Medicaid Reimbursement for Oral Direct Antiviral Agents for the Treatment of Chronic Hepatitis C

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SUPPLEMENTARY MATERIAL is linked to the online version of the paper at http://www.nature.com/ajg

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BACKGROUND

All-oral direct-acting antiviral (DAA) regimens are an excellent modality to treat chronic hepatitis C virus (HCV) infection. Federal Medicaid law requires states to cover all drugs from manufacturers with rebate agreements with the Department of Health and Human Services within their FDA label. However, because of their high cost, many state Medicaid agencies do not cover DAAs for those who have mild liver disease or who abuse substances (1,2). These restrictions persist despite many analyses that confirm that DAA regimens are cost-effective (reduce the cost per quality-adjusted life year) (3,4) and result in savings in healthcare spending (5). We sought to assess whether and how these restrictions have changed since oral DAAs first came on the market. On the basis of our experience and anecdotal evidence, we expected that despite loosening of restrictions, the majority of states have restrictions in excess of those recommended by professional societies.

METHODS

We searched publicly available state fee-for-service (FFS) Medicaid websites from 20 August 2016 to 10 September 2016 to obtain reimbursement criteria for DAAs. We reviewed reimbursement criteria across several domains, including: liver fibrosis, decompensated cirrhosis, biopsy requirement, prescriber specialty, HIV status, renal function, and substance abuse. We documented which DAAs were covered, and in cases in which criteria differed between agents, the most liberal or inclusive criteria were used. Inconsistencies and gaps were resolved by direct phone calls to state Medicaid agencies. We included policy criteria that were in effect or stated on state Medicaid documents to take effect on a future date; future policies reported by media sources without state confirmation were not included. Coverage requirements for DAA regimens were compared with reimbursement criteria for sofosbuvir in 2014 as summarized by Barua *et al.* (1).

RESULTS

Of the 50 states and the District of Columbia (D.C.), we found Medicaid reimbursement criteria published online for all but New Jersey, whose agency provided criteria by direct communication following telephone request, and Hawaii, whose Medicaid representatives were not aware of any formal criteria. Online documentation for the remaining states was not uniform and was found in various documents, including prior authorization forms, preferred drug lists, clinical criteria sheets, and memoranda. Multiple states had discrepancies between prior authorization forms and published clinical criteria. Some criteria and prior authorization forms were not up to date or were incorrect upon review with state administrators.

Many states have loosened restrictions since 2014 (**Table 1**; **Table 2**). Fifteen states loosened restrictions based on fibrosis; none tightened restrictions (**Figure 1**). Twenty-nine states cover patients with decompensated cirrhosis but five explicitly exclude such patients and twenty-two states restrict coverage to patients with a METAVIR score of F3–4. Only South Dakota requires biopsy. Thirty-four states require a specialist (e.g., gastroenterologist, hepatologist, or infectious disease physician) or consultation with a specialist to prescribe DAAs. Some states (Minnesota, Montana, New Hampshire, New York, Rhode Island, and Washington State) allow certain other practitioners with special training to also prescribe DAAs.

Nineteen states require patients to pass a drug screen prior to treatment. Five states require abstinence from alcohol and drugs in patients with a history of abuse, while 20 states require abstinence in all patients. Nine states require periodic drug testing. Seven states cover patients co-infected with HCV and HIV regardless of fibrosis score. Six states require such patients to have HIV under control (e.g., meet a target CD4 or have an HIV viral load under a specified threshold). Six states do not reimburse DAAs for patients with creatinine clearance of <30 ml/min or with end-stage renal disease (ESRD).

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Table 1. Summary of clinical criteria for reimbursement of DAAs (number of states including the District of Columbia)

Minimum fibrosis	2014[a]	2016
F0	N/A	7
F1	1	0
F2	2	14
F3	27	21
F4	4	1
Decompensated Cirrhosis		
Eligible	7	29
Ineligible	1	5
Biopsy		
Not required	0	34
Required	5	1
Drug testing before treatment		
History of abuse[b]	4	3
All patients	21	16
Requires period of abstinence from alcohol and drugs		
History of abuse[b]	9	5
All patients	21	20
Random/periodic drug testing		
History of abuse[b]	N/A	7
All patients	N/A	2
HIV		
Automatic coverage	N/A	7
Requires control	11	6
Other restrictions		
Excluded if CrCl <30 ml/min or ESRD		6
Must be naive to DAAs		6
Prescriber		
By or in consultation with specialist	15	22
By specialist	14	12
Drugs covered		
Daklinza		41
Epclusa		18
Harvoni		47
Olysio		43
Sovaldi		44
Technivie		43
Viekira Pak		39
Zepatier		39

[a]As published by Barua *et al.* (1).
[b]Patients with a history of alcohol abuse or illicit/IV drug use.

The majority of states cover one or more newer combination regimens other than sofosbuvir-ledipasvir (Harvoni). Sofosbuvir-velpatasvir (Epclusa), ombitasvir-paritaprevir-ritonavir (Technivie), ombitasvir-paritaprevir-ritonavir and dasabuvir (Viekira Pak), and elbasvir-grazoprevir (Zepatier) are covered in 18, 43, 39, and 39 states, respectively. A state-by-state representation of all restrictions is provided in **Supplementary Figure 1**. The current analysis is limited to publicly available sources by state Medicaid agency FFS programs, which vary in accuracy and are subject to change. We have provided web address links to publicly available sources in **Supplementary Table 1**.

DISCUSSION

In this study we provide a contemporary update to a survey of state Medicaid criteria for all-oral DAA regimens published by Barua *et al.* (1), expanding the analysis to include all FDA-approved regimens beyond sofosbuvir/ledipasvir, and clarifying reimbursement policies by direct communication with state officials, largely due to confusing, opaque, and/or discordant policy language on publicly available policy documents. We find that although clinical criteria have been loosened by most measures, a substantial number of states continue to restrict access. Nearly all states require some minimum level of fibrosis and nearly half limit reimbursement to patients with advanced fibrosis or cirrhosis.

These restrictions appear to persist despite conflict with federal Medicaid law, major medical society guidelines, legal challenges in federal courts, ongoing improvement and expansion of treatment options, and the significant cost-effectiveness data to support broad treatment of chronic HCV. In November 2015, the Centers for Medicare & Medicaid Services (CMS) released a Program Notice to state Medicaid agencies to clarify that access to all FDA-approved medications for "medically accepted indications" is protected by federal statute (6), likely in response to the emerging data confirming that risk-adjusted likelihood of denial for HCV treatment is four times greater for Medicaid patients compared to those with Medicare or private insurance (7). Several legal challenges to restrictive Medicaid reimbursement criteria are currently in process, and others have already contributed to loosening of criteria (8–11). Similar legal challenges have been raised against private insurers (12).

Guidelines from the American Association for the Study of Liver Disease (AASLD) and the Infectious Diseases Society of America (IDSA) support treatment for all patients with chronic hepatitis C who do not have short life expectancy (13). The continued restriction of appropriate DAA regimens to patients with decompensated cirrhosis or ESRD is particularly concerning, given their higher risk for kidney and liver-related morbidity, mortality, and transplant (14,15). The FDA has approved multiple agents for decompensated cirrhosis (13) and has approved elbasvir-grazoprevir (Zepatier) in renal dysfunction based on safety and efficacy data in patients with CKD stages 4 and 5 (16,17). Surprisingly, two states that exclude patients with renal dysfunction list Zepatier as a preferred agent.

Table 2. Major clinical criteria for reimbursement by state

	Minimum fibrosis		Decompensated cirrhosis		Requires abstinence from drugs and alcohol		Specialist prescriber	
State	2014[a]	2016	2014[a]	2016	2014[a]	2016	2014[a]	2016
Alabama					6 months			
Alaska	F3	F2	Eligible	Eligible	3 months			
Arizona	F3	F3		Ineligible			Consult	Consult
Arkansas	F3	F3						Required
California	F3	F2					Consult	
Colorado	F3	F2	Ineligible	Eligible	6 months	6 months	Consult	Consult
Connecticut	F4	F0					Consult	
Delaware	F4	F3		Eligible	3 months			
D.C.	F3	F2	Eligible	Eligible	3 months		Consult	Consult
Florida	F3	F0		Eligible	1 month	1 month	Required	Consult
Georgia								
Hawaii								
Idaho	F3	F3	Eligible	Eligible		6 months	Consult	Consult
Illinois	F4	F4		Ineligible	12 months	12 months	Consult	Consult
Indiana	F3	F2		Eligible			Required	Consult
Iowa	F3	F3		Eligible	3 months	3 months	Required	Required
Kansas		F3		Eligible		6 months		Consult
Kentucky	F3	F3	Eligible	Ineligible	6 months	6 months	Consult	Consult
Louisiana	F3	F3		Eligible	12 months	12 months	Required	Required
Maine	F1			Eligible		6 months	Required	Consult
Maryland	F2	F2		Eligible			Required	
Massachusetts		F0		Eligible				
Michigan		F3		Eligible				Consult
Minnesota		F0		Ineligible		6 months		Consult
Mississippi				Eligible	6 months	6 months	Consult	Consult
Missouri	F3	F3			3 months			
Montana	F3	F3			6 months	6 months	Consult	Required
Nebraska	F3	F3		Eligible				
Nevada				Eligible				
New Hampshire	F3	F0				Not required	Required	
New Jersey		F2						Required
New Mexico		F2		Eligible				
New York	F3	F0					Required	Consult
North Carolina		F2		Eligible				
North Dakota		F2		Eligible		12 months		Consult
Ohio	F3	F3		Eligible		6 months	Required	Required
Oklahoma	F2	F2	Eligible	Eligible	6 months	6 months	Consult	Consult
Oregon	F4	F3			6 months		Consult	Consult
Pennsylvania	F3	F2			6 months		Required	Required
Rhode Island	F3	F3		Eligible			Required	Required

Table 2 continued on following page

Table 2. Continued

	Minimum fibrosis		Decompensated cirrhosis		Requires abstinence from drugs and alcohol		Specialist prescriber	
State	2014[a]	2016	2014[a]	2016	2014[a]	2016	2014[a]	2016
South Carolina		F3				6 months		
South Dakota	F3	F3			6 months	6 months	Consult	Required
Tennessee	F3	F3	Eligible	Eligible		6 months	Required	Required
Texas		F3		Eligible				Required
Utah				Eligible				Consult
Vermont	F3	F3		Eligible		6 months		Consult
Virginia	F3	F2			6 months		Consult	Consult
Washington	F3	F0	Eligible	Ineligible			Required	Consult
West Virginia	F3	F3		Eligible	6 months	3 months	Consult	Consult
Wisconsin	F3	F2		Eligible	6 months		Required	Required
Wyoming					1 month			

[a]As published by Barua *et al.* (1).

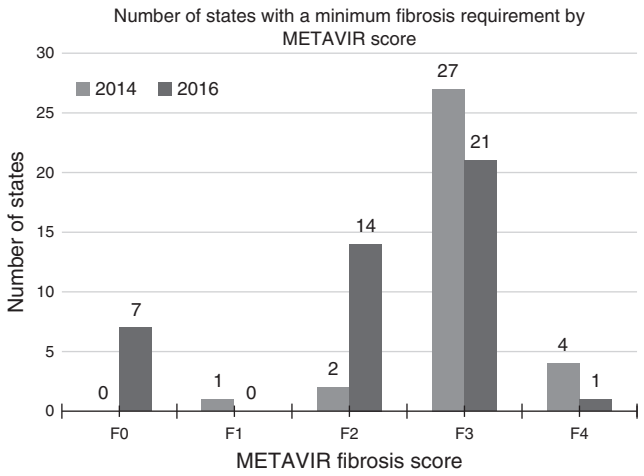

Figure 1. Number of states with a minimum fibrosis requirement by METAVIR score. Data from 2014 as published by Barua *et al.* (1).

Cost-effectiveness studies, which have evaluated models of HCV treatment from payor and societal perspectives and across the lifetime horizon, consistently support broad HCV treatment across all stages of liver fibrosis based on rapid, durable improvement in clinical outcomes, and long-term reduction in liver-related morbidity and mortality (18–20). Even using cost estimates from wholesale acquisition cost (WAC) rather than lower negotiated drug prices, the incremental cost of universal treatment remains below traditional thresholds of willingness to pay (21,22) and is associated with a decrease in overall cost of healthcare over a patient's lifetime (5).

However, even in the face of favorable cost-effectiveness data, the combination of high drug prices (WAC range of $54,600–94,500 for a 12 week course) and high demand for all-oral DAA regimens has generated significant concern by payors regarding the feasibility of covering the cost of HCV treatment for all eligible patients. Prescription drug expenditures by Medicaid rose 24.3% in 2014 when the first all-oral DAA regimen was released, driven in part by uptake of new DAA regimens (23), and directly contributing to restrictive policies, which "prioritize" DAA therapy for patients perceived to have the most urgent need for HCV treatment such as those with advanced fibrosis (24). The combination of increasing market competition, organized advocacy efforts, and shortening of treatment regimen duration may help to decrease drug prices over the next several years, which in turn may improve access to DAA regimens across payors.

The historically rapid pace of drug development and evolution of preferred treatment strategies for hepatitis C between 2013 and 2016 (10 new FDA-approved DAAs) has likely contributed to the chaotic implementation of payor reimbursement policies. In recognition of the need to provide real-time changes in treatment recommendations in response to the emerging clinical trial data and FDA approvals, the AASLD and IDSA HCV guidelines now represent a live online document (www.hcvguidelines.org), which is updated regularly, including three guideline revisions in 2016 alone (13). More efficient models are needed to translate new clinical evidence, FDA labels, and guideline recommendations to facilitate timely reviews and formulary updates by state Medicaid agencies and other payors.

We advocate for rapid and universal coverage of DAA regimens, which are safe and efficacious across all genotypes and stages of fibrosis, including special populations such as decompensated cirrhosis, post-transplant, HIV co-infection, and ESRD. Although some have proposed mandatory licensing and healthcare legislation as a path towards price control (25), this has not been successful in the past (26) and current uncertainty regarding the future of

the Affordable Care Act presents a challenge to efforts to implement important policy changes to entitlement programs including Medicaid (27–29). A combination of patient and provider advocacy, engagement of key medical specialty societies, selective legal actions, increased market competition with approval of new DAA regimens (30), evidence-based practice guidelines, and further strengthening of cost-effectiveness data (payor perspective) (31) is likely needed to support further expansion of drug coverage by public and private payors.

CONCLUSION

Clinical criteria for the reimbursement of DAAs by state Medicaid agencies suggest a loosening of restrictions between 2014 and 2016. Yet significant barriers to hepatitis C drug access remain, largely based on factors such as stage of liver fibrosis, substance abuse, and medical comorbidities. These restrictions appear to be in conflict with federal Medicaid law and national practice guidelines. Coordination of state Medicaid plans to establish evidence-based, transparent, and cost-effective policies are needed to promote a more rational and patient-centered approach to coverage of DAAs for the treatment of HCV.

CONFLICT OF INTEREST

Guarantor of the article: Joseph K. Lim, MD.

Specific author contributions: Kohtaro Ooka designed and planned the study, collected and interpreted the data, drafted the manuscript, and approved the final draft submitted. James J. Connolly collected and interpreted the data, drafted the manuscript, and approved the final draft submitted. Joseph K. Lim designed and planned the study, collected and interpreted the data, drafted the manuscript, and approved the final draft submitted.

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