HEPATITIS C TREATMENT OVERVIEW

BACKGROUND

According to the Centers for Disease Control and Prevention (CDC), Hepatitis C (Hep C) is a blood-borne viral infection of the liver that is most commonly transmitted by the sharing of needles or other percutaneous exposure to infected blood.[1,2] Hep C infection can be an acute illness, but for over half of individuals infected, it develops into a chronic infection. Chronic Hep C infection can lead to long-term health problems and even death.[1] Hep C infection is also a major cause of liver transplants.[3] Between 2013-2016, it was estimated that 2.4 million people were living with Hep C in the United States.[4] There are 6 main genotypes of the hepatitis C virus (HCV) along with subtypes that are based on the virus' genetic makeup.[5] The specific genotype an individual carries determines treatment.

For many years, interferon (IFN)-based therapies combined with ribavirin (RBV) were the mainstay of treatment for chronic hepatitis C (CHC), however, treatment response was suboptimal. In 2013 with the release of the direct-acting antiviral (DAA) sofosbuvir, a new era in HCV treatment began.[6] These second generation DAA agents have been shown to produce high levels of sustained virologic response (SVR) and are now the standard treatment for CHC.[7]

Medicaid's current Universal Preferred Drug List (UPDL) category for Hep C treatments is below (Figure 1). The current preferred DAA agents are branded Mavyret® and sofosbuvir/velpatasvir (generic Epclusa®).

FIGURE 1: MS Medicaid's UPDL for Hepatitis C Treatments.

THERAPEUTIC DRUG CLASS	PREFERRED AGENTS	NON-PREFERRED AGENTS	PA CRITERIA
HEPATITIS C TREATMENTS			
	MAVYRET (glecaprevir/pibrentasvir)∞ PEGASYS (peginterferon alfa-2a) PEG-INTRON (peginterferon alfa-2b) ribavirin tablets sofosbuvir/velpatasvir∞	COPEGUS (ribavirin) DAKLINZA (daclatasvir) ∞ EPCLUSA (sofosbuvir/velpatasvir) ∞ HARVONI (ledipasvir/sofosbuvir)∞ ledipasvir/sofosbuvir∞ MODERIBA (ribavirin) OLYSIO (simeprevir) REBETOL (ribavirin) RIBASPHERE (ribavirin) RIBASPHERE RIBAPAK DOSEPACK (ribavirin) ribavirin capsules	∞ **Daklinza, Epclusa, Harvoni, Mavyret, Sovaldi, Vosevi, Zepatier – MANUAL PA** Note: Harvoni and Sovaldi have FDA pediatric indications
		SOVALDI (sofosbuvir)∞ TECHNIVIE (ombitasvir/paritaprevir/ritonavir) VIEKIRA (ombitasvir/paritaprevir/ritonavir) VIEKIRA XR (ombitasvir/paritaprevir/ritonavir) VOSEVI (sofosbuvir/velpatasvir/voxilaprevir)∞ ZEPATIER (elbasvir/grazoprevir)∞	

MS-DUR was asked to provide a treatment overview of hepatitis C among Medicaid beneficiaries since the introduction of the second generation DAAs in 2013.

METHODS

A retrospective database analysis was conducted using Mississippi Medicaid fee-for-service (FFS) and coordinated care organization [CCOs: Magnolia Health (MAG), Molina Healthcare (MOL), and UnitedHealthcare (UHC)] claims. Beneficiaries prescribed direct-acting antivirals (DAAs) were identified between January 1, 2013 and December 31, 2019.

RESULTS

Descriptive characteristics of beneficiaries who were treated by the DAAs are presented in Table 1. Age and health plan were assessed as of the date for the first DAA claim in the analysis period.

TABLE 1: Demographic Characteristics of Beneficiaries Prescribed Direct-Acting Anti-retroviral (DAA) Therapy (January 2013 - December 2019)

Variable	FFS		UHC		Magnolia		Molina		Total
Age Category (yrs)									
0-17	0	0.0%	5	1.1%	2	0.3%	0	0.0%	**7**
18-25	5	2.1%	8	1.7%	8	1.3%	3	17.6%	**24**
26-44	32	13.7%	114	24.7%	148	23.3%	6	35.3%	**300**
45-64	194	83.3%	334	72.5%	475	74.9%	8	47.1%	**1,011**
65+	2	0.9%	0	0.0%	1	0.2%	0	0.0%	**3**
Total	*233*		*461*		*634*		*17*		***1,345***
Gender									
Female	105	45.1%	258	56.0%	342	53.9%	7	41.2%	**712**
Male	128	54.9%	203	44.0%	292	46.1%	10	58.8%	**633**
Total	*233*		*461*		*634*		*17*		***1,345***
Race									
Caucasian	136	58.4%	281	61.0%	375	59.1%	11	64.7%	**803**
African American	82	35.2%	103	22.3%	160	25.2%	2	11.8%	**347**
Other	15	6.4%	77	16.7%	99	15.6%	4	23.5%	**195**
Total	*233*		*461*		*634*		*17*		***1,345***

Note: Insurance plan at the first DAA treatment.

- A total of 1,345 beneficiaries have been treated with DAAs since January 2013.
- 75.4% (1,014) were 45 years or older.
- 52.9% (712) were female.
- 59.7% (803) were Caucasian.

The overall utilization of DAAs was analyzed using pharmacy point-of-sale (POS) claims data to identify the number of DAA prescription fills as well as the number of treated beneficiaries in each quarter stratified by pharmacy program (Tables 2a/2b). A red line in the tables represents the point in time when the Complex Pharmacy Care (CPC) was initiated in FFS. The CPC program was designed to help ensure that complex and high-cost pharmaceuticals are only used in the correct patient and that they are taken as intended. The agents used in the treatment of Hep C fall under the CPC program management in FFS.

TABLE 2a: Hep C DAA Claims by Quarter and Pharmacy Program *(January 2013 - December 2019)*

Quarter	Pharmacy Program				
	FFS	UHC	MAG	MOL	Total
Q1 2013	0	0	0	0	0
Q2 2013	0	0	0	0	0
Q3 2013	0	0	0	0	0
Q4 2013	0	1	0	0	1
Q1 2014	5	19	7	0	31
Q2 2014	30	31	38	0	99
Q3 2014	18	27	44	0	89
Q4 2014	35	17	41	0	93
Q1 2015	32	27	51	0	110
Q2 2015	26	56	140	0	222
Q3 2015	29	93	142	0	264
Q4 2015	42	74	86	0	202
Q1 2016	29	57	88	0	174
Q2 2016	44	48	122	0	214
Q3 2016	41	52	76	0	169
Q4 2016	31	55	91	0	177
Q1 2017	23	49	70	0	142
Q2 2017	25	51	114	0	190
Q3 2017	20	51	62	0	133
Q4 2017	14	48	56	0	118
Q1 2018	30	92	67	0	189
Q2 2018	39	64	71	0	174
Q3 2018	32	65	86	0	183
Q4 2018	34	67	95	1	197
Q1 2019	26	66	80	12	184
Q2 2019	30	42	73	13	158
Q3 2019	22	46	78	20	166
Q4 2019	22	41	36	7	106
Total	*679*	*1,239*	*1,814*	*53*	*3,785*

Note: Count Rx claims only for DAA.
Red line denotes when CPC was initiated in FFS .

TABLE 2b: Beneficiaries Treated by Hep C DAA Medications by Quarter and Pharmacy Program *(January 2013 - December 2019)*

Quarter	Pharmacy Program				
	FFS	UHC	MAG	MOL	Total
Q1 2013	0	0	0	0	0
Q2 2013	0	0	0	0	0
Q3 2013	0	0	0	0	0
Q4 2013	0	1	0	0	1
Q1 2014	4	17	7	0	28
Q2 2014	20	25	33	0	78
Q3 2014	15	21	41	0	77
Q4 2014	27	11	35	0	73
Q1 2015	32	21	48	0	101
Q2 2015	25	51	133	0	209
Q3 2015	26	89	126	0	241
Q4 2015	39	65	79	0	183
Q1 2016	28	54	71	0	153
Q2 2016	36	48	102	0	186
Q3 2016	28	51	67	0	146
Q4 2016	27	50	83	0	160
Q1 2017	22	47	63	0	132
Q2 2017	21	48	106	0	175
Q3 2017	17	48	56	0	121
Q4 2017	13	47	52	0	112
Q1 2018	28	87	62	0	177
Q2 2018	39	63	64	0	166
Q3 2018	31	63	76	0	170
Q4 2018	32	65	87	1	185
Q1 2019	25	61	77	10	173
Q2 2019	29	37	67	8	141
Q3 2019	19	42	73	16	150
Q4 2019	22	38	35	7	102
Total	*605*	*1,150*	*1,643*	*42*	*3,440*

Note: Count beneficiaries with DAA claims
Red line denotes when CPC was initiated in FFS.

- Although the first breakthrough DAA agent received FDA approval in late 2013, it appears that utilization of DAA therapies for the treatment Hep C in Medicaid substantially increased around Q2 2015.
- On average, 151 beneficiaries have been treated with DAAs each quarter since Q4 2016.

In order to determine the total dollars paid on Hep C treatment, quarterly cost of DAA regimens (DAA plus supplementary drug, e.g. ribavirin and/or interferon) was measured and stratified by pharmacy plans (Table 3). (*Paid amounts represent the amount reported on claims as paid to the pharmacy. These amounts do not reflect final actual costs after rebates, etc.)*

TABLE 3: Total Paid for Hep C Rx Claims by Quarter and Pharmacy Program
(January 2013 - December 2019)

	Pharmacy Program				
Quarter	FFS	UHC	MAG	MOL	Total
Q1 2013	-	-	-	-	-
Q2 2013	-	-	-	-	-
Q3 2013	-	-	-	-	-
Q4 2013	-	$ 30,613.32	-	-	$ 30,613.32
Q1 2014	$ 152,313.20	$ 583,419.78	$ 213,621.33	-	$ 949,354.31
Q2 2014	$ 853,186.08	$ 922,107.55	$ 1,216,935.15	-	$ 2,992,228.78
Q3 2014	$ 552,301.88	$ 776,064.87	$ 1,225,183.56	-	$ 2,553,550.31
Q4 2014	$ 1,044,872.91	$ 442,761.01	$ 1,252,419.35	-	$ 2,740,053.27
Q1 2015	$ 1,029,952.74	$ 881,014.62	$ 1,629,124.85	-	$ 3,540,092.21
Q2 2015	$ 849,230.14	$ 1,839,944.97	$ 4,574,774.19	-	$ 7,263,949.30
Q3 2015	$ 950,815.93	$ 2,994,787.07	$ 4,602,629.95	-	$ 8,548,232.95
Q4 2015	$ 1,382,503.27	$ 2,406,338.90	$ 2,769,166.38	-	$ 6,558,008.55
Q1 2016	$ 943,913.41	$ 1,875,157.19	$ 2,751,787.68	-	$ 5,570,858.28
Q2 2016	$ 1,375,067.69	$ 1,576,193.50	$ 3,765,475.48	-	$ 6,716,736.67
Q3 2016	$ 1,203,145.95	$ 1,700,663.12	$ 2,379,040.07	-	$ 5,282,849.14
Q4 2016	$ 972,026.98	$ 1,625,549.78	$ 2,791,303.15	-	$ 5,388,879.91
Q1 2017	$ 708,870.69	$ 1,480,623.46	$ 2,173,957.87	-	$ 4,363,452.02
Q2 2017	$ 734,202.38	$ 1,468,251.12	$ 3,273,298.43	-	$ 5,475,751.93
Q3 2017	$ 528,108.10	$ 1,421,546.29	$ 1,687,775.15	-	$ 3,637,429.54
Q4 2017	$ 268,393.21	$ 1,334,112.38	$ 1,518,145.00	-	$ 3,120,650.59
Q1 2018	$ 598,363.79	$ 1,877,609.03	$ 1,629,244.63	-	$ 4,105,217.45
Q2 2018	$ 737,588.08	$ 1,253,768.44	$ 1,281,978.32	-	$ 3,273,334.84
Q3 2018	$ 594,435.23	$ 1,159,546.03	$ 1,687,628.06	-	$ 3,441,609.32
Q4 2018	$ 664,260.22	$ 1,288,682.77	$ 2,070,271.26	$ 12,888.85	$ 4,036,103.10
Q1 2019	$ 529,863.63	$ 1,066,486.79	$ 1,297,273.06	$ 171,139.24	$ 3,064,762.72
Q2 2019	$ 656,339.05	$ 517,860.46	$ 1,156,771.79	$ 166,185.53	$ 2,497,156.83
Q3 2019	$ 435,297.68	$ 493,847.22	$ 1,131,714.94	$ 333,151.46	$ 2,394,011.30
Q4 2019	$ 324,625.00	$ 456,153.95	$ 402,571.44	$ 114,645.03	$ 1,297,995.42
Total	*$ 18,089,677.24*	*$ 31,473,103.62*	*$ 48,482,091.09*	*$ 798,010.11*	*$ 100,134,611.00*

Note: Includes overall paid amounts on DAA regimens (DAAs + supplement drugs).
Manufacturer rebates are not reflected in cost reports.
Red line denotes when CPC was initiated in FFS

- There has been a marked decrease in total spend on Hep C treatments across all programs since Q4 2016. This could be the result of patient management programs across pharmacy plans.

The provider types associated with DAA prescription claims are summarized in Table 4. Adjustments were made for some nurse practitioners according to the records of physician-type or practice-type they were affiliated.

- 43.8% (1,658) of DAA claims were associated with gastroenterology.

TABLE 4: Summary of DAA Prescriptions by Provider Type
(January 2013 - December 2019)

Provider Type	Number of Prescriptions	Percent
MD-Gastro - Gastroenterology	1,658	43.8%
NP-FM - Family Medicine	526	13.9%
MD-Nephr - Nephrology	240	6.3%
MD-IM - Internal Medicine	192	5.1%
Prov-Other - Specialist	162	4.3%
MD-Hospit - Hospitalist	160	4.2%
Prov-Other - Student in an Organized Health Care Education/Training Progr	103	2.7%
MD-ID - Infectious Disease	93	2.5%
MD-EM - Emergency Medicine	86	2.3%
PA - Physician Assistant	85	2.2%
PA - Medical	65	1.7%
NP - Acute Care	52	1.4%
NP-Ped - Pediatrics	52	1.4%
MD-Transpl - Transplant Hepatology	47	1.2%
NP - Nurse Practitioner	33	0.9%
MD-Gastro - Pediatric Gastroenterology	30	0.8%
MD-OB/GYN - Obstetrics & Gynecology	27	0.7%
MD-Other - Hepatology	10	0.3%
NP - Adult Health	10	0.3%
MD-FP - Family Medicine	9	0.2%
MD-Card - Cardiovascular Disease	4	0.1%
NP-FM - Dental	3	0.1%
NP-FM - Student Health	2	0.1%
No provider type available	139	3.7%

Note: There were 139 claims without information available for provider type.
Some nurse practitioners were adjusted based on their provider affliation ID.

For individuals receiving DAA therapy, it is recommended they receive quantitative HCV RNA level testing to determine treatment response.[8,9] HCV RNA level testing results cannot be obtained through claims data. As an alternative, MS-DUR examined the number of DAA treatments beneficiaries received (Table 5). It could be assumed that beneficiaries receiving 1 treatment with DAA therapy were more likely to have experienced a positive treatment response.

- 96.1% of beneficiaries received 1 treatment with DAA therapy.

TABLE 5: Number of Treatments for Beneficiaries Prescribed DAA Therapy
(January 2013 - December 2019)

Total number of treatments	Beneficiaries	Percent
1	1,292	96.1%
2	51	3.8%
3	2	0.1%
Total	**1,345**	100.0%

Table 6 displays the overall distribution of beneficiaries across various DAA treatment regimens stratified by program.

TABLE 6: Overall Distribution of Beneficiaries by DAA Therapy and Plan including Retreatments
(January 2013 - December 2019)

Regimen	Plan				Total
	FFS	UHC	MAG	MOL	
Harvoni	101	202	296	0	**599**
Mavyret	47	101	98	3	**249**
Epclusa	48	81	105	10	**244**
Sovaldi	26	42	89	0	**157**
Sofosbuvir-Velpatasvir (Generic for Epclusa)	4	30	34	5	**73**
Zepatier	3	7	13	0	**23**
Viekira Pak	3	4	8	0	**15**
Olysio / Sovaldi	7	5	0	0	**12**
Daklinza / Sovaldi	3	0	8	0	**11**
Vosevi	1	1	5	0	**7**
Epclusa / Sofosbuvir-Velpatasvir	2	2	2	0	**6**
Harvoni / Viekira Pak	0	0	1	0	**1**
Ledipasvir-Sofosbuvir (Generic for Harvoni)	0	1	0	0	**1**
Sovaldi / Daklinza	1	0	0	0	**1**
Viekira XR	0	0	1	0	**1**
Total	**246**	**476**	**660**	**18**	**1400***

*Does not represent unique beneficiaries. Beneficiaires with retreatments are counted multiple times.

Tables 7 and 8 examine completion rates for DAA therapies since 2013. Completion of therapy was based on the number of days supply equal to or exceeding the days supply for the shortest approved regimen for a product. Beneficiaries were excluded if their initiation date did not allow them to complete therapy before the study period ended. Treatment was considered complete if days' supply were at least equal to the minimum days of therapy approved for that product. A 30-day treatment gap was allowed in determining completion. Pharmacy program was flagged at the start and end of each treatment episode. A beneficiary was flagged as plan switching if they were enrolled in different pharmacy programs at the start and end of each treatment episode. Continuous Medicaid eligibility was assessed during each treatment episode.

TABLE 7: Treatment Completion By Regimen for First Hep C Treatment

(January 2013 - December 2019, Includes FFS and CCOs)

Regimen	TOTAL	Minimum Regimen Duration (in days)	Completed		Not Completed	Not Completed Associated With	
						Lost Enrollment	Switched Plans
Epclusa	282	84	251	89.0%	31	6	11
Harvoni	579	56	541	93.4%	38	5	11
Harvoni / Viekira	1	84	0	0.0%	1	0	0
Mavyret	227	56	210	92.5%	17	0	0
Olysio / Sovaldi	12	84	11	91.7%	1	0	0
Sovaldi	150	84	110	73.3%	40	5	11
Sovaldi / Daklinza	11	84	11	100.0%	0	0	0
Viekira	13	84	10	76.9%	3	0	0
Zepatier	22	84	20	90.9%	2	0	0
Total	**1297**		**1164**	**89.7%**	**133**	**16**	**33**

NOTE: Completion of therapy is based on number of days supply equal to or exceeding the days supply for the shortest approved regimen for the product combination.

- Overall, 89.7% of beneficiaries that started DAA during the entire study period completed therapy.
- Of those that did not complete therapy:
  - 16 lost enrollment
  - 33 switched pharmacy plans

In Table 8 completion rates were further analyzed by pharmacy program and time period excluding beneficiaries that lost eligibility during treatment.

TABLE 8: Treatment Completion by Pharmacy Program and Start Time Period

-- Only Includes Beneficiaries With Continuous Enrollment During Expected Treatment Period --

Pharmacy Program	Jan 2013 - Sep 2016					Oct 2016 - Dec 2019				
During Treatment*	Completed		Not completed		Total	Completed		Not completed		Total
FFS	65	86.7%	10	13.3%	75	107	89.9%	12	10.1%	119
MAG	210	86.8%	32	13.2%	242	326	93.9%	21	6.1%	347
UHC	145	92.9%	11	7.1%	156	257	93.8%	17	6.2%	274
MOL	0	0.0%	0	0.0%	0	10	71.4%	4	28.6%	14
FFS-MAG	6	85.7%	1	14.3%	7	3	100.0%	0	0.0%	3
FFS-MOL	0	0.0%	0	0.0%	0	2	100.0%	0	0.0%	2
FFS-UHC	4	44.4%	5	55.6%	9	5	62.5%	3	37.5%	8
MAG-FFS	7	70.0%	3	30.0%	10	6	66.7%	3	33.3%	9
MAG-UHC	0	0.0%	0	0.0%	0	1	100.0%	0	0.0%	1
UHC-FFS	4	80.0%	1	20.0%	5	3	60.0%	2	40.0%	5
UHC-MAG	1	100.0%	0	0.0%	1	0	0.0%	1	100.0%	1
Total	**442**	**87.5%**	**63**	**12.5%**	**505**	**720**	**92.0%**	**63**	**8.0%**	**783**

** Pharmacy program during treatment equals pharmacy program at time of first prescription fill for therapy and pharmacy program at time treatment regimen should be completed.*

NOTE: Completion of therapy is based on number of days supply equal to or exceeding the days supply for the shortest approved regimen for the product combination.

- Overall completion rates improved across all programs from 87.5% to 92% when comparing the 2 time periods. This improvement could be related to patient management programs.
- **Beneficiaries that switched programs during their treatment period had a higher likelihood of not completing therapy.**

A major complication associated with chronic HCV infection is liver transplantation. In the past HCV infection has been cited as the most common indication for liver transplantation.[10] With the introduction of DAA therapy into the treatment landscape for HCV, the leading indications for liver transplantation are shifting toward alcoholic liver disease and nonalcoholic fatty liver disease.[11] By utilizing DAA therapy among chronic HCV patients, it is expected that the need for liver transplantation would be reduced.

Table 9 shows the proportion of beneficiaries diagnosed with Hep C that experienced liver transplant. The proportion of patients diagnosed with Hep C that were not prescribed a DAA and received a liver transplant during the study period was 1.44%, whereas the proportion of patients prescribed DAA therapy that received a liver transplant was 0.74%.

TABLE 9: Proportion of Hep C Patients Experiencing Liver Transplant (Jan 2013- Dec 2019)			
Prescribed DAA therapy	Total number of beneficiaries	Liver transplant	Percentage
No	5,607	81	1.44%
Yes	1,345	10*	0.74%
Note: *Beneficiaries who had liver transplant after the initiation of DAA			

CONCLUSIONS

Chronic HCV infection can be a debilitating and deadly disease. With the introduction of DAA therapy for the treatment of HCV infection, outcomes have changed dramatically. MS Medicaid has treated 1345 beneficiaries with DAA therapy since 2013. Overall completion rates for DAA therapy across all pharmacy programs since 2013 was at 89.7% with overall completion rates since Q4 2016 increasing to 92% across all pharmacy programs. One area with frequent suboptimal completion rates is among those beneficiaries that switch pharmacy programs during DAA therapy. From data analysis, it appears that treatment with DAA therapy reduced the proportion of Hep C positive beneficiaries that received liver transplant during the study period**.**

RECOMMENDATIONS

1. MS-DUR recommends DOM restrict the switching of pharmacy programs by beneficiaries while undergoing DAA therapy.

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