MARYLAND
Department of Health

Larry Hogan, Governor · Boyd K. Rutherford, Lt. Governor · Robert R. Neall, Secretary

January 24, 2018

The Honorable Edward J. Kasemeyer, Chair
Senate Budget and Taxation Committee
3 West Miller Senate Office Bldg.
Annapolis, MD 21401-1991

The Honorable Maggie McIntosh, Chair
House Appropriations Committee
121 House Office Bldg.
Annapolis, MD 21401-1991

Re: 2017 Joint Chairmen's Report (p. 87) – Report on Criteria Used for Individuals to be Eligible for New Therapies Used for Hepatitis C Treatment

Dear Chairs Kasemeyer and McIntosh:

Pursuant to the requirements of the 2017 Joint Chairmen's Report (p. 87), please find enclosed a report on the criteria used for individuals to be eligible for new therapies that are used to treat hepatitis C. The report addresses (1) the clinical literature to assess what is the appropriate Metavir score to begin coverage of the new therapies; (2) an estimate of the number of individuals annually who would be covered if the Metavir score criteria was lowered to 1 and 0; (3) the associated annual cost for covering drug therapies at a Metavir score of 1 and 0, net of drug rebates; (4) the savings associated with starting treatment at an earlier Metavir score of 1 or 0; and (5) the cost implications for the Department of Public Safety and Correctional Services if it chooses to likewise lower the Metavir score to 1 and 0 for individuals in the State correctional system.

Thank you for your consideration of this information. If you have questions or need more information on the subjects included in this report, please contact Webster Ye, Deputy Chief of Staff at (410) 767-6480 or webster.ye@maryland.gov.

Sincerely,

Robert R. Neall
Secretary

Enclosure

cc: Tricia Roddy
Athos Alexandrou
Lisa Burgess
Webster Ye

Joint Chairmen's Report on Hepatitis C Treatment

Submitted by the Maryland Department of Health

2017 Joint Chairmen's Report
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I. Executive Summary

Pursuant to the 2017 Joint Chairmen's Report (JCR) (p. 87), the Maryland Department of Health ("the Department") Medicaid agency respectfully submits this report on new therapies for treating Hepatitis C virus (HCV) in Medicaid participants. This report details research on cost-effectiveness of new therapies, the estimated number of people who would be eligible for therapies if the Department changes its current treatment criteria, and possible financial implications for expanding access.

HCV is a viral infection that leads to liver damage and may, in advanced cases, ultimately cause liver failure or cancer. Approximately 15 percent to 25 percent of persons clear the virus from their bodies without treatment and do not develop chronic infection, while the remainder of persons develop chronic HCV. Most persons with chronic HCV infections are asymptomatic, and progression may occur over a period of decades. Unlike Hepatitis A or B, patients do not develop immunity to HCV and may be re-infected post-recovery or treatment. The Centers for Disease Control and Prevention (CDC) estimates that between 2.7 and 3.9 million people in the United States have chronic HCV. Based on Calendar Year (CY) 2016 data, approximately 22 thousand Medicaid participants in Maryland have received a diagnosis of chronic HCV of any severity.

The severity of HCV in a patient is determined by the degree of liver damage or fibrosis and is often measured using a Meta-analysis of histological data in viral hepatitis (Metavir) score. The scale delineates hepatitis with no fibrosis (F0) to complete cirrhosis (F4). Many state Medicaid programs use the Metavir score to determine treatment, with Maryland providing a more encompassing program by treating those with a Metavir score of F2 or greater (as inclusive as 9 other states, and more inclusive than 23 other states). Liver biopsy is the most accurate yet invasive way to determine disease progression. Alternate methods such as the use of biomarkers are preferred but are less accurate. Data of HCV prevalence overall by Metavir score is extremely limited.

Traditionally, treatment for HCV included a combination of pegylated interferon and ribavirin (PR) with a protease inhibitor. Treatment courses generally took 12 weeks but came with significant side effects that forced almost 25 percent of patients to stop treatment. In 2013, the Food and Drug Administration approved a direct-acting antiviral (DAA) drug, Sovaldi, to cure HCV effectively with little to no side effects in almost all prescribed patients. At the time, Sovaldi cost about $100,000 for a 12-week course of treatment with much less side effects. Newer DAAs have significantly lower costs and some provide a shorter treatment window, but most generally still require 12 weeks. One such drug, Mavyret, costs $26,400 for a full 8-week course of treatment and is approved to treat patients with genotype 1-6 without cirrhosis or with

mild cirrhosis. This may positively impact the cost-effectiveness of treatment with DAAs for people with an F2 Metavir score or lower, but people at F3 or F4 will still require treatment with more expensive medications.

Studies conducted over the past few years indicate the potential for DAAs to be cost-effective by averting some complications of HCV, including liver cancer or liver transplant. Even with drug rebates, however, chronic HCV treatment in CY2016 cost Maryland Medicaid approximately $74 million net of rebates ($139 million before rebates), or about $71,000 per person ($133,000 before rebates) for the 1,041 patients who received treatment. The changing market of DAAs and fluctuating prices means published studies do not account for introduction of new (or cheaper) drugs.

The Department conservatively estimates that lowering the threshold for DAA access from F2 to F1 would result in a State General Fund expenditure of $21 million to $45 million, while lowering the threshold from F2 to F1 and F0 would result in an expenditure of $27 million to $59 million. The ranges are inclusive of rebates and the lower cost of treatment for patients with lower Metavir scores. If all currently estimated participants with a Metavir score of F1 or F0 elected to receive treatment, expenditures could grow by more than $235 million. These estimates assume drug companies will continue to provide rebates at the same level they provide currently. Furthermore, cost projections may increase as awareness of DAA treatment grows and testing for HCV expands.

Currently, the Department recommends maintaining its current HCV coverage policy. Though DAAs are a safe and effective means of treating HCV, the uncertain price market and rapid introduction of new drugs may have a significant impact on the State Medicaid budget. Further, Maryland's current policy of treating participants with a Metavir score of F2 or above is more permissive in access to DAA treatment than 23 other states. The Department is unable to make any additional comments on the costs to the Department of Public Safety and Correctional Services on expanding coverage among incarcerated persons. If circumstances regarding HCV and treatment change, the Department would consider placing lower cost treatments on Medicaid's preferred drug list as well as allowing step therapy to treat patients with lower Metavir scores with more cost-effective drugs as necessary and available.

II. Introduction

Pursuant to the requirements of the 2017 Joint Chairmen's Report (p. 87-88), the Maryland Department of Health ("the Department") Medicaid program respectfully submits this report, which addresses:

1. The clinical literature to assess what is the appropriate Metavir score to begin coverage of the new therapies;
2. An estimate of the number of individuals annually that would be covered if the Metavir score criteria was lowered to F1 and F0;
3. The associated annual cost for covering drug therapies at a Metavir score of F1 and F0, net of drug rebates;
4. The savings associated with starting treatment at an earlier Metavir score of F1 or F0; and
5. The cost implications for the Department of Public Safety and Correctional Services (DPSCS) if it chooses to likewise lower the Metavir score to F1 and F0 for individuals in the State correctional system.

III. Hepatitis C and Treatment Overview

"Hepatitis" refers to an inflammatory condition of the liver and is the name of a group of viral infections that can affect the liver. Common types include Hepatitis A, Hepatitis B, and Hepatitis C. There are vaccines for both Hepatitis A and B, but not for the Hepatitis C virus (HCV). Acute infection occurs within the first 6 months after a person is exposed to HCV, and the majority of people (75 percent to 85 percent) with acute HCV will develop chronic infections as the replication of the virus can surmount the effects of a typical immune response.[1] Chronic HCV infection is a long-term illness that can lead to significant liver problems, including cirrhosis and liver cancer, and it is the leading reason for receiving a liver transplant in the United States.[2]

In 2015, the Centers for Disease Control and Prevention (CDC) estimated that approximately 33,900 people acquired acute HCV; however, most people with acute infections are asymptomatic (70 percent to 80 percent). Additionally, disease progression may occur over a period of decades; therefore, many people may not be screened for the disease. As a result, the actual prevalence of HCV may be higher than estimated. CDC estimates that between 2.7 and 3.9 million people in the United States have chronic HCV and, of those, approximately 1 million are enrolled in Medicaid programs.[3] People with either acute or chronic HCV often do not look or

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[1] Hepatitis C FAQs for health professionals. Centers for Disease Control and Prevention Web site. https://www.cdc.gov/hepatitis/hcv/hcvfaq.htm. Updated 2017.

[2] Hepatitis C FAQs for the public. Centers for Disease Control and Prevention Web site. https://www.cdc.gov/hepatitis/hcv/cfaq.htm. Updated 2016.

[3] NAMD calls on Congress to act on hepatitis C drug costs and access. National Association of Medicaid Directors. July 6, 2016. Available from: http://medicaiddirectors.org/namd-calls-on-congress-to-act-on-hepatitis-c-drug-costs-and-access/.

feel sick and may unintentionally spread the virus to others. The CDC estimates that 19,000 people die each year from HCV-related liver disease.[4]

Baby Boomers (those born between 1945 and 1965) account for approximately 75 percent of all chronic HCV infections.[5] They are five times more likely to have HCV than other adults, and they are believed to have been exposed between 1960 and 1990, when transmission rates were highest.

Transmission of the virus generally occurs when an uninfected person is exposed to the blood of an infected person. Common routes of transmission include injection drug use and sharing needles, unprotected sex, blood transfusions, and organ transplants before blood screening became common in 1992. Today, infection is most commonly spread by sharing needles and drug paraphernalia and less commonly through needle sticks in a health care setting, from mother to baby during childbirth, through sharing personal care items that may be exposed to blood (e.g., razors), or through sexual contact.[6]

HCV occurs in six major strains, or genotypes. Genotype 1 is the most common form of HCV in the United States, affecting about 74 percent of prevalent cases. There is no lasting immunity against HCV. This means that if a person spontaneously clears or is cured of HCV via medication, they may later become re-infected with the same or a different genotype.[7]

Fibrosis, Cirrhosis, and Metavir Score

Fibrosis of the liver accompanies many liver diseases, including HCV, and it leads to inflammation as the result of wound repair. The scar tissue that forms as a result of liver tissue breaking down and repairing can alter the liver's structure and ability to regenerate. Septa (fibers that develop between portals) are indicative of a greater level of damage. Enough septa develop into fibrosis. Liver fibrosis may lead to cirrhosis (long-term damage where healthy tissue is replaced by scar tissue) over a certain period of time, varying from person to person based on other risk factors. Estimates predict that, of the 75 to 85 percent of individuals who are infected with chronic HCV, 60 to 70 percent will develop chronic liver disease, 5 to 20 percent will develop cirrhosis over a period of 20 to 30 years, and 1 to 5 percent will die from the complications of chronic HCV infection.[8]

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[4] Hepatitis C FAQs for the public. Updated 2016.
[5] Centers for Disease Control and Prevention. Hepatitis C: Why people born from 1945 –1965 should get tested. 2016.
[6] Hepatitis C FAQs for the public. Updated 2016.
[7] Hepatitis C FAQs for health professionals. Updated 2017.
[8] Ibid.

Patients with HCV often receive a Metavir (Meta-analysis of histological data in viral hepatitis) score to indicate the liver's stage of fibrosis, determined by a liver biopsy or other testing.[9] As listed in Table 1, the Metavir score has five grades that correspond to degrees of liver fibrosis and give an indication of type of cirrhosis.

Table 1: Metavir Score, Fibrosis, and Cirrhosis Gradation

Metavir Score	Fibrosis Description
F0	Chronic hepatitis without fibrosis
F1	Portal fibrosis without septae
F2	Portal fibrosis with a few septae
F3	Septal fibrosis without cirrhosis
F4	Complete cirrhosis

Data on HCV prevalence by Metavir score is extremely limited. The gold standard to determine the degree of fibrosis is the liver biopsy. Liver biopsies are done infrequently and have been largely replaced with noninvasive methodologies, which can determine the degree of fibrosis in patients infected with chronic HCV. These methodologies employ either the use of biomarkers or evaluation of liver stiffness to make a determination regarding the degree of liver fibrosis.[10,11]

One 2015 study provided estimates of Metavir score at diagnosis based on unpublished data from the CDC, detailed in Table 2 below.[12]

Table 2: Estimate of Prevalence of Metavir Score Category at Initial Diagnosis

Metavir Score Category at Diagnosis	Percent
F0	11%
F1	36%
F2	23%
F3	14%
F4	16%

[9] Bedossa P, Poynard T. An algorithm for the grading of activity in chronic hepatitis C. the METAVIR cooperative study group. Hepatology (Baltimore, Md.). 1996;24(2):289. http://www.ncbi.nlm.nih.gov/pubmed/8690394.
[10] Maryland Department of Health. Clinical criteria for hepatitis C (HCV) therapy. 2017.
[11] Non-invasive tests to determine fibrosis level are not always 100 percent accurate. We note that tests may be overly inclusive, including people who actually have a lower level of fibrosis as an F2 or greater. This may result in people who do not truly have an F2 score to be recorded as F2, thereby allowing them to access treatment.
[12] Rein DB, Wittenborn JS, Smith BD, Liffmann DK, Ward JW. The cost-effectiveness, health benefits, and financial costs of new antiviral treatments for hepatitis C virus. Clinical Infectious Diseases. 2015;61(2):157-168. http://www.ncbi.nlm.nih.gov/pubmed/25778747. doi: 10.1093/cid/civ220.

As these estimates only reflect the level of fibrosis at initial diagnosis, the burden of morbidity associated with HCV may be substantially different in the general population, as fibrosis increases as the disease progresses and may be exacerbated by comorbidities. This report utilizes these unpublished estimates of the proportions of the populations who fall within a given category of Metavir score at initial diagnosis to estimate the burden of HCV on Maryland's Medicaid population.

Advances in Treatment

The benefits of HCV treatment include: decreased liver inflammation; slowed progression of liver fibrosis; and reduced risk of liver cancer, transplantation, or liver-related mortality. [13]

The traditional standard of care for patients has changed in recent years. Treatment advanced from a combination of pegylated interferon and ribavirin (PR) to the triple treatment of PR plus a first generation protease inhibitor. PR treatment was effective in approximately 50 to 70 percent of patients. Triple treatment achieved a 75 percent effectiveness rate after 24 weeks but had significant side effects, numerous drug interactions, and was a highly complex regimen including the need for injection.[14]

More recent advances in HCV treatment include the use of direct-acting antiviral (DAA) drugs approved by the Food and Drug Administration (FDA) in 2011 for treatment of chronic HCV. DAAs are designated as "breakthrough therapies."[15] DAAs present a significant advantage over traditional PR and protease inhibitor treatment because they are nearly 100 percent effective at clearing the virus and, unlike traditional treatments, they have shorter durations, minimal side effects, and fewer drug interactions. Table 3 below delineates the progression of recent DAA approvals and approximate costs per treatment cycle in 2017.

[13] AASLD-IDSA. Recommendations for testing managing and treating hepatitis C. http://www.hcvguidelines.org/ Web site. Accessed June, 2017.

[14] Zhang S, Bastian ND, Griffin PM. Cost-effectiveness of sofosbuvir-based treatments for chronic hepatitis C in the US. BMC Gastroenterology. 2015;15(1):98. http://www.ncbi.nlm.nih.gov/pubmed/26239358. doi: 10.1186/s12876-015-0320-4.

[15] Breakthrough treatments are defined as "drugs that have proved to provide substantial improvement over available therapies for patients with serious or life-threatening diseases".

Table 3: DAA Drug Approval Timeline

Time	Event	Approximate Cost (2017)
December 2013	FDA approved Sovaldi (sofosbuvir) as part of interferon-free oral treatment regimen for patients with genotype 2 or 3 and as part of PR for patients with genotype 1.[16]	~$85,000 (12 weeks)
October 2014	FDA approved Harvoni (ledpasvir-sofosbuvir) for treatment of genotype 1 patients with or without cirrhosis.[17]	~$95,000 (12 weeks)
November 2014	FDA approved Olysio (simeprevir) in combination with sofosbuvir for genotype 1 patients.	~$66,000 (simeprevir alone); ~$150,000 with sofosbuvir (12 weeks)
December 2014	FDA approved Viekira Pak (ombitasvir, paritaprevir, ritonavir, and dasabuvir combination) for treatment of genotype 1 patients.	~$84,000 (12 weeks)
January 2016	FDA approved Zepatier (elbasvir/grazoprevir) for the treatment of genotype 1 and 4.	~$54,600 (12 weeks)
June 2016	FDA approved Epclusa (velpatasvir/sofosbuvir) for the treatment of genotype 1-6.	~$75,000 (12 weeks)
August 2017	FDA approved Mavyret (glecaprevir and pibrentasvir) for treatment of genotype 1-6 patients without cirrhosis or with mild cirrhosis.	~$26,400 (8 weeks)

DAAs are formulated to treat various genotypes of HCV, sometimes in concert with other traditional (interferon-based) medications. Both the American Association for the Study of Liver Disease and the Infectious Diseases Society of America endorse HCV treatment using the all-oral DAA drugs rather than traditional regimens unless a patient has a short life expectancy where any treatment is not expected to eliminate the virus.[18]

Cost of Treatment

Sovaldi and Harvoni, two DAAs, garnered public attention due to their very high costs for a single course of treatment. Treatment duration may range from 8 to 24 weeks depending on patient clinical characteristics and cost $1,000 to $1,125 per day when used in conjunction with

[16] As of September 2017, Sovaldi is approved for treatment of HCV genotypes 1, 2, 3, and 4.
[17] As of September 2017, Harvoni is approved for treatment of HCV genotypes 1, 4, 5, and 6.
[18] AASLD-IDSA. Recommendations for testing managing and treating hepatitis C. Accessed June, 2017.

additional medications. Upon their release in 2014, Gilead Sciences, the developer of both Sovaldi and Harvoni, set the wholesale cost of treatment at approximately $100,000 for 12 weeks.[19]

In light of the substantial cost, public and private health care payers, including Medicaid, restricted access to the medications to the sickest patients (often based on Metavir score). In 2014, Medicaid programs spent $1.3 billion on Sovaldi to treat less than 2.4 percent of the 700,000 participants with HCV. When state Medicaid programs individually sought discounts, Gilead offered rebates of 10 percent under the condition that states remove barriers to allow more people to access treatment, thereby increasing overall spending. Five state Medicaid programs received supplemental rebates in 2014. [20]

Increased competition led to some price decreases. In late 2014, the drug company AbbVie introduced a cheaper HCV treatment: Viekira Pak. The introduction spurred Gilead to offer more significant discounts of approximately 40 percent, but Gilead still had nearly $10.1 billion in sales from January to September 2015 (more than what was spent on all HCV treatment combined in 2014).[21] State Medicaid programs spent $2.2 billion on Harvoni, $618 million on Sovaldi, and $210 million on Viekira Pak in 2015.[22] In comparison, Medicare spent $7 billion on Harvoni and $1.3 billion on Sovaldi in 2015 (spending on Viekira Pak was not reported).[23]

Companies are still developing DAAs to meet patient needs. In August 2017, the FDA approved Mavyret for use in patients with HCV genotypes 1-6. Mavyret is manufactured by AbbVie, and is distinct because it offers a shorter treatment timeline for patients without cirrhosis (8 weeks) and lower cost ($26,400 per course of treatment). Mavyret is only approved to treat patients without cirrhosis or with compensated cirrhosis. This clinical requirement corresponds to a slight decrease in cost of treating patients with a F2 Metavir score and below. However, it will not meaningfully impact potentials costs to treat people at a more advance stage of disease. Because Mavyret is a recent addition to the HCV drug landscape, clinical literature and cost effectiveness research do not yet consider its impact. Additionally, other drug companies may choose to lower their prices to remain competitive.

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[19] Barua S, Greenwald R, Grebely J, Dore GJ, Swan T, Taylor LE. Restrictions for Medicaid reimbursement of sofosbuvir for the treatment of hepatitis C virus infection in the United States. Annals of internal medicine. 2015;163(3):215. http://www.ncbi.nlm.nih.gov/pubmed/26120969. doi: 10.7326/M15-0406.

[20] McCarthy M. Hepatitis C drug maker puts profit ahead of patients, US senate report charges. BMJ (Clinical research ed.). 2015;351. http://www.ncbi.nlm.nih.gov/pubmed/26635239. doi: 10.1136/bmj.h6573.

[21] Ibid.

[22] 2015 Medicaid drug spending dashboard. Centers for Medicare and Medicaid Services Web site. Updated 2016

[23] Ibid.

IV. Clinical Literature

Medical Approval of DAAs

The FDA has approved DAAs for treatment of individuals at various stages of liver disease. Harvoni, Sovaldi, and Viekira Pak were the most commonly prescribed DAAs paid for by state Medicaid agencies, and the clinical considerations of each are detailed and current as of June 2017. Mavyret was not included because it has only gained FDA approval in August 2017.

Harvoni is approved for HCV treatment in adult and pediatric patients with HCV genotype 1, 4, 5, and 6.[24] Based on the FDA's approval, Harvoni is effective at treating HCV in patients across the spectrum of liver damage, from F0 to F4 (when used in combination with other therapies).

Sovaldi is approved for HCV treatment as a component of an antiviral treatment regimen for adult and pediatric patients with HCV genotype 1, 2, 3, or 4.[25] Based on the FDA's approval, Sovaldi is effective at treating HCV in patients across the spectrum of liver damage, from F0 to F4 (when used in combination with other therapies).

Viekira Pak is approved for HCV treatment in adult patients with genotype 1a and 1b.[26] Based on the FDA's approval, Viekira Pak is effective at treating HCV in patients across the spectrum of liver damage, from F0 to F4 (when used in combination with other therapies).

Cost-Effectiveness Research

Cost-effectiveness of DAA treatment is the subject of ongoing debate among medical professionals and policymakers. Professional groups recommend treatment of all patients with HCV regardless of liver disease status (except in people with short life expectancies who should not expect to recover fully with any regimen), and there are several FDA-approved DAA medications to meet patients' needs. However, given the cost of each treatment cycle, policymakers have raised concerns about cost-effectiveness in light of increased demand and skyrocketing health care costs.

Research in this area has been limited due to the newness of DAA therapies and the constantly changing price landscape as additional drugs enter the market. The wholesale cost of the drugs is often cited as evidence of expense but does not take into account any volume discounts or rebates that a purchaser may receive. New drugs enter the market frequently and may treat specific genotypes or a broad range of genotypes, and cost estimates may be outdated months

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[24] US Food and Drug Administration. Prescribing information: HARVONI. Drugs@FDA Web site. https://www.accessdata.fda.gov/scripts/cder/daf/. Updated 2017.
[25] US Food and Drug Administration. Prescribing information: SOVALDI. Drugs@FDA Web site. https://www.accessdata.fda.gov/scripts/cder/daf/. Updated 2017.
[26] US Food and Drug Administration. Prescribing information: VIEKIRA PAK. Drugs@FDA Web site. https://www.accessdata.fda.gov/scripts/cder/daf/. Updated 2017.

after a paper is published. As such, it is difficult to consistently ascertain the cost-effectiveness of the treatments if pricing information is incomplete.

One 2015 study examined the cost-effectiveness of various combinations of sofosbuvir-based treatments compared with traditional interferon-based treatment, as well as relative health benefits of DAA treatments (Harvoni and Viekira Pak were not approved by the FDA at the time of research itself).[27] The study was a microsimulation for HCV among the US adult population (20 years old and older). A brief summary of the findings is illustrated in Table 4 below.

Treatment 2 reduced deaths by over 80,000 in the microsimulation. Treatment 3 further reduced deaths by 164,540, but the relative cost per additional year of life increased. In other words, Treatment 2 reduced deaths, but Treatment 3 reduced deaths at an increased cost per year of life gained. Additionally, patients may progress differently and have different health costs as a result of co-occurring chronic illnesses, which may increase cost per year of full health when treating at a later stage of liver damage.[28]

Table 4: Comparison of Cost-Effectiveness and Health Benefits of Various Treatment Regimens

Treatment	Comparison Treatment	Deaths Reduced	Total Cost	Cost per quality-adjusted life-years (QALY) gained
Treatment 1: Pegylated Interferon and Ribavirin (PR), protease inhibitor for genotype 1; PR alone for genotype 2 and 3	Treatment 2: PR and Sofosbuvir (PRS) for genotype 1 and 4; Sofosbuvir and Ribavirin (SR) for genotype 2 and 3	80,682	$26.2 billion	$47,237
Treatment 2: PRS/SR	Treatment 3: All-oral regimen of Sofosbuvir and Simeprevir (SS) for genotype 1 and 4 and SR for genotype 2 and 3	164,540	$80.1 billion	$72,169

[27] Rein DB, Wittenborn JS, Smith BD, Liffmann DK, Ward JW. The cost-effectiveness, health benefits, and financial costs of new antiviral treatments for hepatitis C virus. Clinical Infectious Diseases. 2015;61(2):157-168. http://www.ncbi.nlm.nih.gov/pubmed/25778747.

[28] Ibid.

Authors noted that the recent approval of Harvoni and Viekira Pak (not factored in the study design) would decrease costs because they had lower list prices than sofosbuvir-based treatments upon approval in 2015. The authors assumed equal effectiveness of the new drugs, and hypothesized decreased cost per year of full health when treated with Harvoni or Viekira Pak compared to Treatment 2 (based on list price of $94,500 for Harvoni and $83,319 for Viekira Pak). The authors further acknowledged that results are based on all patients receiving treatment in the base year of the simulation and exclude the benefit of averting secondary transmissions (from intravenous drug use, for example), which may result in even greater cost-effectiveness. The study overall indicated that treating at a lower Metavir score may be more cost effective than no treatment, and clinical guidelines support prioritizing treatment in patients who are at an F1 Metavir score or greater.[29]

In 2015, the study "Cost-effectiveness of sofosbuvir-based treatments for chronic hepatitis C in the US" was published in the journal *Gastroenterology*.[30] The authors sought to determine the cost-effectiveness of sofosbuvir-involved treatments compared with interferon-based treatments. They considered the effectiveness of each treatment regimen for a particular HCV genotype in patients with and without cirrhosis, as well as the estimated annual transitions to various stages of liver damage. The analysis showed that as compared to sofosbuvir-based treatments, Viekira Pak is more cost-effective for patients who have no cirrhosis and are infected with genotype 1. Harvoni is cost-effective for genotype 1 patients with cirrhosis. According to this study, for sofosbuvir-based treatment to be as cost effective as these other treatment regimens among the aforementioned group of patients a reduction of 30 percent in cost would need to be achieved. However, this study is limited in that costs were based on the 2015 list price of Viekira Pak/Ribavirin at $97,380 and Harvoni at $106,830, and therefore the analysis may not truly assess the current cost-effectiveness of these treatments given changes in the market, increased competition, and the capacity of payers to negotiate discounts or rebates with drug companies. [31]

Researchers have also considered cost-effectiveness of "full access" treatment for the Baby Boomer population. "Full access" treatment allows for access to DAAs at any stage of liver disease as compared to the more common practice of limiting access to treatment by disease severity. Many payers, including Medicaid programs, currently limit access as a means of short-term cost reduction. A 2016 article specifically examined economic impact of restrictions for the Medicaid population and found that restricting treatment is not a cost-effective method of treating HCV in Baby Boomers.[32]

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[29] Ibid.

[30] Zhang S, Bastian ND, Griffin PM. Cost-effectiveness of sofosbuvir-based treatments for chronic hepatitis C in the US. BMC Gastroenterology. 2015;15(1):98. http://www.ncbi.nlm.nih.gov/pubmed/26239358. doi: 10.1186/s12876-015-0320-4.

[31] Ibid.

[32] Chidi AP, Bryce CL, Donohue JM, et al. Economic and public health impacts of policies restricting access to hepatitis C treatment for medicaid patients. *Value in health: the journal of the International Society for*

The study evaluated the cost-effectiveness of restricting HCV treatment in Medicaid enrollees between ages 45 and 55 compared with a policy of "full access" to DAAs. Using various model cohorts, authors estimated treatment and follow-up costs for patients under restricted or full access and evaluated the budgetary impacts on each strategy. They found that "full access" to treatment regardless of Metavir score was cost-effective for Baby Boomer Medicaid enrollees as compared to treatment wherein HCV treatment was restricted to beneficiaries with more advanced disease. The short-term cost of DAA treatment appears to offset the complications that arise in subsequent years of liver disease progression (depending on cohort composition). Authors found that increased access could avoid future complications such as liver cancer and need for liver transplantation and would reduce follow-up costs for patients in early stages of the disease. Cost-savings could further be realized because fewer patients would progress to advanced fibrosis, averting high follow-up costs and potential for progression to more serious stages of disease.[33]

V. Hepatitis C Virus in Maryland

Prevalence in Medicaid

Table 5 presents HCV-related intervention data among Medicaid participants for CY 2015. Of the nearly 1.6 million individuals with any period of Medicaid enrollment in CY 2015, 53,051 received a HCV antibody test and 11,021 received a HCV RNA test for diagnosis of HCV. A total of 21,569 unique participants had a HCV diagnosis code, corresponding to a HCV prevalence of 1.37 percent among all Maryland Medicaid participants. Of the 21,569 participants with HCV diagnoses, 1,707 received non-interferon-based treatment (DAA treatment). Assuming only people with an F2 score or above (54 percent, or 11,647 people) accessed treatment, the overall treatment rate was 14.66 percent.

Pharmacoeconomics and Outcomes Research. 2016;19(4):326-334. http://www.ncbi.nlm.nih.gov/pubmed/27325324.

[33] Ibid.

Table 5: Frequency of Hepatitis C Interventions Among Medicaid Participants with Any Period of Enrollment, CY 2015

Total Number of Unique Participants	Unique Participants with HCV Antibody Test	Unique Participants with HCV RNA Test	Unique Participants with HCV Diagnosis Code	Unique Participants with Prescription for Interferon-Based HCV Treatment	Unique Participants with Prescription for Non-Interferon-Based HCV Treatment
1,570,392	53,051	11,021	21,569	*	1,707

**Not reported due to small cell size.*

Table 6 presents HCV-related intervention data for CY 2016. Of the approximate 1.5 million individuals with any period of Medicaid enrollment in CY 2016, 61,849 received a HCV antibody test and 12,436 received a HCV RNA test for diagnosis of HCV. A total of 22,352 unique participants had a HCV diagnosis code, corresponding to a HCV prevalence of 1.47 percent among all Maryland Medicaid participants. Of the 22,352 participants with HCV diagnoses, 1,041 received non-interferon-based treatment. Assuming only people with an F2 score or above (54 percent, or 12,070 people) accessed treatment, the overall treatment rate was 8.62 percent.

Table 6: Frequency of Hepatitis C Interventions Among Medicaid Participants with Any Period of Enrollment, CY 2016

Total Number of Unique Participants	Unique Participants with HCV Antibody Test	Unique Participants with HCV RNA Test	Unique Participants with HCV Diagnosis Code	Unique Participants with Prescription for Interferon-Based HCV Treatment	Unique Participants with Prescription for Non-Interferon-Based HCV Treatment
1,535,414	61,849	12,436	22,352	*	1,041

**Not reported due to small cell size.*

From CY 2015 to CY 2016, there was an increase in prevalence of HCV among Medicaid participants from 1.37 percent to 1.47 percent. Over the same period, there was a decrease in the proportion of people with an F2 Metavir score and above receiving DAA treatment of 6.03 percentage points, corresponding to 666 fewer people receiving non-interferon-based treatment.

Table 7 indicates the frequencies of testing, prevalence, and treatment among the Baby Boomer population enrolled in Medicaid that occurred between January 1, 2012, and December 31, 2016.

Table 7: Frequency of Hepatitis C Interventions Occurring between CY 2012 – CY 2016 Among Medicaid Participants Born Between 1945 and 1965 with Any Period of Enrollment in CY 2016

Total Number of Unique Participants Born 1945 through 1965	Number of Unique Participants Born 1945 through 1965 Tested for HCV Antibody	Number of Unique Participants Born 1945 through 1965 Tested for HCV RNA	Unique Participants with HCV Diagnosis Code	Unique Participants with Prescription for Interferon-Based HCV Treatment	Unique Participants with Prescription for Non-Interferon-Based HCV Treatment
224,295	36,121	13,340	20,034	371	2,226

The data in Table 7 account only for Baby Boomers with a period of enrollment in CY 2016. The data tabulate five qualifying interventions (antibody test, RNA test, diagnosis code, prescription for interferon-based treatment, and prescription for non-interferon-based treatment) that Baby Boomer participants received over a three-year period: January 1, 2012 to December 31, 2016. As a result, one possible trend not reflected is a likely increase in prescriptions for non-interferon-based treatment over the four-year period corresponding with a decrease in prescriptions for interferon-based treatment as DAA treatments gain popularity.

Treatment Trends Nationally

When DAAs were first introduced, many state Medicaid programs implemented treatment policies, which generally restricted access to sicker patients who met certain criteria. Some states have altered their policies in subsequent years. Table 8 presents information for each state's requirements for accessing DAAs through their fee-for-service (FFS) Medicaid programs in 2014 and 2016.[34] In 2014, 34 states had known Metavir score restrictions for FFS program enrollees. Of those 34 states, 79 percent (27 states) restricted access to patients with a score of F3. In 2016, many states modified policies to provide access for patients with lower Metavir scores. As of 2016, twenty-one states, including Maryland, allowed patients with a F2 Metavir score and below to access DAA treatment. Twenty-three states had more restrictive standards than Maryland in 2016. Notably, some states substantially restrict which types of providers can prescribe DAAs. Maryland allows a variety of providers to prescribe DAAs if they have expertise in HCV management.

[34] NVHR C. Hepatitis C: The state of Medicaid access. Center for Health Law & Policy Innovation. 2016.

Table 8: Comparing 2014 and 2016 Medicaid FFS Liver Disease Requirements[35]

Category	2014 FFS Liver Disease Restriction	States 2014 FFS Liver Disease Restriction	2016 FFS Liver Disease Restriction	States 2016 FFS Liver Disease Restriction
No Restrictions	0 (0%) [a,b]	None	5 (11%) [c]	Connecticut, Florida, Massachusetts, New York, Wyoming
Chronic HCV	0 (0%)	None	4 (9%)	Arizona, Georgia, Nevada, Washington
F1	1 (3%)	Maine	2 (5%)	North Dakota, Utah
F2	2 (6%)	Maryland, Oklahoma	10 (23%)	Alaska, California, District of Columbia, Idaho, Maryland, North Carolina, Oklahoma, Pennsylvania, Virginia, Wisconsin
F3	27 (79%)	Alaska, Arizona, Arkansas, California, Colorado, District of Columbia, Florida, Idaho, Indiana, Iowa, Kentucky, Louisiana, Missouri, Montana, Nebraska, New Hampshire, New York, Ohio, Pennsylvania, Rhode Island, South Dakota, Tennessee, Vermont, Virginia, Washington, West Virginia, Wisconsin	22 (50%)	Arkansas, Colorado, Delaware, Hawaii[c], Indiana, Iowa, Kansas, Louisiana, Michigan, Minnesota, Missouri, Montana, Nebraska, New Jersey, Ohio, Oregon, Rhode Island, South Carolina, South Dakota, Texas, Vermont, West Virginia
F4	4 (12%)	Connecticut, Delaware, Illinois, Oregon	1 (2%)	Illinois
Restrictions Unknown	17	Alabama, Georgia, Hawaii, Kansas, Massachusetts, Michigan, Minnesota, Mississippi, New Jersey, New Mexico, Nevada, North Carolina, North Dakota, South Carolina, Texas, Utah, Wyoming	7	Alabama, Kentucky, Maine, Mississippi, New Hampshire, New Mexico, Tennessee

a: Percentages are calculated using the number of states that had known restrictions in a given year. For 2014 FFS Medicaid programs, 34 states had known restrictions for fibrosis.

b: Due to rounding, percentages in each chart may not add up to 100 percent

c: Percentages are calculated on the number of states that had known restrictions in a given year. For 2016 FFS Medicaid programs, 44 states had known restrictions for fibrosis.

d: Hawaii has confirmed that as of January 1, 2017, both its FFS and managed care programs will only require demonstration of mild fibrosis (F1). As of 2016, both programs require demonstration of advanced fibrosis (F3).

[35] Ibid.

Some states are moving toward expanding access to DAAs at a lower level of liver damage. For example, on January 1, 2018, Delaware, Oklahoma, and Pennsylvania will begin covering treatment for HCV as soon as a patient is diagnosed with chronic HCV. Other states require consultation with a specialist, such as an infectious disease specialist, or will make allowances for accessing DAA treatment if the patient has co-morbidities such as HIV or AIDS.

Maryland Medicaid Program Coverage for Hepatitis C Treatment

The Department has established clinical criteria for HCV treatment, (Appendix A) Chronic Hepatitis C and HCV genotype and sub-genotype documented:

- HCV RNA quantitative within 90 days of application for therapy;
- Liver biopsy or other accepted test demonstrating liver fibrosis corresponding to Metavir score of greater than or equal to F2[36];
- Previous HCV treatment history and outcome;
- HIV status and, if HIV positive, current antiretroviral regimen and degree of viral suppression;
- Adherence evaluation: Providers must assess and document the patient's ability to adhere to therapy; and
- Drug resistance testing as indicated.

Patients are also required to have a treatment plan developed in collaboration with a provider, and, if the patient or partner is of childbearing age, to use two forms of contraception during treatment with ribavirin and 6 months after the regimen is completed.

The Maryland Medicaid Pharmacy Program requires providers to submit prior authorization for DAAs. A patient's entire medical history is considered, including treatment history, history of substance use disorder, history of medication non-adherence, and co-occurring conditions (such as cancer or HIV). If prior authorization is not granted, providers may petition for reconsideration on a case-by-case basis.

Maryland follows genotype treatment recommendations for testing, managing, and treating HCV as directed from the American Association for the Study of Liver Diseases. As of August 16, 2017, the Department covers the recently-approved Mavyret drug, as well as Daklinza, Zepatier, Harvoni, Viekira Pak, Olysio, Epclusa, Sovaldi, Technivie, and Vosevi.[37]

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[36] Non-invasive tests to determine fibrosis level are not always 100 percent accurate. We note that tests may be overly inclusive, including people who actually have a lower level of fibrosis as an F2 or greater. This may result in people who do not truly have an F2 score to be recorded as F2, thereby allowing them to access treatment.
[37] See Appendix A.

VI. Estimate of Treatment Costs Annually

Due to the high cost of treatment, DAA therapies are carved out of MCO capitation rates in Maryland. When a participating provider prescribes a DAA, the MCO receives a one-time "kick" (additional) payment to cover the cost of the drug. Medicaid pays MCOs directly for DAAs prescribed to patients enrolled in FFS Medicaid. Both the FFS program and MCOs are eligible for bulk discounts and rebates, which make estimating the total cost of treatment difficult.

Data on MCO drug rebates is collected as part of the Myers & Stauffer review process. The Department requested that the portion of rebates for HCV drugs be specified independent of other drug rebates. In 2015, MCOs reported $26.6 million in total rebates, with approximately $6.6 million associated with HCV drugs, including: Daklinza, Epclusa, Harvoni, Olysio, Sovaldi, Technivie, Viekira Pak, and Zepatier. This represents approximately 0.15 percent of 2015 MCO net revenues. Preliminary data for 2016 indicates MCOs reported $35.3 million in total rebates, with approximately $4.5 million associated with the same HCV drugs (approximately 0.09 percent of MCO net revenues).

Table 9 shows the estimated net cost of DAA drugs for CY 2016 for MCOs and FFS. There was a total of 4,706 prescriptions (1-month supply each) in CY 2016 and an estimated net cost of approximately $74 million. The net cost is derived using total units reimbursed by all the programs, multiplied by Unit Rebate Amount (URA), minus the Estimated Unit Rebate Offset Amount (UROA) (estimated because not all medication had UROA in the CMS Rebate System).

Table 9: HCV DAA Therapies, Estimated Net Cost for MCOs and FFS, CY 2016

	Paid Units	Number of Rx	Total Reimbursement	Net Cost
All Drug Total	132,817	4,706	$138,912,867	$74,049,797

Using data from CY 2016 about people treated with DAAs, the total cost of treating 1,041 people was $138,912,867, or about $133,000 per person before rebates ($71,000 after rebates). Actual amount per person may be lower if certain individuals required retreatment (if their HCV was not cured by the initial treatment course) or became re-infected. Rebates accounted for 47 percent of the per-person cost.

Table 10 shows projected annual costs of treatment for three scenarios (1) the Department maintains its current policy covering participants with a Metavir score of F2 or higher, (2) the Department changes its policy to also cover individuals with a Metavir score of F1 or higher, and (3) the Department changes its policy to cover individuals irrespective of Metavir score. The calculations make the following assumptions:

- Number of people with HCV increases to 23,134, consistent with the increase of prevalence of 3.5 percent, observed from CY 2015 to CY 2016.
- Percentage of eligible people receiving treatment is 11.64 percent across all Metavir score groups (average of proportion of people with F2 Metavir score or above that received DAA treatment in CY 2015 and CY 2016).
- Costs before rebates remain the same per-person for higher levels of liver damage (F3 and F4) ($133,000). Cost before rebates is lower for lower levels of liver damage (F0, F1, and F2) (using Mavyret cost for reference—$26,400). Not all patients may receive treatment with Mavyret, so assume 1/3 Mavret and 2/3 other treatment mix.
- Rebates cover 47 percent of treatment costs (same as CY 2016). Mavyret rebate is approximately $6,000.
- State General Fund expenditures calculated using a blended Federal Medical Assistance Percentage (FMAP) of 60 percent Federal Funds and 40 percent State General Funds.

Under these assumptions, Table 10 shows the possible cost of treating people at various inclusive levels of Metavir scores.

Table 10: Scenarios of Eligibility and Treatment Cost for Increasing Access to DAAs

Scenario 1: No change (F2+)

Metavir Score	People Eligible for Treatment	People Receiving Treatment	Gross Cost	Net Cost (after rebates)	State General Fund Expenditures
F4	3,701	431	$57,302,733	$30,370,448	$12,148,179
F3	3,239	377	$50,139,891	$26,574,142	$10,629,657
F2	5,321	619	$59,761,688	$32,983,383	$13,193,353
F1	-	-	-	-	-
F0	-	-	-	-	-
Total	12,261	1,427	$167,204,312	$89,927,974	$35,971,190

Scenario 2: F1 and Above Are Eligible for Treatment

Metavir Score	People Eligible for Treatment	People Receiving Treatment	Gross Cost	Net Cost (after rebates)	State General Fund Expenditures
F4	3,701	431	$57,302,733	$30,370,448	$12,148,179
F3	3,239	377	$50,139,891	$26,574,142	$10,629,657
F2	5,321	619	$59,761,688	$32,983,383	$13,193,353
F1	8,328	969	$93,540,033	$51,626,165	$20,650,466
F0	-	-	-	-	-
Total	20,589	2,397	$260,744,346	$141,554,139	$56,621,655
		Total New Costs:	**$93,540,033**	**$51,626,165**	**$20,650,466**

Scenario 3: Open access (F0+)

Metavir Score	People Eligible for Treatment	People Receiving Treatment	Gross Cost	Net Cost (after rebates)	State General Fund Expenditures
F4	3,701	431	$57,302,733	$30,370,448	$12,148,179
F3	3,239	377	$50,139,891	$26,574,142	$10,629,657
F2	5,321	619	$59,761,688	$32,983,383	$13,193,353
F1	8,328	969	$93,540,033	$51,626,165	$20,650,466
F0	2,545	296	$28,581,677	$15,774,661	$6,309,865
Total	23,134	2,693	$289,326,022	$157,328,800	$62,931,520
		Total New Costs:	**$122,121,710**	**$67,400,826**	**$26,960,331**

Savings Associated with DAA Treatment

As previously discussed, the clinical literature indicates that it may be cost effective to treat patients with DAAs upon initial diagnosis of chronic HCV. However, due to the evolving drug price landscape and variations in testing, it is difficult to predict with certainty the cost savings associated with treating at a lower level of Metavir score than F2.

When a full course of treatment is completed, traditional treatment for HCV is approximately 75 percent effective at eliminating the disease but comes with significant side effects that may take a toll on a person's quality of life.[38] DAAs have limited side effects, making them easier to tolerate for many patients. Not all patients with HCV who are prescribed interferon-based treatment are able to adhere to the full course. DAAs consistently have a higher likelihood of

[38] Zhang S, Bastian ND, Griffin PM. Cost-effectiveness of sofosbuvir-based treatments for chronic hepatitis C in the US. BMC Gastroenterology. 2015;15(1):98. http://www.ncbi.nlm.nih.gov/pubmed/26239358. doi: 10.1186/s12876-015-0320-4.

adherence to treatment regimens (96.2 percent) compared to interferon-based therapies (77.6 percent).[39]

Costs for a full course of treatment have decreased as new therapies were introduced. With increased competition, prices may fall further, enabling greater purchasing power of DAA medications. Mavyret, which costs $26,400 for a full 8-week course of treatment, is significantly less expensive than other similar medications, and is approved to treat patients with genotype 1-6 without cirrhosis and with mild cirrhosis. This may impact the cost-effectiveness of treatment with DAAs for people with an F2 Metavir score or lower, but people at F3 or F4 will still require treatment with more expensive medications.

Table 11 indicates the new State General Fund expenditures based on treating the hypothetical 23,134 newly-diagnosed people in CY 2018 at different Metavir score thresholds. Lowering the threshold for treatment to F1 and above would increase costs to nearly $21 million after rebates and 60 percent FMAP. Opening treatment to all newly diagnosed (F0 and above) would increase General Fund expenditures by almost $27 million.

Table 11: Annual Costs of Treatment for Hypothetical CY 2018 HCV Cases, Based on Coverage at Various Metavir Scores

Metavir Score Threshold	Number of People Eligible	Additional State General Fund Expenditure	Percentage Increase in State General Fund Cost of Treatment From F2 Threshold
F2	12,261	-	-
F1	20,589	$20,650,466	57%
F0	23,134	$26,960,331	75%

These costs are calculated under the assumption that rebate availability remains the same. The calculations also assume that 33 percent of patients at F2 are treated with Mavyret and 66 percent of patients with F2 are treated with a different DAA. If a greater percentage of patients were to receive more expensive medications, annual costs would sharply increase. Additionally, if there is a greater uptake of treatment than the anticipated 11.64 percent, costs would increase.

The cost for treatment also does not take into account the savings realized by externalities such as decreasing transmission, increasing quality of life, and avoiding treating with a more expensive medication later. In other words, if a person is diagnosed in 2018 with HCV and has a Metavir score of F1, treating him or her at F1 is less expensive than waiting until the person

[39] Younossi ZM, Stepanova M, Henry L, Nader F, Younossi Y, Hunt S. Adherence to treatment of chronic hepatitis C: From interferon containing regimens to interferon and ribavirin free regimens. *Medicine*. 2016;95(28):e4151. http://www.ncbi.nlm.nih.gov/pubmed/27428205.

reaches F2 or above to begin treatment. Treatment at F1 may cost as little as $26,400, while treatment at F2 and above may cost $133,000. However, because disease progression may take place over decades, cost-savings may not accrue for many years. Additionally, individuals cured of HCV are still susceptible to subsequent reinfection by the same or a different genotype of HCV.

The assumptions presented in Tables 10 and 11 reflect more conservative estimates of possible outcomes of expanding access in a hypothetical first year. Table 12 compares these estimates with another scenario assuming slightly higher prevalence and treatment uptake rates. If, in the second year there is an increase in HCV prevalence in the population (5 percent) and more people seek treatment than anticipated (25 percent), new State General Fund expenditures costs could increase to $45-$59 million.

Table 12: Annual Costs of Treatment for Hypothetical CY 2018 HCV Cases, Based on Coverage at Various Metavir Scores: Comparison of Prevalence Rates and Treatment Uptake

Metavir Score Threshold	Table 10 Estimate		Alternative Estimate		Difference Between Estimates
	Net New Cost Assuming 3.5% Prevalence and 11.64% Uptake	State General Fund Expenditures	Net New Cost Assuming 5% Prevalence and 25% Uptake	State General Fund Expenditures	
F1	$51,626,165	$20,650,466	$121,491,381	$44,996,553	$24,346,087
F0	$67,400,826	$26,960,331	$146,863,748	$58,749,499	$31,789,168

Finally, if Maryland elects to expand coverage of HCV treatment to participants with lower Metavir scores, the Department could also consider placing lower cost treatments (e.g., Mavyret) on the preferred drug list for participants with lower Metavir scores (F1, F0) or adopting similar step-therapy requirement, for instance, requiring treatment with lower cost therapies at F1 and F0 before initiating higher cost drugs. Implementing such measures could help control costs.

VII. Incarcerated Individuals

The Bureau of Justice Statistics (BJS) estimates that in CY 2015 there were approximately 1.5 million individuals under the jurisdiction of state or federal correctional authorities. The rate of HCV among incarcerated individuals is approximately 30 times higher than in the general

population.[40] Based on estimates of general population prevalence, there may be between 370,000 and 540,000 people living with chronic HCV under the jurisdiction of state or federal correctional authorities.

Like Medicaid programs, prison systems have responded to the high cost of treating a large population of people with HCV using DAAs by restricting access to drugs to people at more advanced stages of disease. The Federal Bureau of Prisons issued updates to clinical guidance for new therapies including prioritization for treatment and updates to recommended courses of treatment.[41] Interferon-based treatments are no longer recommended or suggested as alternatives except in very limited cases.

Maryland Medicaid is actively pursuing initiatives that improve access to health care and services for justice-involved individuals statewide. If incarcerated individuals meet all the requirements of Medicaid, they may enroll in Medicaid at any time. Medicaid will only pay for inpatient hospital stays when an individual is incarcerated. During incarceration, an individual's medical needs are coordinated by the Department of Public Safety and Correctional Services (DPSCS). Costs such as outpatient health services and prescription drug services are borne by DPSCS.

The Department supports efforts to connect justice-involved individuals to Medicaid services. The Department cannot comment on the costs that may be incurred by DPSCS by expanding access to new HCV therapies because their costs systems and medical requirements are independent of the Department's policies. However, formerly incarcerated people may later enroll in Medicaid and gain access to DAAs.

Maryland Medicaid is also working with its health and correctional partners to boost efforts to ensure eligible individuals have Medicaid coverage close to the time of release, so they may access services when they return home. LHDs are valuable resource for the justice-involved population because upon release, they assist the person in enrolling in an MCO and accessing needed services, such as behavioral health or substance use disorder services.

VIII. Conclusion

While DAAs provide a safe and effective way to cure HCV for a variety of patients, research addressing their cost-effectiveness is limited. Complicating matters, the treatment landscape continues to shift. New drugs are entering the market and cost changes are ongoing. As more drugs are approved and the market becomes more competitive, prices may fluctuate, and

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[40] Ollove M. Are states obligated to provide expensive hepatitis C drugs? The Pew Charitable Trusts Web site. http://www.pewtrusts.org/en/research-and-analysis/blogs/stateline/2016/02/09/are-states-obligated-to-provide-expensive-hepatitis-c-drugs. Updated 2016.

[41] Federal Bureau of Prisons. Evaluation and management of chronic hepatitis C virus (HCV) infection: Clinical practice guidelines. 2016:53.

companies may choose to offer more discounts or rebates. However, the Department has also observed an upward trend in the prevalence of HCV in Maryland Medicaid population between CY 2015 and CY 2016. This trend may be driven by increased awareness and testing for the disease. Additionally, data on distribution of Metavir score within a diagnosed population is limited. The analysis in this report also does not account for the fact that individuals cured of HCV are still susceptible to subsequent reinfection by the same or a different genotype of HCV. As such, the calculations in this report likely underestimate the actual cost of expanding coverage of DAAs in the Maryland Medicaid population.

Conservatively, the Department estimates that the State General Fund cost to expand treatment coverage would be substantial—requiring between $21 million and $45 million to expand coverage to participants with a Metavir score of F1, and $27 million to $59 million annually to expand coverage to participants with a Metavir score of F1 and F0 —while cost savings in the near term would be limited. Notably, projected costs could dramatically increase as more people are diagnosed with HCV and seek various treatment options. Additionally, rebates may change and are not guaranteed from year to year. If *all* participants currently estimated to be diagnosed with an F1 or F0 Metavir score elected to receive treatment, State General Fund expenditures could grow by $235 million or more in subsequent years, and possibly higher if rebates are decreased or discontinued. If circumstances regarding HCV and treatment change in the future, the Department could also consider placing lower cost treatments (e.g., Mavyret) on the preferred drug list for participants with lower Metavir scores (F1, F0) or adopting similar step-therapy requirements such as requiring treatment with lower cost therapies at F1 and F0 before initiating higher cost drugs. Implementing such measures could help control costs if coverage is expanded.

Given these considerations, the Department recommends maintaining its current policy for access to DAA therapies. With the available resources and other options for managing liver disease progression and HCV diagnosis, decreasing the threshold for access is not financially sustainable or medically necessary at this time and would create a substantial fiscal impact for the State.

Appendix A

MARYLAND Department of Health

Clinical Criteria for Hepatitis C (HCV) Therapy

Pre-Treatment Evaluation

- Must have chronic hepatitis C and HCV genotype and sub-genotype documented;
- HCV RNA quantitative within 90 days of application for therapy;
- Liver biopsy or other accepted test (Appendix A) demonstrating liver fibrosis corresponding to Metavir score of greater than or equal to 2;
- Previous HCV treatment history and outcome;
- HIV status and, if HIV positive, current antiretroviral regimen and degree of viral suppression;
- Adherence evaluation: Providers must assess and document the patient's ability to adhere to therapy;
- Drug resistance testing as indicated; and

Patient Treatment Plan

- It is required that the patient have a treatment plan developed by, or in collaboration with, a provider with expertise in Hepatitis C management. Sample treatment plan documents are available for use.
- If the patient or their partner is of childbearing age, at least two (2) forms of contraception must be used (by the patient or their partner) if a RBV -containing regimen is prescribed throughout the duration of therapy and for 6 months after the regimen is completed.

Drug Therapy

- Must be in accordance with FDA approved indications.

Treatment Options[1]:

Genotype 1a:

- **Daclatasvir (Daklinza®) and Sofosbuvir (Sovaldi®)[2]**
  - Prior to requesting/initiating therapy with this agent, documentation of eGFR ≥30 mL/min is required for approval.

Patient characteristics	Treatment length
Treatment naïve, without cirrhosis	12 weeks
Treatment naïve, with cirrhosis*	24 weeks

Treatment experienced, without cirrhosis	12 weeks
Treatment experienced with cirrhosis*	24 weeks

*Providers may add weight-based ribavirin to this regimen with the same treatment length.

- **Elbasvir/grazoprevir (Zepatier™)[3]**
  - Prior to requesting/initiating therapy with this agent, genotype testing for baseline NS5A polymorphisms is REQUIRED, in order to determine treatment length.
  - Prior to requesting/initiating therapy with this agent in a patient with cirrhosis (stage F4 by Metavir), documentation of Child-Pugh status of A is required.

Patient characteristics	Treatment	Treatment length
Treatment naïve, without baseline NS5A polymorphisms	Zepatier	12 weeks
Treatment naïve, with baseline NS5A polymorphisms	Zepatier + weight based ribavirin	16 weeks
Treatment experienced (PegIFN/RBV), without baseline NS5A polymorphisms	Zepatier	12 weeks
Treatment experienced (PegIFN/RBV), with baseline NS5A polymorphisms	Zepatier + weight based ribavirin	16 weeks

- **Glecaprevir/pibrentasvir (Mavyret ™)**
  - Prior to requesting/initiating therapy with this agent in a patient with cirrhosis (stage F4 by Metavir), documentation of Child-Pugh status of A is required.

Patient characteristics	Treatment length
Treatment naïve, without cirrhosis	8 weeks
Treatment naïve, with compensated cirrhosis	12 weeks
Treatment experienced, without cirrhosis	8 weeks
Treatment experienced, with compensated cirrhosis	12 weeks

- **Ledipasvir/sofosbuvir (Harvoni®)[4]**
  - Prior to requesting/initiating therapy with this agent, documentation of eGFR ≥30 mL/min is required for approval.

Patient characteristics	Treatment length
Treatment naïve, without cirrhosis*	12 weeks
Treatment naïve, with cirrhosis	12 weeks
Treatment experienced, without cirrhosis	12 weeks
Treatment experienced, with cirrhosis**	24 weeks

*8 weeks of treatment can be considered in treatment naive patients without cirrhosis who have pretreatment HCV RNA levels less than 6 million IU/mL.

**A 12 week regimen with weight-based ribavirin may be considered.

- **Paritaprevir/ritonavir/ombitasvir plus dasabuvir (Viekira Pak/ Viekira XR®) with Weight Based Ribavirin[5]**
  - Prior to requesting/initiating therapy with this agent in a patient with cirrhosis (stage F4 by Metavir), documentation of Child-Pugh status of A is required.

Patient characteristics	Treatment length
Treatment naïve, without cirrhosis	12 weeks
Treatment naïve, with cirrhosis	24 weeks
Treatment experienced, without cirrhosis	12 weeks
Treatment experienced, with cirrhosis	24 weeks

- **Simeprevir (Olysio®) and Sofosbuvir (Sovaldi®)[5]**
  - Negative Q80K polymorphism test REQUIRED.
  - Prior to requesting/initiating therapy with this agent, documentation of eGFR ≥30 mL/min is required for approval.

Patient characteristics	Treatment length
Treatment naïve, without cirrhosis	12 weeks
Treatment naïve, with cirrhosis*	24 weeks
Treatment experienced, without cirrhosis	12 weeks
Treatment experienced, with cirrhosis*	24 weeks

*Providers may add weight-based ribavirin to this regimen with the same treatment length.

- **Sofosbuvir/velpatasvir (Epclusa®)**
  - Prior to requesting/initiating therapy with this agent, documentation of eGFR ≥ 30 mL/min is required for approval.

Patient characteristics	Treatment	Treatment length
Patient without cirrhosis and with compensated cirrhosis (Child-Pugh A)	Epclusa	12 weeks
Patients with decompensated cirrhosis (Child-Pugh B and C)	Epclusa + weight based ribavirin	12 weeks

- **Sofosbuvir/velpatasvir/voxilaprevir (Vosevi ™)**
  - Prior DAA experience with an NS5A inhibitor or sofosbuvir
  - Prior to requesting/initiating therapy with this agent in a patient with cirrhosis (stage F4 by Metavir), documentation of Child-Pugh status of A is required.
  - Prior to requesting/initiating therapy with this agent, documentation of eGFR ≥ 30 mL/min is required for approval.

Genotype 1b:

- **Daclatasvir (Daklinza®) and Sofosbuvir (Sovaldi®)[2]**
  - Prior to requesting/initiating therapy with this agent, documentation of eGFR ≥30 mL/min is required for approval.

Patient characteristics	Treatment length
Treatment naïve, without cirrhosis	12 weeks
Treatment naïve, with cirrhosis*	24 weeks
Treatment experienced, without cirrhosis	12 weeks
Treatment experienced with cirrhosis*	24 weeks

*Providers may add weight-based ribavirin to this regimen with the same treatment length.

- **Elbasvir/grazoprevir (Zepatier™)[3]**
  - Prior to requesting/initiating therapy with this agent in a patient with cirrhosis (stage F4 by Metavir), documentation of Child-Pugh status of A is required.

Patient characteristics	Treatment length
Treatment naïve	12 weeks
Treatment experienced (PegIFN/RBV)	12 weeks

- **Glecaprevir/pibrentasvir (Mavyret ™)**
  - Prior to requesting/initiating therapy with this agent in a patient with cirrhosis (stage F4 by Metavir), documentation of Child-Pugh status of A is required.

Patient characteristics	Treatment length
Treatment naïve, without cirrhosis	8 weeks
Treatment naïve, with compensated cirrhosis	12 weeks
Treatment experienced, without cirrhosis	8 weeks
Treatment experienced, with compensated cirrhosis	12 weeks

- **Ledipasvir/sofosbuvir (Harvoni®)[4]**
  - Prior to requesting/initiating therapy with this agent, documentation of eGFR ≥30 mL/min is required for approval.

Patient characteristics	Treatment length
Treatment naïve, without cirrhosis*	12 weeks
Treatment naïve, with cirrhosis	12 weeks
Treatment experienced, without cirrhosis	12 weeks
Treatment experienced, with cirrhosis**	24 weeks

*8 weeks of treatment can be considered in treatment naive patients without cirrhosis who have pretreatment HCV RNA levels less than 6 million IU/mL.

**A 12 week regimen with weight-based ribavirin may be considered.

- **Paritaprevir/ritonavir/ombitasvir plus dasabuvir (Viekira Pak/ Viekira XR®)[5]**
  - Prior to requesting/initiating therapy with this agent in a patient with cirrhosis (stage F4 by Metavir), documentation of Child-Pugh status of A is required.

Patient characteristics	Treatment length
Treatment naïve, with or without cirrhosis	12 weeks
Treatment experienced, with or without cirrhosis*	12 weeks

*Providers may add weight-based ribavirin to this regimen with the same treatment length.

- **Simeprevir (Olysio®) and Sofosbuvir (Sovaldi®)[6]**
  - Negative Q80K polymorphism test REQUIRED.
  - Prior to requesting/initiating therapy with this agent, documentation of eGFR ≥30 mL/min is required for approval.

Patient characteristics	Treatment length
Treatment naïve, without cirrhosis	12 weeks
Treatment naïve, with cirrhosis*	24 weeks
Treatment experienced, without cirrhosis	12 weeks
Treatment experienced, with cirrhosis*	24 weeks

*Providers may add weight-based ribavirin to this regimen for the same treatment length.

- **Sofosbuvir/velpatasvir (Epclusa®)[7]**
  - Prior to requesting/initiating therapy with this agent, documentation of eGFR ≥ 30 mL/min is required for approval.

Patient characteristics	Treatment	Treatment length
Patient without cirrhosis and with compensated cirrhosis (Child-Pugh A)	Epclusa	12 weeks
Patients with decompensated cirrhosis (Child-Pugh B and C)	Epclusa + weight based ribavirin	12 weeks

- **Sofosbuvir/velpatasvir/voxilaprevir (Vosevi ™)**
  - Prior DAA experience with an NS5A inhibitor
  - Prior to requesting/initiating therapy with this agent in a patient with cirrhosis (stage F4 by Metavir), documentation of Child-Pugh status of A is required.
  - Prior to requesting/initiating therapy with this agent, documentation of eGFR ≥ 30 mL/min is required for approval.

Genotype 2:

- **Glecaprevir/pibrentasvir (Mavyret ™)**
  - Prior to requesting/initiating therapy with this agent in a patient with cirrhosis (stage F4 by Metavir), documentation of Child-Pugh status of A is required.

Patient characteristics	Treatment length
Treatment naïve, without cirrhosis	8 weeks
Treatment naïve, with compensated cirrhosis	12 weeks
Treatment experienced, without cirrhosis	8 weeks
Treatment experienced, with compensated cirrhosis	12 weeks

- **Sofosbuvir (Sovaldi®) and weight based ribavirin[8]**
  - Prior to requesting/initiating therapy with this agent, documentation of eGFR ≥30 mL/min is required for approval.

Patient characteristics	Treatment length
Treatment naïve, without cirrhosis	12 weeks
Treatment naïve, with cirrhosis	16 weeks
Treatment experienced, without cirrhosis*	16 weeks
Treatment experienced, with cirrhosis**	16 weeks

*Providers may add PegIFN to this regimen to shorten treatment length to 12 weeks.
**Providers may request and extension to 24 weeks if medically necessary.

- **Sofosbuvir/velpatasvir (Epclusa®)[7]**
  - Prior to requesting/initiating therapy with this agent, documentation of eGFR ≥ 30 mL/min is required for approval.

Patient characteristics	Treatment	Treatment length
Patient without cirrhosis and with compensated cirrhosis (Child-Pugh A)	Epclusa	12 weeks
Patients with decompensated cirrhosis (Child-Pugh B and C)	Epclusa + weight based ribavirin	12 weeks

- **Sofosbuvir/velpatasvir/voxilaprevir (Vosevi ™)**
  - Prior DAA experience with an NS5A inhibitor
  - Prior to requesting/initiating therapy with this agent in a patient with cirrhosis (stage F4 by Metavir), documentation of Child-Pugh status of A is required.

Prior to requesting/initiating therapy with this agent, documentation of eGFR ≥ 30 mL/min is required for approval

Genotype 3:

- **Daclatasvir (Daklinza®) and Sofosbuvir (Sovaldi®)[2]**
  - Prior to requesting/initiating therapy with this agent, documentation of eGFR ≥30 mL/min is required for approval.

Patient characteristics	Treatment length
Treatment naïve, without cirrhosis	12 weeks
Treatment naïve, with cirrhosis*	24 weeks
Treatment experienced, without cirrhosis	12 weeks
Treatment experienced with cirrhosis*	24 weeks

*Providers may add weight-based ribavirin to this regimen with the same treatment length.

- **Glecaprevir/pibrentasvir (Mavyret ™)**
  - Prior to requesting/initiating therapy with this agent in a patient with cirrhosis (stage F4 by Metavir), documentation of Child-Pugh status of A is required.

Patient characteristics	Treatment length
Treatment naïve, without cirrhosis	8 weeks
Treatment naïve, with compensated cirrhosis	12 weeks
Treatment experienced, without cirrhosis	16 weeks
Treatment experienced, with compensated cirrhosis	16 weeks

- **Sofosbuvir/velpatasvir (Epclusa®)[7]**
  - Prior to requesting/initiating therapy with this agent, documentation of eGFR ≥ 30 mL/min is required for approval.

Patient characteristics	Treatment	Treatment length
Patient without cirrhosis and with compensated cirrhosis (Child-Pugh A)	Epclusa	12 weeks
Patients with decompensated cirrhosis (Child-Pugh B and C)	Epclusa + weight based ribavirin	12 weeks

- **Sofosbuvir/velpatasvir/voxilaprevir (Vosevi ™)**
  - Prior DAA experience with an NS5A inhibitor or sofosbuvir
  - Prior to requesting/initiating therapy with this agent in a patient with cirrhosis (stage F4 by Metavir), documentation of Child-Pugh status of A is required.
  - Prior to requesting/initiating therapy with this agent, documentation of eGFR ≥ 30 mL/min is required for approval.

Genotype 4:

- **Elbasvir/grazoprevir (Zepatier™)[3]**
  - Prior to requesting/initiating therapy with this agent in a patient with cirrhosis (stage F4 by Metavir), documentation of Child-Pugh status of A is required.

Patient characteristics	Treatment	Treatment length
Treatment naïve	Zepatier	12 weeks
Treatment experienced (PegIFN/RBV)	Zepatier + weight based ribavirin	16 weeks

- **Glecaprevir/pibrentasvir (Mavyret ™)**
  - Prior to requesting/initiating therapy with this agent in a patient with cirrhosis (stage F4 by Metavir), documentation of Child-Pugh status of A is required.

Patient characteristics	Treatment length
Treatment naïve, without cirrhosis	8 weeks
Treatment naïve, with compensated cirrhosis	12 weeks
Treatment experienced, without cirrhosis	8 weeks
Treatment experienced, with compensated cirrhosis	12 weeks

- **Ledipasvir/sofosbuvir (Harvoni®)[4]**
  - Prior to requesting/initiating therapy with this agent, documentation of eGFR ≥30 mL/min is required for approval.

Patient characteristics	Treatment length
Treatment naïve, with or without cirrhosis	12 weeks
Treatment experienced, with or without cirrhosis	12 weeks

- **Ombitasvir/paritaprevir/ritonavir (Technivie®) and weight based ribavirin[9]**
  - Prior to requesting/initiating therapy with this agent in a patient with cirrhosis (stage F4 by Metavir), documentation of Child-Pugh status of A is required.

Patient characteristics	Treatment length
Treatment naïve, with or without cirrhosis	12 weeks
Treatment experienced, with or without cirrhosis	12 weeks

- **Sofosbuvir/velpatasvir (Epclusa®)[7]**
  - Prior to requesting/initiating therapy with this agent, documentation of eGFR ≥ 30 mL/min is required for approval.

Patient characteristics	Treatment	Treatment length

Patient without cirrhosis and with compensated cirrhosis (Child-Pugh A)	Epclusa	12 weeks
Patients with decompensated cirrhosis (Child-Pugh B and C)	Epclusa + weight based ribavirin	12 weeks

- **Sofosbuvir/velpatasvir/voxilaprevir (Vosevi ™)**
  - Prior DAA experience with an NS5A inhibitor
  - Prior to requesting/initiating therapy with this agent in a patient with cirrhosis (stage F4 by Metavir), documentation of Child-Pugh status of A is required.
  - Prior to requesting/initiating therapy with this agent, documentation of eGFR ≥ 30 mL/min is required for approval.

Genotype 5 and 6:

- **Glecaprevir/pibrentasvir (Mavyret ™)**
  - Prior to requesting/initiating therapy with this agent in a patient with cirrhosis (stage F4 by Metavir), documentation of Child-Pugh status of A is required.

Patient characteristics	Treatment length
Treatment naïve, without cirrhosis	8 weeks
Treatment naïve, with compensated cirrhosis	12 weeks
Treatment experienced, without cirrhosis	8 weeks
Treatment experienced, with compensated cirrhosis	12 weeks

- **Ledipasvir/sofosbuvir (Harvoni®)[4]**
  - Prior to requesting/initiating therapy with this agent, documentation of eGFR ≥30 mL/min is required for approval.

Patient characteristics	Treatment length
Treatment naïve, with or without cirrhosis	12 weeks
Treatment experienced, with or without cirrhosis	12 weeks

- **Sofosbuvir/velpatasvir (Epclusa®)[7]**
  - Prior to requesting/initiating therapy with this agent, documentation of eGFR ≥ 30 mL/min is required for approval.

Patient characteristics	Treatment	Treatment length
Patient without cirrhosis and with compensated cirrhosis (Child-Pugh	Epclusa	12 weeks

A)		
Patients with decompensated cirrhosis (Child-Pugh B and C)	Epclusa + weight based ribavirin	12 weeks

- **Sofosbuvir/velpatasvir/voxilaprevir (Vosevi ™)**
  - Prior DAA experience with an NS5A inhibitor
  - Prior to requesting/initiating therapy with this agent in a patient with cirrhosis (stage F4 by Metavir), documentation of Child-Pugh status of A is required.
  - Prior to requesting/initiating therapy with this agent, documentation of eGFR ≥ 30 mL/min is required for approval.

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Appendix A: Acceptable tests for determination of fibrosis in HCV

Noninvasive methods for determination of liver disease

Numerous noninvasive methodologies have been developed to determine the degree of fibrosis in patients infected with chronic HCV. These methodologies employ either the use of biomarkers or evaluation of liver stiffness to make a determination regarding the degree of liver fibrosis.[1] Below is a table of acceptable noninvasive testing and the score which is equivalent to metavir stage F2.

Noninvasive test	Score equivalent to metavir stage F2
FibroScan (transient elastography)	7.9 kPa[2]
Point shear wave elastography (pSWE) Acoustic radiation force impulse imaging (AFRI)	1.34 m/s[3]
MR elastography	3.66 kPa[4]
Hepascore ®/Fibroscore ®	0.2
Fibrosure®	0.48

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