CALIFORNIA TECHNOLOGY ASSESSMENT FORUM℠

Next Steps for *Clinicians*: An Action Guide on the Newest Treatments for Chronic Hepatitis C Infection

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Introduction

About This Guide

Evidence from clinical research, which informs effectiveness reviews, provides a critical foundation for judgments that patients, clinicians, and health insurers must make about treatment choices and coverage policies. Yet that evidence is often not translated in a way that is helpful to inform health care decisions. This document is a companion action guide designed to help clinicians make use of the results of a recent technology assessment entitled "*The Comparative Clinical Effectiveness and Value of Novel Combination Therapies for the Treatment of Patients with Genotype 1 Chronic Hepatitis C Infection*" developed by the Institute for Clinical and Economic Review (ICER) and faculty/researchers at the University of California, San Francisco. This report formed the basis for the deliberations and votes of the California Technology Assessment Forum (CTAF) Panel – an independent committee of medical evidence experts from across California, with a mix of practicing clinicians, methodologists, and leaders in patient engagement and advocacy, who evaluate evidence and vote on the comparative clinical effectiveness and value of medical interventions. All CTAF Panel members meet strict conflict of interest policies.

CTAF held its public meeting on the newest treatments for hepatitis C on December 18, 2014 in Oakland, California. A full report summarizing the discussion and votes taken is available on the CTAF website. We have developed this Action Guide to provide a list of specific action steps that clinicians can take to improve patient outcomes and the overall value of treating patients with chronic hepatitis C, genotype 1. This guide serves as a companion to the evidence review and meeting results. The content provided here is for informational purposes only, and it is not designed to replace professional medical advice.

A Note on CTAF Evidence Voting

Each public meeting of CTAF involves deliberation and voting on key questions on the comparative clinical effectiveness and value of the various diagnosis and treatment options discussed. When voting, the CTAF Panel members are asked to assume the perspective of a state Medicaid program making resource allocation decisions within a relatively fixed budget.

Action Steps for Clinicians

This guide is intended to provide clinicians with a series of action steps that can be taken to improve patient outcomes and the overall value of treating patients with chronic hepatitis, genotype 1. These action steps reflect 1) the CTAF Panel's judgment of published evidence as of December 2014, and 2) best practices discussed by subject matter experts during a policy roundtable discussion at the CTAF meeting.

1. **For patients that would benefit from and desire treatment, select from several highly-effective and safe new treatments for hepatitis C, taking into account patient insurance coverage/out-of-pocket expenses.**

Research evidence shows that several treatment regimens for patients with hepatitis C, genotype 1 are equivalent in terms of clinical effectiveness – the newest combination direct-acting antiviral agents (DAAs)[1] eliminate the virus from the bloodstream for at least 12 weeks following the end of treatment in up to 95-100% of participants enrolled in clinical trials. The new combination DAA therapies have fewer side effects than older regimens containing interferon. The new therapies differ in terms of number of daily pills (1, 2 or 4), treatment duration (8, 12, 24 or 48 weeks), and the addition of ribavirin (typically two pills daily).

Ideally, all patients who seek and would benefit from treatment would be able to obtain the newest therapies. Given treatment capacity constraints and limits on financial resources, however, priority for treatment may still need to be given to patients with advanced liver disease or those who are at high risk of infecting others with hepatitis C through injection drug use or sex without using a condom.

Given the cost of these treatments, clinicians should talk with patients who express concerns about cost or insurance coverage and refer them to available resources such as health insurance programs or patient assistance programs offered by manufacturers (see action step #6). Several health plans and pharmacy benefit managers (PBMs) have selected one drug regimen as the preferred therapy among the various FDA-approved treatments, so clinicians should consider the patient's insurance coverage and/or other cost considerations when prescribing one of the therapies over another.

Examples of the preferred therapies for some public and private payers are described here:

- http://www.nytimes.com/2015/02/04/business/sales-of-sovaldi-new-gilead-hepatitis-c-drug-soar-to-10-3-billion.html?_r=0

[1] FDA-approved combination DAAs for the treatment of hepatitis C genotype 1, as of December 19, 2014, were ledipasvir/sofosbuvir, simeprevir + sofosbuvir, and paritaprevir/ritonavir/ ombitasvir + dasabuvir (3D) with or without ribavirin.

- http://www.stltoday.com/news/special-reports/mohealth/missouri-to-drop-expensive-hepatitis-c-drug-sovaldi-use-alternative/article_0f2a8964-d4bc-5362-8d41-b10e65d13408.html

2. Consider creating a system to screen and identify patients with hepatitis C, track them over time, and prioritize treatment in the short term with an ultimate goal of treating all infected patients.

To better understand and address the needs of patients with hepatitis C, clinicians and provider groups should consider developing a comprehensive system to identify these patients; assess their need for treatment, including tracking them to see how those needs evolve over time; and treat patients to the extent possible given system resources, with a priority given to patients with advanced liver fibrosis or who are at high risk of infecting others. Individual clinicians play an important role in recommending screening and following up with patients, as well as discussing treatment options and timing.

Our analyses showed that a strategy of treating patients at all fibrosis stages rather than waiting to treat patients until they reached fibrosis levels F3 or F4 provided a net clinical benefit for the population and met commonly accepted cost-effectiveness thresholds. Given the slow progression of fibrosis in most patients, especially among those who have been infected for many years and have remained at fibrosis levels F0-F2, priority should be given to efforts to identify and treat patients with more advanced liver disease. Some systems of care are prioritizing treatment in this way and not recommending treatment for patients with F0-F2 fibrosis; other systems, however, are treating patients at any level of fibrosis who present and desire treatment.

Some integrated care systems have registries with data on their patients with hepatitis C. To date, these registries have been used primarily for tracking patients and conducting analyses on outcomes after treatment, but their use could be expanded to prioritize patients for treatment based on patient characteristics.

Kaiser Permanente Northern California has a viral hepatitis registry that includes administrative and clinical data for all patients with chronic hepatitis C. More information may be found at these links:

- http://share.kaiserpermanente.org/article/successful-hepatitis-c-treatment-lowers-subsequent-medical-costs/
- http://amcp.org/WorkArea/DownloadAsset.aspx?id=16750

The Department of Veterans Affairs (VA) has a hepatitis C Clinical Case Registry (CCR) that contains data from electronic medical records, is available at each VA facility, and is accessible to HCV clinicians by request. Providers can generate facility-specific reports on patients with hepatitis C

stratified by cirrhosis, genotype, prior treatment experience, and other clinical considerations. This can be used to identify patients with the most urgent need for treatment. The VA's February 2015 updated treatment considerations document addressing the newest DAA therapies describes the CCR on page 8:

- http://www.hepatitis.va.gov/pdf/treatment-considerations-2015-02.pdf

Additional information on the CCR can be found at these links:

- http://www.va.gov/vhapublications/ViewPublication.asp?pub_ID=2420
- http://archinte.jamanetwork.com/article.aspx?articleid=1763967

3. **Because the new, all-oral treatments for hepatitis C are easier to administer and monitor, it is reasonable over time for some primary care physicians to prescribe these therapies, as long as they have ready access to specialists in treating patients with hepatitis C.**

Prior hepatitis C treatments were prescribed primarily by specialists. After there is more experience using the new, all-oral therapies, a broader group of health care providers, including primary care physicians who have been educated and trained in hepatitis C treatment, may be able to safely prescribe them. However, it is important that primary care physicians can readily access experts in treating hepatitis C for guidance on questions that arise during treatment. Bringing nurse practitioners and pharmacists into the care process is also reasonable, as they can supplement the information provided by physicians and provide additional resources. Pharmacists, for example, can perform comprehensive reviews of all prescriptions and over-the-counter medications/supplements to identify any drug-drug interactions and ensure that it is safe for the patient to take their various drugs, explain how medicines and supplements may interact with each other, and review the importance of taking all of the prescribed pills.

More information on a national PBM that recently changed its coverage policies to allow primary care physicians to prescribe the new combination DAAs is available here:

- http://www.nytimes.com/2014/12/22/business/pharmacy-deal-heralds-changed-landscape-for-hepatitis-drugs.html?_r=0

The VA's February 2015 hepatitis C treatment considerations document indicates that, in addition to specialists, treatment can be provided by non-specialists, including general internist or family medicine physicians, who have been educated and trained in hepatitis C therapy and have access to specialists for support. See page 7 for more information:

- http://www.hepatitis.va.gov/pdf/treatment-considerations-2015-02.pdf

4. **Participate in programs to help build treatment capacity so that more health care providers can prescribe these new, all-oral hepatitis C therapies, allowing more patients to access them.**

Expanding the types of providers prescribing these new treatments is one step toward a goal of getting more patients access to care sooner. To advance this goal, provider groups and specialists in treating hepatitis C should work together to train more primary care providers to care for patients with this condition. Care teams that pair a specialist who has extensive experience in treating hepatitis C patients with a primary care physician, social worker, nurse practitioner, pharmacist, and other personnel could greatly increase treatment capacity.

One example of a program that helps build treatment capacity is Project ECHO® (Extension for Community Healthcare Outcomes), which is a collaborative model of medical education and care management using telemedicine. Its long-standing program based in New Mexico increases access to specialty treatment in *rural*, underserved areas by providing front-line clinicians with the knowledge and support they need to manage patients with complex conditions such as hepatitis C. This model has been shown to be extremely effective in terms of patient outcomes and is very popular with primary care physicians. More information may be found at these links:

- http://echo.unm.edu/
- http://echo.unm.edu/nm-teleecho-clinics/hepatitis-c-community-clinic/

In 2014, The University of Chicago Medicine received a grant from the Centers for Disease Control and Prevention (CDC) to lead a public health collaboration aimed at reducing hepatitis C infections in Chicago through education, testing, and treatment. The ECHO-Chicago program seeks to significantly increase the number of community-based primary care providers trained to diagnose and treat HCV, particularly in *urban*, underserved communities. More information is available here:

- http://www.uchospitals.edu/news/2014/20141009-hepccatt.html
- http://www.echo-chicago.org/

5. **Select patients who are most likely to adhere to the treatment regimen associated with the new, all-oral therapies for hepatitis C, and emphasize the importance of adherence to achieving successful outcomes.**

The high success rates of treatment with the newest therapies were achieved in clinical trials with highly motivated and adherent patients. To achieve the full benefit of all-oral hepatitis C therapies and avoid development of treatment-resistant strains of the virus, clinicians should identify those patients most likely to be adherent to the treatment protocol for its entire duration (8-48 weeks). Providers may wish to talk with patients about the need to plan ahead so they can afford the copayments for the entire treatment period.

Provider groups may wish to implement programs, or partner with payers to implement programs, that involve patient outreach to improve adherence; these may involve phone calls from members of the patient's care team, text messages, support groups, etc.

Some examples of patient support tools to enhance adherence to hepatitis C treatment regimens may be found at these links:

- AbbVie (for patients with a prescription for Viekira only, designed to provide personalized treatment support): https://www.viekira.com/proceed-program
- Accredo Plus C (free iPhone application designed to help hepatitis C patients manage treatment): https://itunes.apple.com/us/app/accredo-plus-c/id885883930?ls=1&mt=8

6. Provide psychosocial supports and resources to help patients through treatment.

Although there are far fewer reported side effects from the newest treatments for hepatitis C, the treatment process can still be challenging for patients, particularly those with advanced liver disease. Patients and their families may benefit from connections to social workers or other care coordinators who can help address medical and psychosocial needs. Patients and their families experiencing a significant financial burden associated with the new treatments may need help from other social service agencies for assistance with housing, food, employment, etc. as the patient is going through treatment.

While public and private health plans may be able to negotiate discounts on the price of the all-oral treatments, patients who are uninsured and without significant financial resources may have difficulties accessing treatment. Individuals with low income may be eligible to enroll in public health insurance programs, or they may be able to obtain assistance from the patient assistance programs that manufacturers of these drugs offer. Patients who have health insurance but who cannot afford high out-of-pocket costs (deductibles, copayments, coinsurance) that would effectively limit their access to these treatments may also seek assistance from manufacturers' patient assistance programs.

More information on health insurance and patient assistance programs may be found at these links:

Health Insurance:

- California Department of Health Care Services: http://www.dhcs.ca.gov/Pages/default.aspx
- Covered California: http://www.coveredca.com/

Patient assistance programs:

- AbbVie: https://www.viekira.com/proceed-program
- Gilead: http://www.mysupportpath.com/
- Janssen/Johnson & Johnson: https://support.olysio.com/co-pay-assistance

- Partnership for Prescription Assistance: https://www.pparx.org/
- Patient Access Network (PAN) Foundation: www.panfoundation.org

7. Clinician groups that manage financial risk should partner with health plans and PBMs to develop payment/pricing and policy mechanisms that support appropriate and financially sustainable use of highly effective, expensive treatments for hepatitis C and other conditions.

The newest treatments for hepatitis C, and similarly effective, expensive therapies for other conditions, at the individual patient level, represent a high care value.[2] However, when large numbers of patients are eligible for treatment, the potential budget impact raises stark financial challenges for health systems. Policy action is needed to design mechanisms that can achieve lower drug prices and/or create new payment models to moderate short-term budget impacts. Several examples of innovative payment and policy approaches are described below. The overall goals of these various policy and payment mechanisms include sustaining innovation, linking prices to the underlying degree of benefit (care value), and helping to identify budget impact problems ahead of time so collaborative solutions can be implemented.

Payment/Pricing

- Pay for outcomes rather than for the treatment (e.g., if a patient doesn't achieve the desired clinical benefit, the manufacturer refunds the payment; alternatively, the manufacturer receives payment only when a patient achieves the desired clinical outcome)
- Negotiate price volume agreements with manufacturers so that prices continue to decrease with increasing volume. When alternatives exist in the marketplace, consider making one of them the preferred treatment in order to move market share and lower price. For clinicians, this would require frank dialogue about clinical equivalency and safety, as well as willingness to change practice in pursuit of affordability.

Policy

- Engage other stakeholders including the public in a broad discussion of manufacturer pricing and encourage advocacy for more affordable prices
- Use data to collaboratively identify opportunities to disinvest from low value care and eliminate waste in the health care system, so that the savings can be redirected to higher value options now and in the future

[2] Care value is a judgment comparing the clinical outcomes, average per-patient costs, and broader health effects of two alternative interventions or approaches to care.

- Develop a mechanism that would allow more anticipatory, collaborative policymaking between manufacturers, payers, and other stakeholders so that preventive policy actions can be taken when drugs that will have large budget impacts are on the horizon

More information on cost issues and potential solutions for Medicaid programs (specific to hepatitis C treatments, but applicable to specialty drugs in general) are available here:

National Association of Medicaid Directors letter to Congressional leaders on policy options:

- http://medicaiddirectors.org/sites/medicaiddirectors.org/files/public/namd_sovaldi_letter_to_congress_10-28-14.pdf

American Academy of Actuaries letter to the Centers for Medicare & Medicaid Services (CMS) on challenges related to cost uncertainties for breakthrough therapies:

- http://actuary.org/files/Medicaid_capitation_rates_and_BTD_medications_Letter_to_CMS_Nov%2011.pdf

More information on *payment/pricing* mechanisms, including risk-sharing arrangements, in the US and other countries may be found at these links:

- Health Affairs article: http://content.healthaffairs.org/content/30/12/2329.abstract
- International Society For Pharmacoeconomics and Outcomes Research conference presentation: http://www.ispor.org/meetings/montreal0614/presentations/IP9-AllSpeakers.pdf
- VA presentation: http://www.amsus.org/wp-content/uploads/2014/05/RxRiskSharingAgreements_Good1.pdf

More information on *policy* mechanisms may be found at these links:

Initiative to make drugs more affordable:

- National Coalition on Health Care (NCHC): http://www.nchcbeta.org/
- NCHC Campaign for Sustainable Drug Pricing: http://www.csrxp.org/

Disinvestment in health care services (in the UK and Australia):

- Journal of Health Organization and Management article on efforts in the UK: http://www.ncbi.nlm.nih.gov/pubmed/24422258
- Implementation Science article on efforts in Australia: http://www.implementationscience.com/content/7/1/101