

**Department of  
Veterans Affairs**

# Memorandum

Date: May 20, 2015

From: Acting Executive Director, National Center for Ethics in Health Care (10P6)

Subj: Protocol for Prioritizing HCV Treatment: An Ethical Framework

To: ADUSHOM for Clinical Operations, ADUSH for Patient Care Services

Cc: Interim Under Secretary for Health; Deputy Under Secretary for Health for Policy and Services; Deputy Chief, Public Health; Chief Consultant, Pharmacy Benefits Management; Director, HIV/HCV & Public Health Pathogens Program; National Director of Gastroenterology; Dr. Douglas Heuman; Dr. Timothy Morgan

Based on VA's mission and I CARE core values and characteristics which are ethically imperative and established by regulation, the most appropriate approach to resolving resource scarcity for Hepatitis C (HCV) treatment is for the agency to make exhaustive attempts to secure sufficient resources to treat all patients prior to implementing plans to deny or delay treatment to any patients for whom treatment is clinically indicated.

Since prioritizing patients is ethically challenging, and far inferior to augmenting resources to accommodate all patients for whom treatment is indicated, the details of the attempts to secure additional resources should be made **public**. This provides **accountability** for the decision-makers at all levels of the organization. These efforts should be **clearly and candidly** described to the Veterans, providers, and staff who would be asked to participate in a prioritization plan.

Should the attempts to secure sufficient resources fail, this memorandum provides recommendations concerning an ethical framework that should guide resource allocation decisions for HCV treatment in VHA. A protocol for **consistent, fair, and transparent** decision making regarding initiation of antiviral therapy in patients with confirmed HCV when resources are insufficient to treat all patients for whom the treatment is clinically indicated is included in the Appendix.

## **Ethical Framework:**

1. All activities related to resource allocation decisions for Hepatitis C treatment in VHA should be **informed** by a wide-range of relevant subject matter experts, **transparent** to all involved parties and stakeholders, and **consistently implemented** system-wide.

2. Efforts should be made to **augment** resources to meet clinical needs prior to implementing practices that limit patient access to clinically indicated treatments or procedures. For Hepatitis C treatment in VHA, this might include:

- a. Assuring that all resources allocated for Hepatitis C treatment are being used for that purpose,
- b. Redistributing Hepatitis C resources if there are areas in the system that are not using their allocation,
- c. Seeking an increase in appropriation for Hepatitis C treatment funds, and
- d. Providing patients Hepatitis C treatment under all legal authorities granted to the Veterans Health Administration (e.g., via VA community partners through the Choice Act).

3. If attempts to augment resources have been exhausted, and there are more patients who have clinical indication for treatment than resources to treat them, a protocol for **prioritization** of patients for treatment should be developed, made known to all involved parties and stakeholders, and consistently implemented system-wide. This protocol (Appendix) should be frequently reviewed and adjusted if needed to account for new information regarding either resource availability or clinical information that would impact the rationale for prioritization. The protocol for patient prioritization is based on development/implementation of a set of exclusion and inclusion criteria for use system-wide:

a. Clinical Exclusion Criteria

Consistent with **respect for patient self-determination**, patients who do not want the treatment should not receive it. Consistent with effective resource **stewardship** and the principle of **utility**, the treatment should be allocated to achieve the greatest good for the greatest number. The treatment should not be offered to patients who would not benefit from it or to patients for whom it would be of limited benefit when it can be more effectively used to treat others. However, based on the principles of **equity** and **human dignity**, patients determined to meet an exclusion criterion should be provided all other appropriate medical care and support.

b. Clinical Inclusion Criteria

The use of inclusion criteria is based on the principles of **beneficence and utility**; that is, obtaining the maximum benefit from the available resources.

- i. Patients who have clinical indication for the treatment and are not excluded by the aforementioned criteria need to be further stratified into a hierarchy for treatment (e.g., priority groups). This hierarchy should be

based on which patients are most likely to benefit from the treatment, and which patients would be least harmed by delaying treatment.

- ii. A fair and consistent process for use of limited resources requires that patients be treated by order of priority group. If there are more patients in a priority group than there are resources to treat, then a transparent and consistent method of further prioritizing patients within each group is needed. Since patients within each group will be clinically similar, prioritization within a group that cannot be completely accommodated should be based on non-clinical criteria (e.g., first-come, first-served or randomization, such as ranking by last 2 digits of the patient's social security number).

c. At present, we are aware that groups at the VISN/facility level are developing and implementing criteria on their own. This *ad hoc* approach will unquestionably lead to inconsistency, lack of fairness, and ethically challenging practices, exposing VA not only to media and reputational risk, but also to pressure from stakeholders (e.g., members of Congress, VSOs) seeking to satisfy the requests of their individual constituents. An ethically informed and transparent protocol for scarce HCV resource allocation will be the basis for **consistent**, **defensible**, and **accountable** decision making across the system.

d. Implementing the protocol for scarce HCV resource allocation will require establishing HCV treatment prioritization teams that function at the highest organizational level practical to ensure **accountability** in maintaining information on the population of patients appropriate for HCV treatment and prioritizing those patients based on the protocol.

e. An appeals process based on claims of failure to adhere to the established allocation protocol, rather than appeals for an exception to the protocol itself, should be established to ensure **fairness** and **procedural justice** for prioritization decisions. Additional appeals for exceptions to the protocol should follow the normal clinical appeals process with input from the National HIV, HCV, and Public Health Pathogens Programs, and the National Center for Ethics in Health Care.

4. **Stewardship of resources** is an important ethical principle that should be considered when choosing between the various available Hepatitis C regimens since both cost and the burden on patients varies considerably among the treatments. If one regimen is clearly clinically better for a patient, he/she should receive it irrespective of differential cost. If the regimens are essentially clinically equivalent (e.g., equivalent efficacy and equivalent potential for significant) then, and only then, is cost justifiable as a factor to use when deciding among available treatments.

5. **Transparent, timely communications.** Health care resource allocation decisions, especially those that limit clinically indicated treatments or procedures for some patients based solely on lack of available resources, are among the most ethically complex and

nuanced health care decisions. The importance of **including all relevant parties' values and perspectives** at all levels of decision-making, the ability to provide rationale/justification for all decisions, complete **honesty** and **transparency** throughout the process, and consistent implementation system-wide are essential to maintain **trust and integrity** in our system. Without clear communication about why prioritization is necessary, it can be very controversial and damaging. To this end, implementing the recommendations in this document will require development of a communication plan to include messages from the highest level of VA leadership to VISNs, VAMCs, field staff, providers and patients as well as scripting for consistent communication by clinicians to patients who cannot be prioritized for HCV treatment at this time.

6. The protocol recommended here (Appendix) was developed on a very short timeline. The process for developing it included engagement of relevant clinical stakeholders throughout the organization. Stakeholders generally agreed with the clinical exclusion criteria – which are based on the principle that limited benefit to these patients does not justify using a resource that is scarce when it can be more effectively used to treat others. There was also general agreement that the clinical inclusion criteria should be structured to enable the **sickest patients who will benefit from the treatment** to receive priority over those who are less ill. Those patients will derive immediate benefit from the treatment and would be harmed most by delaying treatment. This approach is consistent with triage decision making where clinical assessment is used to optimize the use of resources that are insufficient to meet the needs of all patients concurrently. The presumption of triage, applicable in the case of HCV drugs as well, is that everyone will eventually be treated, but those who are less ill will wait longer for the treatment. This principle was expressed in the April 22, 2015 letter from VA practitioners to the VA Secretary and Under Secretary for Health that VA should focus on “treating every hepatitis C infected Veteran with advanced liver disease within the next 6-12 months and the remaining hepatitis C infected Veterans over the next three years.”

During development of the prioritization protocol, there were differences of opinion about the clinical validity and usefulness of the Model for End-stage Liver Disease (MELD) scores and criteria used by the American Association for the Study of Liver Disease and Infectious Diseases Society of America as a basis for patient inclusion.<sup>1</sup> As a result, and in an effort to provide guidance that can be used as soon as possible, we have provided a set of inclusion criteria targeted to the patients with advanced liver disease. The inclusion criteria were developed with input from subject matter experts on the National VA Hepatitis C Technical Advisory Group (TAG) and the Gastroenterology Field Advisory Group (FAC). Due to the short timeframe available for development of these recommendations, it was not possible to allow reiterative rounds of revision of the document prior to voting. Only a minority of members of the TAG and FAC voted, but the consensus vote was to approve these recommendations as an initial prioritization scheme.

To develop further prioritization levels, we recommend that a workgroup of clinical subject matter experts be established to deliver additional clinical criteria within no more than 60 days of their charge. That group's charge should include consideration of:

- (A) How/whether the MELD score should be used
- (B) Prioritization related to HCV patients requiring intensive immunosuppression either now or in the future (e.g. transplantation but also transplant candidates, chemotherapy, etc.)
- (C) Prioritization related to patients with extrahepatic immune complex mediated complications of hepatitis C (e.g. cryoglobulinemia, glomerulonephritis)
- (D) Prioritization related to patients with B cell lymphoma associated with HCV (viral antigen may drive cell proliferation and SVR may lead to remission)
- (E) Prioritization related to patients with HIV co-infection
- (F) Prioritization related to patients who are at higher risk of transmission of HCV to others (e.g., Females of childbearing age who desire to conceive a child in the next 12 months, patients with substance use disorders)
- (G) Prioritization related to HCV patients in research protocols

7. I would like to thank all of the subject matter experts who provided comments on how best to define the highest priority groups for treatment. I would especially like to acknowledge Dr. Jason Dornitz, Dr. Timothy Morgan, Dr. Douglas Heuman, and Dr. Virginia A. Sharpe for their contributions to the document.

8. Please feel free to contact me at [Kenneth.berkowitz@va.gov](mailto:Kenneth.berkowitz@va.gov) or 212-951-3385 if you need further information or have questions.

Kenneth A. Berkowitz, MD, FCCP/es

Attachment

## APPENDIX - PROTOCOL

### **Initiation of Hepatitis C Virus (HCV) Treatment: Protocol for Prioritization When Resources Are Insufficient to Treat All Patients for Whom the Treatment is Clinically Indicated May 20, 2015**

In keeping with VA's mission and I CARE core values and characteristics, this protocol for treatment prioritization is the basis for **consistent, fair, and transparent** decision making regarding initiation of antiviral therapy in patients with confirmed HCV who are eligible for medical benefits under 38 C.F.R. 17.38 and other legal authorities granted to the Veterans Health Administration and for whom the treatment is clinically indicated. (NOTE: The process for developing this protocol included engagement of subject matter experts (SME) from VHA. A SME workgroup is being established to continue to refine the prioritization levels based on clinical criteria).

Since prioritizing patients is ethically challenging, and far inferior to augmenting resources to accommodate all patients for immediate treatment, this protocol is to be applied only when resources are not sufficient to immediately treat all patients for whom the treatment is clinically indicated. Attempts to augment resources must be ongoing and **transparent**.

The complete ethical analysis and framework that served as the basis for this protocol – and that should guide resource allocation decisions for HCV treatment in VHA – can be found on the intranet site of the VHA National Center for Ethics in Health Care at [http://www.ethics.va.gov/activities/hcv\\_framework.asp](http://www.ethics.va.gov/activities/hcv_framework.asp). Please also check this link for updates to this prioritization protocol.

#### **1) Clinical Exclusion Criteria**

Patients with any of the following clinical exclusion criteria will not be eligible for initiation of antiviral HCV therapy. This approach is based on the principles of resource **stewardship** and **utility**, i.e., that a scarce resource should be allocated to achieve the greatest good for the greatest number. However, based on the principles of **equity** and **human dignity**, patients assessed to have an exclusion criterion should be provided all other appropriate medical care and support. As in situations where resources are sufficient, HCV treatment should also not be provided to patients who decline to consent to the HCV treatment (i.e., who do not want the treatment).

- Patients with confirmed presence of any advanced disease with average life expectancy of 12 months or less (e.g., severe end-stage congestive heart failure, widely metastatic carcinoma with less than 12 months average survival, or hepatocellular carcinoma with less than 12 months average survival).

- Patients with confirmed severe irreversible cognitive impairment (e.g., persistent vegetative state or advanced dementia).
- Patients with an HCV strain that is resistant to all antiviral treatments.
- Patients with a Model for End-stage Liver Disease (MELD) score >30.<sup>2</sup>

## 2) Clinical Inclusion Criteria

The use of clinical inclusion criteria is based on the principles of **beneficence and utility**; that is, obtaining the maximum benefit from the available resources. The inclusion criteria are structured to enable the **sickest patients who will benefit from the treatment** to receive priority over those who are less ill. Patients with clinical indication for HCV treatment who do not have any of the exclusion criteria should be prioritized for treatment in the following order:

A) Patients who are currently undergoing antiviral HCV therapy (i.e., their therapy should be continued, as long as it remains clinically indicated)

B) Patients with evidence of cirrhosis or at high risk for rapid progression of disease, including:

**Any one** or more of the following criteria for cirrhosis:

- Biopsy evidence of cirrhosis (METAVIR fibrosis Stage F4 or Ishak fibrosis stage 5-6/6)
- Clinical evidence of portal hypertension related to cirrhosis (ascites, gastroesophageal varices)
- Cirrhosis diagnosis based on direct visualization of a nodular liver (surgical or laparoscopic)
- Measured portal hypertension (i.e. hepatic venous pressure gradient  $\geq 6$  mmHg)
- Liver stiffness measurement (FibroScan®) >15 kPa

**Or at least 2** of the following criteria for advanced fibrosis/cirrhosis:

- Biopsy evidence of advanced fibrosis (METAVIR fibrosis Stage F3 or Ishak fibrosis stage 4/6)
- Radiographic evidence of cirrhosis (e.g. nodular liver, portal-systemic collaterals, recanalized umbilical vein or splenomegaly)
- Liver stiffness measurement (FibroScan®) between 10-15 kPa
- Fib-4 score > 3.25
- Synthetic dysfunction, defined as any of the following (only one point allowed)
  - a. albumin <3.5 mg/dL, OR
  - b. direct bilirubin >1.0 mg/dL, OR
  - c. total bilirubin >2.0 mg/dL (not explainable by another cause such as Gilbert syndrome, hemolysis, acute liver injury, biliary obstruction or atazanavir) OR
  - d. INR >1.2 (not receiving warfarin).
- Platelets < 150,000 per ul

- AST > ALT
- HIV/HCV co-infection

**Or patients with any one** of the following criteria:

- Requiring intensive immunosuppression (e.g. status post transplantation, on chemotherapy, etc.)
- On an organ transplant list or if the transplant center requires antiviral treatment prior to listing
- Extrahepatic immune complex mediated complications of hepatitis C (e.g. cryoglobulinemia, glomerulonephritis)
- B cell lymphoma associated with HCV

C) Patients without advanced fibrosis/cirrhosis or the other conditions outlined above.

Further prioritization will be determined by a workgroup of clinical subject matter experts who will provide additional clinical criteria within no more than 60 days of their charge. Those criteria will be included in a revised protocol that will be provided through the DUSHOM to the field.

### **3) Team Structure and Process to Implement This Protocol**

To ensure an **impartial** process, this protocol is to be implemented by HCV treatment prioritization teams that function at the highest organizational level practical, such as the VISN-level, with access to the most comprehensive data on the population of patients with HCV and the funds available for HCV treatment. The population of patients in this case includes HCV patients who have indication for treatment at the time of the team's review.

Placing the responsibility for making difficult resource decisions on a team not only preserves the clinicians role as advocate in the clinician-patient relationship but also helps to ensure a **fair, consistent and transparent** decision making process.

HCV treatment prioritization team review should occur at least every 45 days and be based on patient information provided by clinicians. The team should consist of individuals who have knowledge of the HCV patient population and resource availability, clinicians experienced in care of HCV patients, ethics experts, and other appropriate experts as needed.

To avoid decision making that is based on real or perceived conflict of interest, preferential treatment, or nepotism, the team must adhere to the protocol. Likewise, when providing information to the team, clinicians must not attempt to manipulate the exclusion or inclusion criteria to give an advantage to their patients.

#### 4) Appeals Process

Depending on the organizational level of the HCV treatment prioritization team, leadership at that organizational level or higher should also establish an appeals process to ensure **fairness** and **procedural justice** for prioritization decisions made by the team. Whether the appeal is initiated by the Veteran or by a VA clinician on the Veteran's behalf, valid appeals will generally be based on claims of the teams' failure to adhere to the established prioritization protocol, rather than an appeal for an exception to the protocol itself. Appeals for exceptions to the protocol should follow the normal clinical appeals process with input from the Office of Public Health and the National Center for Ethics in Health Care. Adjudication of appeals must not be conducted by anyone who serves on the prioritization team or by any clinician responsible for the care of the patient whose case is under appeal.

#### 5) References

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<sup>1</sup> American Association for the Study of Liver Disease and Infectious Diseases Society of America. Recommendations for Testing, Managing, and Treating Hepatitis C. Available at [www.hcvguidelines.org](http://www.hcvguidelines.org), accessed 22 April 2015; Bruno S, Zuin M, Crosignani A, Rossi S, Zadra F, Roffi L, Borzio M, Redaelli A, Chiesa A, Silini EM, Almasio PL, Maisonneuve P. Predicting mortality risk in patients with compensated HCV-induced cirrhosis: a long-term prospective study. *Am J Gastroenterol*. 2009 May;104(5):1147-58; Said A, Williams J, Holden J et al. Model for end stage liver disease score predicts mortality across a broad spectrum of liver disease. *J Hepatol* 2004; 40:897-903.

<sup>2</sup> MELD calculator available at <http://optn.transplant.hrsa.gov/converge/resources/MeldPeldCalculator.asp?index=98>