

HCV Treatment Process

Management of HCV

Hepatitis C virus infection represents a potentially serious problem within the correctional environment. It is widely recognized that Hepatitis C infection may result in chronic infection. However, currently there is no risk stratification data to assist in predicting the outcome of Hepatitis C infection in any individual case. Most studies show that at least 80% of persons with chronic Hepatitis C infection will experience a mild course of the disease without the development of cirrhosis or death from the infection. The remaining 20% will develop some form of cirrhosis, mild to severe. Additionally, a small percentage of persons with severe cirrhosis will develop liver cancer. It is this small percentage of persons with severe cirrhosis and cancer that are most likely to benefit from current available interventions. Unfortunately, at this time there is no way to predict how an individual will respond to the Hepatitis C infection or the available treatments.

Medication treatments currently available for Hepatitis C infection are fraught with side effects and complications. The side effects can be incapacitating and even fatal. Individuals with certain medical and mental health conditions are at a high risk for serious and potentially fatal complications. Therefore, inclusion and exclusion criteria have been established to facilitate the selection of individuals who are least likely to be harmed or experience serious complications from the Hepatitis C medication treatment.

Stage I – Surveillance and Education

STEP 1

Intake Screening - Patients are screened for specific communicable diseases at the time of intake screening.

STEP 2

Health Assessment- Patients are screened for Hepatitis C risk factors at the time of the intake health assessment or annual health appraisal. Hepatitis C risk factors will be determined by addressing the following:

- History of injection drug use.
- Blood transfusions received prior to 1992.
- Solid organ transplantation from an infected donor.
- Occupational exposure to infected blood.
- Birth from an infected mother.
- Sex with an infected person.
- High-risk sexual practices.
- Intranasal cocaine use.

If a patient has a positive response to any of the above risk factors, a referral to the chronic care clinic will be recommended. If the patient declines the chronic care visit, the declination will be documented in the patient's health record.

STEP 3

Chronic Care Scheduled Visit – The chronic care encounter will be scheduled to take place within 90 days of the health assessment. Patients will receive education and counseling and may be offered a screening test for Hepatitis C, based on a more comprehensive assessment of risk factors and medical appropriateness. The HCV Patient Information/Education document is signed by the patient and provider. (Attachment A)

STEP 4

Hepatitis C Antibody Testing - The Hepatitis C antibody test is recommended for screening and is sufficient to exclude a diagnosis of chronic Hepatitis C infection in most individuals with intact immune systems. A false negative Hepatitis C antibody test may occur in a small number of inmates who are immune-deficient (i.e., HIV/AIDS). In patients with immune deficiency who have an elevated ALT (indicating possible Hepatitis C infection) and a negative Hepatitis C antibody test, a Hepatitis C RNA polymerase chain reaction (PCR) should be performed.

STEP 5

Hepatitis C Antigen Testing – It has been demonstrated that approximately 10 to 15% of patients who contract Hepatitis C will spontaneously clear the virus. A PCR HCV RNA antigen test will be completed. If the test is positive the evaluation will continue. If the test is negative, the patient should be instructed to have the test repeated in five years.

STEP 6

Hepatitis A & B Vaccine - Patients who are HCV antibody positive will be offered the Hepatitis A and B vaccines as indicated.

- Administer Hepatitis A vaccine series unless it is known that the patient has Hepatitis A disease or previous vaccination.
- Administer Hepatitis B vaccine series unless the patient was previously vaccinated or serology indicates previous infection.

Stage II - Eligibility for Medication Treatment

STEP 1

Baseline eligibility screening will be done pursuant to the comprehensive surveillance, educational and vaccination program in Stage 1. Eligibility will be considered for inmates that have at least a 24-month sentence remaining. The reason for stipulating this minimum length of time is because:

1. Complex and time-consuming educational and clinical evaluation requirements,
2. Adherence to treatment is essential to maximize successful outcomes, and
3. Side effects should be monitored for at least 6 months post treatment.

STEP 2

Consent and Education Attestation – The patient will review and sign the HCV Patient/Education Information document. (Attachment A) The patient will review and sign the HCV Evaluation and Treatment Consent form in the "determining eligibility" section. (Attachment C) CDC patient education material will also be used to provide inmates with a more complete understanding of the disease process.

STEP 3

Determining Eligibility - Patients with the conditions listed as absolute exclusion criteria will be excluded from the eligibility pool because the risks outweigh the benefits of therapy. Following is a list of absolute and relative exclusion criteria. Patients who have an absolute exclusion criteria will not have further evaluation or testing unless the condition(s) resolves or improves (example pregnancy and anemia) in which case they will be reevaluated within 90 days of resolution.

Absolute Exclusion Criteria

- Age ≤ 18 or ≥ 60
- Remaining incarceration time ≤ 24 months.
- Presence of an Axis I diagnosis that is not controlled and stable as determined by the treating psychiatrist.
- History of solid organ transplant.
- Presence or history of an autoimmune disorder.
- Presence or history of decompensated cirrhosis, presence or history of ascites or encephalopathy (albumin ≤ 3.2 gm/dl, bilirubin > 3.0 gm/dl).
- CBC results outside acceptable limits (Hgb ≤ 12 females, ≤ 13 for males; WBC $> 3,000$; ANC $\leq 1,500$ & platelets $\leq 100,000$ /mm).
- Creatinine ≥ 1.7 or creatinine clearance ≤ 50 ml/minute.
- Normal ALT (< 2.0 times normal at 0, 3 and 6 months).
- Positive pregnancy test.
- Active TB
- Auto Immune Disease e.g. – Lupus, Graves Disease, R.A., M.S., Myasthenia Gravis
- Cancer – not in remission
- Hemoglobinopathies

"No further evaluation should be completed so long as the absolute criterion exists."

Relative Exclusion Criteria

- Hepatitis B Co-infection
- Diabetes – poorly controlled with Hgb. A1C \geq 9.0
- Ischemic Cardiac Disease or Cerebrovascular Disease
- Hypertension – poorly controlled
- CHF
- Peripheral Vascular Disease – Symptomatic
- COPD – severe
- Seizures – poorly controlled
- Active Thyroid Disease
- Active Gout
- Significant CNS Trauma – recent within the past six months
- Poor adherence to treatment including \leq 80% of clinic visits and medications, to the extent the inmate made the choices.
- Alcohol and illicit drug use within one year.
- Interferon/Ribavirin sensitivity.
- Life expectancy < 10 years.

The provider is required to review relative exclusion criteria with the Regional Medical Director prior to proceeding with further evaluation.

STEP 4

Liver Biopsy – Liver biopsy provides a unique source of information on fibrosis and assessment of histology. The information obtained on liver biopsy allows affected individuals to make a more informed choice about the initiation or postponement of antiviral treatment. Thus, the liver biopsy is a useful part of the informed consent process.

In general, a baseline assessment of liver histology offers a valuable standard for subsequent comparisons. However, the appropriate interval for subsequent evaluations is yet to be determined. A biopsy will be required prior to initiating medication for patients with Hepatitis C viremia with genotype 1A or 1B. A biopsy will not be required for genotypes 2, 3 & 4 and for patients with compensated cirrhosis.

Stage III - Medication Treatment

The provider will initiate a treatment plan including medication treatment if the patient is determined to be eligible and the patient consents for medical treatment by signing patient education document and the HCV consent form in the medication initiation section.

HCV Disease: Evaluating patient new to a facility on medication for HCV disease

Patients arriving at a ADOC facility, either from the community or another ADOC facility, who are on antiviral therapy for HCV disease will be evaluated within 72 hours for consideration of continuing or resuming medication therapy. There should be a low threshold for continuing the medication for the first week while evaluating the appropriateness of the medication regimen. As a part of this evaluation, patients should be reviewed for the following:

1. Absolute exclusion criteria (but not the minimum remaining sentence since they have already been on therapy).
2. Response to therapy as measured by viral load.
3. Dosing adjustment due to anemia.
4. Adherence

Continuing Therapy

Patients who are already on a potent antiretroviral regimen and who are adherent to therapy should have the HVC medications continued by the physician during the intake process. A complete medical record review and clinic visit should be done within one week to review:

1. Medication adherence
2. Response to therapy
3. Medication side effects
4. Assure patient education material has been reviewed and consent forms signed.

Resuming Therapy

Patients who are non-adherent to therapy or who have had an interruption in medication for greater than 2 weeks should be evaluated in consult with the State Medical Director prior to restarting antiretroviral therapy. If there is any question about the adherence pattern the treatment should be continue for a week while the information is being reviewed.

HCV - Patient Information/Education

Adopted from the Schering-Plough medication guide and labeling document.

HEPATITIS C VIRUS

The Hepatitis C virus can and does damage the liver. However, the majority of patients never experience symptoms while others can take from 10 to 15 years before symptoms develop. The damage caused by the Hepatitis C virus may range from none to mild, moderate or life threatening. Symptoms may include:

- Fatigue
- Jaundice (yellowing of the eyes)
- Nausea
- Pain in the abdomen
- Fever
- Muscle Aches
- Joint Pain
- Loss of appetite
- Diarrhea
- Vision Loss

HEPATITIS C TREATMENT

At the present time there is a medication treatment strategy that is FDA approved for the treatment of the Hepatitis C infection: Pegylated Interferon and Ribavirin combination treatment.

Patients are treated for 24-48 weeks and are followed for 24 weeks post-treatment. The goal of treatment is to achieve sustained virologic clearance. Response to treatment is defined as undetectable HCV RNA and normalization of ALT at 24 weeks post-treatment.

It is important to note that there is no data regarding whether Pegylated Interferon treatment will prevent transmission of HCV infection to others. Additionally, it is not known if treatment with Pegylated Interferon will cure Hepatitis C or prevent cirrhosis, liver failure, or liver cancer that may be the result of infection with the Hepatitis C virus. Approximately 10-14% of patients discontinued treatment due to side effects. It is recommended that patients receiving Pegylated Interferon, alone or in combination with Ribavirin, be discontinued from treatment if HCV viral levels do not show an improvement at 12 weeks or are absent at 24 weeks.

INDICATIONS

Pegylated Interferon is a treatment for some people who are infected with the Hepatitis C virus. However, Pegylated Interferon/Ribavirin combination treatment can have serious side effects that may cause death. Therefore the treatment is not for everyone. Prior to beginning treatment, patients should discuss the risks and benefits so that they are prepared to make an informed decision.

CONTRAINDICATIONS

Pegylated Interferon/Ribavirin combination treatment is contraindicated in:

- Patients with hypersensitivity to ribavirin or any other component of the product.

- Women who are pregnant, planning to become pregnant or are breast-feeding.
- Men whose female partners are pregnant.
- Patients that have Hepatitis Caused by your immune system attacking your liver or unstable liver disease.
- Patients that have abnormal red blood cells such as sickle-cell anemia or thalassemia major.
- Patients with a history of significant or unstable cardiac disease should not be treated with Pegylated Interferon/Ribavirin combination treatment.

Serious consideration and thought should occur before taking Pegylated Interferon/Ribavirin, is you have any of the following conditions:

Conditions that may effect Treatment	
Depression or anxiety	Alcoholism
High blood pressure	Drug abuse or addiction
Previous heart attack, or heart problems	Any kind of autoimmune disease
Liver problems other than Hepatitis C	Hepatitis B infection
HIV infection	Thyroid problems
Diabetes	Sleep problems
Colitis	Cancer
Kidney problems	Body organ transplants
Bleeding problems	

SIDE EFFECTS

Patients may present with side effects within the first 12 weeks of treatment and many continue to experience adverse events several months after discontinuation of treatment.

In the combination treatment trial, dose reductions due to adverse reactions occurred in 42% of patients receiving Pegylated Interferon. In the Pegylated Interferon/Ribavirin combination trial the most common adverse events were psychiatric which occurred among 77% of the patients and included most commonly depression, irritability, and insomnia. Pegylated Interferon/Ribavirin induced fatigue or headache was also found in approximately two-thirds of patients and induced fever or rigors in approximately half of the patients. Following is a description of the side effects experienced by patients taking Interferon/Ribavirin treatment.

Mental Health And Suicide - Pegylated Interferon/Ribavirin therapies may cause mood and behavior problems. Behavioral problems include irritability and depression. Some patients become more aggressive and some think about hurting or killing themselves or others.

Heart Problems - Some patients taking Pegylated Interferon/Ribavirin therapies may develop problems with low blood pressure, fast heart rate and very rarely, heart attacks.

Blood Problems - Pegylated Interferon/Ribavirin therapies commonly lower two types of blood cells, white blood cells and platelets. The therapies have also been shown to decrease red blood cells, resulting in anemia. Anemia can be dangerous, especially if a person has heart or circulatory problems.

Body Organ Problems - Pegylated Interferon/Ribavirin therapies have been shown to cause damage to internal organs. Symptoms of severe abdominal pain can indicate internal organ damage.

Birth Defects - Ribavirin may cause birth defects and/or death of the unborn child. Extreme care must be taken to avoid pregnancy in female patients and in female partners of male patients.

Endocrine Disorders - Pegylated Interferon causes or aggravates hypothyroidism and hyperthyroidism. Hyperglycemia has been observed in patients treated with Pegylated Interferon. Diabetes mellitus has been observed in patients treated with alpha interferons.

Colitis - Fatal and nonfatal ulcerative or hemorrhagic/ischemic colitis have been observed within 12 weeks of the start of alpha interferon treatment. Abdominal pain, bloody diarrhea, and fever are the typical manifestations. The colitis usually resolves within 1-3 weeks of discontinuation of alpha interferons.

Autoimmune Disorders - Pegylated Interferon treatment may cause the development or exacerbation of autoimmune disorders such as thrombocytopenia, rheumatoid arthritis, systematic lupus, and psoriasis.

Pancreatitis - Fatal and nonfatal pancreatitis has been observed in patients treated with alpha interferon. Pegylated Interferon treatment should be suspended in patients with signs and symptoms suggestive of pancreatitis and discontinued in patients diagnosed with pancreatitis.

Common, Less Serious Side Effects

Flu symptoms:	Including headache, muscle aches, tiredness and fever.
Appetite:	Including nausea, loss of appetite, and weight loss.
Thyroid:	Some patients develop changes in the function of their thyroid. Symptoms include inability to concentrate, feeling cold or hot all the time, a change in weight and skin changes.
Skin reactions:	Redness, swelling, and itching are common at the injection site.
Hair Thinning:	Hair loss stops and hair growth returns after treatment is stopped.

On-Going Side Effects

A study showed that by the end of the 6-month follow-up period the incidence of ongoing adverse events by body class in the PEG-INTRON 1.5/REBETOL groups was:

- 33% (psychiatric),
- 20% (musculoskeletal), and

➤ 10% (for endocrine and for GI).

In addition, approximately 10-15% of patients weight loss, fatigue and headache had not resolved.

DOCUMENTATION OF EDUCATION

Education Session 1 - Screening

I understand that I have risk factors for Hepatitis C. I have been provided with the HCV-Patient Information/Education material is adapted from the "Medication Guide" established by Schering-Plough Research Institute. The information in this document has been reviewed with me and I have that the opportunity to ask questions.

PATIENT'S SIGNATURE	DATE SIGNED
PROVIDER'S SIGNATURE	DATE SIGNED

Education Session 2 – HCV Positive

I understand that I have tested positive for the Hepatitis C virus. I have been provided with the HCV-Patient Information/Education material is adapted from the "Medication Guide" established by Schering-Plough Research Institute. The information in this document has been reviewed with me and I have that the opportunity to ask questions.

PATIENT'S SIGNATURE	DATE SIGNED
PROVIDER'S SIGNATURE	DATE SIGNED

Education Session 3 - Treatment

I understand that I am eligible to receive Interferon/Ribavirin treatment. I have been provided with the HCV-Patient Information/Education material is adapted from the "Medication Guide" established by Schering-Plough Research Institute. The information in this document has been reviewed with me and I have that the opportunity to ask questions.

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HCV – Provider Reference

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HEPATITIS C VIRUS

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- Fatigue
- Jaundice (yellowing of the eyes)
- Nausea
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INDICATIONS

Pegylated Interferon, peginterferon alfa-2b, is indicated for use alone or in combination with REBETOL (ribavirin, USP) for the treatment of chronic hepatitis C in patients with compensated liver disease who have not been previously treated with interferon alpha and are at least 18 years of age.

However, Pegylated Interferon/Ribavirin combination treatment can have serious side effects that may cause death. Therefore the treatment is not for everyone. Prior to beginning treatment, patients should discuss the risks and benefits so that they are prepared to make an informed decision.

CONTRAINDICATIONS

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- Appetite:** Including nausea, loss of appetite, and weight loss.
- Thyroid:** Some patients develop changes in the function of their thyroid. Symptoms include inability to concentrate, feeling cold or hot all the time, a change in weight and skin changes.
- Blood Sugar:** Some patients may develop diabetes.

Skin reactions: Redness, swelling, and itching are common at the injection site.
Hair Thinning: Hair loss stops and hair growth returns after treatment is stopped.

On-Going Side Effects

A study showed that by the end of the 6-month follow-up period the incidence of ongoing adverse events by body class in the PEG-INTRON 1.5/REBETOL groups was:

- 33% (psychiatric),
- 20% (musculoskeletal), and
- 10% (for endocrine and for GI).

In addition, approximately 10-15% of patients weight loss, fatigue and headache had not resolved.

MONITORING

It is recommended that patients receiving Pegylated Interferon, alone or in combination with ribavirin, be discontinued from treatment if HCV viral levels remain high after 6 months of treatment.

Pegylated Interferon treatment should be suspended in patients with signs and symptoms suggestive of pancreatitis and discontinued in patients diagnosed with pancreatitis.

Patients were treated for 48 weeks and were followed for 24 weeks post-treatment.

Patients should receive an eye examination at baseline. Patients with preexisting ophthalmologic disorders (e.g. diabetic or hypertensive retinopathy) should receive periodic ophthalmologic exams during interferon alpha treatment. Any patient who develops ocular symptoms should receive a prompt and complete eye examination. Pegylated Interferon treatment should be discontinued in patients who develop new or worsening ophthalmologic disorders.

Patients should undergo monthly pregnancy tests during treatment and for six months post-treatment.

OUTCOME

Mono-therapy – A randomized study compared treatment with Pegylated Interferon to treatment with INTRON A. The patients were not previously treated with interferon alfa, had compensated liver disease, detectable HCV RNA, elevated ALT, and liver histopathology consistent with chronic hepatitis. Patients were treated for 48 weeks and were followed for 24 weeks post-treatment.