2019)

Characteristics	Category	Fee for Service		United Health Care		Magnolia		Molina		Total (across all plans)	
		N	%	N	%	N	%	N	%	N	%
Race	White	138	40.8%	101	37.4%	135	35.2%	12	38.7%	386	37.8%
	African American	151	44.7%	124	45.9%	170	44.4%	11	35.5%	456	44.6%
	Other	49	14.5%	45	16.7%	78	20.4%	8	25.8%	180	17.6%
	Total	338	100.0%	270	100.0%	383	100.0%	31	100.0%	1022	100.0%
Gender											
Male	CHA_2DS_2-VASc score < 2	45	23.6%	31	20.3%	48	25.1%	6	27.3%	130	23.3%
	CHA_2DS_2-VASc score ≥ 2	146	76.4%	122	79.7%	143	74.9%	16	72.7%	427	76.7%
	Total	191	100.0%	153	100.0%	191	100.0%	22	100.0%	557	100.0%
Female	CHA_2DS_2-VASc score < 3	42	28.6%	41	35.0%	55	28.6%	7	77.8%	145	31.2%
	CHA_2DS_2-VASc score ≥ 3	105	71.4%	76	65.0%	137	71.4%	2	22.2%	320	68.8%
	Total	147	100.0%	117	100.0%	192	100.0%	9	100.0%	465	100.0%
Age (as of index AF diagnosis in the study analysis period)	< 18 years	0	0.0%	0	0.0%	3	0.7%	1	3.3%	4	0.4%
	18-44 years	35	10.4%	41	15.2%	42	11.0%	9	29.0%	127	12.4%
	45-64 years	276	81.7%	229	84.8%	338	88.3%	21	67.7%	864	84.5%
	65-74 years	18	5.3%	0	0.0%	0	0.0%	0	0.0%	18	1.8%
	≥ 75 years	9	2.6%	0	0.0%	0	0.0%	0	0.0%	9	0.9%
	Total	338	100.0%	270	100.0%	383	100.0%	31	100.0%	1022	100.0%
Prior Bleeding Event (in the 12 months prior to the first Afib diagnosis in the study analysis period)											
Yes	Anticoagulant use	68	57.6%	69	71.9%	80	63.0%	5	50.0%	222	63.2%
	No anticoagulant use	50	42.4%	27	28.1%	47	37.0%	5	50.0%	129	36.8%
	Total	118	100.0%	96	100.0%	127	100.0%	10	100.0%	351	100.0%
No	Anticoagulant use	121	55.0%	116	66.7%	181	71%	13	61.9%	431	64.2%
	No anticoagulant use	99	45.0%	58	33.3%	75	29%	8	38.1%	240	35.8%
	Total	220	100.0%	174	100.0%	256	100%	21	100.0%	671	100.0%

Note: Patients with Afib were identified using the CMS Chronic Conditions warehouse algorithm of at least 1 inpatient or 2 outpatient claims for Afib in the first two diagnosis codes

History of bleeding was identified from medical claims (inpatient and outpatient) using all diagnosis codes for any of the three following categories: major gastrointestinal bleeding, intracranial hemorrhage, other bleeding events

Anticoagulant drugs included: warfarin, apixaban, dabigatran, rivaroxaban, betrixaban*, and edoxaban (*No claims were found for betrixaban)

- A total of 1022 beneficiaries had a diagnosis of AFib during the study period.
- Of the 1022 beneficiaries, 54.5% (557) were males and 45.5% (465) were females.

- 73.1% (747) of beneficiaries with Afib diagnosis were calculated to have a high CHA_2DS_2-VASc risk score ($\geq$ 2 for males or $\geq$ 3 for females).
- The majority of beneficiaries (84.5%) were ages 45-64 years.
- 65.7% (671) of beneficiaries with an Afib diagnosis had no history of bleeding events with 35.8% (240) of those beneficiaries not having a claim for anticoagulant therapy.

Table 2 combines CHA_2DS_2-VASc risk scores and history of prior bleeding events to identify beneficiaries that are candidates for anticoagulant therapy based on claims data.

TABLE 2: Current Anticoagulant Use Among Medicaid Beneficiaries with Afib with High CHA_2DS_2-VASc Risk Score and No Prior History of Bleeding (Dec 2018 - Nov 2019)

Plan (at index AF diagnosis)	Gender	High CHA_2DS_2-VASc Risk Score*	No prior bleeding**	Anticoagulant use***	
				Yes	No
Fee for Service	Male	146	82	51	31
	Female	105	67	39	28
	Total	251	149	90	59
United Health Care	Male	122	73	52	21
	Female	76	41	30	11
	Total	198	114	82	32
Magnolia	Male	143	89	66	23
	Female	137	87	60	27
	Total	280	176	126	50
Molina	Male	16	11	8	3
	Female	2	1	1	0
	Total	18	12	9	3
Total		747	451	307	**144**

*High CHA_2DS_2-VASc risk score = $\geq$ 2 for males, $\geq$ 3 females.

**History of prior bleeding events were checked for during the 12-month period prior to the index AFib diagnosis date among those that had high CHA_2DS_2-VASc risk scores.

***Anti-thrombin use in the current analysis period was assessed for those that had high CHA_2DS_2-VASc risk scores and no prior bleeding events.

- For the 747 Afib beneficiaries with a high CHA_2DS_2-VASc risk score, 451 had no prior bleeding events identified.
- **Of those with a high CHA_2DS_2-VASc risk score and no prior bleeding events identified, 144 beneficiaries had no anticoagulant claim during the study period.**

For additional analysis, MS-DUR examined hospitalization events experienced by beneficiaries with Afib who had a high CHA_2DS_2-VASc risk score, no history of bleeding events, and no anticoagulant drug use during the analysis period. (Table 3)

TABLE 3: Hospitalizations Among Afib Beneficiaries with High CHA_2DS_2-VASc Risk Score, No Prior Bleeding, and No Anticoagulant Use (Dec 2018 - Nov 2019)

Gender	Any hospitalization	FFS	UHC	MAG	MOL	Total
Female	Yes	16	3	14	-	33
	No	12	8	13	-	33
Male	Yes	17	11	6	3	37
	No	14	10	17	0	41

- 48.6% (70) of beneficiaries with high risk scores, no prior bleeding events identified, and no anticoagulant use were hospitalized during the study.
- Regardless of the reason for the hospitalizations, these hospitalizations represent opportunities for transitions of care services to recognize and initiate oral anticoagulant therapy for these 70 beneficiaries.

CONCLUSIONS

Although a small number of Medicaid beneficiaries have a diagnosis of Afib, these individuals are at a significantly increased risk of lifetime stroke compared to those without Afib. Afib-associated strokes have been shown to be more debilitating, have higher mortality, and are associated with higher costs than strokes of other etiologies. Preventing even a small number of Afib-associated strokes can have a significant impact. Opportunities exist for beneficiaries diagnosed with Afib to be properly treated with anticoagulants for stroke prophylaxis.

RECOMMENDATIONS

1) DOM should implement an educational intervention notifying prescribers of those beneficiaries diagnosed with Afib that are potential candidates for anticoagulant therapy.

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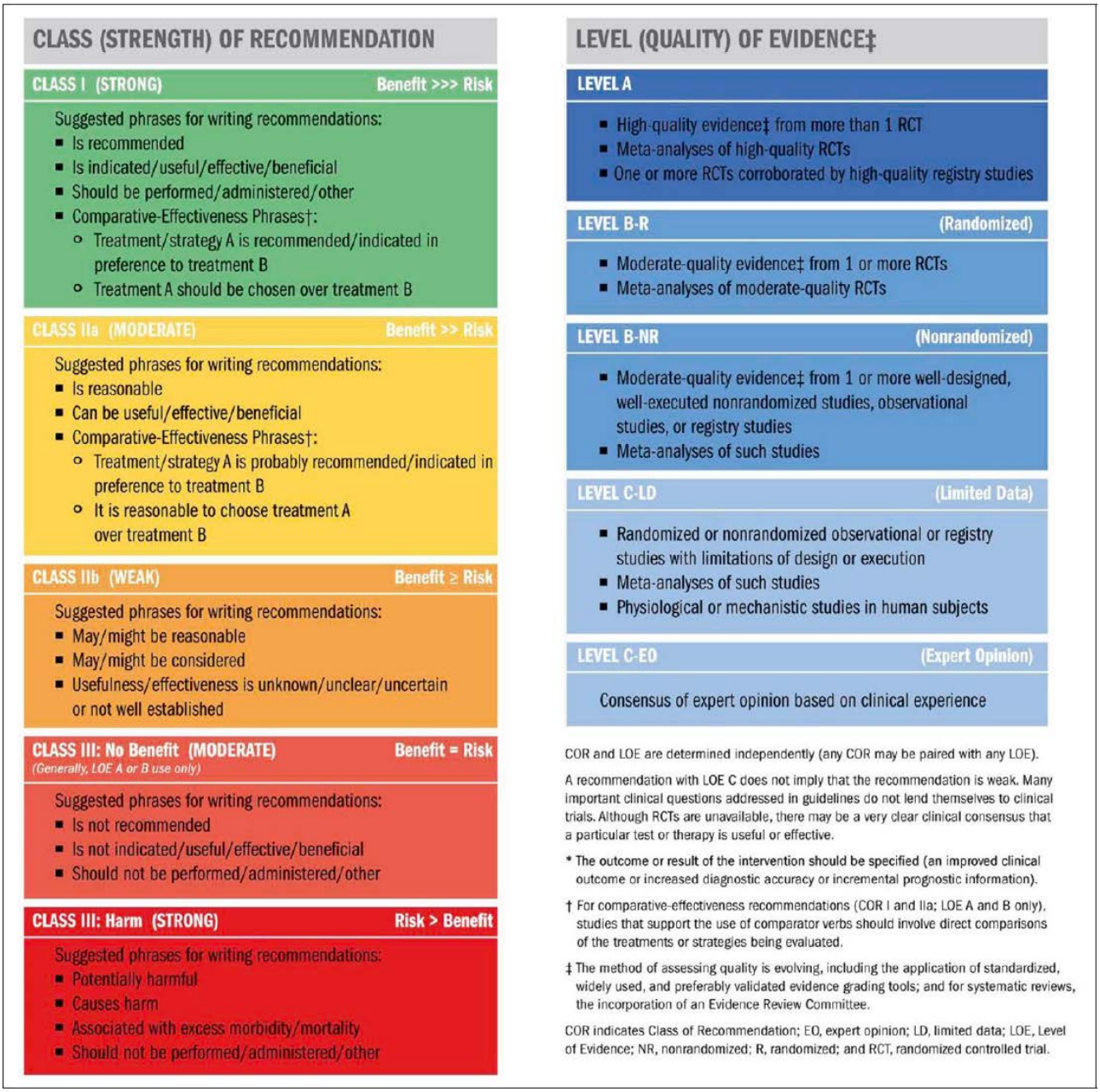
APPENDIX A



CLASS (STRENGTH) OF RECOMMENDATION

CLASS I (STRONG) — **Benefit >>> Risk**

Suggested phrases for writing recommendations:
- Is recommended
- Is indicated/useful/effective/beneficial
- Should be performed/administered/other
- Comparative-Effectiveness Phrases†:
  - Treatment/strategy A is recommended/indicated in preference to treatment B
  - Treatment A should be chosen over treatment B

CLASS IIa (MODERATE) — **Benefit >> Risk**

Suggested phrases for writing recommendations:
- Is reasonable
- Can be useful/effective/beneficial
- Comparative-Effectiveness Phrases†:
  - Treatment/strategy A is probably recommended/indicated in preference to treatment B
  - It is reasonable to choose treatment A over treatment B

CLASS IIb (WEAK) — **Benefit ≥ Risk**

Suggested phrases for writing recommendations:
- May/might be reasonable
- May/might be considered
- Usefulness/effectiveness is unknown/unclear/uncertain or not well established

CLASS III: No Benefit (MODERATE) — **Benefit = Risk**
(Generally, LOE A or B use only)

Suggested phrases for writing recommendations:
- Is not recommended
- Is not indicated/useful/effective/beneficial
- Should not be performed/administered/other

CLASS III: Harm (STRONG) — **Risk > Benefit**

Suggested phrases for writing recommendations:
- Potentially harmful
- Causes harm
- Associated with excess morbidity/mortality
- Should not be performed/administered/other

LEVEL (QUALITY) OF EVIDENCE‡

LEVEL A
- High-quality evidence‡ from more than 1 RCT
- Meta-analyses of high-quality RCTs
- One or more RCTs corroborated by high-quality registry studies

LEVEL B-R (Randomized)
- Moderate-quality evidence‡ from 1 or more RCTs
- Meta-analyses of moderate-quality RCTs

LEVEL B-NR (Nonrandomized)
- Moderate-quality evidence‡ from 1 or more well-designed, well-executed nonrandomized studies, observational studies, or registry studies
- Meta-analyses of such studies

LEVEL C-LD (Limited Data)
- Randomized or nonrandomized observational or registry studies with limitations of design or execution
- Meta-analyses of such studies
- Physiological or mechanistic studies in human subjects

LEVEL C-EO (Expert Opinion)

Consensus of expert opinion based on clinical experience

COR and LOE are determined independently (any COR may be paired with any LOE).

A recommendation with LOE C does not imply that the recommendation is weak. Many important clinical questions addressed in guidelines do not lend themselves to clinical trials. Although RCTs are unavailable, there may be a very clear clinical consensus that a particular test or therapy is useful or effective.

* The outcome or result of the intervention should be specified (an improved clinical outcome or increased diagnostic accuracy or incremental prognostic information).

† For comparative-effectiveness recommendations (COR I and IIa; LOE A and B only), studies that support the use of comparator verbs should involve direct comparisons of the treatments or strategies being evaluated.

‡ The method of assessing quality is evolving, including the application of standardized, widely used, and preferably validated evidence grading tools; and for systematic reviews, the incorporation of an Evidence Review Committee.

COR indicates Class of Recommendation; EO, expert opinion; LD, limited data; LOE, Level of Evidence; NR, nonrandomized; R, randomized; and RCT, randomized controlled trial.

Note: COR – Class of Recommendation; LOE – Level of Evidence

Recommendations for Selecting an Anticoagulant Regimen—Balancing Risks and Benefits *(1 of 3)*

COR	LOE	Recommendations
I	A	1. For patients with AF and an elevated CHA_2DS_2-VASc score of 2 or greater in men or 3 or greater in women, oral anticoagulants are recommended. Options include: • Warfarin [Coumadin, Jantoven] - (LOE: A) • Dabigatran [Pradaxa] - (LOE: B) • Rivaroxaban [Xarelto] - (LOE: B) • Apixaban [Eliquis] - (LOE: B) or • Edoxaban [Savaysa] - (LOE: B-R) MODIFIED: This recommendation has been updated in response to the approval of edoxaban, a new factor Xa inhibitor. More precision in the use of CHA_2DS_2-VASc scores is specified in subsequent recommendations. The LOEs for warfarin, dabigatran, rivaroxaban, and apixaban have not been updated for greater granularity as per the new LOE system. (Section 4.1. in the 2014 AF Guideline) The original text can be found in Section 4.1 of the 2014 AF guideline. Additional information about the comparative effectiveness and bleeding risk of NOACs can be found in Section 4.2.2.2.
I	A	2. NOACs (dabigatran, rivaroxaban, apixaban, and edoxaban) are recommended over warfarin in NOAC-eligible patients with AF (except with moderate-to-severe mitral stenosis or a mechanical heart valve). NEW: Exclusion criteria are now defined as moderate-to-severe mitral stenosis or a mechanical heart valve. When the NOAC trials are considered as a group, the direct thrombin inhibitor and factor Xa inhibitors were at least noninferior and, in some trials, superior to warfarin for preventing stroke and systemic embolism and were associated with lower risks of serious bleeding.
I	A	3. Among patients treated with warfarin, the international normalized ratio (INR) should be determined at least weekly during initiation of anticoagulant therapy and at least monthly when anticoagulation (INR in range) is stable. MODIFIED: "Antithrombotic" was changed to "anticoagulant."
I	B	4. In patients with AF (except with moderate-to-severe mitral stenosis or a mechanical heart valve), the CHA_2DS_2-VASc score is recommended for assessment of stroke risk. MODIFIED: Exclusion criteria are now defined as moderate-to-severe mitral stenosis or a mechanical heart valve. Patients with AF with bioprosthetic heart valves are addressed in the supportive text. (Section 4.1. in the 2014 AF guideline)
I	B	5. For patients with AF who have mechanical heart valves, warfarin is recommended. MODIFIED: New information is included in the supportive text.
I	B	6. Selection of anticoagulant therapy should be based on the risk of thromboembolism, irrespective of whether the AF pattern is paroxysmal, persistent, or permanent. MODIFIED: "Antithrombotic" was changed to "anticoagulant."

Recommendations for Selecting an Anticoagulant Regimen—Balancing Risks and Benefits *(2 of 3)*

I	B-NR	**7. Renal function and hepatic function should be evaluated before initiation of a NOAC and should be reevaluated at least annually.** **MODIFIED**: Evaluation of hepatic function was added. LOE was updated from B to B-NR. New evidence was added. (Section 4.1. in the 2014 AF Guideline)
I	C	**8. In patients with AF, anticoagulant therapy should be individualized on the basis of shared decision-making after discussion of the absolute risks and relative risks of stroke and bleeding, as well as the patient's values and preferences.** **MODIFIED: "**Antithrombotic" was changed to "anticoagulant."
I	C	**9. For patients with atrial flutter, anticoagulant therapy is recommended according to the same risk profile used for AF.** **MODIFIED: "**Antithrombotic" was changed to "anticoagulant."
I	C	**10. Reevaluation of the need for and choice of anticoagulant therapy at periodic intervals is recommended to reassess stroke and bleeding risks.** **MODIFIED: "**Antithrombotic" was changed to "anticoagulant."
I	C-EO	**11. For patients with AF (except with moderate-to-severe mitral stenosis or a mechanical heart valve) who are unable to maintain a therapeutic INR level with warfarin, use of a NOAC is recommended.** **MODIFIED:** Exclusion criteria are now defined as moderate-to-severe mitral stenosis or a mechanical heart valve, and this recommendation has been changed in response to the approval of edoxaban. (Section 4.1. in the 2014 AF Guideline)
IIa	B	**12. For patients with AF (except with moderate-to-severe mitral stenosis or a mechanical heart valve) and a CHA_2DS_2-VASc score of 0 in men or 1 in women, it is reasonable to omit anticoagulant therapy.** **MODIFIED**: Exclusion criteria are now defined as moderate-to-severe mitral stenosis or a mechanical heart valve. (Section 4.1. in the 2014 AF Guideline)
IIb	B-NR	**13. For patients with AF who have a CHA_2DS_2-VASc score of 2 or greater in men or 3 or greater in women and who have end-stage chronic kidney disease (CKD; creatinine clearance [CrCl] <15 mL/min) or are on dialysis, it might be reasonable to prescribe warfarin (INR 2.0 to 3.0) or apixaban for oral anticoagulation.** **MODIFIED**: New evidence has been added. LOE was updated from B to B-NR. (Section 4.1. in the 2014 AF Guideline)

Recommendations for Selecting an Anticoagulant Regimen—Balancing Risks and Benefits *(3 of 3)*

IIb	B-R	**14. For patients with AF (except with moderate-to-severe mitral stenosis or a mechanical heart valve) and moderate-to-severe CKD (serum creatinine ≥1.5 mg/dL [apixaban], CrCl 15 to 30 mL/min [dabigatran], CrCl ≤50 mL/min [rivaroxaban], or CrCl 15 to 50 mL/min [edoxaban]) with an elevated CHA_2DS_2-VASc score, treatment with reduced doses of direct thrombin or factor Xa inhibitors may be considered (e.g., dabigatran, rivaroxaban, apixaban, or edoxaban).** **MODIFIED**: Exclusion criteria are now defined as moderate-to-severe mitral stenosis or a mechanical heart valve, and this recommendation has been changed in response to the approval of edoxaban. LOE was updated from C to B-R. (Section 4.1. in the 2014 AF Guideline)
IIb	C- LD	**15. For patients with AF (except with moderate-to-severe mitral stenosis or a mechanical heart valve) and a CHA_2DS_2-VASc score of 1 in men and 2 in women, prescribing an oral anticoagulant to reduce thromboembolic stroke risk may be considered.** **MODIFIED**: Exclusion criteria are now defined as moderate-to-severe mitral stenosis or a mechanical heart valve, and evidence was added to support separate risk scores by sex. LOE was updated from C to C-LD. (Section 4.1. in the 2014 AF Guideline)
III: No Benefit	C-EO	**16. In patients with AF and end-stage CKD or on dialysis, the direct thrombin inhibitor dabigatran or the factor Xa inhibitors rivaroxaban or edoxaban are not recommended because of the lack of evidence from clinical trials that benefit exceeds risk.** **MODIFIED**: New data have been included. Edoxaban received FDA approval and has been added to the recommendation. LOE was updated from C to C-EO. (Section 4.1. in the 2014 AF Guideline)
III: Harm	B-R	**17. The direct thrombin inhibitor dabigatran should not be used in patients with AF and a mechanical heart valve.** **MODIFIED**: Evidence was added. LOE was updated from B to B-R. Other NOACs are addressed in the supportive text. (Section 4.1. in the 2014 AF Guideline)

AN UPDATE TO DUR RECOMMENDATIONS FOR PROTON PUMP INHIBITOR DEPRESCRIBING IN MISSISSIPPI MEDICAID

BACKGROUND

During the March 2018 DUR Board meeting the use of proton pump inhibitors (PPIs) in the Medicaid population was reviewed examining the potential of deprescribing these products. The Board recommended the implementation of a maximum days supply edit of 90 days in a 12-month period for the use of PPIs based on diagnosis. Due to the prioritized implementation of opioid criteria, the implementation of the PPI maximum days supply edit was postponed. At this time the Division of Medicaid is requesting the DUR Board reevaluate the previous DUR recommendations based on a review of current literature regarding PPI chronic therapy and evaluation of current prescribing trends in Medicaid.

Upper gastrointestinal disorders are increasingly common worldwide. In 2018, 18% to 27% of adults in the United States (US) had gastroesophageal reflux disease (GERD).[1] Increasing incidence of GERD may result in increasing numbers of related complications which include erosive esophagitis (EE), Barrett's esophagus, gastroesophageal strictures, and adenocarcinoma.[2] Proton pump inhibitors (PPIs) are commonly used in clinical practice to treat upper gastrointestinal disorders, including GERD, EE, and gastric ulcers, and make up more than half of the drugs utilized in that market.[3,4] PPIs provide successful symptom relief for 57% to 80% of patients with EE, and over 85% of EE lesions are successfully healed with PPI therapy.[5] In addition to excellent clinical success, patient-reported adverse events of PPIs are mild.[4]

High therapeutic success rates, good tolerability, and patient satisfaction with PPI use have led to high utilization of the drug class.[6] In 2012, PPIs were the second-most commonly prescribed medication class by dollar amount within the US and accounted for $11 billion of the United States' drug expenditure.[3] Despite common use, concerns with overprescribing and potential long-term adverse events exist. Chronic use of PPIs has been associated with increased risk of osteoporotic fractures, *Clostridium difficile* infection, community-acquired pneumonia, vitamin B12 deficiency, acute gastroenteritis, and dementia.[7–9] Inappropriate use of PPIs carries the potential for both clinical and economic ramifications. In 2010 a large, single-center study found that as many as 36% of patients prescribed PPIs lacked appropriate documentation for PPI therapy with the estimated cost of inappropriate use of PPIs totaled over 1.7 million dollars.[10] Furthermore, unnecessary use places patients at higher risks for adverse events and drug-drug interactions.

Demand for appropriate management of PPI therapy has grown as concerns for these adverse events has risen. Recently, the *Canadian Family Physician* published guidelines that detailed deprescribing practices for patients on potentially unnecessary PPI therapy.[11] However, there is conflicting evidence regarding the causal effect between PPIs and adverse event profiles. Recent studies have suggested that PPI use is not associated with the incidence of dementia, and instead

suggest high body mass index may instead be a predicting factor of dementia onset.[12,13] One study found that antibiotic use, rather than PPI use, was the greatest contributing factor to the incidence of *C. diff* in hospitalized populations.[14] Lack of conclusive evidence regarding adverse events along with potential worsening patient quality of life with tapering PPI therapy may compound provider unwillingness to deprescribe PPIs. Providers have cautioned that rebound acid hypersecretion may occur in some patients, particularly those who have been on long-term PPI therapy. This rebound phenomenon may be partially responsible for chronic PPI use.[15] Intermittent, low-dose, or on-demand PPI use may help minimize cost or adverse event burden in patients who are unable or unwilling to stop therapy.[11] Patients are encouraged to step down from PPI use to histamine-2 receptor antagonist (H2 antagonist) therapy for control of mild upper gastrointestinal disease, as H2 antagonist uses overlap significantly with those of PPIs.[2] While H2 antagonists are less effective and have greater drug tolerance than PPIs, their safety and drug-drug interaction profiles are superior.[2] PPI deprescribing practices promoting utilizing H2 antagonists may be disrupted by recent manufacturing instability among this medication class. In 2019, the H2-antagonists nizatidine and ranitidine were found to contain unacceptable levels of N-nitrosodimethylamine (NMDA), a probable carcinogen.[16] Both products have experienced nationwide recalls in response to manufacturing contamination.[17] Given this news, concern exists that physicians will shift prescribing back to PPIs in spite of risks associated with chronic PPI therapy.

MS-DUR conducted the following:

- An update to the March 2018 DUR Board analyses of prescribing trends for PPIs among Medicaid beneficiaries.
- An analysis for H2 antagonist utilization to assess the impact of market disruption caused by the recent FDA safety notices.

METHODS

A retrospective database analysis was conducted using Medicaid point-of-sale (POS) and medical claims data for fee-for-service (FFS) and coordinated care organizations (CCOs): UnitedHealthcare (UHC), Magnolia Health (MAG) and Molina Healthcare (MOL). Beneficiaries prescribed PPIs and H2 antagonists were identified during the period of September 1, 2018 to August 31, 2019. Descriptive characteristics are presented in Tables 1a and 1b. Pharmacy claims data for the period of September 2018 – November 2019 were analyzed to determine the number of prescription fills for PPIs and H2 antagonists identifying potential prescribing trends (Tables 2a and 2b). For PPI users, length of PPI therapy was identified by measuring days supply after adjusting for early refills with a maximum persistence gap 60 days allowed. The index event was defined as the first paid claim in the study period. Beneficiaries were stratified into two groups based on length of PPI therapy ($\leq$ 90 days and > 90 days). To allow a follow-up period of at least 90 days for all beneficiaries prescribed PPIs during the study period, POS claims through November 2019 were analyzed to measure length of therapy (Tables 3a and 3b). A 24-month look back period was used to identify target diagnoses for PPI use (Table 4).

Occurrences of two common acute conditions that have been associated with PPI use, *Clostridium difficile (C. diff)* and acute gastroenteritis (AGE), were identified among beneficiaries after initiating PPI therapy. The ICD-10 codes used to identify *C. difficile* infections were A04.71 and A04.72. The ICD-10 codes used to identify AGE were K52.0, K52.1, K52.21-29, K52.89 and K52.9. Results were stratified by age of the beneficiary and length of PPI therapy (Tables 5 and 6). Recent hospitalizations prior to initiation of PPI therapy were also examined to assess the impact hospitalizations had on PPI therapy initiation. A 30-day look back period prior to the index PPI prescription was used to identify hospitalizations (Table 7).

RESULTS

Tables 1a/1b display demographic characteristics of beneficiaries prescribed PPIs and H2 antagonists between September 2018 and August 2019.

TABLE 1a: Demographic Characteristics of Beneficiaries Prescribed PPI Therapy (Sep 2018 - Aug 2019)

Variable	FFS		UHC		Magnolia		Molina		Total
Age Category (yrs)									
0-17	1,868	29.0%	3,299	31.4%	3,461	24.8%	408	27.7%	**9,036**
18-35	1,053	16.4%	2,114	20.1%	2,852	20.4%	658	44.7%	**6,677**
36-50	1,108	17.2%	2,356	22.4%	3,338	23.9%	253	17.2%	**7,055**
51-64	2,405	37.4%	2,743	26.1%	4,324	30.9%	152	10.3%	**9,624**
Total	*6,434*		*10,512*		*13,975*		*1,471*		***32,392***
Gender									
Female	3,945	61.3%	7,065	67.2%	9,708	69.5%	1,116	75.9%	**21,834**
Male	2,489	38.7%	3,447	32.8%	4,267	30.5%	355	24.1%	**10,558**
Total	*6,434*		*10,512*		*13,975*		*1,471*		***32,392***
Race									
African American	2,823	43.9%	4,673	44.5%	6,737	48.2%	613	41.7%	**14,846**
Caucasian	3,042	47.3%	4,423	42.1%	5,526	39.5%	632	43.0%	**13,623**
Hispanic	61	0.9%	145	1.4%	134	1.0%	16	1.1%	**356**
Other	508	7.9%	1,271	12.1%	1,578	11.3%	210	14.3%	**3,567**
Total	*6,434*		*10,512*		*13,975*		*1,471*		***32,392***

PPIs:

- 32,392 unique beneficiaries were prescribed PPIs during the study period.
- There was no specific age category that contributed to the majority of prescribing of PPIs.
- Approximately twice as many females received PPIs as compared to males.

TABLE 1b: Demographic Characteristics of Beneficiaries Prescribed H2 Antagonists (Sep 2018 - Aug 2019)									
Variable	**FFS**		**UHC**		**Magnolia**		**Molina**		**Total**
Age Category (yrs)									
0-17	2,543	56.6%	6,270	69.9%	6,970	62.4%	1,413	64.76%	**17,196**
18-35	705	15.7%	1,249	13.9%	1,679	15.0%	586	26.86%	**4,219**
36-50	387	8.6%	708	7.9%	1,131	10.1%	125	5.73%	**2,351**
51-64	859	19.1%	749	8.3%	1,392	12.5%	58	2.66%	**3,058**
Total	*4,494*		*8,976*		*11,172*		*2,182*		***26,824***
Gender									
Female	2,601	57.9%	5,365	59.8%	6,825	61.1%	1,427	65.40%	**16,218**
Male	1,893	42.1%	3,611	40.2%	4,347	38.9%	755	34.60%	**10,606**
Total	*4,494*		*8,976*		*11,172*		*2,182*		***26,824***
Race									
African Amer	1,916	42.6%	3,396	37.8%	4,938	44.2%	746	34.19%	**10,996**
Caucasian	1,948	43.3%	2,973	33.1%	3,423	30.6%	576	26.40%	**8,920**
Hispanic	59	1.3%	165	1.8%	162	1.5%	12	0.55%	**398**
Other	571	12.7%	2,442	27.2%	2,649	23.7%	848	38.86%	**6,510**
Total	*4,494*		*8,976*		*11,172*		*2,182*		***26,824***

H2 antagonists:

- 26,824 unique beneficiaries were prescribed H2 antagonists during the study period.
- Children age 17 and under received 64.1% (n=17,196) of the H2 antagonists prescribed.

With increased awareness surrounding PPI deprescribing in general among healthcare professionals in recent years, a downward trend in PPI prescribing could potentially be expected. Table 2a depicts PPI prescription fills by month.

TABLE 2a: PPI Prescription Fills by Month and Plan (Sep 2018 - Nov 2019)					
Month	**Plan**				**Total**
	FFS	**UHC**	**Magnolia**	**Molina**	
Sep-18	2,009	3,336	4,924	0	**10,269**
Oct-18	2,139	3,347	5,212	13	**10,711**
Nov-18	2,030	3,227	4,979	2	**10,238**
Dec-18	1,942	3,073	4,760	2	**9,777**
Jan-19	2,059	3,308	5,079	2	**10,448**
Feb-19	1,901	3,046	4,635	1	**9,583**
Mar-19	2,013	3,048	4,809	120	**9,990**
Apr-19	2,107	3,164	4,862	443	**10,576**
May-19	2,093	3,076	4,887	483	**10,539**
Jun-19	1,912	2,908	4,548	476	**9,844**
Jul-19	2,078	3,231	4,896	594	**10,799**
Aug-19	2,144	3,123	4,891	661	**10,819**
Sep-19	2,032	2,922	4,671	606	**10,231**
Oct-19	2,209	3,127	4,910	698	**10,944**
Nov-19	2,083	2,916	4,830	750	**10,579**
Total	***30,751***	***46,852***	***72,893***	***4,851***	***155,347***

- Previous March 2018 DUR Board Report analyses indicated the average number of PPI prescriptions filled monthly for calendar year 2017 was 10,563.[18]

- Current March 2020 DUR Board report analyses indicate the average number of PPI prescriptions filled monthly between September 2018 and November 2019 was **10,356.**

- Minimal change was noted in the monthly volumes of PPI prescribed for the two analyses timeframes.

H2-Antagonist Prescribing

Due to manufacturing issues with the presence of unacceptable issues and subsequent FDA recalls initiated in September 2019, the use of H2 antagonists could be impacted. Table 2b illustrates a decline in H2 antagonist prescription numbers correlating with the FDA recalls.

TABLE 2b: H2 Antagonist Prescription Fills by Month and Plan (Sep 2018 - Nov 2019)

Month	Plan				Total
	FFS	UHC	Magnolia	Molina	
Sep-18	1,084	1,674	2,244	0	**5,002**
Oct-18	1,198	1,759	2,421	8	**5,386**
Nov-18	1,024	1,601	2,183	1	**4,809**
Dec-18	958	1,474	2,097	3	**4,532**
Jan-19	1,140	1,808	2,377	0	**5,325**
Feb-19	1,051	1,518	2,076	3	**4,648**
Mar-19	1,056	1,561	2,164	123	**4,904**
Apr-19	1,130	1,524	2,122	380	**5,156**
May-19	1,112	1,430	2,102	457	**5,101**
Jun-19	1,006	1,256	1,867	459	**4,588**
Jul-19	1,156	1,429	2,003	619	**5,207**
Aug-19	1,151	1,483	2,093	727	**5,454**
Sep-19	1,097	1,377	1,914	713	**5,101**
Oct-19	1,085	1,350	1,877	652	**4,964**
Nov-19	899	981	1,434	469	**3,783**
Total	***16,147***	***22,225***	***30,974***	***4,614***	***73,960***

- H2 antagonist prescription claims began decreasing in November 2019.
    - The number of prescription fills in November 2019 (3,783) represented a 24.5% decrease from the average number of monthly prescription fills between September 2018 and October 2019.

**It should be noted that the analysis period ended early during the FDA recall period for ranitidine. However with the data available, it does not appear the recall of ranitidine products corresponded to an immediate increase in PPI prescribing.*

PPI Prescribing Trends

Table 3 describes characteristics of beneficiaries prescribed PPIs based on length of therapy.

- 65.6% (N=21,325) of beneficiaries prescribed PPIs during the study period had a length of therapy ≤ 90 days.
- As the age of beneficiaries increased, the percent with a length of therapy > 90 days increased overall.
- Although Molina had the highest percentage of beneficiaries with a length of therapy ≤ 90 days at 82.5%, there was a significantly smaller number of beneficiaries who received PPIs during the study period in Molina compared to the other plans. Molina's initial Mississippi Medicaid implementation date of 10-01-2018 yielded smaller total PPI numbers and less initial beneficiaries enrolled for comparison purposes during the study period.

TABLE 3: Demographic Characteristics of Beneficiaries Prescribed PPIs Stratified by Length of Therapy (Sep 2018 - Aug 2019)

Characteristic	Length of Therapy ≤ 90 days (N=21,325)		Length of Therapy > 90 days (N= 11,067)		Total (N=32,392)
Age Category					
0-17	7,045	78.0%	1,991	22.0%	9,036
18-35	5,101	76.4%	1,576	23.6%	6,677
36-50	4,278	60.6%	2,777	39.4%	7,055
51-64	4,901	50.9%	4,723	49.1%	9,624
Sex					
Female	14,683	67.2%	7,151	32.8%	21,834
Male	6,642	62.9%	3,916	37.1%	10,558
Race					
Caucasian	8,355	61.3%	5,628	41.3%	13,623
Other	2,223	62.3%	1,344	37.7%	3,567
Hispanic	296	83.1%	60	16.9%	356
African American	10,451	70.4%	4,395	29.6%	14,846
Plan					
Fee-for-service	3,977	61.8%	2,457	38.2%	6,434
UHC	7,275	69.2%	3,237	30.8%	10,512
Magnolia	8,860	63.4%	5,115	36.6%	13,975
Molina	1,213	82.5%	258	17.5%	1,471

Various PPIs available along with their FDA-approved and compendia supported indications for use are provided in Figure 1. Indications for PPI use influence duration of therapy.

FIGURE 1 – PPI FDA-approved and compendia supported indications

Micromedex® Recommendations for PPI Medications		
Generic (Brand) Product	**FDA Indications**	**Compendia-Supported Indication**
Omeprazole (Prilosec)	• Erosive esophagitis • Gastric hypersecretion • Acute gastric ulcer • Symptomatic GERD • Acute duodenal ulcer	• Duodenal ulcer maintenance • Indigestion • Giant duodenal ulcer • GI hemorrhage • Refractory GERD • *H. pylori*-induced duodenal ulcer • Esophageal stricture • Prophylaxis of NSAID-induced gastric ulcer
Esomeprazole (Nexium)	• Erosive esophagitis • Prophylaxis of NSAID-induced gastric ulcer • Symptomatic GERD • Zollinger-Ellison syndrome • *H.pylori*-induced duodenal ulcer	• Post-procedure endoscopic application of hemostyptics to gastric lesion
Pantoprazole (Protonix)	• Erosive esophagitis • Gastric hypersecretion • Zollinger-Ellison syndrome	• Prophylaxis of NSAID-induced gastric ulcer • *H. pylori* GI tract infection • Acute duodenal ulcer
Lansoprazole (Prevacid)	• Erosive esophagitis • Acute gastric ulcer • Treatment of NSAID-induced gastric ulcer • Prophylaxis of NSAID-induced gastric ulcer • Symptomatic GERD • *H. pylori* GI tract infection • Acute duodenal ulcer • Zollinger-Ellison syndrome • Duodenal ulcer maintenance	• Barrett's esophagus • Gastric ulcer maintenance • Indigestion
Dexlansoprazole (Dexilant)	• Erosive esophagitis • Non-erosive symptomatic GERD	• Refractory GERD
Rabeprazole (Aciphex)	• Gastric hypersecretion • Symptomatic GERD • Acute duodenal ulcer • *H. pylori*-induced duodenal ulcer	• Acute gastric ulcer • Indigestion • Laryngopharyngeal reflux • *H. pylori*-induced peptic ulcer

Based on manufacturer recommendations and published research, recommended lengths of therapy for FDA-approved and compendia supported indications are displayed in Figure 2.

FIGURE 2: Recommended lengths of therapy with PPI treatment according to indication.[6,19–24]

Common Length of Therapy	FDA and Compendium-Supported Indications for PPI
Long-term (> 90 days)	Los Angeles Grade C or D erosive esophagitis (Moderate-Severe)
	Esophageal stricture
	Gastric hypersecretion
	Zollinger-Ellison syndrome
	Refractory GERD
	Prophylaxis of NSAID-induced gastric ulcer
	Barrett's esophagus
	Gastric ulcer maintenance
	Duodenal ulcer maintenance
Short-term (≤ 90 days)	Los Angeles Grade A or B Erosive Esophagitis (Mild)
	H. pylori GI tract infection
	H. pylori-induced duodenal ulcer
	H. pylori-induced peptic ulcer
	Acute gastric ulcer
	Acute duodenal ulcer
	Symptomatic GERD
	Giant duodenal ulcer
	Post-procedure endoscopic application of hemostyptics to gastric lesion
	Treatment of NSAID-induced gastric ulcer
	Indigestion
	GI hemorrhage
	Non-erosive symptomatic GERD
	Laryngopharyngeal reflux

GI = gastrointestinal; GERD = Gastroesophageal reflux disease; *H. pylori* = *Helicobacter pylori*; NSAID = nonsteroidal anti-inflammatory drug

Table 4 includes information about the presence of target diagnoses present for beneficiaries prescribed PPIs during the study period. To determine the presence of target diagnoses, a medical claim had to occur with associated diagnoses within 24 months prior to the index prescription date.

- Approximately 27.3% (n=8847) of beneficiaries prescribed PPIs did not have a target diagnosis present in medical claims data. **This is a major improvement from the data reported in the March 2018 DUR report where 62.5% of beneficiaries did not have a target diagnosis present**.
- Of the beneficiaries prescribed PPIs with diagnoses indicating short-term therapy, 38.7% took PPIs for > 90 days.

TABLE 4: Presence of Target Diagnosis and Length of Time on Therapy for Beneficiaries Prescribed PPI Therapy (Sep 2018 - Aug 2019)

Target Diagnosis*	FFS (n=6,434)					UHC (n=10,512)					Magnolia (n=13,975)					Molina (n=1,471)				
	Total with Dx	Length of Therapy ≤ 90 days		Length of Therapy > 90 days		Total with Dx	Length of Therapy ≤ 90 days		Length of Therapy > 90 days		Total with Dx	Length of Therapy ≤ 90 days		Length of Therapy > 90 days		Total with Dx	Length of Therapy ≤ 90 days		Length of Therapy > 90 days	
Esophagitis (GERD)	3,493	1,939	55.5%	1,554	44.5%	7,310	4,745	64.9%	2,565	35.1%	9,918	5,826	58.7%	4,092	41.3%	744	596	80.1%	148	19.9%
GERD	3,275	1,811	55.3%	1,464	44.7%	6,828	4,395	64.4%	2,434	35.6%	9,414	5,484	58.3%	3,930	41.7%	699	558	79.8%	141	20.2%
GI bleed	330	200	60.6%	130	39.4%	362	242	66.9%	120	33.1%	410	242	59.0%	168	41.0%	32	25	78.1%	7	21.9%
H. pylori infection	199	137	68.8%	62	31.2%	467	352	75.4%	115	24.6%	689	510	74.0%	179	26.0%	41	38	92.7%	3	7.3%
Stress ulcer	194	103	53.1%	91	46.9%	359	251	69.9%	108	30.1%	413	229	55.4%	184	44.6%	15	13	86.7%	2	13.3%
Gastric ulcer	164	103	62.8%	61	37.2%	315	201	63.8%	114	36.2%	373	233	62.5%	140	37.5%	23	18	78.3%	5	21.7%
NSAID use	149	91	61.1%	58	38.9%	289	186	64.4%	103	35.6%	439	249	56.7%	193	44.0%	17	11	64.7%	6	35.3%
Barett's esophagus	50	26	52.0%	24	48.0%	99	46	46.5%	53	53.5%	152	71	46.7%	81	53.3%	2	1	50.0%	1	50.0%
Erosive esophagitis	13	8	61.5%	5	38.5%	20	13	65.0%	7	35.0%	21	14	66.7%	7	33.3%	6	6	100.0%	0	0.0%
Zollinger-Ellison	1	0	0.0%	1	100.0%	1	1	100.0%	0	0.0%	1	1	100.0%	0	0.0%	0	0	0.0%	0	0.0%
Other target dianoses**	560	323	57.7%	245	43.8%	1,277	855	67.0%	422	33.0%	1,747	1,078	61.7%	669	38.3%	91	76	83.5%	15	16.5%
NO TARGET DIAGNOSIS	**2,105**	**1,440**	68.4%	**665**	31.6%	**2,681**	**2,108**	78.6%	**573**	21.4%	**3,411**	**2,518**	73.8%	**893**	26.2%	**650**	**549**	84.5%	**101**	15.5%

NOTE 1: Beneficiaries taking PPIs may be be included in more than one diagnosis category, except the 'no target diagnosis' category.
NOTE 2: 585 beneficiaries did not have medical claims to record target diagnoses.
NOTE 3: Green highlight represents target diagnoses with indications for long-term PPI use. Orange highlight represents target diagnoses with indication for short-term therapy where beneficiaries received PPI therapy > 90 days.
*Diagnosis code was recorded in a medical claim within 24 months of starting PPI therapy.
** Other diagnoses include achalasia and cardiospasm, duodenal ulcer, dyskinesia esophagus, esophageal hemorrhage, gastritis and duodenitits, gastroesophageal laceration-hemorrhage syndrome, gastrojejunal ulcer, malignant mast cell tumors, multiple endocrine neoplasia, neoplasm of uncertain behavior of other and unspecified endocrine glands, peptic ulcer unspecified, perforation of esophagus, stricture and stenosis of esophagus

Chronic use of PPIs has been associated with an increased risk of multiple adverse events (AE). Two acute AEs associated with chronic PPI use are *clostridium difficile* (*C.diff*) infection and acute gastroenteritis (AGE). A recent study published in the Journal of the American Medical Association found that continuous PPI use was associated with an increased risk of developing AGE of viral origin.[9] Approximately 19-21 million cases of AGE annually can be linked to viral infections in the US.[25,26] An estimated 500,000 Americans are infected with *C.diff* annually, of which approximately 41% are community-acquired cases.[27] Using the June 2019 US Census estimate of 328,234,721 for the US population[28], the calculated incidence proportion of AGE was approximately 6.4%, all-cause *C.diff* was approximately 0.15% and community-acquired *C.diff* was 0.062% in 2019. In Tables 5 and 6, the number of beneficiaries that experienced *C.diff* infections and AGE after being prescribed PPI therapy was examined.

TABLE 5: Number of Beneficiaries with Claims for *Clostridium difficile* Infection After Prescription for PPI (Sep 2018 - Nov 2019)

Age Category	FFS (n=6,434)		UHC (n=10,512)		Magnolia (n=13,975)		Molina (n=1,471)		Total
	Length of Therapy		Length of Therapy		Length of Therapy		Length of Therapy		
	≤ 90 days	> 90 days	≤ 90 days	> 90 days	≤ 90 days	> 90 days	≤ 90 days	> 90 days	
0-17 years	3	0	3	4	5	4	1	0	20
18-35 years	4	2	1	2	3	1	1	1	15
36-50 years	8	2	4	4	4	8	0	0	30
51-64 years	19	10	12	6	11	5	1	0	64
Total	**34**	**14**	**20**	**16**	**23**	**18**	**3**	**1**	**129**

TABLE 6: Number of Beneficiaries with Claims for Acute Gastroenteritis After Prescription for PPI (Sep 2018 - Nov 2019)

Age Category	FFS (n=6,434)		UHC (n=10,512)		Magnolia (n=13,975)		Molina (n=1,471)		Total
	Length of Therapy		Length of Therapy		Length of Therapy		Length of Therapy		
	≤ 90 days	> 90 days	≤ 90 days	> 90 days	≤ 90 days	> 90 days	≤ 90 days	> 90 days	
0-17 years	54	22	236	74	229	91	30	10	746
18-35 years	47	14	107	29	148	59	21	7	432
36-50 years	41	27	90	57	121	94	8	3	441
51-64 years	54	52	91	59	90	130	4	3	483
Total	**196**	**115**	**524**	**219**	**588**	**374**	**63**	**23**	**2,102**

NOTE for Table 4 and Table 5: 1,453 beneficiaries (4.48%) did not have medical claims available for outcome evaluation. Outcome evaluation was conducted in period following first prescription of PPI till Nov 2019

- Of the total cohort of 32,392 beneficiaries prescribed PPI therapy,
  - 129 (0.4%) had *C. diff* infection and
  - 2,102 (6.5%) had AGE during the study period.
    - There was virtually no difference in proportions experiencing *C.diff* infections or AGE based of length of PPI therapy (≤ 90 days or > 90 days).

PPIs are commonly prescribed in the inpatient setting as a continuation of outpatient use or for stress ulcer prophylaxis. Upon discharge from the hospital, PPIs are often continued even when there is no indication for continued use. Table 7 examines the presence of a recent inpatient hospitalization prior to an initial PPI prescription during the study period.

TABLE 7: Summary of Hospitalizations in a 30-day Period Prior to PPI Therapy Index Date (Sep 2018 - Aug 2018)

Age Category	FFS		UHC		Magnolia		Molina		Total
	Prior Hospitalization		Prior Hospitalization		Prior Hospitalization		Prior Hospitalization		
	0- 14 days	15 - 30 days	0- 14 days	15 - 30 days	0- 14 days	15 - 30 days	0- 14 days	15 - 30 days	
0-17 years	16	16	32	34	47	35	14	12	206
18-35 years	43	30	57	21	92	48	18	13	322
36-50 years	61	38	64	23	98	42	9	3	338
51-64 years	162	105	120	44	174	102	21	5	733
Total	**282**	**189**	**273**	**122**	**411**	**227**	**62**	**33**	**1599**

- A total of 1,599 beneficiaries (4.9%) with 1,712 hospitalizations initiated PPI therapy within 30 days after a hospitalization.
    - *For the 113 beneficiaries with multiple hospitalizations in a 30-day period prior to initiation of a PPI, the hospitalization closest to the PPI index date was used in determining the number of days.*
- 1,028 (64.3%) of the total 1,599 beneficiaries had a hospitalization within a 14-day period prior to initiating PPI therapy.

CONCLUSIONS

Based on the analysis presented, there remains multiple opportunities for PPI deprescribing in MS Medicaid. During the study period, 34.2% of beneficiaries prescribed PPI therapy received them for > 90 days. Approximately 27.3% of beneficiaries receiving PPI therapy did not have a target diagnosis present in claims data. For beneficiaries with a diagnosis indicating short-term PPI therapy, 37.8% received > 90 days of PPI therapy. There also appears to be opportunities to encourage appropriate deprescribing of PPIs through transitions of care upon hospital discharge. Additionally, initial data did not indicate prescribers were switching beneficiaries to PPIs in the wake of drug recalls related to the H2 antagonist ranitidine.

RECOMMENDATIONS

The DUR Board is asked to reaffirm the recommendations from the March 2018 DUR Board meeting or alter those recommendations.

The recommendations from the March 2018 DUR Board meeting are below:

1. *DOM should set an electronic PA edit to limit the maximum days supply for PPI therapy to 90 days in a 12 month period before a PA is required.*

2. *For therapy exceeding the 90 day limit, DOM should implement electronic or manual PA requirements for the maximum number of days supply based on diagnoses.*

3. *MS-DUR should implement an educational initiative notifying providers of the new PPI prescribing criteria and guidance on deprescribing.*

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FDA DRUG SAFETY COMMUNICATIONS

DECEMBER 2019 – MARCH 2019

- 3/4/2020 FDA requires Boxed Warning about serious mental health side effects for asthma and allergy drug montelukast (Singulair); advises restricting use for allergic rhinitis
- 2/13/2020 - FDA requests the withdrawal of the weight-loss drug Belviq, Belviq XR (lorcaserin) from the market
- 1/28/2020 - FDA strengthens warning that untreated constipation caused by schizophrenia medicine clozapine (Clozaril) can lead to serious bowel problems
- 1/14/2020 - Safety clinical trial shows possible increased risk of cancer with weight-loss medicine Belviq, Belviq XR (lorcaserin)
- 12/19/2019 - FDA warns about serious breathing problems with seizure and nerve pain medicines gabapentin (Neurontin, Gralise, Horizant) and pregabalin (Lyrica, Lyrica CR)

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