

<b>SUMMARY</b>	<b>DECISION SUPPORT</b>	<b>PATIENT EDUCATION/SELF MANAGEMENT</b>
----------------	-------------------------	--

## GOALS

- Identify Hepatitis C Virus (HCV) infected patients
- Monitor HCV patients on treatment per guidelines
- Stop treatment when indicated (futility rules)
- Monitor all HCV patients for signs of cirrhosis
- Manage End Stage Liver Disease (ESLD)

## ALERTS

### HCV TREATMENT

- HCV treatment **for all genotypes** requires approval from the HQ CCHCS HCV Oversight Committee
- Closely monitor hemoglobin, platelets, and ANC during treatment
- **DO NOT USE any agent as monotherapy**

### CIRRHOTICS

- Screen for hepatocellular carcinoma and varices
- Identify decompensated cirrhosis (evidenced by encephalopathy, ascites, variceal hemorrhage, spontaneous bacterial peritonitis, hepatopulmonary or hepatorenal disease or a Child-Pugh score of  $\geq 7$ )

## TREATMENT OPTIONS

### PATIENT SELECTION: Who to treat?

In CCHCS, treatment eligibility is based on estimated disease severity.

- Every patient with chronic HCV does **not** need treatment.
- Only 10-20% of people with chronic HCV develop severe liver disease; only 1- 5% will die from complications of liver disease. There is no single test that can absolutely predict who will progress to severe liver disease.
- Treatment in CCHCS is deferred for those with minimal liver disease or low likelihood of significant liver disease (see page 5).
- **All genotypes** now require treatment preapproval through the HQ CCHCS HCV Oversight Committee.

HCV evaluation and treatment is generally not initiated in reception centers. HCV treatment, when indicated, will begin after the patient has transferred to a mainline institution.

Patients deferred for any of the new HCV treatments according to the criteria outlined in this care guide may not receive the older pegylated interferon / ribavirin regimen as an alternative to no treatment.

### TREATMENT

The recommended medication regimen depends on genotype and other factors. These regimens are changing rapidly as many new agents are now being released for treatment of HCV. (See page 6)

## MONITORING

### **ALL CHRONIC HCV INFECTED PATIENTS:**

- Annual clinical assessment: consider labs including platelets (Plt), INR, albumin, AST/ALT, and total bilirubin every 6-12 months to assess progression of liver disease, determine FIB4 or Child-Pugh score (see page 3) as indicated.
- Vaccines: Offer and document HAV, HBV, pneumococcal vaccination. Encourage annual influenza vaccination.

### **HCV PATIENTS RECEIVING ANTIVIRAL THERAPY:**

- See HCV treatment tracking flowsheets<sup>1</sup> regarding intervals for CBC, creatinine, LFT, TSH, high sensitivity HCV VL.
- Assess for depression and other side effects at each visit.
- Follow up as clinically indicated, usually every 1-4 weeks during active treatment.

### **CHRONIC HCV INFECTED PATIENTS WITH CIRRHOSIS**

- Ultrasound every 6 months with clinically diagnosed or biopsy proven cirrhosis to screen for hepatocellular carcinoma.
- Monitor Child-Pugh score (page 3) as indicated. See CCHCS ESLD Care Guide.

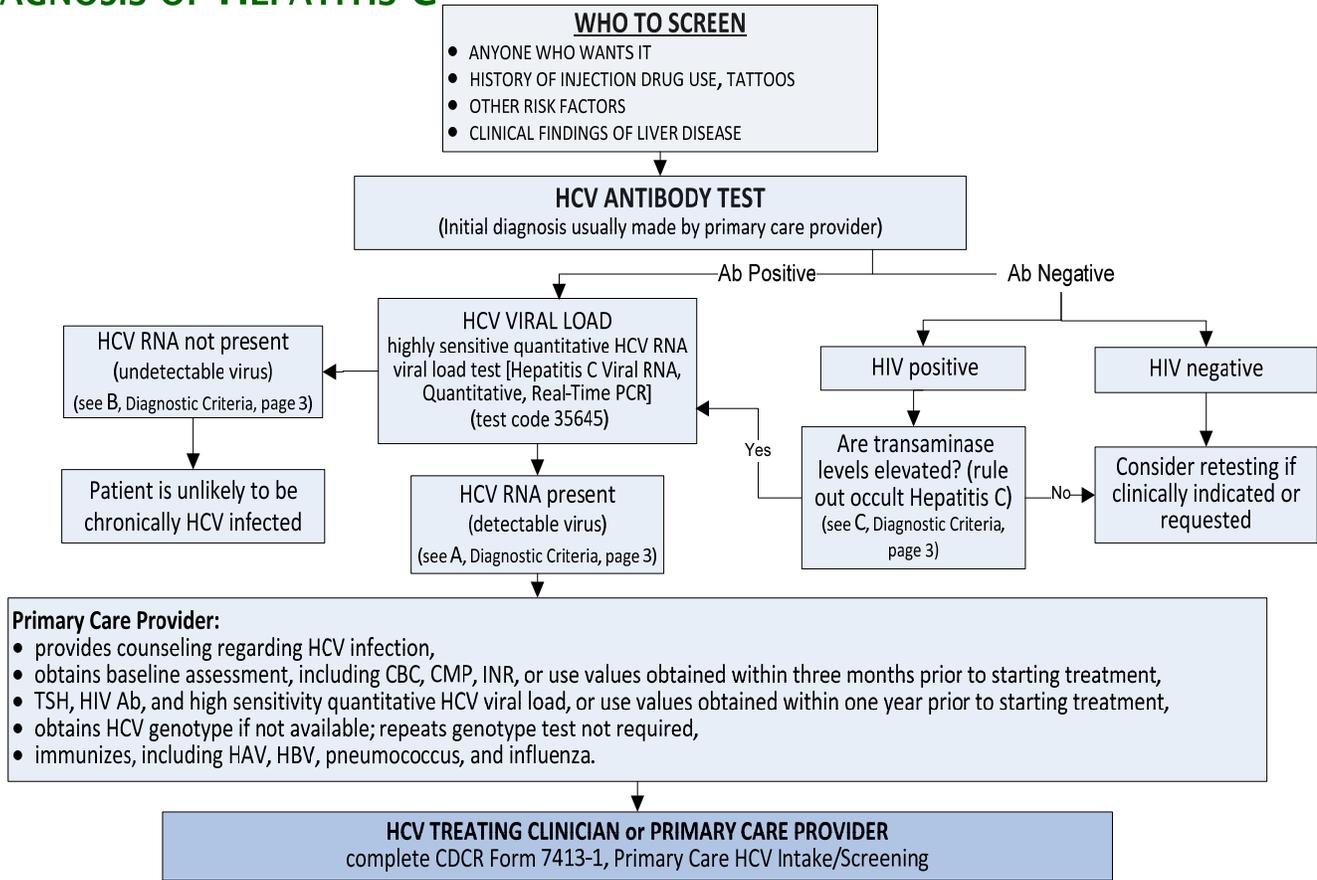
<sup>1</sup>All HCV Care Guide related forms are available on CCHCS Lifeline at <http://lifeline/PolicyandAdministration/PolicyandRiskManagement/IMSPP/Pages/Resources.aspx>

### TABLE OF CONTENTS

EXCLUSION CRITERIA	PAGE 2
DIAGNOSIS ALGORITHM	PAGE 2
DIAGNOSTIC CRITERIA	PAGE 3
CHILD-PUGH SCORING	PAGE 3
ACUTE HCV	PAGE 4
CHRONIC HCV STAGING ALGORITHM	PAGE 5
CHRONIC HCV TREATMENT	PAGE 6
MEDICATION DOSING AND SIDE EFFECTS	PAGE 7-9
MANAGEMENT OF SIDE EFFECTS	PAGE 10-11
FDA DRUG SAFETY COMMUNICATION	PAGE 12
DRUG INTERACTIONS	PAGE 12
PATIENT EDUCATION	PAGE PE-1
PATIENT EDUCATION (SPANISH)	PAGE PE-2

**SUMMARY**      **DECISION SUPPORT**      **PATIENT EDUCATION/SELF MANAGEMENT**

**DIAGNOSIS OF HEPATITIS C**



All HCV forms are available on CCHCS Lifeline at <http://lifeline/PolicyandAdministration/PolicyandRiskManagement/IMSPP/Pages/Resources.aspx>

EXCLUSION CRITERIA		INTERFERON EXCLUSION CRITERIA																			
<p><b>Release Date Exclusion :</b></p> <p><b>Treatment Naïve:</b></p> <table border="1"> <tr> <th>Genotype</th> <th>Min. # of Months*</th> </tr> <tr> <td>1, 2, 3 and 4</td> <td>5</td> </tr> <tr> <td>5 and 6</td> <td>14</td> </tr> </table> <p><b>Interferon ineligible:</b></p> <table border="1"> <tr> <th>Genotype</th> <th>Min. # of Months*</th> </tr> <tr> <td>1 and 2</td> <td>5</td> </tr> <tr> <td>3, 4, 5, 6</td> <td>8</td> </tr> </table> <p><b>Treatment experienced:</b></p> <table border="1"> <tr> <th>Genotype</th> <th>Min. # of Months*</th> </tr> <tr> <td>1a</td> <td>5</td> </tr> <tr> <td>1b, 2, 3, 4, 5, 6</td> <td>8</td> </tr> </table>		Genotype	Min. # of Months*	1, 2, 3 and 4	5	5 and 6	14	Genotype	Min. # of Months*	1 and 2	5	3, 4, 5, 6	8	Genotype	Min. # of Months*	1a	5	1b, 2, 3, 4, 5, 6	8	<p><b>Other Exclusion Criteria :</b></p> <ul style="list-style-type: none"> <li>• Poorly controlled cardiopulmonary, cerebrovascular, or thyroid disease, blood dyscrasias, seizures, cancer, diabetes mellitus (hemoglobin A1C &gt; 8.5)</li> <li>• HIV infection with CD4 count &lt; 200 cells/ml or undergoing treatment for opportunistic infection</li> <li>• Kidney, lung, heart transplant</li> <li>• Anemia, hemoglobin &lt; 11 g/dl or hematocrit &lt; 33%</li> <li>• Allergy to ribavirin</li> <li>• Inability to cooperate with treatment</li> <li>• Inability to give informed consent</li> <li>• Ongoing illicit drug or alcohol use</li> <li>• Pregnancy or inability to practice contraception</li> </ul>	<p><b>INTERFERON EXCLUSION CRITERIA</b></p> <ul style="list-style-type: none"> <li>• WBC &lt; 1,500 cells/μl or Plt &lt; 75,000/μl</li> <li>• History of decompensated cirrhosis, evidenced by either variceal hemorrhage, (esophageal varices with no history of variceal hemorrhage are not a contraindication) ascites, hepatic encephalopathy, spontaneous bacterial peritonitis, hepatopulmonary disease, hepatorenal disease, or a Child-Pugh score of ≥ 7 (Child-Pugh ≥ 6 if HIV/HCV coinfectd)</li> <li>• Severe or acute autoimmune disease (recommend consultation)</li> <li>• Poorly controlled depression</li> <li>• Serious suicidal behavior in the past 12 months</li> </ul>
Genotype	Min. # of Months*																				
1, 2, 3 and 4	5																				
5 and 6	14																				
Genotype	Min. # of Months*																				
1 and 2	5																				
3, 4, 5, 6	8																				
Genotype	Min. # of Months*																				
1a	5																				
1b, 2, 3, 4, 5, 6	8																				

\*Patients will be excluded from treatment consideration in CCHCS if they will be released before the evaluation and course of treatment can be completed. The 'months' noted above show the minimum number of months of incarceration needed to be eligible for consideration of HCV therapy based on genotype and other patient factors. More time may be required in some cases.

SUMMARY	DECISION SUPPORT	PATIENT EDUCATION/SELF MANAGEMENT
---------	------------------	-----------------------------------

## DIAGNOSTIC CRITERIA

FROM PAGE 2	HCV AB	HCV RNA VIRAL LOAD	DIAGNOSIS	COMMENT
A	Pos	Pos	<ul style="list-style-type: none"> <li>Chronic HCV (80% of those initially infected)</li> </ul>	<ul style="list-style-type: none"> <li>Order genotype if no prior result available</li> <li>Assess for treatment eligibility</li> </ul>
B	Pos	Neg	<ul style="list-style-type: none"> <li>Resolved HCV (up to 20% of those infected)</li> <li>Acute HCV with transient viral clearing (see page 4)</li> <li>False positive HCV Ab</li> </ul>	<ul style="list-style-type: none"> <li>Consider rechecking high sensitivity VL at 6-12 months to confirm that patient is not chronically infected</li> </ul>
C	Neg	Pos	<ul style="list-style-type: none"> <li>Early acute HCV (see page 4)</li> <li>Chronic HCV in immunosuppressed patient (e.g., HIV)</li> <li>False positive viral load</li> </ul>	<ul style="list-style-type: none"> <li>If acute HCV, consider consultation with HCV specialist at CDCR CPHCS HCV QUESTIONS @cdc.ca.gov and see Acute HCV Diagnosis, Staging, and Treatment (page 4).</li> </ul>

## CHILD-PUGH SCORING

COMPONENT	POINTS SCORED		
	1	2	3
Encephalopathy <sup>†</sup>	None	Grade 1-2	Grade 3-4
Ascites	None	Mild or controlled with diuretics	Moderate or refractory despite diuretics
Albumin	> 3.5 g/dl	2.8-3.5 g/dl	< 2.8 g/dl
Total bilirubin or Modified total bilirubin <sup>§</sup>	< 2 mg/dl	2-3 mg/dl	> 3 mg/dl
	< 4 mg/dl	4-7 mg/dl	> 7 mg/dl
Prothrombin time (seconds prolonged) or International normalized ratio (INR)	< 4	4-6	> 6
	< 1.7	1.7-2.3	> 2.3

<sup>†</sup> Encephalopathy: grade 1: mild confusion, anxiety, restlessness, fine tremor, slowed coordination  
 grade 2: drowsiness, disorientation, asterixis  
 grade 3: somnolent but arousable, marked confusion, incomprehensible speech, incontinence, hyperventilation  
 grade 4: coma, decerebrate posturing, flaccidity

<sup>§</sup> modified total bilirubin used to score patients who have Gilbert's syndrome or who are taking atazanavir or indinavir

CHILD PUGH CLASS <sup>2,3</sup>	POINTS	ESTIMATED 2 YEAR SURVIVAL
Class A	5-6	85%
Class B	7-9	60%
Class C	>9	35%

1. Child CG, Turcotte JG. The Liver and Portal Hypertension. Philadelphia, WB Saunders Co. 1964.  
 2. Pugh RN, Murray-Lyon IM, Dawson JL, et. al. Transection of the oesophagus for bleeding oesophageal varices. Br J Surg. 1973; 60:646.  
 3. Trey C, Burns DG, Saunders SJ. Treatment of hepatic coma by exchange blood transfusion. NEJM. 1966; 274:473

## SUMMARY

## DECISION SUPPORT

## PATIENT EDUCATION/SELF MANAGEMENT

**ACUTE HCV: DIAGNOSIS, STAGING AND TREATMENT****DEFINITION**

- Positive HCV viral load with negative HCV antibody, OR
- Documented change in HCV antibody from negative to positive within a 6 month time period, OR
- A new (within the last 3 months) positive HCV antibody accompanied by:
  - a new elevation of ALT (defined as at least 5x prior baseline level obtained within the last 24 months), or
  - an increase of ALT to more than 5 times > normal ALT levels if no baseline labs in last 24 months, and
  - no other concomitant conditions to explain the rise in liver enzymes.

**EVALUATION**

- The majority of patients are asymptomatic. Clinical presentation may include jaundice, dark urine, fatigue, and/or right upper quadrant abdominal pain.
- “Time Zero” is date of first signs and symptoms of acute hepatitis, or first lab abnormalities or, if none of the above are present, most recent date of IV drug use or tattooing can be used to determine waiting time to see if HCV will spontaneously resolve.
- Obtain baseline labs: quantitative HCV VL, HCV genotype, HIV antibody, CBC, complete metabolic panel (CMP), TSH, and PT/INR.
- **Not required** for pre-treatment work up of acute HCV: interleukin 28B (IL28B) genotyping (CC, CT, TT), amylase, lipase, urinalysis, abdominal ultrasound or CT
- Confirm that HCV hasn't resolved spontaneously: recheck quantitative HCV viral load 8-10 weeks after the first identified seroconversion. If HCV VL is negative, confirm that virus has cleared by rechecking HCV VL in 4 weeks. If HCV VL is detectable at any recheck, consider treatment. No Treatment Authorization is needed.
- Consult the HCV warmline at [CDCR CPHCS HCV Questions@cdcr.ca.gov](mailto:CDCR_CPHCS_HCV_Questions@cdcr.ca.gov) if the diagnosis (acute or chronic) is uncertain.
- Screen patient using exclusion criteria listed on page 2. High risk behavior that led to this seroconversion is not an absolute contraindication to treatment of acute HCV. Counsel patient regarding risk reduction.

**TREATMENT**

**GOAL:** start acute HCV treatment no later than 24 weeks after exposure

**Treatment Regimen**

**Pegylated interferon, 180 mcg subcutaneous weekly, WITH  
Ribavirin weight based (Genotype 1,4,5 or 6;see page 12 for dosing) OR  
Ribavirin 400 mg BID (Genotype 2 or 3)**

**Stopping Rules**

Treatment week 4: Check quantitative HCV VL  
If genotype 2 or 3, and week 4 HCV VL is undetectable, treatment duration is 16 weeks.

Treatment week 12: Check quantitative HCV VL at 12 weeks  
If VL does not decrease by at least 2 log, stop all treatment.

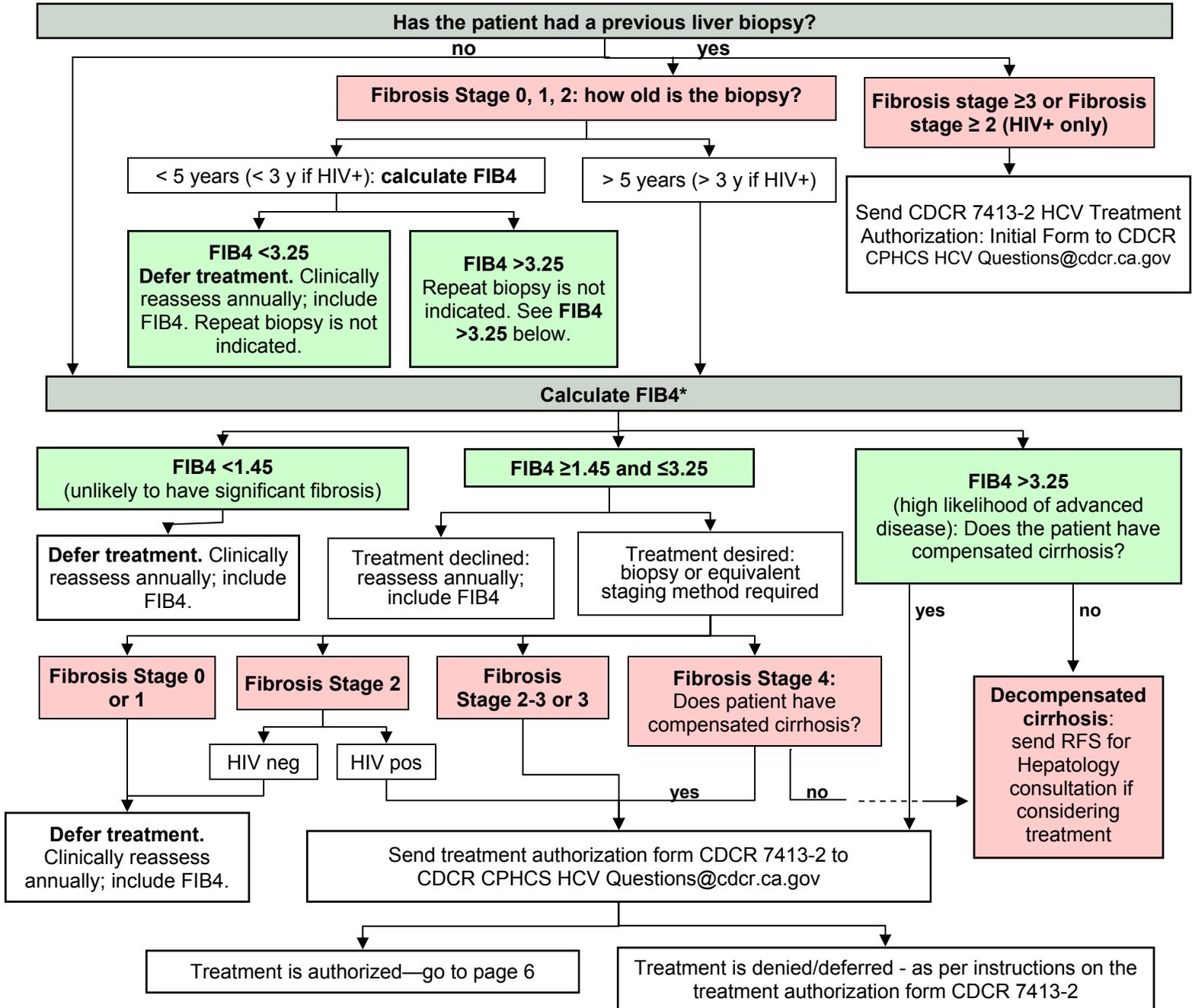
**Total Treatment Duration**

**Genotype 1,4,5 and 6:** 24 weeks

**Genotype 2 and 3:**

- If week 4 HCV VL is undetectable treatment ends after 16 weeks.
- If week 4 HCV VL is not undetectable treatment ends after 24 weeks.

**CHRONIC HCV: PATIENT SELECTION FOR TREATMENT**



**LIVER BIOPSY**

- Adequate biopsy defined as 15 mm in length with a minimum of 6-8 portal tracts seen.
- If indicated and if treatment is being considered, repeat biopsy if stage ≤2 every 5 years if HIV negative, every 3 years if HIV positive. Liver biopsy is not necessary if prior biopsy stage 3 or 4 fibrosis, or if clinically cirrhotic.
- Biopsy not required for patients with FIB4 < 1.45 or > 3.25 unless clinical condition is unclear.

**\*FIB4 = [Age(y) x AST(U/L)] / [PLT(10<sup>9</sup>/L) x ALT(U/L)<sup>1/2</sup>]**

FIB4 < 1.45 - unlikely to have significant fibrosis;

FIB4 1.45 to 3.25 - FIB4 in this range is not an accurate predictor of fibrosis stage, biopsy or equivalent staging method required;

Vallet-Pichard, A et al, FIB-4: an Inexpensive and Accurate Marker of Fibrosis in HCV Infection. Comparison with Liver Biopsy and FibroTest. Hepatology 2007;46:32-36.

SUMMARY	DECISION SUPPORT	PATIENT EDUCATION/SELF MANAGEMENT
---------	------------------	-----------------------------------

## CHRONIC HCV TREATMENT

Chronic HCV treatment is advancing at a pace more rapid than CCHCS Care Guide revision cycles. In order to avoid the publication of outdated HCV treatment regimens in this Hepatitis C Care Guide, the provider is referred to the CCHCS Hepatitis C warmline ([CDCR CPHCS HCV Questions@cdcr.ca.gov](mailto:CDCR_CPHCS_HCV_Questions@cdcr.ca.gov)) or [www.hcvguidelines.org](http://www.hcvguidelines.org) (American Association for the Study of Liver Diseases/ Infectious Diseases Society of America/ International Antiviral Society USA) for information regarding specific recommended treatment regimens for each HCV genotype and associated clinical condition[s]. Treatment protocols are available for each HCV genotype both for initial HCV treatment as well as for chronic HCV patients requiring retreatment.

**NOTE: Evaluation by HQ CCHCS HCV Oversight Committee required before initiating therapy.**  
 Email questions to [CDCR CPHCS HCV Questions@cdcr.ca.gov](mailto:CDCR_CPHCS_HCV_Questions@cdcr.ca.gov)

LAB EVALUATION: BEFORE TREATMENT DURING TREATMENT AFTER TREATMENT		LAB TESTS (OBTAIN FROM QUEST)					
		CBC	CMP	PT/INR	HCV viral load	HIV test	TSH *
Pre-treatment	Within past 12 months				✓	✓	✓
	Within past 3 months	✓	✓	✓			
During Treatment	Week 2	✓	✓				
	Week 4	✓	✓		✓		
	Week 12	✓ **	✓ **		✓ **		✓ **
End of treatment		✓	✓		✓		
After treatment	3 months after treatment is over				✓		

\*if pegylated interferon treatment is considered

\*\*Obtain these labs every 4 weeks until end of treatment

## MONITORING DURING TREATMENT AND STOPPING RULES

Rx week	Result	Sofosbuvir (SOF) containing regimens (includes ledipasvir/SOF, simeprevir/SOF)	Pegylated interferon/ ribavirin only
Week 4	ALT: >10 fold increase	<b>Stop treatment</b>	<b>Stop treatment</b>
	HCV VL: detectable	Check HCV VL at week 6	n/a
Week 6	HCV VL: 1 log increase from week 4	<b>Stop treatment</b>	n/a
	HCV VL: not undetectable but <1 log increase from week 4	Continue treatment	n/a
Week 12	HCV VL: < 2 log decrease	n/a	<b>Stop treatment</b>
	HCV VL: >2 log decrease	n/a	Check HCV VL at week 24
Week 24	HCV VL: detectable	n/a	<b>Stop treatment</b>
	HCV VL: undetectable	n/a	Continue treatment

<b>SUMMARY</b>	<b>DECISION SUPPORT</b>	<b>PATIENT EDUCATION/SELF MANAGEMENT</b>
----------------	-------------------------	--

**MEDICATIONS**

<b>DIRECT ACTING ORAL AGENTS</b>	<ul style="list-style-type: none"> <li>• <b>Do not prescribe any single agent as monotherapy.</b> If treatment interruption occurs or is anticipated, contact the HCV warmline ASAP.</li> <li>• Multiple drug-drug interactions may occur. Consult pharmacy or HCV warmline prior to initiating new medications during HCV treatment course. (See page 12)</li> </ul>
----------------------------------	---

<b>MEDICATION/DOSE</b>	<b>COMMENTS/SIDE EFFECTS</b>
------------------------	------------------------------

<p>Dasabuvir 250 mg tablet Ombitasvir/paritaprevir/ritonavir 12.5/75/50 mg [co-packaged as Viekira Pak®]</p> <p>Dasabuvir: NS5B polymerase inhibitor Ombitasvir: NS5A inhibitor Paritaprevir: NS3/4A protease inhibitor Ritonavir: CYP3A inhibitor</p> <p>Dose: two ombitasvir/paritaprevir/ritonavir twice daily with one dasabuvir twice daily</p>	<ul style="list-style-type: none"> <li>• ALT ELEVATIONS &gt;5x upper limit of normal (ULN) WITHIN 1ST 4 WEEKS OF TREATMENT             <ul style="list-style-type: none"> <li>• d/c if ALT persistently &gt;10x ULN;</li> <li>• Consider d/c if ALT elevation is accompanied by signs/symptoms of liver inflammation or increasing conjugated bilirubin, alkaline phosphatase, or INR</li> </ul> </li> <li>• CONTAINS RITONAVIR; HIV patients must be on suppressive HIV regimen to prevent development of HIV resistant mutations</li> <li>• FATIGUE</li> <li>• NAUSEA</li> <li>• PRURITIS and skin reactions including rash</li> <li>• INSOMNIA</li> </ul>
--	--

*Activity in genotypes 1 and 4*

<p><b>Ledipasvir/sofosbuvir (HAR)</b> [Harvoni®] 90/400 mg tablet</p> <p>NS5A/NS5B inhibitor</p> <p>Dose: one tablet once daily with or without food</p>	<ul style="list-style-type: none"> <li>• FATIGUE</li> <li>• HEADACHE</li> <li>• NAUSEA</li> <li>• Significant drug-drug interaction with acid lowering agents.</li> <li>• AVOID USE IN ESRD ON HEMODIALYSIS AND/OR CREATININE CLEARANCE &lt;30 ML/MIN</li> </ul>
--	--

*Activity in genotypes 1, 4, and 6*

<p><b>SOFOSBUVIR (SOF)</b> [SOVALDI®] 400 mg tablet</p> <p>NS5B Polymerase Inhibitor</p> <p>Dose: one tablet once daily with or without food</p>	<ul style="list-style-type: none"> <li>• FATIGUE AND HEADACHE</li> <li>• MONOTHERAPY IS CONTRAINDICATED: Do not use SOF without the rest of the HCV combination as HCV resistance will develop.</li> <li>• ESRD ON HEMODIALYSIS AND/OR CREATININE CLEARANCE &lt;30 ML/MIN: SOF is contraindicated</li> </ul>
--	--

*Activity in all genotypes*

<p>SIMEPREVIR (SMV) [OLYSIO®] 150 mg capsule</p> <p>NS3/4A Protease Inhibitor</p> <p>Dose: one 150 mg capsule once daily with food</p>	<ul style="list-style-type: none"> <li>• NAUSEA AND MYALGIA</li> <li>• PHOTOSENSITIVITY: Wear protective clothing and protect skin from sun. Discontinue if serious photosensitivity is noted.</li> <li>• RASH: if severe, treatment should be discontinued</li> <li>• DO NOT USE IN PATIENTS WHO HAVE PREVIOUSLY FAILED BOCEPREVIR OR TELAPREVIR.</li> </ul>
--	---

*Activity in genotypes 1 and 4*

<b>SUMMARY</b>	<b>DECISION SUPPORT</b>	<b>PATIENT EDUCATION/SELF MANAGEMENT</b>
----------------	-------------------------	--

**MEDICATIONS**

MEDICATION/DOSE	COMMENTS/SIDE EFFECTS										
<b>RIBAVIRIN (RBV)</b> 200 mg tablet/capsule	<p><b>ANEMIA:</b></p> <ul style="list-style-type: none"> <li>The primary clinical toxicity of ribavirin is hemolytic anemia (see anemia management, page 10).</li> <li>After about 2 weeks of ribavirin treatment, approximately 10% of people develop severe anemia; this may result in worsening of cardiac disease and has led to fatal and nonfatal myocardial infarctions.</li> </ul> <p><b>TERATOGENICITY (PREGNANCY):</b></p> <ul style="list-style-type: none"> <li>Due to the risk of fetal malformations and fetal death with ribavirin, a negative pregnancy test is required before treatment consideration.</li> <li>Women of childbearing potential must use 2 forms of effective contraception during treatment and for 6 months after treatment.</li> <li>Men whose female partners are pregnant or may become pregnant must use barrier contraception during treatment and for 6 months after treatment.</li> </ul> <p><b>HISTAMINE-LIKE SIDE EFFECTS:</b> nasal stuffiness, itching, skin irritation, asthma-like syndrome.</p>										
<table border="1" style="width: 100%;"> <tr> <td style="width: 50%;"><b>Weight:</b></td> <td style="width: 50%;"><b>Dose: (total daily, divided two times a day)</b></td> </tr> <tr> <td>&lt;75 kg:</td> <td>1000 mg/day</td> </tr> <tr> <td>&gt;75 kg:</td> <td>1200 mg/day</td> </tr> </table>		<b>Weight:</b>	<b>Dose: (total daily, divided two times a day)</b>	<75 kg:	1000 mg/day	>75 kg:	1200 mg/day				
<b>Weight:</b>		<b>Dose: (total daily, divided two times a day)</b>									
<75 kg:		1000 mg/day									
>75 kg:		1200 mg/day									
<i>All genotypes</i>											
<b>RBV DOSE ADJUSTMENT FOR RENAL IMPAIRMENT</b>											
<table border="1" style="width: 100%;"> <thead> <tr> <th style="width: 50%;">Creatinine Clearance</th> <th style="width: 50%;">RBV Dose (daily)</th> </tr> </thead> <tbody> <tr> <td>&gt; 50 ml/min</td> <td>No additional dosage adjustment needed</td> </tr> <tr> <td>30 to 50 ml/min</td> <td>Alternating doses, 200 mg and 400 mg every other day</td> </tr> <tr> <td>Less than 30 ml/min</td> <td>200 mg daily</td> </tr> <tr> <td>Hemodialysis</td> <td>200 mg daily</td> </tr> </tbody> </table>		Creatinine Clearance	RBV Dose (daily)	> 50 ml/min	No additional dosage adjustment needed	30 to 50 ml/min	Alternating doses, 200 mg and 400 mg every other day	Less than 30 ml/min	200 mg daily	Hemodialysis	200 mg daily
Creatinine Clearance	RBV Dose (daily)										
> 50 ml/min	No additional dosage adjustment needed										
30 to 50 ml/min	Alternating doses, 200 mg and 400 mg every other day										
Less than 30 ml/min	200 mg daily										
Hemodialysis	200 mg daily										
<b>PEGYLATED INTERFERON (PEG) [PEGASYS®]</b> Alfa 2a-given by subQ injection  Usual Dose: 180 mcg subQ once weekly	<ul style="list-style-type: none"> <li><b>FLU-LIKE SYMPTOMS:</b> fever, chills, headache, myalgia, fatigue, nausea, and anorexia. Symptoms are usually worse right after the weekly injection and can be reduced by taking analgesic medications an hour or two before each injection.</li> <li><b>DEPRESSION AND RELATED SYMPTOMS:</b> anxiety, irritability, insomnia, confusion, and difficulty with concentration and memory are common during treatment. While less common, other psychiatric side effects include aggressive behavior, psychosis, hallucinations, and mania; a few cases of suicide have been reported.</li> <li><b>NEUTROPENIA AND THROMBOCYTOPENIA:</b> see page 11 for management.</li> <li><b>ADDITIONAL SIDE EFFECTS:</b> colitis, pancreatitis, vision problems, pruritus, hair loss, and injection site reactions.</li> <li><b>WARNINGS:</b> Pegylated interferon should not be used in those with the following conditions:                             <ul style="list-style-type: none"> <li>kidney, lung, or heart transplants</li> <li>known hypersensitivity to pegylated interferon components</li> <li>decompensated cirrhosis</li> <li>autoimmune hepatitis</li> <li>uncontrolled major depression</li> </ul> </li> <li>Pegylated interferon should be used with caution, preferably by a specialist, in people with heart and thyroid problems, pulmonary disorders, and other autoimmune diseases.</li> <li><b>DOSE ADJUSTMENT FOR RENAL IMPAIRMENT:</b></li> </ul>										
<i>All genotypes</i>											
<table border="1" style="width: 100%;"> <thead> <tr> <th style="width: 50%;">Creatinine Clearance</th> <th style="width: 50%;">PEG Alfa 2a dose (once weekly)</th> </tr> </thead> <tbody> <tr> <td>&gt; 50 ml/min</td> <td>No dosage adjustment needed</td> </tr> <tr> <td>30 to 50 ml/min</td> <td>180 mcg</td> </tr> <tr> <td>Less than 30 ml/min</td> <td>135 mcg</td> </tr> <tr> <td>Hemodialysis</td> <td>135 mcg</td> </tr> </tbody> </table>		Creatinine Clearance	PEG Alfa 2a dose (once weekly)	> 50 ml/min	No dosage adjustment needed	30 to 50 ml/min	180 mcg	Less than 30 ml/min	135 mcg	Hemodialysis	135 mcg
Creatinine Clearance	PEG Alfa 2a dose (once weekly)										
> 50 ml/min	No dosage adjustment needed										
30 to 50 ml/min	180 mcg										
Less than 30 ml/min	135 mcg										
Hemodialysis	135 mcg										

SUMMARY	DECISION SUPPORT	PATIENT EDUCATION/SELF MANAGEMENT
<b>MEDICATIONS</b>		
<b>MEDICATION/DOSE</b>		<b>COMMENTS / SIDE EFFECTS</b>
<b>COLONY STIMULATING FACTORS (EPOETIN ALFA AND FILGRASTIM)</b>		
<p><b>EPOETIN ALFA</b>                      10,000 units/ml, 20,000 units/ml,                      40,000 units/ml, 4,000 units/ml,                      3,000 units/ml, 2,000 units/ml                      Usual Dose:                      50-100 units/kg subQ,                      (IV preferred if dialysis)                      three times weekly                      150-300 units/kg subQ once                      weekly (maximum 40,000                      units weekly)                      Titrate to maintain                      Hgb 10-12 g/dl</p>	<ul style="list-style-type: none"> <li>• Epoetin alfa does not have a U.S. Food and Drug Administration (FDA) indication for the treatment of ribavirin associated anemia although it is commonly used for this complication of treatment.</li> <li>• Epoetin alfa is associated with significant toxicities, including pure red cell aplasia and cardiovascular risks such as thromboembolic events and strokes.</li> <li>• Use with caution in patients with malignancies, hypertension, cardiovascular disease, hypercoagulable conditions, sickle cell disorders and seizures.</li> <li>• Health care professionals who prescribe epoetin alfa to patients with anemia from causes other than cancer chemotherapy are required to provide a copy of the <i>Medication Guide</i> to each patient. Please see <a href="http://www.fda.gov/downloads/Drugs/Drugsafety/ucm088988.pdf">http://www.fda.gov/downloads/Drugs/Drugsafety/ucm088988.pdf</a> for a copy of this medication guide.</li> <li>• Prior to the initiation of epoetin for the correction of anemia in the patient receiving HCV treatment, a consultation with the CCHCS HCV warmline is <i>strongly</i> recommended at CDCR CPHCS HCV Questions@cdcr.ca.gov.</li> <li>• Frequent Hgb monitoring is required</li> <li>• Avoid increase of Hgb &gt; 1g/dl over a two week period</li> </ul>	
<p><b>FILGRASTIM</b>                      300 mcg vial                      480 mcg vial                      Usual Dose:                      Dose required to reach target                      Absolute neutrophil count                      (ANC) varies, but is generally                      150 to 300 mcg subQ one to                      three times weekly. Frequent                      CBC monitoring is required.</p>	<p><b>Management of Neutropenia</b></p> <ul style="list-style-type: none"> <li>• Filgrastim does not have an FDA indication for the treatment of pegylated interferon associated neutropenia. Prior to the initiation of filgrastim for the correction of neutropenia in the patient receiving HCV treatment, a consultation with the CCHCS HCV warmline is <i>strongly</i> recommended at CDCR CPHCS HCV Questions@cdcr.ca.gov.</li> <li>• Signs/symptoms of neutropenic fever require emergent evaluation.</li> <li>• For <u>non-febrile patients</u>, filgrastim should be used only in consultation with a specialist and should be limited to patients who have:                             <ol style="list-style-type: none"> <li>1. failed to respond to dose reductions of interferon (from 180 mcg/wk to 135 mcg/wk).</li> <li>2. persistent severe neutropenia. (See page 11)</li> <li>3. an excellent response to therapy (as measured by HCV viral load) such that continued treatment is desirable.</li> <li>4. been counseled regarding the increased risk for infectious complications, and have signed informed consent that they desire to continue with both HCV treatment and filgrastim.</li> </ol> </li> </ul>	

**Bold = Formulary**

<b>SUMMARY</b>	<b>DECISION SUPPORT</b>	<b>PATIENT EDUCATION/SELF MANAGEMENT</b>
----------------	-------------------------	--

**MANAGEMENT OF SIDE EFFECTS OF HEP C TREATMENT**

**ANEMIA - CONSIDER CONSULTATION WITH HCV WARMLINE AT CDCR CPHCS HCV QUESTIONS@CDCR.CA.GOV**

HEMOGLOBIN g/dl	ACTION
< 10 g/dl in patients with no history of cardiac disease	<ul style="list-style-type: none"> <li>Decrease ribavirin (RBV) to 600 mg/day*</li> <li>Recheck Hgb weekly</li> </ul>
≥ 2 g/dl decrease during any 4 week period and history of stable cardiovascular disease	<ul style="list-style-type: none"> <li>Decrease RBV to 600 mg/day*</li> <li>Recheck Hgb weekly</li> </ul>
Hgb 8.6-9.0 g/dl	<ul style="list-style-type: none"> <li>RBV dose reduction to 600 mg/day if not already done</li> <li>Weekly Hgb monitoring</li> <li>Consider epoetin alfa if the dose has been reduced to 600 mg/day for at least two weeks with continued drop in Hgb                             <ul style="list-style-type: none"> <li>Careful review with patient of risks/benefits of epoetin alfa vs. stopping HCV treatment.** † Provide the epoetin alfa medication guide (see page 12).</li> <li>If the patient agrees to treatment with epoetin alfa, start at 150-300 units/kg/week                                     <ul style="list-style-type: none"> <li>If follow-up Hgb is 9.0-9.9 g/dl, decrease epoetin alfa to 100 units/kg once weekly and continue RBV at 600 mg/day.</li> <li>If follow up Hgb is 10.0 g/dl or above, stop epoetin alfa. If the next weekly Hgb remains at 10.0 g/dl or above, increase RBV by 200 mg at two week intervals until initial RBV dose is reached.</li> </ul> </li> </ul> </li> <li>Symptomatic anemia: discontinue HCV treatment** †</li> </ul>
Hgb 8.0-8.5 g/dl	<ul style="list-style-type: none"> <li>RBV dose reduction to 600 mg/day if not already done</li> <li>Weekly Hgb monitoring</li> <li>Careful review with patient of risks/benefits of epoetin alfa vs. stopping HCV treatment.** †</li> <li>If considered clinically stable to continue HCV treatment and if the patient agrees, provide epoetin alfa medication guide (see page 12) and start epoetin alfa at 150-300 units/kg/week                             <ul style="list-style-type: none"> <li>If follow-up Hgb is 9.0-9.9 g/dl, decrease epoetin alfa to 100 units/kg once weekly and continue RBV at 600 mg/day.</li> <li>If follow-up Hgb is 10.0 g/dl or above, epoetin alfa can be discontinued. If the next weekly Hgb remains at 10.0 g/dl or above, increase RBV by 200 mg at two week intervals until the initial RBV dose is reached.</li> </ul> </li> <li>Symptomatic anemia: consider inpatient management and RBC transfusion and consider discontinuing HCV treatment** †</li> </ul>
Hgb 7.5-7.9 g/dl	<ul style="list-style-type: none"> <li>Review with patient the risks of anemia and stopping HCV treatment vs. the risk of continuing HCV treatment and epoetin alfa.** † Provide epoetin alfa medication guide to patients starting epoetin alfa (see page 12).</li> <li>Stop RBV (If on DAA, discontinue medication and contact the HCV warmline)</li> <li>Weekly CBC monitoring</li> <li>If considered clinically stable and if patient agrees to continue HCV treatment and treatment with epoetin alfa, continue epoetin alfa at 150-300 units/kg/week                             <ul style="list-style-type: none"> <li>If Hgb is 9.0-9.9 g/dl, decrease epoetin alfa to 100 units/kg once weekly and continue RBV at 600 mg/day.</li> <li>If Hgb is 10.0 g/dl or above, epoetin alfa can be discontinued. If the next weekly Hgb remains at 10.0 g/dl or above, increase RBV by 200 mg at two week intervals until the initial RBV dose is reached.</li> </ul> </li> <li>Symptomatic anemia: discontinue HCV treatment** † and consider inpatient management and RBC transfusion.</li> </ul>
Hgb < 7.5 g/dl or symptomatic anemia	<ul style="list-style-type: none"> <li>Terminate HCV treatment†</li> </ul>

\* If RBV dose is reduced for anemia:  
 • Once Hgb has increased to > 10.0 g/dl, increase the dose by 200 mg/day at two week intervals until the initial dose is reached

\*\* If RBV is temporarily stopped due to anemia:  
 • Recheck Hgb within two weeks and at two week intervals until stable  
 • If Hgb is > 10.0 g/dl, restart RBV at a dose of 600 mg/day if patient's weight < 75 kg; 800 mg/day if patient's weight ≥ 75 kg  
 • If hemoglobin remains > 10.0 g/dl, increase dose by 200 mg/day at two week intervals until the initial dose is reached

§ If the patient is taking protease or polymerase inhibitor, urgent consultation with the CCHCS HCV warmline is *strongly* recommended prior to stopping PEG or RBV as resistance can develop rapidly. CDCR CPHCS HCV Questions@cdcr.ca.gov.

† If genotype 1, and treatment is discontinued, submit CDCR 7413-4, HCV Treatment Referral: End of Treatment Evaluation to CDCR CPHCS HCV Questions@cdcr.ca.gov

<b>SUMMARY</b>	<b>DECISION SUPPORT</b>	<b>PATIENT EDUCATION/SELF MANAGEMENT</b>
----------------	-------------------------	--

**MANAGEMENT OF SIDE EFFECTS OF HEP C TREATMENT (CONT'D)**

<b>THROMBOCYTOPENIA</b>	
<i>CONSIDER CONSULTATION WITH HCV WARMLINE AT CDCR CPHCS HCV QUESTIONS@CDCR.CA.GOV</i>	
PLATELET COUNT	ACTION
< 50,000 / $\mu$ l	<ul style="list-style-type: none"> <li>• Decrease PEG to 135 mcg/week</li> </ul>
< 25,0000 / $\mu$ l	<ul style="list-style-type: none"> <li>• Discontinue PEG<sup>§†</sup></li> </ul>

<b>LEUKOPENIA/NEUTROPENIA -</b>	
<i>CONSIDER CONSULTATION WITH HCV WARMLINE AT CDCR CPHCS HCV QUESTIONS@CDCR.CA.GOV</i>	
COUNT	ACTION
WBC < 1000 cells/ $\mu$ l	<ul style="list-style-type: none"> <li>• Discontinue PEG<sup>§†</sup></li> </ul>
ANC < 750 cells / $\mu$ l	<ul style="list-style-type: none"> <li>• Decrease PEG to 135 mcg/week</li> </ul>
ANC < 500 cells/ $\mu$ l	<ul style="list-style-type: none"> <li>• Consider filgrastim [granulocyte colony stimulating factor-GCSF] (see dosing, page 9) if asymptomatic and:                             <ul style="list-style-type: none"> <li>◦ ANC &lt; 500 cells/<math>\mu</math>l and                                     <ul style="list-style-type: none"> <li>&gt; HIV positive</li> <li>&gt; cirrhotic</li> <li>&gt; age &gt; 55</li> </ul> </li> <li>◦ ANC &lt; 400 cells/<math>\mu</math>l and                                     <ul style="list-style-type: none"> <li>&gt; HIV negative</li> <li>&gt; not cirrhotic</li> <li>&gt; age &lt; 55</li> </ul> </li> </ul> </li> <li>• Monitor patient weekly to assess for signs of infection, provide education regarding warning signs of acute illness or fever and weekly WBCs.</li> <li>• Stop HCV treatment if:                             <ul style="list-style-type: none"> <li>◦ Patient presents with a neutropenic fever, acute illness or infection. Emergent evaluation recommended.</li> <li>◦ ANC drops to &lt; 250 cells/<math>\mu</math>l</li> <li>◦ ANC declines from prefilgrastim nadir after two or more weekly doses of filgrastim</li> </ul> </li> <li>• If ANC rises to over 750 cells/<math>\mu</math>l, reduce weekly dose of filgrastim by 50%                             <ul style="list-style-type: none"> <li>◦ If subsequent weekly ANC is &gt; 750 cells/<math>\mu</math>l, discontinue filgrastim</li> <li>◦ If subsequent weekly ANC is &lt; 750 cells/<math>\mu</math>l, increase filgrastim to original dose</li> </ul> </li> <li>• If ANC increases to &gt; 2000 cells/<math>\mu</math>l, discontinue filgrastim</li> </ul>

<sup>§</sup> If the patient is taking protease or polymerase inhibitor, urgent consultation with the CDCR CCHCS HCV warmline is *strongly* recommended prior to stopping PEG or RBV as resistance can develop rapidly. CDCR CPHCS HCV Questions@cdcr.ca.gov.

<sup>†</sup> If treatment is discontinued, submit CDCR 7413-4 HCV Treatment Referral: End of Treatment Evaluation to CDCR CPHCS HCV Questions@cdcr.ca.gov

## SUMMARY

## DECISION SUPPORT

## PATIENT EDUCATION/SELF MANAGEMENT

**Summary of “FDA Drug Safety Communication: Erythropoiesis-Stimulating Agents (ESAs): Epogen® and Aranesp®” as it pertains to the use of Epogen® (epoetin alfa) for Hepatitis C patients who have become anemic from HCV treatment.**

### Safety Announcement

The FDA said in a safety announcement dated 02/16/2010, that it is requiring all ESAs to be prescribed and used under a risk management program to ensure the safe use of these drugs. Epogen®, which we may prescribe to our hepatitis C patients who have become anemic due to their use of ribavirin or interferon, is an ESA.

According to the safety announcement, studies have shown that ESAs can increase the risk of heart attack, heart failure, stroke, and blood clots in patients who use these drugs for conditions other than cancer.

This announcement was primarily focused on cancer patients and oncologists.

The announcement said that **health care professionals** who prescribe ESAs to patients who have anemia from causes other than cancer chemotherapy **are**:

- Required to provide a copy of the *Medication Guide* to each patient or his/her representative when an ESA is dispensed
- Not required to enroll in the ESA APPRISE Oncology program.

The announcement added that **patients** with chronic kidney failure, including those on dialysis and those not on dialysis, who are using ESAs **should**:

- Know that the use of ESAs can increase the risk for stroke, heart attack, heart failure, blood clots, and death.
- Read the *Medication Guide* to understand the benefits and risks of using an ESA (which can be found at <http://www.fda.gov/downloads/Drugs/Drugsafety/ucm088988.pdf> )
- Get blood tests while using ESAs. The test results help guide the course of therapy and lower the risks of using these drugs. A patient’s health care professional should make them aware of how often to have blood tests.
- Talk with their health care professional about any questions they have about the risks and benefits of using ESAs.

### DRUG-DRUG INTERACTIONS

Multiple drug-drug interactions exist between the direct acting HCV medications and other medication classes, including, but not limited to, certain antimicrobials, analgesics, antiarrhythmics, oral contraceptives, anxiolytics, lipid lowering agents, acid lowering agents, antiretrovirals, herbal preparations, corticosteroids, and anticonvulsants and specific medications such as rifampin, salmeterol, and warfarin.

For more information on drug-drug interactions:

- › **Contact the HCV warmline at [CDCR CPHCS HCV Questions@cdcr.ca.gov](mailto:CDCR_CPHCS_HCV_Questions@cdcr.ca.gov)**
- › **<http://www.hep-druginteractions.org>**

**PATIENT EDUCATION/SELF MANAGEMENT**



**WHAT YOU SHOULD KNOW: HEPATITIS C VIRUS**

**WHAT IS HEPATITIS C?**

- Hepatitis C is a virus that causes swelling and irritation of the liver.
- The liver helps with digestion and filters waste products out of the blood. Hepatitis C can cause serious damage to the liver.
- There is no vaccination for hepatitis C, but you can be vaccinated for hepatitis A and B to prevent more damage to your liver.

**HOW DO YOU GET HEPATITIS C?**

You can get hepatitis C from:

- Dirty needles (tattoos or piercing)
- Snorting drugs with infected equipment
- Sharing needles to inject drugs
- Unprotected sex (rarely)
- A blood transfusion if you got one in the United States before 1992. (All blood is now tested for hepatitis C before it is used for transfusion)



**HOW DO YOU KNOW IF YOU HAVE HEPATITIS C?**

- |   |   |
|---|---|
| <ul style="list-style-type: none"> <li>➢ Most people who have hepatitis C look and feel fine.</li> <li>➢ You can have hepatitis C for a long time and not know it.</li> <li>➢ Usually hepatitis C is found by doing blood tests.</li> <li>➢ If hepatitis C damages the liver, it can cause scarring. This is called cirrhosis (sir-oh-sis).</li> <li>➢ Your health care provider may order more tests to see how much liver damage you have.</li> </ul> | <ul style="list-style-type: none"> <li>➢ Some people with hepatitis C can have:                             <ul style="list-style-type: none"> <li>• Fatigue</li> <li>• Stomach pain</li> <li>• Joint pain</li> <li>• Night sweats</li> <li>• Loss of appetite or nausea</li> </ul> </li> </ul> |
|---|---|



**WHAT CAN YOU DO TO TAKE CARE OF YOURSELF?**

- Get vaccinated for hepatitis A and B. Get yearly vaccinations for pneumonia and the flu.
- Do not drink alcohol or use illegal drugs - these will damage your liver more.
- Do not take a lot of medications like acetaminophen (Tylenol®) and Motrin®. Talk to your health care provider about all medications, including over-the-counter medications, vitamins, and herbs to be sure they will not damage your liver. Ask your health care provider before you take any pain medicine.
- Do not get tattoos in prison to avoid blood borne infections.
- Do not share your toothbrush, razor, or other personal items.
- Try to lose weight if you are overweight.
- Eat a healthy diet.
- Drink plenty of water.
- Get plenty of rest and regular exercise.
- Quit smoking cigarettes.
- Follow your health care provider's instructions about medications for hepatitis C treatment.
- See your health care provider regularly.



**DOES EVERYONE WITH HEPATITIS C NEED TREATMENT?**

- Most people with hepatitis C do not need treatment.
- A few people may develop severe liver damage and can die from problems with hepatitis C.
- Who needs treatment depends on many things and these are different for each person. You should discuss your case with your health care provider.

## EDUCACIÓN DEL PACIENTE/MANEJO PERSONAL



### ¿QUÉ DEBE USTED SABER: HEPATITIS C

#### ¿QUÉ ES LA HEPATITIS C?

- La hepatitis C es un virus que produce inflamación e irritación del hígado.
- El hígado ayuda a la digestión y filtra los productos de desecho fuera de la sangre. La hepatitis C puede causar daños serios al hígado.
- No existe vacuna para prevenir la hepatitis C, pero usted puede vacunarse contra la hepatitis A y B para evitar dañar más su hígado.

#### ¿CÓMO SE PUEDE CONTRAER LA HEPATITIS C?

La hepatitis C se puede contraer de las siguientes maneras:

- Agujas contaminadas (tatuajes o perforaciones).
- Inhalar drogas usando un equipo infectado.
- Compartir agujas para inyectarse drogas.
- Practicar sexo sin protección (raras veces).
- Mediante transfusión de sangre si se realizó en EE.UU. antes de 1992.  
(Actualmente, toda transfusión de sangre es sometida a la prueba de hepatitis C antes de realizarse.)



#### ¿CÓMO SABER SI USTED SUFRE DE HEPATITIS C?

- La mayoría de las personas enfermas lucen y se sienten sanas.
- Se puede sufrir de hepatitis C por un tiempo largo y no saberlo.
- Usualmente se puede detectar la hepatitis C mediante un examen de sangre.
- Si la hepatitis C daña el hígado, puede producir cicatrices. Esto se conoce como cirrosis. Su médico puede indicarle otros exámenes para verificar el daño que tiene su hígado.
- Algunas personas que sufren de hepatitis C presentan:
  - Fatiga
  - Dolor estomacal
  - Dolor en las articulaciones
  - Sudoración nocturna
  - Pérdida del apetito o náuseas



#### ¿QUÉ PUEDE HACER USTED PARA CUIDARSE?

- Hágase vacunar contra la hepatitis A y B. Vacúnese anualmente contra la neumonía y la gripe.
- No consuma alcohol ni use drogas ilícitas - estas producirán más daño al hígado.
- No ingiera gran cantidad de medicamentos como el acetaminofén (Tylenol®) y Motrin®. Consulte con su médico acerca de todos los medicamentos, incluyendo los medicamentos de venta sin prescripción, vitaminas y hierbas para evitar dañar el hígado. Consulte con su médico antes de ingerir cualquier medicamento analgésico.
- No se realice tatuajes en la prisión para evitar enfermedades de transmisión sanguínea.
- No comparta su cepillo dental, rasuradora u otros objetos personales.
- Trate de adelgazar si tiene sobrepeso.
- Mantenga una dieta sana.
- Ingiera abundante cantidad de agua.
- Tenga mucho descanso y realice ejercicio con regularidad.
- Abandone el hábito de fumar cigarrillos.
- Siga las instrucciones de su médico acerca de los medicamentos para tratar la hepatitis C.
- Consulte con regularidad con su médico.



#### ¿TODA PERSONA QUE SUFRE DE HEPATITIS C NECESITA TRATAMIENTO?

- La mayoría de las personas que sufren de hepatitis C no requieren tratamiento.
- Solo pocas personas pueden desarrollar serios problemas del hígado y morir debido a complicaciones causadas por la hepatitis C.
- La necesidad de tratamiento depende de muchos factores y estos varían en cada persona. Discuta su caso con su médico.