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

MISSISSIPPI DIVISION OF
MEDICAID

April 27, 2017 at 2:00pm

Woolfolk Building, Room 145

Jackson, MS

Prepared by:

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

Drug Utilization Review Board

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

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

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

Antoinette M. Hubble, MD
McComb Children's Clinic
300 Rawls Dr. Ste 100
McComb, MS 39648
Term Expires: June 30, 2017

Cherise McIntosh, PharmD
UMC Dept of Pharmacy
2500 North State St.
Jackson, MS 39216
Term Expires: June 30, 2017

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

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

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

Dennis Smith, RPh
Polk's Discount Pharmacy
1031 Star Rd
Brandon, MS 39042
Term Expires: June 30, 2017

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

Cynthia Undesser, MD
MS Children's Home Services
402 Wesley Ave
Jackson, MS 39202
Term Expires: June 30, 2017

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

2017 DUR Board Meeting Dates

February 2, 2017
April 27, 2017
July 27, 2017
November 9, 2017 (new date)

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
April 27, 2017

Welcome — Pearl Wales, PharmD (Chair)

Old Business — Pearl Wales, PharmD (Chair)

Approval of September 2016 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

Pharmacy Program Update — Terri Kirby, RPh; Sara (Cindy) Noble, PharmD, MPH

Feedback and Discussion from the Board

New Business

Special Analysis Projects

Unique Hepatitis C Treatment Regimens Used Since 2015 In Mississippi Medicaid — page 21
Celexa® (Citalopram) Utilization and Dosing Management — page 26
Type 2 Diabetes Treatment Patterns In Mississippi Medicaid — page 33

FDA Drug Safety Information Updates January - March 2017 — page 43

Next Meeting Information — Pearl Wales, PharmD (Chair)

DUR Board Meeting Minutes

MISSISSIPPI DIVISION OF MEDICAID
DRUG UTILIZATION REVIEW (DUR) BOARD
MINUTES OF THE FEBRUARY 2, 2017 MEETING

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

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

Also Present:

Division of Medicaid (DOM) Staff:
Terri Kirby, RPh, CPM, Pharmacy Director Cindy Noble, PharmD, MPH, DUR Coordinator, Gail McCorkle, RPh, Clinical Pharmacist; Tami Brooks, MD, Medical Director; Bonlitha Windham, Mental Health Director; Gay Gipson, RN, Mental Health; Dorthy Young, PhD, MHSA, Deputy Administrator for Health Services

MS-DUR Staff:
Ben Banahan, PhD, 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

Coordinated Care Organization Staff:
Shana Bush, PharmD, Director of Community and State Pharmacy, United Healthcare; Conor Smith, RPh, Director of Pharmacy, Magnolia Health

Visitors:
John Meynardie, Deputy Criminal Chief, Narcotics, Unites States Attorney General's Office; Judy Clark, Consultant; Rachel Strait, University of Mississippi Pharmacy Student, Phil Hecht, Abbvie; Kris Harrell, University of Mississippi School of Pharmacy; Jason Swartz, Otsuka; Tim Hambacher, Otsuka; Kelli Heathman, Biogen; Brian Berhow, Sunovian; Kim Clark, ViiV; Wendy Phillabaum, Supernus; Leigh Turner, Indivior; Bruce Wallace, Silvergate Pharmaceuticals

Call to Order:
Dr. Wales called the meeting to order at 2:00 pm.

Old Business:
Dr. Banahan distributed revised minutes for the September 29, 2016 DUR Board Meeting. He explained that some edits had been made to clarify and correct a few issues. It was moved by Dr. Hubble and seconded by Dr. Bell. The revised minutes were approved unanimously by the DUR Board.

Pharmacy Program Update:
Ms. Kirby recognized several special attendees in the audience including the guest speaker, John Meynardie with the United States Attorney General's Office. She then asked for the members of the board to introduce themselves and provide a brief description of their practices. Ms. Kirby's update included DOM's proposed reimbursement changes to comply with the Affordable Care Act Medicaid Program Covered Outpatient Drugs with final comments (CMS-2345-FC). This rule addresses regulations that pertain to reimbursement for covered outpatient drugs in the Medicaid program. The state is required to implement the new reimbursement methodology by April 1, 2017. The state plan amendment (SPA) was posted for public comment. Following the end of public comments and upon signature by the Governor, the SPA will be submitted to CMS. MS Kirby stated that Drs. Banahan and Noble will represent DOM at the national American Drug Utilization Review Society (ADURS). Ms. Kirby emphasized that the work of the DUR Board has allowed Mississippi Division of Medicaid to take a leadership role with other states and to effectively address major issues identified by CMS and other national organizations. DOM and MS-DUR are working to promote achievements through poster presentations at national conferences. MS DUR/DOM posters have been accepted for presentation at the following conferences: ADURS, Academy of Managed Care Pharmacy (AMCP) Annual Meeting and at the International Society for Pharmacoeconomic and Outcomes Research (ISPOR) thus far for 2017.

Special Presentation by Prosecutor for U.S. Attorney General
John Meynardie, the Deputy Criminal Chief, Narcotics for Mississippi's US Attorney General's Office provided background information on the US Attorney General's (AG) office involvement in the state's Opioid and Heroin Work Group. Work efforts from three sub-groups held in December of 2016 focused on law enforcement, medical issues, and treatment/prevention. Recommendations from these workgroups were compiled into a report to be shared publicly and turned over the Governor's State Heroin/Opioid Task Force for consideration. Mr. Meynardie provided an overview of the strategy and role of the US AG's office in prosecuting and eliminating illegitimate pain clinics. A description of his educational programs for intermediate and high schools which focus on illicit drug use was provided. Mr. Meynardie emphasized the national problem of counterfeit narcotics that look exactly like the real products, and as an example conveyed the varying toxic levels of fentanyl that have been discovered. He noted that the U.S. AG's office wishes to share resources with other groups and state agencies. In particular, he welcomes requests for presentations at local schools and made a plea for more public service announcements to help educate everyone about the severity of the problem. When Dr. Noble asked his opinion about naloxone availability for first responders, Mr. Meynardie indicated increased naloxone access was an important strategy for reducing overdose deaths.

Resource Utilization Review:
Dr. Banahan informed the board that encounter data from the coordinated care plans appears to be complete for this report. He noted that enrollment has been fairly consistent during the last six months. Average cost per prescription being higher in the fee-for-service (FFS) program than in the two

coordinated care plans can be attributed to differences in the FFS population vs CCO population. Dr. Banahan stated while the top drug categories have been consistent with respect to claim volume, the immune globulins have had an increase in rank order to the number 10 position with respect to dollars paid (Table D). Also highlighted was that the beginning of the Synagis season accounted for a sharp increase in utilization/dollars paid. Synagis information appears in several tables examining paid amounts (Tables F, G, and H). Overall, most of the products which appear in the volume and amount paid tables are seasonal items and do not represent significant utilization issues. Dr. Banahan stated that Exjade and Jadenu expenditures continue to increase (Table H). DOM and MS-DUR are continuing to monitor and track Jadenu utilization. Dr. Hubble asked about the trend regarding beneficiaries being treated for hepatitis-C. Dr. Noble informed the board that Ms. Hardwick, the Complex Pharmaceutical Care (CPC) Pharmacist with Change Healthcare, will provide an overview of the CPC program at the next DUR Board meeting and would address hepatitis C.

Feedback and Discussion from the Board

Dr. Hubble reported that her patients with ringworm have experienced a problem obtaining the preferred product. Ms. Kirby responded that the prior authorization (PA) unit was addressing this issue. Dr. Hubble also reported problems with getting coverage from some of the products listed on the OTC list. Ms. Kirby indicated DOM would look into the examples discussed. When Dr. Wales asked about the outcome of the insulin vials vs. pen safety issue in long term care that was discussed last year, Dr. Noble reported that DOM had investigated the safety issue. Only one safety related event had been reported related to dosing of insulin from vials and this one issue was attributed to a nursing student. As no other reports of safety related to insulin dosing in long term care were discovered, the restriction on coverage of insulin pens for use in long term care was not changed.

N**EW BUSINESS**

Research Reports:

Mississippi Medicaid Pharmacy Programs: Demographics, Utilization and Comorbidities

The MS-DUR analysis comparing FFS and the two coordinated care programs on beneficiary characteristics and prevalence of comorbidities should help provide a background for understanding differences that might exist in treatment patterns due to the populations included in each pharmacy program. Dr. Banahan explained that the CMS Chronic Condition Warehouse criteria for identifying chronic conditions were used in the analysis.

As noted previously in resource utilization reports, the average amount paid per prescription in the FFS program is significantly higher than the averages for the two CCOs (Table 2). This is due to the older age (Table 3) and the greater number (Tables 4-14) of chronic conditions in the FFS population. Dr. Banahan noted that for almost every condition examined, the prevalence was significantly higher in FFS than in the two CCOs. Dr. Young highlighted that the analysis needs to exclude some eligibility codes that only include care for selected conditions, such as family planning, in order to have more accurate prevalence estimates. Dr. Banahan indicated that overall the two CCO populations were very similar but the FFS population had almost twice as many chronic conditions than did the populations in the CCOs. He assured the board that when MS-DUR compares utilization trends across the three programs, these differences are always taken into account and when appropriate, this difference is noted in the DUR Board reports.

CMS Adult Core Set Quality Measure: Antidepressant Medication Management

Dr. Banahan summarized a MS-DUR analysis examining performance on the Antidepressant Medication Management quality measure included in the CMS Adult Care Set. This measure is taken from the HEDIS measures, which is used in the evaluation of health care plans. The quality measure specifications are designed to be conservative about selecting only patients starting antidepressant therapy related to a diagnosis of major depression. Appropriate medication management required continuation of therapy (persistence) for an appropriate length of time and taking the medication as indicated (compliance) was emphasized. Dr. Banahan reported results for performance measure during calendar year 2015 using the measure specifications. Overall, 30% of beneficiaries included in the measure were classified as having appropriate management during the acute phase of treatment (first 12 weeks) and only 14% had appropriate management through the continuation phase (first 6 months). Overall, 48% of patients stopped taking their medication (lack of persistence) during the acute phase with another 20% remaining on therapy but not meeting the compliance measure to be classified as "appropriate management." Dr. Banahan asked for any comments or suggestions the board could provide for improving performance on this quality measure. Dr. Simmons suggested that letters informing providers that of their patients not refilling their medication could help providers address the issue. Other suggestions included encouraging pharmacist interventions with patients and also providing prescription synchronization. It was suggested that pharmacists should be actively involved in addressing the adherence and persistence issues.

Use of Multiple Providers for Opioids: Impact of Cash Prescriptions and Affiliate Provider Identifiers on Identifying At Risk Beneficiaries

Dr. Banahan reviewed an MS-DUR study which examined the impact of including cash prescriptions and affiliate provider identifiers on the number of beneficiaries identified as using multiple providers for opioid prescriptions. Cash prescriptions were obtained from the Prescription Monitoring Program data. Affiliate provider identifiers were computed by MS-DUR by assigning the same identifier to all prescribers practicing in the same physical site and to all chain pharmacies in the same zip code. The inclusion of cash prescriptions from the Prescription Monitoring Program increased the number of beneficiaries classified as provider shopping for opioids by approximately 10%. The use of affiliate provider identifiers decreased the number by about 20%. Although the change in the actual number of beneficiaries classified as using multiple providers may not appear to be meaningful, these adjustments will help more accurately identify beneficiaries that are at high risk for abuse. Dr. Banahan explained that these methods will be incorporated into the quarterly high risk beneficiary reports being prepared for DOM's Program Integrity to identify beneficiaries at risk for substance use disorder and the need for potential lock-in.

Update on Previous Board Recommendations:

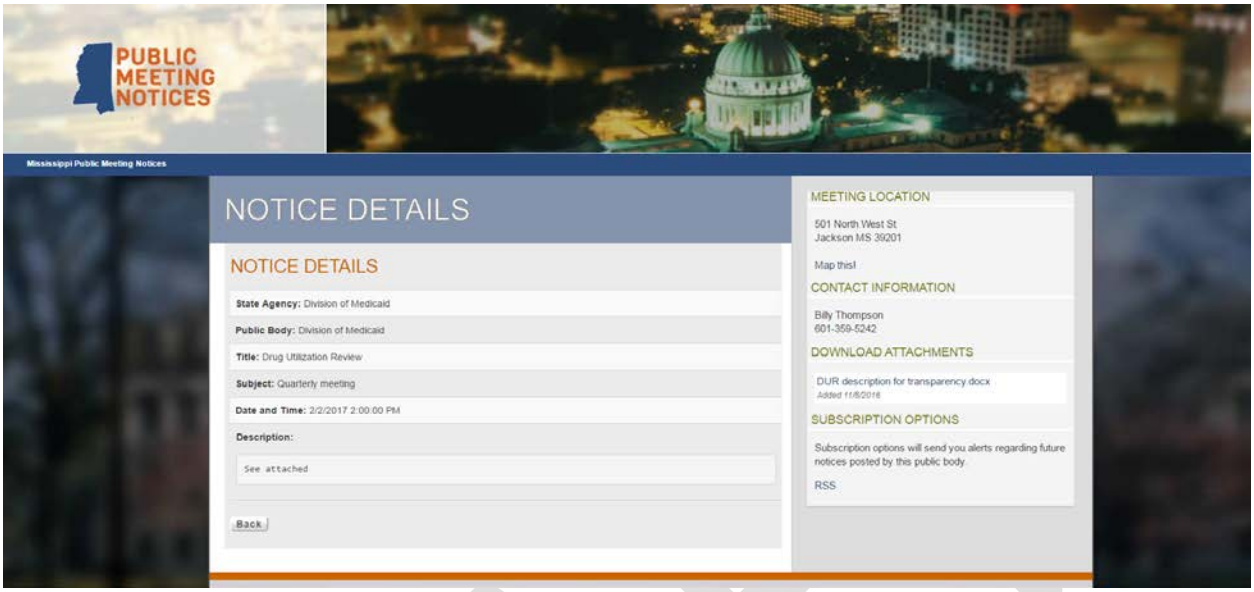
Dr. Noble provided an update on the board recommendations regarding the Centers for Disease Control (CDC) guidelines for opioid prescribing. She indicated that programming changes for the DOM electronic PA process, although underway, will take time to address the recommended edits. Dr. Noble stressed the need for provider education on all of these changes as they are being implemented. The board was informed that the issue of changing the temazepam clinical edit criteria was tabled previously by the board due to concerns about the limited treatment options available for insomnia. Dr. Noble reported that DOM had commissioned a clinical report to review the issue. The report recommended that DOM set criteria for temazepam consistent with FDA labeling and warnings regarding limiting it to short term use only. DUR Board members indicated their agreement with this recommendation.

Next Meeting Information:
Dr. Wales announced that the next meeting of the DUR Board will take place on April 27, 2017 at 2:00 p.m. Dr. Wales thanked everyone for their attendance and participation at the February DUR Board meeting. The meeting adjourned at 4:09 pm.

Submitted,

Benjamin F. Banahan, III, PhD
Evidence-Based DUR Initiative, MS-DUR

PUBLIC MEETING NOTICES



MISSISSIPPI DIVISION OF
MEDICAID

Drug Utilization Review

Board Meeting

February 2, 2017

2:00 P.M.

Woolfolk Building - Room 145

Resource Utilizaton Review

TABLE A: ENROLLMENT STATISTICS FOR LAST 6 MONTHS September 1, 2016 through February 28, 2017							
		Sep-16	Oct-16	Nov-16	Dec-16	Jan-17	Feb-17
Total enrollment		746,820	743,768	741,770	737,342	738,062	734,438
Dual-eligibles		156,054	155,926	155,724	153,538	155,138	154,936
Pharmacy benefits		639,750	636,216	633,628	630,074	629,265	624,953
LTC		17,492	17,451	17,438	17,230	17,179	16,941
PLAN %	FFS	23.2%	23.3%	23.1%	22.5%	22.2%	21.8%
	MSCAN-UHC	38.2%	38.1%	38.1%	38.3%	37.8%	38.0%
	MSCAN-Magnolia	38.6%	38.6%	38.8%	39.1%	40.0%	40.2%

TABLE B: PHARMACY UTILIZATION STATISTICS FOR LAST 6 MONTHS September 1, 2016 through February 28, 2017							
		Sep-16	Oct-16	Nov-16	Dec-16	Jan-17	Feb-17
# Rx Fills	FFS	93,741	93,549	94,226	92,771	92,562	91,208
	MSCAN-UHC	202,110	192,631	205,303	198,883	206,241	204,608
	MSCAN-Mag	231,980	235,135	239,101	234,061	247,467	250,209
# Rx Fills / Bene	FFS	0.6	0.6	0.6	0.7	0.7	0.7
	MSCAN-UHC	0.8	0.8	0.9	0.8	0.9	0.9
	MSCAN-Mag	0.9	1.0	1.0	1.0	1.0	1.0
$ Paid Rx	FFS	$11,330,690	$11,687,669	$11,108,725	$11,899,183	$11,398,366	$12,781,928
	MSCAN-UHC	$15,150,083	$14,508,386	$15,620,773	$15,287,774	$16,769,082	$16,422,993
	MSCAN-Mag	$16,899,124	$17,242,852	$17,574,760	$17,468,723	$19,044,339	$19,225,471
$ /Rx Fill	FFS	$120.87	$124.94	$117.89	$128.26	$123.14	$140.14
	MSCAN-UHC	$74.96	$75.32	$76.09	$76.87	$81.31	$80.27
	MSCAN-Mag	$72.85	$73.33	$73.50	$74.63	$76.96	$76.84
$ /Bene	FFS	$76.34	$78.84	$75.90	$83.93	$81.59	$93.82
	MSCAN-UHC	$61.99	$59.85	$64.71	$63.35	$70.50	$69.15
	MSCAN-Mag	$68.43	$70.21	$71.49	$70.91	$75.66	$76.53

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 FEB 2017 (FFS AND CCOs)

Category	Month Year	Rank Volume	# RXs	$ Paid	# Unique Benes
CNS stimulants	Feb 2017	1	24,428	$5,650,272	21,336
	Jan 2017	1	27,129	$6,180,774	23,396
	Dec 2016	1	24,147	$5,231,691	20,762
aminopenicillins	Feb 2017	2	22,172	$234,932	21,750
	Jan 2017	3	19,395	$199,522	19,036
	Dec 2016	3	19,698	$203,878	19,356
narcotic analgesic combinations	Feb 2017	3	21,949	$506,580	20,410
	Jan 2017	2	24,362	$555,572	22,249
	Dec 2016	2	23,532	$544,591	21,487
macrolides	Feb 2017	4	18,269	$442,663	17,818
	Jan 2017	7	15,056	$373,538	14,678
	Dec 2016	5	16,025	$398,736	15,628
nonsteroidal anti-inflammatory agents	Feb 2017	5	17,396	$216,910	16,811
	Jan 2017	5	17,104	$222,178	16,472
	Dec 2016	7	15,264	$190,577	14,673
neuraminidase inhibitors	Feb 2017	6	16,518	$3,246,652	16,453
	Jan 2017	23	6,689	$1,310,350	6,664
	Dec 2016	50	2,786	$570,370	2,774
adrenergic bronchodilators	Feb 2017	7	16,503	$1,236,281	14,661
	Jan 2017	4	17,140	$1,290,956	15,137
	Dec 2016	4	17,346	$1,244,850	15,331
antihistamines	Feb 2017	8	16,103	$344,689	15,626
	Jan 2017	6	15,401	$337,320	14,877
	Dec 2016	6	15,293	$334,236	14,780
glucocorticoids	Feb 2017	9	13,670	$309,274	13,232
	Jan 2017	8	13,172	$292,718	12,716
	Dec 2016	8	14,158	$317,515	13,733
SSRI antidepressants	Feb 2017	10	10,966	$109,831	10,478
	Jan 2017	10	11,870	$112,180	11,207
	Dec 2016	10	11,209	$94,964	10,508

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

Category	Month Year	Rank Paid Amt	# RXs	$ Paid	# Unique Benes
CNS stimulants	Feb 2017	1	24,428	$5,650,272	21,336
	Jan 2017	1	27,129	$6,180,774	23,396
	Dec 2016	1	24,147	$5,231,691	20,762
factor for bleeding disorders	Feb 2017	2	114	$3,315,890	82
	Jan 2017	5	85	$1,842,105	67
	Dec 2016	3	100	$2,537,351	67
neuraminidase inhibitors	Feb 2017	3	16,518	$3,246,652	16,453
	Jan 2017	7	6,689	$1,310,350	6,664
	Dec 2016	15	2,786	$570,370	2,774
antiviral combinations	Feb 2017	4	742	$2,947,496	711
	Jan 2017	2	797	$2,863,116	737
	Dec 2016	2	783	$3,158,412	742
insulin	Feb 2017	5	4,397	$2,323,248	3,379
	Jan 2017	3	4,793	$2,498,221	3,590
	Dec 2016	4	4,586	$2,372,547	3,467
atypical antipsychotics	Feb 2017	6	10,914	$1,758,412	9,998
	Jan 2017	4	12,098	$1,912,765	10,825
	Dec 2016	5	11,725	$1,893,160	10,250
antirheumatics	Feb 2017	7	326	$1,419,606	308
	Jan 2017	6	335	$1,424,177	305
	Dec 2016	6	341	$1,321,861	311
adrenergic bronchodilators	Feb 2017	8	16,503	$1,236,281	14,661
	Jan 2017	8	17,140	$1,290,956	15,137
	Dec 2016	7	17,346	$1,244,850	15,331
bronchodilator combinations	Feb 2017	9	3,101	$1,000,442	2,895
	Jan 2017	10	3,283	$1,045,240	3,057
	Dec 2016	9	3,036	$912,057	2,828
inhaled corticosteroids	Feb 2017	10	3,028	$955,668	2,988
	Jan 2017	9	3,353	$1,060,110	3,274
	Dec 2016	8	3,220	$1,032,057	3,151

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

Drug Molecule Therapeutic Category	Jan 2017 # Claims	Feb 2017 # Claims	Feb 2017 $ Paid	Feb 2017 # Unique Benes
amoxicillin / aminopenicillins	19,292	22,047	$230,878	21,637
azithromycin / macrolides	14,249	17,332	$339,459	16,948
oseltamivir / neuraminidase inhibitors	6,687	16,516	$3,246,519	16,452
albuterol / adrenergic bronchodilators	16,573	15,951	$919,794	14,245
acetaminophen-hydrocodone / narcotic analgesic combinations	16,848	14,913	$155,480	14,089
montelukast / leukotriene modifiers	11,013	10,567	$457,149	10,441
cetirizine / antihistamines	9,743	10,364	$235,953	10,241
ibuprofen / nonsteroidal anti-inflammatory agents	8,444	9,395	$86,596	9,234
lisdexamfetamine / CNS stimulants	9,293	8,618	$2,466,913	8,421
amoxicillin-clavulanate / penicillins/beta-lactamase inhibitors	6,988	7,704	$365,649	7,582
prednisolone / glucocorticoids	7,012	7,280	$250,471	7,055
gabapentin / gamma-aminobutyric acid analogs	7,454	6,970	$109,915	6,701
fluticasone nasal / nasal steroids	6,374	6,767	$329,579	6,738
amlodipine / calcium channel blocking agents	7,027	6,731	$28,544	6,592
omeprazole / proton pump inhibitors	6,948	6,488	$76,574	6,380
cefdinir / third generation cephalosporins	5,843	6,285	$425,370	6,180
ondansetron / 5HT3 receptor antagonists	5,408	6,055	$80,730	5,929
methylphenidate / CNS stimulants	6,294	5,682	$1,346,001	5,124
amphetamine-dextroamphetamine / CNS stimulants	6,503	5,542	$490,900	4,838
clonidine / antiadrenergic agents, centrally acting	5,895	5,310	$112,530	5,103
sulfamethoxazole-trimethoprim / sulfonamides	5,270	4,562	$75,825	4,483
lisinopril / angiotensin converting enzyme inhibitors	4,750	4,390	$13,442	4,318
ranitidine / H2 antagonists	4,619	4,060	$202,880	3,964
guanfacine / antiadrenergic agents, centrally acting	4,347	4,050	$81,860	3,899
ethinyl estradiol-norgestimate / contraceptives	4,516	4,043	$94,281	3,929

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

Drug Molecule Therapeutic Category	Jan 2017 $ Paid	Feb 2017 $ Paid	Feb 2017 # Claims	Feb 2017 # Unique Benes
oseltamivir / neuraminidase inhibitors	$1,310,217	$3,246,519	16,516	16,452
lisdexamfetamine / CNS stimulants	$2,658,531	$2,466,913	8,618	8,421
antihemophilic factor / factor for bleeding disorders	$841,977	$1,648,809	39	23
methylphenidate / CNS stimulants	$1,530,810	$1,346,001	5,682	5,124
anti-inhibitor coagulant complex / factor for bleeding disorders	$598,461	$1,243,155	9	3
ledipasvir-sofosbuvir / antiviral combinations	$898,153	$1,031,212	31	28
adalimumab / antirheumatics	$931,546	$933,258	163	151
albuterol / adrenergic bronchodilators	$962,007	$919,794	15,951	14,245
insulin glargine / insulin	$850,631	$791,303	1,736	1,688
dexmethylphenidate / CNS stimulants	$802,321	$680,102	2,864	2,439
deferasirox / chelating agents	$714,822	$668,721	77	70
somatropin / growth hormones	$726,501	$660,855	148	143
insulin aspart / insulin	$705,410	$655,136	1,148	1,119
budesonide / inhaled corticosteroids	$702,680	$628,350	1,363	1,348
pregabalin / gamma-aminobutyric acid analogs	$651,577	$597,540	1,357	1,322
palivizumab / immune globulins	$669,446	$586,582	221	168
aripiprazole / atypical antipsychotics	$577,174	$527,794	2,631	2,519
lurasidone / atypical antipsychotics	$528,890	$521,062	437	420
amphetamine-dextroamphetamine / CNS stimulants	$535,613	$490,900	5,542	4,838
montelukast / leukotriene modifiers	$468,933	$457,149	10,567	10,441
esomeprazole / proton pump inhibitors	$476,025	$440,678	2,057	2,011
fluticasone-salmeterol / bronchodilator combinations	$451,507	$431,986	1,111	1,098
cobicistat/elvitegravir/emtricitabine/tenofov / antiviral combinations	$422,823	$425,903	148	144
cefdinir / third generation cephalosporins	$397,281	$425,370	6,285	6,180
atomoxetine / CNS stimulants	$407,022	$380,157	872	818

TABLE G: TOP 25 DRUG MOLECULES
BY CHANGE IN NUMBER OF CLAIMS FROM DEC 2016 TO FEB 2017 (FFS and CCOs)

Drug Molecule	Dec 2016 # Claims	Jan 2017 # Claims	Feb 2017 # Claims	Feb 2017 $ Paid	Feb 2017 # Unique Benes
oseltamivir / neuraminidase inhibitors	2,783	6,687	16,516	$3,246,519	16,452
amoxicillin / aminopenicillins	19,603	19,292	22,047	$230,878	21,637
azithromycin / macrolides	15,097	14,249	17,332	$339,459	16,948
ibuprofen / nonsteroidal anti-inflammatory agents	7,401	8,444	9,395	$86,596	9,234
ondansetron / 5HT3 receptor antagonists	5,303	5,408	6,055	$80,730	5,929
fluticasone nasal / nasal steroids	6,079	6,374	6,767	$329,579	6,738
amoxicillin-clavulanate / penicillins/beta-lactamase inhibitors	7,086	6,988	7,704	$365,649	7,582
triamcinolone topical / topical steroids	2,971	3,579	3,436	$53,246	3,330
prednisone / glucocorticoids	3,277	3,414	3,690	$24,078	3,603
cetirizine / antihistamines	9,984	9,743	10,364	$235,953	10,241
lisdexamfetamine / CNS stimulants	8,250	9,293	8,618	$2,466,913	8,421
promethazine / antihistamines	3,447	3,622	3,807	$41,059	3,633
codeine-guaifenesin / upper respiratory combinations	1,981	1,917	2,318	$31,010	2,292
dextromethorphan-promethazine / upper respiratory combinations	1,170	1,121	1,490	$11,675	1,462
methylphenidate / CNS stimulants	5,379	6,294	5,682	$1,346,001	5,124
benzonatate / antitussives	1,310	1,330	1,582	$14,913	1,556
acetaminophen-codeine / narcotic analgesic combinations	2,655	2,961	2,917	$20,507	2,828
cephalexin / first generation cephalosporins	2,903	3,117	3,143	$56,457	3,104
amphetamine / CNS stimulants	50	187	270	$85,485	262
dextroamphetamine / CNS stimulants	344	511	538	$174,560	524
methylprednisolone / glucocorticoids	1,957	2,213	2,145	$27,247	2,122
brompheniramine/dextromethorphan/pse / upper respiratory combinations	728	645	908	$19,514	897
ciprofloxacin-dexamethasone otic / otic steroids with anti-infectives	853	1,074	1,014	$214,961	992
fluconazole / azole antifungals	2,758	3,193	2,904	$28,036	2,742
metronidazole / miscellaneous antibiotics	2,141	2,367	2,283	$18,680	2,221

TABLE H: TOP 25 DRUG MOLECULES
BY CHANGE IN AMOUNT PAID FROM DEC 2016 TO FEB 2017 (FFS and CCOs)

Drug Molecule	Dec 2016 $ Paid	Jan 2017 $ Paid	Feb 2017 $ Paid	Feb 2017 # Claims	Feb 2017 # Unique Benes
oseltamivir / neuraminidase inhibitors	$570,175	$1,310,217	$3,246,519	16,516	16,452
antihemophilic factor / factor for bleeding disorders	$914,117	$841,977	$1,648,809	39	23
lisdexamfetamine / CNS stimulants	$2,168,057	$2,658,531	$2,466,913	8,618	8,421
esomeprazole / proton pump inhibitors	$272,743	$476,025	$440,678	2,057	2,011
methylphenidate / CNS stimulants	$1,216,771	$1,530,810	$1,346,001	5,682	5,124
corticotropin / corticotropin	$179,708	$151,203	$302,403	4	4
dexmethylphenidate / CNS stimulants	$586,037	$802,321	$680,102	2,864	2,439
dasatinib / BCR-ABL tyrosine kinase inhibitors	$55,987	$119,032	$140,258	12	11
fluticasone-salmeterol / bronchodilator combinations	$356,743	$451,507	$431,986	1,111	1,098
adalimumab / antirheumatics	$860,517	$931,546	$933,258	163	151
amphetamine / CNS stimulants	$15,559	$59,432	$85,485	270	262
ledipasvir-sofosbuvir / antiviral combinations	$964,688	$898,153	$1,031,212	31	28
interferon beta-1a / interferons	$170,893	$188,085	$236,754	32	30
sorafenib / multikinase inhibitors	$23,950	$53,180	$87,018	7	6
liraglutide / GLP-1 receptor agonists	$22,847	$66,272	$75,625	111	109
dextroamphetamine / CNS stimulants	$127,182	$163,983	$174,560	538	524
coagulation factor ix / factor for bleeding disorders	$88,091	$106,284	$134,288	5	4
fluticasone nasal / nasal steroids	$283,565	$299,361	$329,579	6,767	6,738
elosulfase alfa / lysosomal enzymes	$46,003	$46,003	$92,007	2	1
ciprofloxacin-dexamethasone otic / otic steroids with anti-infectives	$175,731	$221,224	$214,961	1,014	992
azithromycin / macrolides	$300,281	$277,684	$339,459	17,332	16,948
dolutegravir / integrase strand transfer inhibitor	$224,516	$248,167	$260,839	141	137
empagliflozin / SGLT-2 inhibitors	$4,146	$17,872	$39,993	88	88
cobicistat/elvitegravir/emtricitabine/tenofov / antiviral combinations	$390,822	$422,823	$425,903	148	144
pimecrolimus topical / miscellaneous topical agents	$85,016	$130,615	$119,300	281	276

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 DEC 2016 TO FEB 2017 (FFS and CCOs)

Drug Product Therapeutic Category	Feb 2017 # Claims	Feb 2017 $ Paid	Feb 2017 Avr. Paid Per Rx	Feb 2017 Avr. Units Per Rx	Dec 2016 Paid Per Unit	Jan 2017 Paid Per Unit	Feb 2017 Paid Per Unit	Percent Change
esomeprazole 40 mg delayed release capsule / proton pump inhibitors (P)	1,022	$199,468	$195.17	31	$1.17	$5.85	$6.13	425.2%
esomeprazole 20 mg delayed release capsule / proton pump inhibitors (P)	313	$42,547	$135.93	31	$1.56	$4.24	$4.25	172.7%
NexIUM (esomeprazole) 40 mg delayed release capsule / proton pump inhibitors (P)	169	$41,495	$245.53	32	$4.43	$7.58	$7.43	67.5%
tacrolimus 1 mg capsule / calcineurin inhibitors (P)	107	$40,082	$374.60	163	$1.46	$1.23	$2.23	52.0%
guanfacine 4 mg tablet, extended release / antiadrenergic agents, centrally acting (P)	398	$20,212	$50.78	30	$1.09	$1.29	$1.53	40.8%
cefprozil 500 mg tablet / second generation cephalosporins (P)	242	$8,348	$34.50	19	$1.18	$1.49	$1.55	31.5%
Tri-Lo-Sprintec (ethinyl estradiol-norgestimate) triphasic 25 mcg tablet / contraceptives (P)	114	$4,754	$41.71	28	$1.11	$1.45	$1.35	21.4%
sumatriptan 100 mg tablet / antimigraine agents (P)	155	$3,021	$19.49	9	$1.43	$1.73	$1.66	16.3%
Focalin XR (dexmethylphenidate) 5 mg capsule, extended release / CNS stimulants (P)	122	$36,582	$299.86	29	$8.77	$10.61	$10.17	16.0%
ethinyl estradiol-norgestimate triphasic 25 mcg tablet / contraceptives (P)	356	$13,479	$37.86	29	$1.01	$1.25	$1.16	14.5%
Adderall XR (amphetamine-dextroamphetamine) 20 mg capsule, extended release / CNS stimulants (N)	136	$32,105	$236.07	31	$6.48	$5.37	$7.42	14.5%
quetiapine 400 mg tablet / atypical antipsychotics (P)	394	$62,785	$159.35	43	$3.44	$3.06	$3.87	12.4%
oxcarbazepine 600 mg tablet / dibenzazepine anticonvulsants (P)	258	$23,032	$89.27	70	$1.07	$1.14	$1.20	11.7%
Zetia (ezetimibe) 10 mg tablet / cholesterol absorption inhibitors (P)	104	$34,370	$330.48	30	$9.88	$10.50	$10.95	10.8%
Lyrica (pregabalin) 50 mg capsule / gamma-aminobutyric acid analogs (P)	157	$69,427	$442.21	67	$5.98	$6.55	$6.59	10.1%

New Business

Special Analysis Projects

UNIQUE HEPATITIS C TREATMENT REGIMENS USED SINCE 2015 IN MISSISSIPPI MEDICAID

BACKGROUND

Eight new drugs have been approved for the treatment of hepatitis C since November 2013 (Table 1). These new drugs have provided significant improvement in the cure rate of the disease. Nationally, Medicaid programs and other payers have expressed concerns that a large number of patients had been "warehoused" while waiting for the introduction of new "improved" treatment options and the potential financial impact. Many state Medicaid programs restricted access to the new drugs by requiring documentation of existing hepatic fibrosis with varying levels being required by states. The Mississippi Division of Medicaid (DOM) established and has maintained prior authorization (PA) guidelines based on the American Association For The Study Of Liver Diseases (AASLD) / Infectious Diseases Society of America (ISDA) Recommendations for Testing, Managing, and Treating Hepatitis C.[1] The treatment recommendations in these guidelines do not include clinical criteria based on hepatic fibrosis level.

TABLE 1: New Drugs Approved for Hepatitis C Treatment

Hepatitis C drug	FDA Approval Date
Olysio	November 2013
Sovaldi	December 2013
Harvoni	October 2014
Viekira Pak	December 2014
Technivie	July 2015
Daklinza	July 2015
Zepatier	January 2016
Epclusa	June 2016

During the February 2017 DUR Board Meeting a board member requested an update on the treatment trend for hepatitis C in Medicaid. In response to this inquiry, MS-DUR conducted an analysis to examine the number of beneficiaries treated and the specific regimens used for treatment of hepatitis C during the last two years.

METHODS

MS-DUR conducted a retrospective analysis using Division of Medicaid (DOM) pharmacy claims from all the pharmacy programs including fee-for-service (FFS) and coordinated care organizations (CCOs) for the period July 1, 2014 – February 28, 2017. Data from 2014 was used as a "wash out" period so that new treatment starts could be identified in January of 2015.

Identifying treatment regimens: Recommended regimens consist of using one, and sometimes two, of the new medications listed in Table 1. Some recommended regimens include the addition of pegylated interferon and/or ribavirin. MS-DUR used refill patterns for each medication option to determine regimens used to treat beneficiaries. Regimens were identified as the combination of drugs used concomitantly. The length of treatment was determined by the total days supply of the major drug used in the regimen. Refill gaps resulting in lack of possession of the major drug in the regimen for 30 days or more were classified as breaks in therapy with the next prescription fill considered to be a restart of therapy.

[1] American Association for The Study of Liver Diseases (AASLD) / Infectious Diseases Society of America (ISDA) Recommendations for Testing, Managing, and Treating Hepatitis C. http://www.hcvguidelines.org/full-report-view

RESULTS

Table 2 shows the number of beneficiaries starting hepatitis C treatment regimens during each quarter since January 2015. There was a sharp increase in the number of beneficiaries starting treatment during the first quarter of 2015. Since that time, there has been a slow decline in the number of beneficiaries starting treatment with approximately 50-60 currently initiating treatment each quarter. Harvoni monotherapy has been the dominant treatment regimen since it was introduced to the market. Recently there has been an increase in Epclusa use.

TABLE 2: Number of Beneficiaries Starting Hepatitis C Treatment Regimens by Quarter Started										
	Quarter When Regimen Started*									
Regimen	Q1 2015	Q2 2015	Q3 2015	Q4 2015	Q1 2016	Q2 2016	Q3 2016	Q4 2016	Q1 2016	Total
ALL PHARMACY PROGRAMS										
Epclusa							3	17	5	25
Harvoni	33	86	69	49	53	45	39	35	21	430
Harvoni / Viekira Pak	0	0	0	1	0	0	0	0	0	1
Harvoni / ribavirin	0	0	0	0	0	3	0	2	1	6
Sovaldi	0	0	0	0	1	1	0	0	0	2
Sovaldi / Daklinza			0	1	3	3	2	0	0	9
Sovaldi / Daklinza / ribavirin			0	0	0	1	0	0	0	1
Sovaldi / peg-interferon / ribavirin	0	0	0	0	0	0	1	0	0	1
Sovaldi / ribavirin	7	13	15	8	5	19	3	2	0	72
Viekira Pak / ribavirin	0	6	2	0	1	0	2	0	1	12
Zepatier					0	0	1	3	3	7
TOTAL STARTS	40	105	86	59	63	72	51	59	31	566
FFS										
Epclusa							2	3	0	5
Harvoni	10	7	10	11	11	8	7	9	4	77
Harvoni / ribavirin	0	0	0	0	0	1	0	2	1	4
Sovaldi / Daklinza			0	0	1	1	2	0	0	4
Sovaldi / ribavirin	2	1	1	3	1	0	0	0	0	8
Viekira Pak / ribavirin	0	1	0	0	0	0	0	0	0	1
Zepatier					0	0	0	0	1	1
TOTAL STARTS	12	9	11	14	13	10	11	14	6	100
UHC										
Epclusa							0	6	4	10
Harvoni	10	24	25	18	18	20	16	10	5	146
Sovaldi	0	0	0	0	1	0	0	0	0	1
Sovaldi / peg-interferon / ribavirin	0	0	0	0	0	0	1	0	0	1
Sovaldi / ribavirin	1	3	7	2	0	2	1	2	0	18
Viekira Pak / ribavirin	0	3	0	0	0	0	0	0	0	3
Zepatier					0	0	1	1	0	2
TOTAL STARTS	11	30	32	20	19	22	19	19	9	181
MAG										
Epclusa							1	8	1	10
Harvoni	13	55	34	20	24	17	16	16	12	207
Harvoni / Viekira Pak	0	0	0	1	0	0	0	0	0	1
Harvoni / ribavirin	0	0	0	0	0	2	0	0	0	2
Sovaldi	0	0	0	0	0	1	0	0	0	1
Sovaldi / Daklinza			0	1	2	2	0	0	0	5
Sovaldi / Daklinza / ribavirin			0	0	0	1	0	0	0	1
Sovaldi / ribavirin	4	9	7	3	4	17	2	0	0	46
Viekira Pak / ribavirin	0	2	2	0	1	0	2	0	1	8
Zepatier					0	0	0	2	2	4
TOTAL STARTS	17	66	43	25	31	40	21	26	16	285

** Data for 2017 Q1 are not complete.*

The length of time (in weeks) that beneficiaries remained on therapy with their initial treatment is shown in Table 3." Beneficiaries who began regimens after November 2016 are not included since these regimens may not be completed by the data cutoff for the analysis. Harvoni is the only product with a recommended regimen as short as 8 weeks. The shortest recommended regimen for all other products is 12 weeks. Cases where beneficiaries remained on therapy for shorter than the minimum recommended time for the regimen are highlighted in orange.

TABLE 3: Number of Weeks Beneficiary Remained on Treatment Regimen (Initial Treatments Starting January 1, 2015 - November 30, 2016)

Regimen	Number of Weeks On Therapy						
	4 weeks	8 weeks	12 weeks	16 weeks	20 weeks	24 weeks	> 24 weeks
ALL PROGRAMS							
Epclusa	0	1	13	0	0	0	0
Harvoni	43	190	171	2	2	16	0
Harvoni / Viekira Pak	1	0	0	0	0	0	0
Harvoni / ribavirin	0	0	5	0	0	0	0
Sovaldi	1	0	0	1	0	0	0
Sovaldi / Daklinza	0	0	7	0	0	2	0
Sovaldi / Daklinza / ribavirin	0	0	1	0	0	0	0
Sovaldi / peg-interferon / ribavirin	0	0	1	0	0	0	0
Sovaldi / ribavirin	7	6	36	3	2	17	1
Viekira Pak / ribavirin	1	2	6	0	0	2	0
Zepatier	0	0	4	0	0	0	0
FFS							
Epclusa	0	0	3	0	0	0	0
Harvoni	10	19	34	0	0	5	0
Harvoni / ribavirin	0	0	3	0	0	0	0
Sovaldi / Daklinza	0	0	2	0	0	2	0
Sovaldi / ribavirin	2	1	1	0	0	4	0
Viekira Pak / ribavirin	0	1	0	0	0	0	0
UHC							
Epclusa	0	1	3	0	0	0	0
Harvoni	5	76	52	0	0	3	0
Sovaldi	0	0	0	1	0	0	0
Sovaldi / peg-interferon / ribavirin	0	0	1	0	0	0	0
Sovaldi / ribavirin	2	0	10	1	1	4	0
Viekira Pak / ribavirin	0	1	2	0	0	0	0
Zepatier	0	0	2	0	0	0	0
MAG							
Epclusa	0	0	7	0	0	0	0
Harvoni	15	80	81	2	2	8	0
Harvoni / Viekira Pak	1	0	0	0	0	0	0
Harvoni / ribavirin	0	0	2	0	0	0	0
Sovaldi	1	0	0	0	0	0	0
Sovaldi / Daklinza / ribavirin	0	0	1	0	0	0	0
Sovaldi / ribavirin	3	5	25	2	1	9	1
Viekira Pak / ribavirin	1	0	2	0	0	2	0
Zepatier	0	0	2	0	0	0	0

Weeks on therapy less than shortest recommended regimen

Beneficiaries receiving more than one treatment regimen were identified in order to evaluate effectiveness of the new treatment regimens. Only seven (7) beneficiaries were identified as having two treatment regimens. In each of these cases, the beneficiary initiated treatment with Harvoni monotherapy and had a more than 30-day lapse in therapy before filling a second prescription for Harvoni. All of these cases occurred in 2015. These cases could indicate poor compliance and a decision to not approve continued treatment after the second prescription fill. However, these cases could also have been 8-week treatment regimens where the patients did not start the medication until several weeks after the first prescription fills.

CONCLUSIONS

The number of beneficiaries being treated for hepatitis C spiked in early 2015 and has declined to around 50-60 beneficiaries per quarter at this time. Some problems have occurred with beneficiaries not completing their regimens. Hepatitis C regimens are expensive. When patients do not complete their regimens, a successful outcome (cure) is highly unlikely. Hepatitis C is one of the initial disease categories being addressed by DOM's new Complex Pharmacy Care program.

CELEXA® (CITALOPRAM) UTILIZATION AND DOSING MANAGEMENT

BACKGROUND

In May 2007, the FDA issued a notice that the agency was updating the black box warning for antidepressants to include warnings about increased risks of suicidal thinking and behavior, known as suicidality, in young adults ages 18 to 24 during initial treatment (generally the first one to two months).[1] FDA's black box warning in Celexa's package insert is shown 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 Celexa 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. Celexa is not approved for use in pediatric patients. (See WARNINGS: Clinical Worsening and Suicide Risk, PRECAUTIONS: Information for Patients, and PRECAUTIONS: Pediatric Use.)**

Also in 2007, a study that was partially funded by the National Institute of Mental Health was published reporting results of a comprehensive review of pediatric clinical trials conducted between 1988 and 2006.[2] The study suggested that the benefits of antidepressant medications likely outweigh their risks to children and adolescents with major depression and anxiety disorders. More recent studies have supported these conclusions. Antidepressant-induced suicidality appears to be an uncommon occurrence but also a legitimate phenomenon that needs to be monitored.[3,4]

1 U.S. Food and Drug Administration. FDA Proposes New Warnings About Suicidal Thinking, Behavior in Young Adults Who Take Antidepressant Medications. May 2, 2007. https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/2007/ucm108905.htm

2 Bridge JA, Iyengar S, Salary CB, Barbe RP, Birmaher B, Pincus HA, Ren L, Brent DA, MD. Clinical Response and Risk for Reported Suicidal Ideation and Suicide Attempts in Pediatric Antidepressant Treatment: A Meta-analysis of Randomized Controlled Trials. *JAMA*. 2007;297:1683-1696.

3 Wijlaars LPMM, Nazareth I, Whitaker HJ, et al. Suicide-related events in young people following prescription of SSRIs and other antidepressants: a self-controlled case series analysis. *BMJ Open* 2013;3:e003247. doi: 10.1136/bmjopen-2013-003247

4 Reeves RR, Ladner ME. Antidepressant-induced suicidality: An update. CNS Neurosci Ther 2010;16:227-234. Doi: 10.1111/j.1755-5949.2010.00160.x

In February 2016, the Food and Drug Administration (FDA) issued a clarification about safety issues related to Celexa (citalopram) dosing and warning recommendations.[5] Based on the possibility that high doses of citalopram can cause dangerous abnormalities in the electrical activity of the heart, the FDA made the following warnings and recommendations to providers:

- Citalopram causes dose-dependent QT interval prolongation, which can cause Torsades de Pointes, ventricular tachycardia, and sudden death.
- Citalopram is not recommended for use at **doses greater than 40 mg per day** because such doses cause too large an effect on the QT interval and confer no additional benefit.
- Citalopram is not recommended for use in patients with congenital long QT syndrome, bradycardia, hypokalemia, or hypomagnesemia, recent acute myocardial infarction, or uncompensated heart failure. Citalopram use is also not recommended in patients who are taking other drugs that prolong the QT interval.
- The maximum recommended dose of citalopram is **20 mg per day** for patients with hepatic impairment, **patients who are greater than 60 years of age**, patients who are CYP 2C19 poor metabolizers, or patients who are taking concomitant cimetidine (Tagamet®) or another CYP2C19 inhibitor. These factors may lead to increased blood levels of citalopram and increase the risk of QT interval prolongation and Torsade de Pointes.
- Citalopram should be discontinued in patients found to have persistent QTc measurements greater than 500 ms.

Some antidepressants are FDA approved to treat pediatric patients diagnosed with major depressive disorder (MDD), obsessive-compulsive disorder (OCD), or childhood enuresis. The results of a survey conducted by the Centers for Disease Control and Prevention (CDC) and the National Center for Health Statistics (NCHS) showed during 2007-2008 that 4.8 percent of adolescents (12 to 19 years old) took antidepressant medications.[6]

5 U.S. Food and Drug Administration. Clarification of dosing and warning recommendations for Celexa. January 5, 2016. https://www.fda.gov/Drugs/ResourcesForYou/SpecialFeatures/ucm297764.htm

6 Gu, Q., Dillon, C. F., & Burt, V. L. (2010, September). Prescription Drug Use Continues to Increase: U. S. Prescription Drug Data for 2007–2008. NCHS Data Brief, No. 42. (DHHS Publication No. [PHS] 2010-1209). http://www.cdc.gov/nchs/data/databriefs/db42.pdf

A fact sheet published by the Centers for Medicare and Medicaid (CMS) in 2013 provided guidance on the use of antidepressants in pediatric patients.[7] As shown in this table from the fact sheet, two of the tricyclic antidepressants (TCAs) – clomipramine and imipramine -- and only four of the selective serotonin reuptake inhibitors (SSRIs) -- escitalopram, fluoxetine, fluvoxamine, and sertraline -- have FDA-approved indications in pediatric patients.

Figure 1. FDA-Approved Pediatric Age Ranges and Indications for Antidepressant Medications

*Fluoxetine is FDA approved for the treatment of MDD in pediatric patients up to 18 years old.

According to the Celexa prescribing information, Celexa was studied in 407 pediatric patients in two placebo-controlled clinical trials. There was insufficient evidence to support a pediatric indication for the treatment of MDD.[8]

As shown in the Universal Preferred Drug List (UPDL) excerpt below, generic citalopram is a preferred product. In 2010, the Division of Medicaid (DOM) implemented an electronic prior authorization (PA) for SSRI antidepressants that included minimum age limits. The current age limit in the UPDL for citalopram is 9 years. All other age limits are consistent with the current FDA labeling for these products.

ANTIDEPRESSANTS, SSRIs SmartPA			
	citalopram escitalopram fluoxetine fluvoxamine paroxetine CR paroxetine IR sertraline	CELEXA (citalopram) fluoxetine DR fluvoxamine ER LEXAPRO (escitalopram) LUVOX (fluvoxamine) LUVOX CR (fluvoxamine) paroxetine suspension PAXIL CR (paroxetine) PAXIL SUPENSION (paroxetine) PAXIL Tablets (paroxetine) PEXEVA (paroxetine) PROZAC (fluoxetine) SARAFEM (fluoxetine) ZOLOFT (sertraline)	**Minimum Age Limits** • **6 years** - Zoloft • **7 years** – Prozac • **8 years** - Luvox • **9 years** - Celexa • **12 years** - Lexapro • **18 years** - Luvox CR, Paxil, Prozac 90 mg **Non Preferred Criteria** • Have tried 2 different preferred agents in the past 6 months **OR** • 90 consecutive days on the requested agent in the past 105 days

7 Centers for Medicare and Medicaid Service. Antidepressant Medications: Use in Pediatric Patients – Fact Sheet. https://www.cms.gov/Medicare-Medicaid-Coordination/Fraud-Prevention/Medicaid-Integrity-Education/Pharmacy-Education-Materials/Downloads/ad-pediatric-factsheet11-14.pdf

8 Celexa® (citalopram) prescribing information. (2017, January 4). http://www.accessdata.fda.gov/drugsatfda_docs/label/2017/020822s047lbl.pdf

MS-DUR examined citalopram utilization to address the following research questions:

- How well is the current age edit working to restrict use in young children?
- What would be the potential impact of raising the age edit to 18?
- How often are the recommended maximum daily dose limits being exceeded?

METHODS

MS-DUR conducted a retrospective analysis using DOM's pharmacy claims for all programs (fee-for-service (FFS) and coordinated care organizations (CCOs)) for the period January 2016 – January 2017.

RESULTS

The **numbers of citalopram prescriptions claims** that DOM paid for each month are listed by the beneficiaries' ages in Table 1. Table 2 shows details on the number of prescriptions by month and beneficiary age for each pharmacy program. Overall utilization of citalopram has remained consistent during 2016 at approximately 3,000 fills per month while there was an increase of prescription claims during January 2017.

TABLE 1: Citalopram Prescription Claims by Month and Age of Beneficiary
(FFS and CCOs)

	Age at Fill					
Fill Month	**5 or less**	**6 - 8**	**9 - 17**	**18 - 59**	**60 +**	**Total**
2016- 1	1	5	425	2,335	282	3,048
2016- 2	0	6	401	2,286	277	2,970
2016- 3	1	5	442	2,380	311	3,139
2016- 4	0	2	392	2,121	273	2,788
2016- 5	1	5	403	2,239	296	2,944
2016- 6	2	1	401	2,244	305	2,953
2016- 7	2	4	364	2,170	279	2,819
2016- 8	0	3	456	2,259	280	2,998
2016- 9	0	4	445	2,149	293	2,891
2016-10	1	5	422	1,996	274	2,698
2016-11	1	3	419	1,929	289	2,641
2016-12	0	6	462	2,205	294	2,967
2017-01	1	6	504	2,899	405	3,815
Total	9	49	5,032	29,212	3,858	34,856

During 2016, 58 prescriptions for citalopram were filled for beneficiaries under the age of 9. The number of prescriptions claims for children under age 9 in the three pharmacy programs appeared to be proportional to the enrollment in each program. All three programs also had prescriptions filled for beneficiaries age 60 and over.

TABLE 2: Citalopram Prescription Claims by Month, Age and Pharmacy Program																		
	FFS						UHC						MAG					
Fill Month	Age at Fill						Age at Fill						Age at Fill					
	5 or less	6 - 8	9 - 17	18 - 59	60 +	Total	5 or less	6 - 8	9 - 17	18 - 59	60 +	Total	5 or less	6 - 8	9 - 17	18 - 59	60 +	Total
2016- 1	0	1	95	415	141	652	0	0	164	817	59	1,040	1	4	166	1,103	82	1,356
2016- 2	0	2	79	398	128	607	0	1	160	804	54	1,019	0	3	162	1,084	95	1,344
2016- 3	0	0	96	452	139	687	0	1	159	820	71	1,051	1	4	187	1,108	101	1,401
2016- 4	0	0	84	408	130	622	0	1	137	653	53	844	0	1	171	1,060	90	1,322
2016- 5	0	0	74	421	130	625	0	2	158	765	68	993	1	3	171	1,053	98	1,326
2016- 6	0	0	85	418	134	637	1	1	150	755	66	973	1	0	166	1,071	105	1,343
2016- 7	0	0	71	391	132	594	1	2	135	758	66	962	1	2	158	1,021	81	1,263
2016- 8	0	0	101	407	127	635	0	2	185	805	57	1,049	0	1	170	1,047	96	1,314
2016- 9	0	1	97	404	136	638	0	3	173	705	57	938	0	0	175	1,040	100	1,315
2016-10	0	3	86	377	125	591	0	2	162	674	49	887	1	0	174	945	100	1,220
2016-11	0	1	91	352	135	579	0	2	157	673	52	884	1	0	171	904	102	1,178
2016-12	0	3	85	367	124	579	0	2	195	907	69	1,173	0	1	182	931	101	1,215
2017-01	0	5	115	457	152	729	0	0	37	212	21	270	1	1	352	2,230	232	2,816
Total	0	11	1,044	5,267	1,733	7,446	2	19	1,935	9,348	742	11,813	7	19	2,053	14,597	1,383	15,597

Table 3 reports the **number of beneficiaries** by age and citalopram maximum total daily dose.

- Only 27 beneficiaries had maximum total daily doses that exceeded 40 mg/day. The majority of these beneficiaries were 18 to 59 years of age.
- 264 (39.5%) of beneficiaries age 60 or greater were prescribed greater than 20 mg/day.

TABLE 3: Maximum Daily Dose for Beneficiaries by Age
(FFS and CCOs - January 2016 - January 2017)

	Maximum Daily Dose*							
Age	**5mg**	**10mg**	**15mg**	**20mg**	**30mg**	**40mg**	**50mg +**	**Total**
5 or less	0	1	0	0	0	1	0	2
6 - 8	2	6	0	0	0	0	2	10
9 - 17	4	492	9	765	40	125	5	1,440
18 - 59	11	689	13	4,196	125	2,235	20	7,289
60 +	5	77	1	374	12	252	0	721
Total	22	1,265	23	5,335	177	2,613	27	9,462

** Daily dose calculated as (quantity dispensed / days supply * strength dispensed). Doses are rounded.*

Table 4 depicts the **number of prescriber**s writing prescriptions for targeted patient groups classified by age. Results were as follows:

- 30 different prescribers wrote prescriptions for children < 9 years of age.
- 26 different prescribers wrote prescriptions for daily doses exceeding 40 mg/day.
- 269 different prescribers wrote prescriptions for beneficiaries > 60 years old with daily doses exceeding 20 mg/day.

Overall, 314 different prescribers wrote prescriptions for one or more situations that were considered to be potential safety concerns.

TABLE 4: Number of Prescribers by Target Patient Groups
(FFS and CCOs - January 2016 - January 2017)

Children < Age 9		Adults Age 60+		Adults Age 60+ Prescribed > 20 mg/day		Beneficiaries Prescribed Daily Dose > 40 mg	
# Benes	**Number of Prescribers**	**# Benes**	**Number of Prescribers**	**# Benes**	**Number of Prescribers**	**# Benes**	**Number of Prescribers**
0	2,553	0	1,954	0	2,314	0	2,557
1	11	1	140	1	63	1	8
2	6	2	86	2	42	2	3
3	4	3	70	3	33	3	2
4	3	4	61	4	29	4	4
5+	6	5+	272	5+	102	5+	9

CONCLUSIONS AND RECOMMENDATIONS

The current age edit of 9 years appears to be effective with only a few prescriptions claims for children under age 9. Increasing the minimum age limit for citalopram to 18 years would have impacted 1,440 children and adolescent beneficiaries in 2016 (Table 3). However, fluoxetine, fluvoxamine, and sertraline which are preferred on the current universal PDL have pediatric indications for ≥ 9 years.

For adults, prescribing daily doses greater than 40 mg/day occurred infrequently and a hard edit for this population would have affected only 27 beneficiaries last year. Prescribing daily doses > than 20 mg/day for beneficiaries age ≥60 years would be somewhat more problematic. A hard edit for this daily dose would have affected 264 beneficiaries in 2016.

Recommendations:

1. DOM should implement an electronic PA edit to limit daily doses of citalopram to a maximum of 40 mg/day for beneficiaries less than age 60 years.
2. DOM should implement an electronic PA edit to limit daily doses of citalopram to a maximum of 20 mg/day for beneficiaries age ≥ 60 years.
3. DOM should raise the minimum age limit for citalopram in the SSRI electronic PA to 18 years to be consistent with the FDA approved citalopram label.
4. MS-DUR should conduct a one-time educational mailing reminding prescribers about age specific risks associated with citalopram and the FDA dosing recommendations. This mailing should include all prescribers writing citalopram prescriptions during the last year that were (a) for children and adolescents <18 years of age, (b) for adults age ≥ 60 years with daily doses > 20 mg, or (c) for adults age < 60 years with daily doses exceeding 40 mg.

TYPE 2 DIABETES TREATMENT PATTERNS IN MISSISSIPPI MEDICAID

BACKGROUND

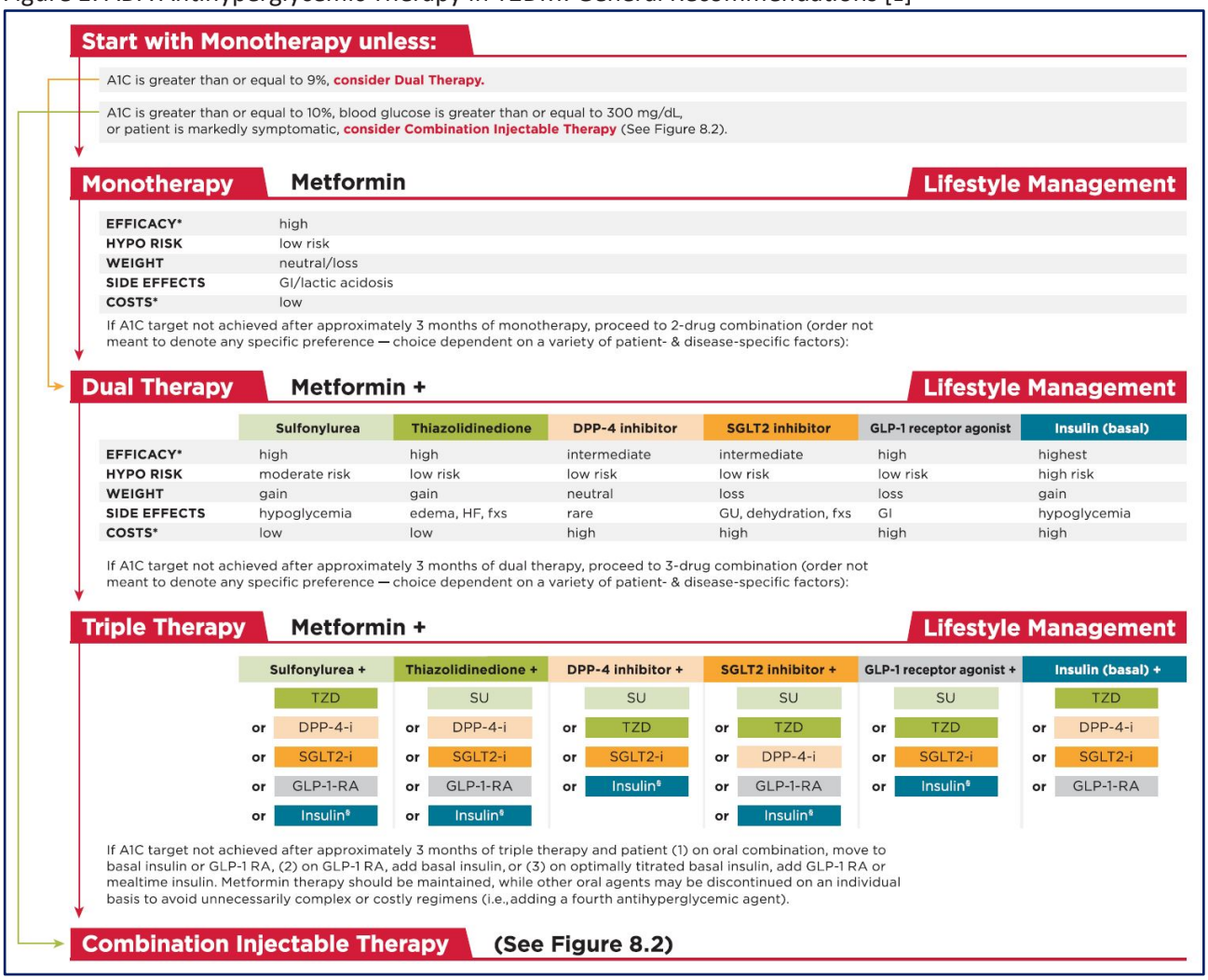
The American Diabetes Association's (ADA's) annually updated "Standards of Medical Care in Diabetes," referred to as the "Standards of Care," is intended to provide clinicians, patients, researchers, payers, and other interested individuals with the components of diabetes care, general treatment goals, and tools to evaluate the quality of care. The Standards of Care recommendations are not intended to preclude clinical judgement and must be applied in the context of excellent clinical care, with adjustments for individual preferences, comorbidities, and other patient factors. The "Standards of Medical Care in Diabetes – 2017" [1] recommend the following regarding pharmacologic therapy for Type 2 diabetes (T2DM):

- Metformin, if not contraindicated and if tolerated, is the preferred initial pharmacologic agent for the treatment of T2DM.
- Long-term use of metformin may be associated with biochemical vitamin B12 deficiency, and periodic measurement of vitamin B12 levels should be considered in metformin-treated patients, especially in those with anemia or peripheral neuropathy.
- Consider initiating insulin therapy (with or without additional agents) in patients with newly diagnosed T2DM who are symptomatic and/or have A1C ≥ 10% (86 mmol/mol) and/or blood glucose levels ≥300 mg/dL (16.7 mmol/L).
- If noninsulin monotherapy at maximum tolerated dose does not achieve or maintain the A1C target after 3 months, add a second oral agent, a glucagon-like peptide 1 receptor agonist, or basal insulin.
- A patient-centered approach should be used to guide the choice of pharmacologic agents. Considerations include efficacy, hypoglycemia risk, impact on weight, potential side effects, cost, and patient preferences.
- For patients with type 2 diabetes who are not achieving glycemic goals, insulin therapy should not be delayed.
- In patients with long-standing suboptimally controlledT2DM and established atherosclerotic cardiovascular disease, the sodium glucose cotransportor-2 inhibitors (SGOT-2) empagliflozin (Jardiance) or liraglutide should be considered as they have been shown to reduce cardiovascular and all-cause mortality when added to standard care. Ongoing studies are investigating the cardiovascular benefits of other agents in these drug classes.

As noted above, metformin if not contraindicated and if tolerated, is the preferred agent for the treatment of T2DM. In patients with metformin contraindications or intolerance, providers should consider an initial drug from another class depicted in Figure 1 under "Dual Therapy" and proceed accordingly. When A1C is ≥9%, initiating dual combination therapy should be considered to achieve the target A1C more expeditiously.

1 American Diabetes Association. Standards of Medical Care in Diabetes – 2017. *Diabetes Care* Volume 40, Supplement 1, January 2017. http://professional.diabetes.org/sites/professional.diabetes.org/files/media/dc_40_s1_final.pdf

Figure 1: ADA Antihyperglycemic Therapy in T2DM: General Recommendations [1]



Although there are numerous trials comparing dual therapy with metformin alone, few directly compare drugs as add-on therapy. A comparative effectiveness metaanalysis [2] suggested that each new class of non-insulin agents added to initial therapy generally lowers A1C approximately 0.9–1.1%. Other noninsulin products should be added if necessary to achieve appropriate treatment goals. The order of products in each row of the chart was determined by historical availability and the route of administration, with injectables to the right. It is not meant to denote any specific preference within each line of therapy. Potential sequence of antihyperglycemic therapy for patients with Type 2 diabetes are displayed, with the usual transition moving vertically from top to bottom (although horizontal movement within therapy stages is also possible, depending on the circumstances). Drug choice is based on patient preferences, various patient disease, and drug characteristics with the goal of reducing blood glucose levels while minimizing side effects, especially hypoglycemia.

2 Bennett WL, Maruthur NM, Singh S, et al. Comparative effectiveness and safety of medications for type 2 diabetes: an update including new drugs and 2-drug combinations. Ann Intern Med 2011;154:602–613

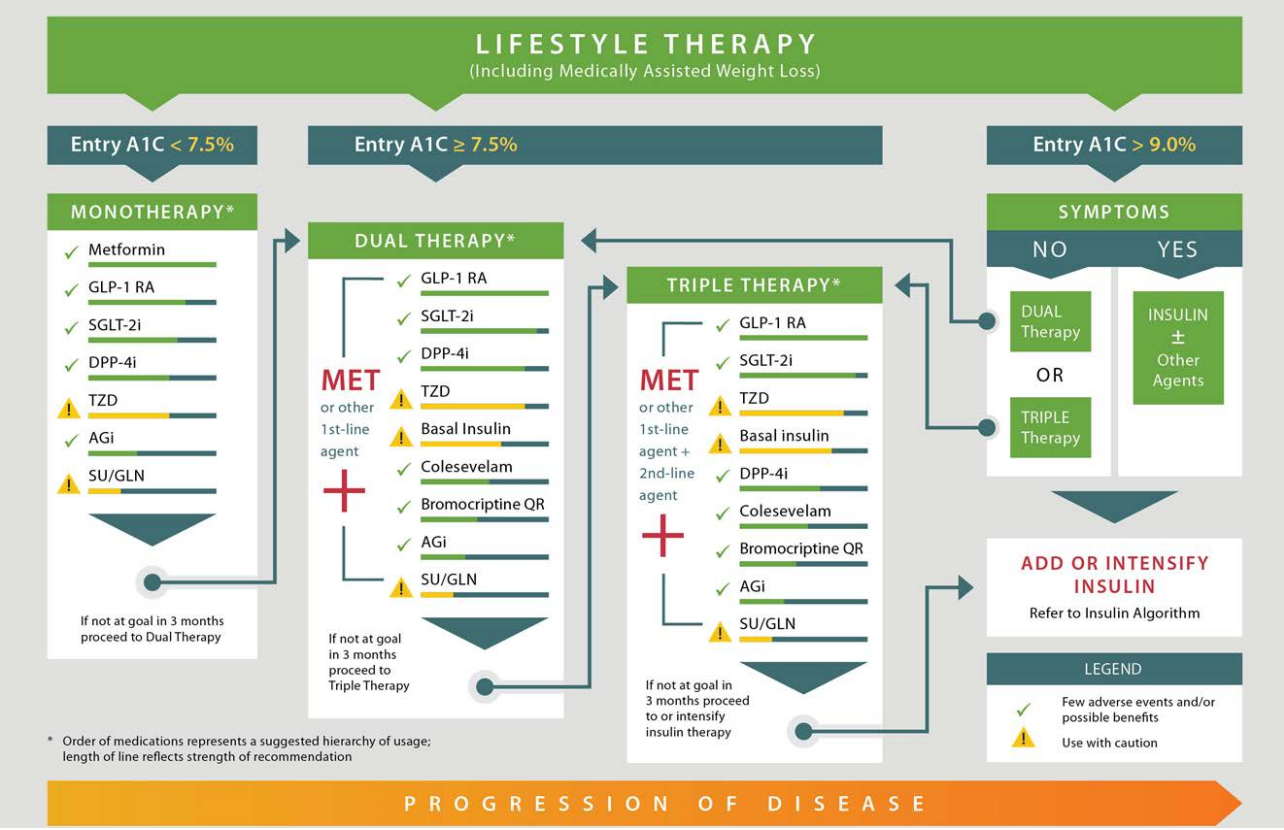
As noted in the triple therapy section in Figure 1, the ADA's Standards of Care recommend that if the A1C target is not achieved after approximately three months of triple therapy and the patient is:

1. On oral combination, should move to basal insulin or GLP-1 receptor agonist (RA)
2. On combination with GLP-1RA, should add basal insulin
3. On combination with optimally titrated basal insulin, should add GLP-1RA or mealtime insulin.

ADA's Standards of Care recommend upon advancing to next line of therapy, metformin therapy should be maintained while other oral agents may be discontinued on an individual basis to avoid unnecessarily complex or costly regimens (i.e., adding a fourth antihyperglycemic agent).

The American Association of Clinical Endocrinologists/American College of Endocrinology (AACE/ACE) 2017 algorithm for glycemic control is shown in Figure 2.[3] This algorithm stratifies choice of therapies based on initial A1C level. It provides guidance as to what therapies to initiate and add but respects individual circumstances that could lead to different choices.

Figure 2: AACE/ACE Glycemic Control Algorithm-2017[3]



3 Consensus Statement by The American Association Of Clinical Endocrinologists And American College Of Endocrinology On The Comprehensive Type 2 Diabetes Management Algorithm – 2017 Executive Summary. Endocrine Practice Vol 23 No. 2 February 2017.

The AACE/ACE algorithm recognizes that combination therapy is usually required and should involve agents with complementary mechanisms of action. The order of agents in each column of the Glycemic Control Algorithm (Figure 2) suggests a hierarchy of recommended usage, and the length of each line reflects the strength of the expert consensus recommendation. Each medication's properties should be considered when selecting a therapy for individual patients.

MS-DUR examined the regimens used to treat beneficiaries with T2DM during 2016 in order to determine how treatment patterns may need to change based on the 2017 ADA Standards of Care and the AACE/ACE algorithm. The objectives were:

1. To evaluate how well recent treatment patterns comply with recommendations in the ADA Standards of Care and the AACE/ACE treatment algorithm.

2. To identify any utilization management actions that may be needed to improve compliance with the current recommendations.

METHODS

MS-DUR conducted a retrospective analysis using Division of Medicaid (DOM) pharmacy and medical claims from all programs including fee-for-service (FFS) and coordinated care organizations (CCOs) for the period July 1, 2015 – December 31, 2016.

Beneficiaries meeting the following criteria were included in the analyses:

- Had at least one medical claim with a diagnosis code for Type 2 diabetes during 2016, and
- Were enrolled in Medicaid for three or more months in 2016.

Claims from the last six months of 2015 and the first half of 2016 were used to identify beneficiaries that were "**new starts**" on antihyperglycemic medications. Beneficiaries were classified as new starts in 2016 if they met the following criteria:

- Had one or more claims for antihyperglycemic medications in 2016,
- Were enrolled in Medicaid for the six months prior to their first antihyperglycemic medication claim in 2016, and
- Had no previous claim for an antihyperglycemic medication during the six months prior to their first prescription in 2016.

Identifying treatment regimens: MS-DUR used refill patterns for medications in each antihyperglycemic drug class to determine regimens used to treat beneficiaries. This was accomplished by determining drug coverage patterns for each day during the observation period for 2016. For each prescription dispensed, the beneficiary was considered to be on treatment with the medication from the date of the prescription fill through the fill date plus the number of days supply dispensed. Coverage from prescription fills for drugs in the same class were combined so

that beneficiaries were considered to be "treated" with a drug class from the date of the first prescription fill in the class to (1) the end of medication possession for the last prescription fill in the class or (2) the beginning of a gap in coverage for the class of 45 days or more. Coverage gaps of 45 days or more were classified as non-persistence and beneficiaries were not considered to be on treatment during these periods. During coverage gaps less than 45 days, beneficiaries were considered to still be treated with the drug class. For each day during the observation year, coverage for each class was combined to identify the regimen being used to treat the patient. Transitioning from one regimen to another can produce short periods of false regimen combinations. Regimens that were continuously used for less than 30 days were eliminated from the analysis.

RESULTS

Demographic characteristics of beneficiaries having medical claims with diagnosis codes for T2DM are summarized in Table 1. Beneficiaries with T2DM were twice as likely to be female and more likely to be African American and the majority were age ≥45 years. However, 5,455 beneficiaries between the ages of 19 to 44 were identified as having T2DM. Almost all of the beneficiaries age 65 and older were in FFS and represent dual-eligible beneficiaries for whom DOM may not have complete prescription records due to coverage for most drugs through Medicare Part D.

TABLE 1: Characteristics of Beneficiaries Having Medical Claims Including Type 2 Diabetes Diagnoses in 2016

		FFS	UHC	MAG	TOTAL
Total		11,220	5,987	8,195	25,402
Gender*	Female	7,501	4,227	6,028	17,756
	Male	3,718	1,760	2,167	7,645
Age at End of Year	12 or less	24	111	108	243
	13 - 18	87	307	311	705
	19 - 44	892	1,978	2,585	5,455
	45 - 64	5,083	3,482	5,015	13,580
	65+	5,134	109	176	5,419
Race	Caucasian	3,584	1,723	2,263	7,570
	Afr. Amer.	6,813	3,648	5,017	15,478
	Hispanic	75	37	43	155
	Amer. Indian	112	12	15	139
	Other	636	567	857	2,060

** Gender categories do not sum to TOTAL for some programs due to missing data.*

Table 2 summarizes all of the regimen combinations that appeared as treatments in 2016. Green highlighted regimens include metformin. The ADA guidelines recommend combinations of no more than 3 antihyperglycemic drug classes; therefore, regimens including four or more classes are marked with red borders. It is unlikely that the combination of a GLP-1 receptor agonist and a DPP-4inhibitor would have an additive benefit due to that both classes affect GLP-1 concentrations though it has not been directly studied in trials. This is extremely unlikely to be cost effective. Regimens including this combination are highlighted in orange.

If it is assumed that non-insulin regimen combinations without metformin occurred due to contraindications or intolerance of metformin in the beneficiary, the majority of the treatment regimens utilized in 2016 were consistent with the ADA guidelines. Very few regimen combinations were used that directly conflicted with the ADA Standards of Care-2017 (highlighted in orange and red). Possible areas for improvement may exist that would require more detailed analyses of individual patient cases. These areas include:

1. The large number of beneficiaries (n = 719) treated with insulin only when the ADA guidelines recommend metformin as initial therapy and its use be continued when possible.
2. Medications in one class being titrated to maximum doses prior to the addition of a drug from a different pharmacological class.
3. The use of sulfonylureas as monotherapy especially in the newly diagnosed and treated T2DM beneficiary.

TABLE 2: All Antihyperglycemic Regimens* Used to Treat Type 2 Diabetics in 2016

Regimen*	FFS	UHC	MAG	TOTAL
MTF	1,570	209	258	2,037
MTF / DPP	248	27	27	302
MTF / DPP / GLP	2	0	1	3
MTF / GLP	11	0	3	14
MTF / SLF	283	34	49	366
MTF / SLF / DPP	39	5	1	45
MTF / SLF / DPP / GLP	0	0	1	1
MTF / SLF / GLP	2	0	0	2
MTF / SLF / TZD	3	1	0	4
MTF / SLF / TZD / DPP	3	0	0	3
MTF / SLF / TZD / DPP / AGI	1	0	0	1
MTF / TZD	19	0	3	22
MTF / TZD / DPP	5	1	0	6
SLF	564	65	90	719
SLF / DPP	48	9	5	62
SLF / DPP / GLP	5	0	0	5
SLF / GLP	3	1	0	4
SLF / TZD	18	0	2	20
SLF / TZD / DPP	1	0	0	1
TZD	53	4	0	57
TZD / DPP	4	0	0	4
TZD / GLP	1	0	0	1
AGI	2	0	0	2
DPP	246	24	38	308
DPP / AGI	5	0	0	5
DPP / GLP	2	2	0	4
GLP	46	6	6	58
INS	1,972	229	392	2,593
INS / DPP	104	5	4	113
INS / DPP / GLP	1	0	0	1
INS / GLP	28	1	2	31
INS / **MTF**	319	24	41	384
INS / **MTF** / DPP	64	5	6	75
INS / **MTF** / DPP / GLP	4	0	0	4
INS / **MTF** / GLP	4	1	0	5
INS / **MTF** / SLF	70	2	2	74
INS / **MTF** / SLF / DPP	9	0	2	11
INS / **MTF** / SLF / TZD / DPP / AGI	1	0	0	1
INS / **MTF** / TZD / DPP	6	0	0	6
INS / SLF	122	5	8	135
INS / SLF / DPP	9	2	0	11
INS / SLF / GLP	2	0	0	2
INS / SLF / TZD	1	0	0	1
INS / TZD	15	0	1	16
INS / TZD / DPP	3	0	0	3
INS / TZD / GLP	1	0	0	1

Includes metformin

Includes DPP and GLP

Includes more than 3 classes

Drug Class Abbreviations Used	
AGI	alpha-glucosidase inhibitors
DPP	DPP-4 inhibitor
GLP	GLP-1 receptor agonist
INS	insulin (all types)
MET	metformin
SGLT	SGLT-2 inhibitors
SLF	sulfonylureas
TZD	thiazolidineiones

** Only includes drug therapy coverage combinations used to treat patients continuously for 30 or more days.*

Table 3 lists the regimen combinations used as **first line therapy** for beneficiaries classified as "new starts" on pharmacologic treatment in 2016. The 2017 ADA guidelines recommend that when A1C is ≥ 9% (75 mmol/mol) dual combination therapy should be considered for first line to more expeditiously achieve the target A1C level. They also note that insulin should be considered as part of any initial combination regimen when blood glucose is ≥ 300 mg/dL (16.7 mmol/L), or A1C is ≥ 10% (86 mmol/mol), or if the patient has symptoms of hyperglycemia (i.e., polyuria or polydipsia). The first line regimens included in Table 3 appear to be consistent with the ADA Standards of Care with the possible exception of a large number of patients starting on insulin without metformin.

TABLE 3: Antihyperglycemic Regimens*
Used FIRST LINE To Treat NEW STARTS in 2016

Regimen*	FFS	UHC	MAG	TOTAL
MTF	228	64	90	382
MTF / DPP	27	7	9	43
MTF / DPP / GLP	1	0	0	1
MTF / GLP	1	0	2	3
MTF / SLF	36	10	11	57
MTF / SLF / DPP	1	1	0	2
MTF / SLF / TZD	0	1	0	1
MTF / TZD	0	0	1	1
SLF	83	13	24	120
SLF / DPP	3	4	2	9
SLF / TZD	0	0	1	1
TZD	5	2	0	7
DPP	18	6	12	36
GLP	5	1	3	9
INS	196	77	119	392
INS / DPP	6	3	2	11
INS / **MTF**	22	7	12	41
INS / **MTF** / DPP	5	3	1	9
INS / **MTF** / SLF	1	0	2	3
INS / **MTF** / SLF / DPP	2	0	1	3
INS / SLF	10	1	3	14
INS / SLF / DPP	0	1	0	1
INS / TZD	1	0	1	2
INS / TZD / GLP	1	0	0	1

** Only includes drug therapy coverage combinations used to treat patients continuously for 30 or more days.*

Includes metformin
Includes DPP and GLP
Includes more than 3 classes

Drug Class Abbreviations Used	
AGI	alpha-glucosidase inhibitors
DPP	DPP-4 inhibitor
GLP	GLP-1 receptor agonist
INS	insulin (all types)
MET	metformin
SGLT	SGLT-2 inhibitors
SLF	sulfonylureas
TZD	thiazolidineiones

In assessing the potential for utilization management actions to improve treatment, it is important to determine the number of providers and beneficiaries that could be affected by any action. Table 4 shows the number of unique beneficiaries and prescribers associated with the three criteria considered to be inconsistent with the ADA Standards of Care or not cost effective.

- Only 10 beneficiaries and 10 prescribers were associated with regimens including a GLP-1 and a DPP-4.
- Only 14 beneficiaries and 15 prescribers were associated with regimens including 4 or more drug classes.
- The use of regimens that do not include metformin affected the greatest number of beneficiaries (1,939) and prescribers (239).

TABLE 4: Number of Beneficiaries and Prescribers Associated With Regimens Not Consistent With ADA Guidelines

	Beneficiaries	Prescribers
Regimen with GLP and DPP	10	10
Regimen with 4+ drug classes	14	15
Regimen without MET	1,939	239

Although the large number of regimens that did not include metformin may represent an area of concern, it is not possible from claims data to determine how often metformin is contraindicated or could not be tolerated.

CONCLUSIONS AND RECOMMENDATIONS

It appears that most of the regimens currently being used to treat beneficiaries with Type 2 diabetes are consistent with the ADA Standards of Care-2017 recommendations for pharmacological management of T2DM. The major area of concern is whether metformin is being used as often as possible. The use of regimens including both GLP-1 and DPP-4 and the use of regimens with four or more drug classes appear to be infrequent problems.

Recommendations:

1. DOM should implement an electronic edit to require manual prior authorization (PA) for concomitant use of GLP-1 and DPP-4.
2. DOM should implement an electronic edit to require manual PA for addition of fourth concurrent antihyperglycemic agents.
3. DOM should investigate regimens that do not include metformin.
4. DOM should investigate further T2DM treatment with only a sulfonylurea agent.

5. MS-DUR should conduct a one-time educational mailing highlighting the new ADA guidelines directed to prescribers who have had patients in the last year with regimens that were not consistent with the ADA Standards of Care recommendations.
6. MS-DUR should explore collaboration with the Mississippi Diabetes Coalition for educational initiatives.

FDA DRUG SAFETY INFORMATION UPDATES
JANUARY - MARCH 2017

1. **Concomitant administration of Sporanox (itraconazole) with Corlanor (ivabradine).**

   Message: In March 2017, the FDA approved labeling changes for Sporanox (itraconazole) to include a contraindication that Sporanox should not be co-administered with Corlanor.

2. **Concomitant administration of Viekira XR/Pak (dasabuvir sodium, ombitasvir, paritaprevir, ritonavir) with the following medications: atorvastatin (Caduet, Lipitor, Liptruzet), everolimus (Afinitor, Zortress), sirolimus (Rapamune), and tacrolimus (Astagraf XL, Envarsus XR, Prograf).**

   Message: In March 2017, the FDA approved labeling changes for Viekira XR/Pak (dasabuvir sodium, ombitasvir, paritaprevir, ritonavir) to include a contraindication that Viekira XR/Pak should not be given with the following medications: atorvastatin (Caduet, Lipitor, Liptruzet), everolimus (Afinitor, Zortress), sirolimus (Rapamune), and tacrolimus (Astagraf XL, Envarsus XR, Prograf).

3. **Prescribing of Viberzi (eluxadoline) in patients without a gallbladder.**

   Message: In March 2017, the FDA recommended healthcare professionals not prescribe Viberzi (eluxadoline) in patients who do not have a gallbladder due to an increased risk of developing serious pancreatitis.

4. **Concomitant administration of promethazine/codeine combination products with benzodiazepines and other CNS depressants in children.**

   Message: In January 2017, the FDA approved labeling changes for promethazine/codeine combination products (Phenergan VC w/ Codeine, Phenergan w/Codeine) to include a boxed warning against the concomitant use of promethazine/codeine combination products with benzodiazepines and other CNS depressants in children. The concomitant use of these medications in children may result in profound sedation, respiratory depression, coma, and death.