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## **Primary Care Case Management Clinical Pathway For the Treatment of Hepatitis C ©**

### **Version 6.0c**

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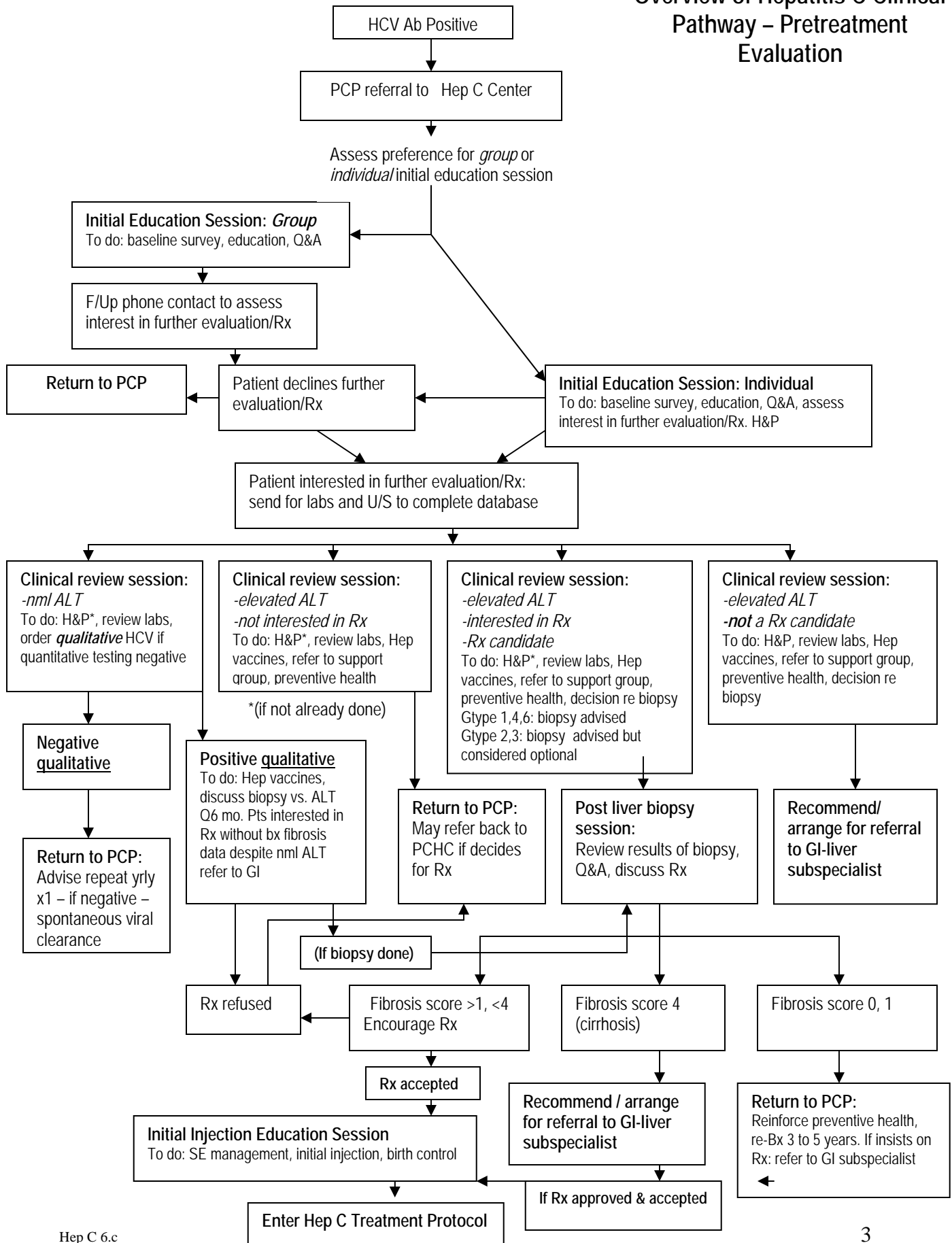
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# Overview of Hepatitis C Clinical Pathway – Pretreatment Evaluation



# Hepatitis C Primary Care Case Management Clinical Pathway

## *Pretreatment Evaluation Protocol*

### **1. Session One – Initial Education Session**

**Format:** *Group education session – lecture, followed by question and answer session. If referred patient declines to participate in a group session due to privacy concerns, then individual education sessions should be scheduled. The 1:1 session will incorporate the H&P in addition to the tasks listed below)*

**Participants:** *Clinic Physician, Nurse Case Manager (NCM), Health Educator; Patients testing positive for hepatitis C referred by PCP. Concerned family and friends may also attend.*

**Timing:** *Monthly or as needed based on referral frequency*

1. Patients learn about (see appendix 1: “Baseline Education Session Outline”);
  - a. HVC epidemiology, clinical course, treatment (see appendix 2: “Hepatitis C General Information Sheet,” and appendix 3: “Side Effects of Interferon and Ribavirin” as well as Hepatitis C Information Resource Guide for Santa Cruz County, interested patients may be given info on managing HCV symptoms with acupuncture)
  - b. Patients complete “Patient Baseline Datasheet” (see appendix 4) that captures: basic demographics, relative and absolute contraindications to treatment, subspecialist referral indications, patient preference for communication, and risk criteria as follows:
    - i. Transfusion of blood products prior to 1992
    - ii. Injection illicit drug use: past or present, (any number of injections, and subcutaneous or intravenous site)
    - iii. Unequivocal blood exposure on or through skin (or mucous membrane) for health care workers, combat casualty care, needle stick injury
    - iv. Sexual partner positive for HCV
    - v. Multiple (>50) life time sexual partners, past or present
    - vi. Hemodialysis
    - vii. Tattoo or body piercing
    - viii. Intranasal cocaine use, past or present
    - ix. Alcohol use:
      1. years daily (or nearly daily)
      2. average daily quantity
      3. last alcohol date
      4. history of binge drinking
    - x. Past history of jaundice.
    - xi. Ever tested positive for hepatitis B, A
2. Ever tested positive for HIV  
If individual education session, then initial physical exam performed (see appendix 5: “ Hep C Center - Initial H&P Template” at this session and baseline studies ordered (see phone contact to initial education session). Referral to local support group as desired by patient.

## 2. Session Two – Follow up phone contact to initial group education session

**Format:** *Phone conversation*

**Participants:** *NCM*

*Referred patients who participated in initial education session*

**Timing:** *During week following initial education session*

1. NCM reviews patient initial database survey: identifies: missing data, potential contraindications to treatment, interest in pursuing further evaluation and treatment
2. NCM contacts each patient by phone to complete initial database, go over possible contraindications to treatment at the primary care level (see appendix 7), permit further questions to be asked/answered, and to assess interest in pursuing further workup and possible treatment. All patients are encouraged to at least complete the “Initial Hep C Workup” (see below) and to attend session 3 (initial clinical visit) in order to assess for advanced liver disease detect co-morbidities, and to receive education regarding preventive health measures (ETOH abstinence, hepatitis A, B vaccines as appropriate).
3. If a patient has no interest whatsoever in pursuing further workup and treatment of Hep C, The NCM attempts to clarify the reason(s) for this decision, and the patient is strongly advised to follow up with their PCP. A summary letter is sent to PCP that encourages referral back to the Hep C Center should the patient change his/her mind, outlines the known clinical history/data, documents the patient’s decision to forego further evaluation, and makes recommendations for PCP management of the patient as follows:
  - a. Minimalist lab assessment:
    - i. Obtain HCV viral load – quantitative or qualitative (confirms active infection)
    - ii. Obtain (or review previous values) “surrogate” markers for cirrhosis; bilirubin, albumin, platelets, cholesterol, INR, AFP. Note: these are all very insensitive indicators of advanced liver fibrosis.
    - iii. Serologic testing for evidence of immunity against Hepatitis A, B, and vaccinate against each as indicated. Offer vaccination empirically against both if patient refuses serologic testing.
  - b. Physical exam with attention to signs of cirrhosis: spider angioma, palpable spleen tip, ascites, peripheral edema, asterixis, etc.
  - c. Reinforcement of importance of abstinence from alcohol
4. Patients who are interested in further workup and treatment are scheduled for initial clinical visit and are instructed to go for the following additional bloodwork/testing (note, some of these studies may already be available on referral):

### ***Initial Hep C Laboratory Workup:***

- a. HCV genotype
- b. HCV viral load – quantitative
- c. INR
- d. CBC with platelets
- e. AFP
- f. HIV if appropriate
- g. TSH
- h. U/A
- i. Ferritin, FE/TIBC

- j. Comprehensive chemistry panel
- k. HBsAg, anti-HBs, anti-HBc, anti-HAV
- l. Lipid panel or total cholesterol
- m. Ceruloplasmin if <50 years old
- n. ANA if globulin (total protein-albumin) greater than 4 g/dL
- o. Pregnancy test (urine) if female of childbearing capacity
- p. AMA if pruritus is a major symptom, or if Alk Phos known to be >1.5x ULN
- q. Rheumatoid factor

ABDOMINAL ULTRASOUND to assess liver surface nodularity and r/o incidental mass, check for splenic enlargement and ask for spleen size. (If positive for signs of cirrhosis or liver mass, refer to GI subspecialist.)

### 3. Session Three – Initial Clinical Review

**Format:** *Clinic visit (phone not acceptable)*

**Participants:** *Clinic physician +/- NCM*

*Patients expressing interest in further workup and treatment of Hep C infection, interested family and friends*

**Timing:** *After “Initial Hep C Workup” completed. Goal is to schedule within 2 weeks of initial education session.*

1. Database, labs, studies reviewed.
2. If not already done, initial physical exam is performed and documented on template (see appendix 5: “ Hep C Center – Initial H&P Template”)
3. Next steps determined according to patient category as follows:
  - a. Patients ***with normal ALT***, [normal defined as >17 for women and >24 for men] order HCV viral load :
    - i. If qualitative or quantitative TMA viral load is *negative*:
      1. Return to PCP with summary letter that includes a recommendation for:
        - a. HCV qualitative TMA viral load yearly x2 years. If remains negative, consider Hep C infection resolved naturally, and discontinue follow up testing.
    - ii. If qualitative TMA viral load is *positive*:
      1. obtain quantitative NAT test such as bDNA or PCR
      2. counsel patient that although likelihood of significant fibrosis is lower than in patients with elevated ALT, significant fibrosis is possible. Liver biopsy is the definitive test to assess whether or not fibrosis is present to the degree that would warrant treatment. Discuss risks and benefits of treatment (see appendix 2 and 3).
      3. If patient desires liver biopsy, schedule procedure.
      4. If patient is not interested in liver biopsy, explore non-histologic indications for treatment:
        - a. Medical: possible HCV-related symptoms; fatigue, cryoglobulinemia-related disease (rash, renal disease), etc.

- b. Psychosocial: stress/worry re: label of chronic viral infection, infectiousness, barriers to normal sexual function, relationships
    - c. Financial: inability to obtain health or life insurance, anticipated loss of health insurance coverage, etc.
    - d. Obstetrical: concern over even low risk of passing HCV to newborn.
    - e. Occupational: contagion risk to others in line of work (health or sporting careers).
  - 5. Encourage vaccination for Hep B and Hep A as appropriate (consider “Twinrix” vaccine if susceptible to both A and B)
  - 6. If not interested in treatment, return to PCP with summary letter that includes recommendations for:
    - a. Appropriate hepatitis vaccination series
    - b. ongoing counseling for ETOH abstinence
    - c. ALT testing Q 6–12 months until elevation of liver enzymes Interested persons may be referred to HCV specialist acupuncturist for management of extra-hepatic symptoms, test ALT more often if there is the use of liver toxic medications
- b. Patients ***with elevated ALT***, who are appropriate ***candidates for treatment*** in the Hep C Center, ***but are not interested*** in treatment at the current time:
  - i. Review clinical course of Hep C, preventive health measures for Hep C infected persons.
  - ii. Review risks and benefits of treatment (appendix 2 and 3).
  - iii. Clarify and document reasons for decision not to pursue treatment.
  - iv. Encourage vaccination for Hep B and Hep A as appropriate (consider “Twinrix” vaccine if susceptible to both A and B)
  - v. Offer referral to ongoing endorsed Hep C support group, endorsed complementary medicine practitioners (acupuncturist, etc.)
  - vi. Return to PCP with summary letter that:
    - 1. offers to see patient again should a preference for treatment are expressed.
    - 2. recommends completion of hepatitis vaccination series
    - 3. advises ongoing encouragement of ETOH abstinence
- c. Patients ***with elevated ALT***, who are appropriate ***candidates for treatment*** in the Hep C Center, ***and interested*** in treatment:
  - i. Review risks and benefits of treatment (appendix 2 and 3).
  - ii. Encourage vaccination for Hep A and Hep B as appropriate (consider “Twinrix” vaccine if susceptible to both A and B)
  - iii. For HCV Genotypes 1,4,6:
    - 1. Discuss risks and benefits of liver biopsy – see appendix 6 “Liver Biopsy in Pretreatment Evaluation of Hepatitis C Infection” (Note;

- given reduced efficacy and prolonged treatment time with these genotypes, biopsy is strongly recommended)
2. Schedule liver biopsy by Radiology under ultrasonographic guidance. Notify Radiology if iron overload suspected (requires additional specimens for special processing)
  3. If patient declines liver biopsy, and treatment still planned, prescriptions for interferon and ribavirin written (see session four) and NCM assists patient in obtaining insurance approval for therapy. When medication available, appointment for session 5 - “Initial Injection Education Session” made.
- iv. For HCV Genotypes 2,3
1. Discuss risks and benefits of liver biopsy – see appendix 6 (note: liver biopsy is optional for genotypes 2,3)
  2. If patient agrees, schedule liver biopsy by Radiology under ultrasonographic guidance. Notify Radiology if iron overload suspected. Obtain sufficient tissue for quantitative iron.
  3. If patient declines liver biopsy, and treatment still planned, discuss risk of life threatening or fatal events that have been reported with interferon/ ribavirin treatment including all side effects listed in the appendix on side effects, then, if the patient continues to decline a liver biopsy, and there are no absolute or relative contraindications for interferon and ribavirin, provide prescriptions for interferon and ribavirin written (see session 4) and NCM assists patient in obtaining insurance approval for therapy. When medication available, appointment for session 5 - “Initial Injection Education Session” made.
- v. Obtain additional labs if indicated to complete pretreatment database:
1. If gamma globulin >4 g/dL, obtain ANA, Anti-SMA (if not done already), mandate liver biopsy to rule out autoimmune liver disease
  2. If glucose elevated, obtain repeat fasting glucose and HGB a 1 c.
- vi. Schedule post liver biopsy case review appointment.
- d. Patients with elevated ALT, but who have contraindications to Hep C Center treatment (see appendix 7: “Clinical Exclusion Criteria for HCV Treatment”) should be offered vaccination for Hep B and Hep A (consider vaccination with “Twinrix” vaccine if susceptible to both A and B), and managed as follows:
- i. Patients with clinical exclusion criteria that are not permanent (may be treated in Hep C Center if improvement occurs):
    1. Counselor regarding the barrier to current treatment candidacy
    2. Given follow up appointment in 6 months for reassessment.
    3. Offered referral to ongoing endorsed Hep C support group
    4. Clinical summary letter sent to PCP that:
      - a. Outlines contraindications to current treatment
      - b. Recommends completion of hepatitis vaccine series
      - c. Recommends ongoing abstinence from ETOH and other hepatotoxins

- ii. Patients with comorbidities that complicate the treatment of Hep C (may be treated at subspecialist level):
  - 1. Should be referred to GI and other subspecialists (see appendix 7: “Clinical Exclusion Criteria for HCV Treatment – special clinical issues”) as appropriate with accompanying clinical summary (note: PCP may be required to make these referrals).
  - 2. Clinical summary letter sent to PCP that:
    - a. Outlines reason for referral to subspecialist(s).
    - b. Recommends completion of hepatitis vaccine series
    - c. Recommends abstinence from ETOH/ hepatotoxins.
  - 3. Offer referral to ongoing endorsed Hep C support group.
- iii. Patients with absolute contraindications to treatment (see appendix 7):
  - 1. should be referred to GI subspecialists with accompanying clinical summary (note: PCP may be required to make the referral).
  - 2. Clinical summary letter sent to PCP that:
    - a. Outlines reason for referral to GI
    - b. Recommends completion of hepatitis vaccine series
    - c. Recommends ongoing abstinence from ETOH and other hepatotoxins.
  - 3. Offer referral to ongoing endorsed Hep C support group, endorsed complementary medicine practitioners (acupuncturist, etc.)

**4. Session Four – Post-Liver Biopsy Case Review (note: patients who are not undergoing liver biopsy go directly to session five)**

*Format: Clinic visit (phone contact optional)*

*Participants: Clinic physician +/- NCM*

*Patients who have undergone liver biopsy, interested family and friends*

*Timing: After liver biopsy. Goal is to schedule within 2 weeks of liver biopsy.*

- 1. Results of liver biopsy discussed
- 2. Discuss indicated therapy as follows:
  - a. Fibrosis score, F0 or F1 [low likelihood of progression to cirrhosis];
    - i. Explore non-histologic indications for treatment:
      - 1. Medical: possible HCV-related symptoms; fatigue, cryoglobulinemia-related disease (rash, renal disease), etc.
      - 2. Psychosocial: stress/worry re: label of chronic viral infection, infectiousness, barriers to normal sexual function, relationships
      - 3. Financial: inability to obtain health or life insurance, anticipated loss of health insurance coverage, etc
      - 4. Obstetrical: concern over even low risk of passing HCV to newborn.
      - 5. Occupational: contagion risk to others in line of work (health or sporting careers).
- 3. Discuss new Ishak scoring system: Stage 1 to 6 if used in the patients biopsy report
- 4. In patients without non-histologic indications for treatment, advocate expectant follow up.
- 5. Offer referral patient to ongoing, endorsed Hep C support group, and endorsed complementary medicine practitioner (acupuncturist, etc.)



Calculate MELD score at MEDCALC.com: refer for liver transplant evaluation if score over 6

9. Calculate medication doses by weight (see appendix 11: Treatment Flow Sheets)

***PEG-Intron (alfa-2b) 1.5 micrograms/kg SQ injection WEEKLY #***

Rebetol or generic ribavirin 13+/-2 mg/kg, round up to next multiple of 200 mg, orally DAILY for genotype 1,4,5,6, patients with cirrhosis or other difficult to treat patients, 800 mg fixed dose for genotypes 2,3 with dose adjustment if renal insufficiency

-or-

***Pegasys (alfa-2a) 180ug SQ injection WEEKLY #***

Copegus or generic ribavirin 13+/-2 mg/kg, round up to next multiple of 200 mg, orally DAILY for genotype 1,4,5,6, patients with cirrhosis or other difficult to treat patients, 800 mg fixed dose for genotypes 2,3 with dose adjustment if renal insufficiency

Patients with genotypes 1, 4, 6 treat for minimum of 48 wks; genotypes 2 and 3 may be treated for 14-24-48 weeks.

Protocol:

- Genotype 1: treat 9 months beyond HCV negative by TMA; minimum of 12 months maximum 18 months
- Genotype 2: treat for 16 weeks if TMA negative at 1 month ; 24 weeks if TMA positive at one month
- Genotype 3: viral load < 500 K IU
  - Treat for 14 weeks if TMA negative at 1 month
  - Treat for 24 weeks if TMA positive at 1 month
- Genotype 3: viral load >500 K IU
  - Treat for 24 weeks if TMA negative at 1 month
  - Treat for 48 weeks if TMA positive at 1 month
- Cirrhosis: treat 9 months beyond HCV negative by TMA minimum of 12 months; maximum 18 months
- HIV HCV coinfection: treat 9 months beyond HCV negative by TMA, minimum of 12 months; maximum 18 months
- Dialysis: treat 9 months beyond HCV negative by TMA, minimum of 12 months maximum; 18 months
- Liver transplant recipients: treat 9 months beyond HCV negative by TMA or use maintenance, minimum of 12 months; maximum 18 months
- Genotype 4,5,6 : treat as a G 1
- On treatment nonresponders: i.e. HCV RNA positive and less than 2 logs at 3 months or HCV RNA positive at 6 months; change to consensus interferon 15mcg per day with ribavirin at 12 mg/kg/day for additional 48 weeks

# = If compensated cirrhosis by biopsy consider step-wise approach in conjunction with GI consult:  
Step 1: 45 - 50 micrograms Peg interferon/ week for 2 weeks (week 1 and 2)  
Step 2: 90 - 100 micrograms / week for 2 weeks (week 3 and 4) if tolerated  
Step 3: full dose = 120-180 micrograms depending on weight (week 5 and beyond) if tolerated  
initiate ribavirin at 800 mg a day (2 x200mg BID) and titrate upward by 200 mg each week until full weight-adjusted dose reached.

Weekly labs

10. Prescriptions for interferon and ribavirin written and NCM assists patient in obtaining

insurance approval for therapy. Pharmaceutical assistance programs accessed as needed. When medication available, appointment for session 5 - "Initial Injection Education Session" made.

11. Arrange for pregnancy test in females (urine HCG) to be obtained just prior to starting treatment
12. Refer to ongoing endorsed Hep C Support Clinic and/or pharmaceutical company support program (e.g.: Schering's "Be in Charge" or Roche's "Pegassist" program).
13. Assure any hepatitis vaccination series continues to completion.
14. Offer referral to endorsed complementary medicine practitioner (acupuncturist, etc.)
15. Ask for ophthalmological consult if history of diabetes, visual disturbances, history of any retinal disease, history of uncontrolled hypertension

#### **4. Session Five – Initial Injection Education Session**

**Format:** *Education one-on-one or small group session*

**Participants:** *Hep C Health Educator +/- NCM*

*Patients ready to start treatment, interested family and friends*

**Timing:** *After medications are available.*

1. Patients are educated on Management of treatment side effects (see appendix 9: "Side Effects Module for the Patient") Interested patients given information on role of complementary medicine (acupuncture, etc.) in management of treatment side effects.
  - c. Technique of SQ injection abdomen, upper legs, upper arms
  - d. Initial injection of interferon given under supervision
  - e. Importance of birth control
  - f. Importance of lab monitoring and clinical follow-up
  - g. Options for communication with Hep C Center staff
2. Standing orders for ongoing lab monitoring (CBC with diff, plts, liver panel – see appendix 16) given to patient.
3. Patient involvement in ongoing endorsed Hep C support group and/or pharmaceutical company support program (e.g.: Schering's "Be in Charge" or Roche's "Pegassist") encouraged
4. Follow up clinic appointment given for two weeks.
5. "Pretreatment Checklist" completed (see appendix 10)
6. Complete Hepatitis Patient Teaching Documentation Tool (see appendix 18)

**Primary Care Hepatitis C Center  
Case Management Baseline Education Session  
– Outline –**

- I. Welcome and introductions
- II. Assurance of confidentiality, inform of aggregate data use.
- III. Overview of Hepatitis C Center
- IV. Natural History of Hepatitis C (Appendix 2)
- V. Risk factors for Hepatitis C infection
- VI. Benefits of treatment
- VII. Drawbacks of treatment (Appendix 2)
- VIII. Who shouldn't be treated by the Primary Care Hep C Center
- IX. Completion of "Baseline Patient Database" form
- X. Next steps – anticipate NCM follow up call

**Decision re: interest in further evaluation/treatment**

## Hepatitis C General Information Sheet

### Natural History of Hepatitis C

Hepatitis C exposure

- IV drug use
- Blood transfusion (pre-1992)
- “Snorting” cocaine
- ▼ unsterile tattooing/ body piercing
- High risk sexual behavior

### Risk Factors for Hep C Infection

Incubation period

-“hands on” health care work

Usually 6-7 weeks

- ▼ Risk of transmission by sexual or household contact low, accounting for <10% of cases. In 3-6 months
  - Perinatal (mother to baby) transmission less than 5%.
- ▼ 20-30% of patients have no risk factors identified

55-80% develop chronic infection

20-30yrs (shorter with alcohol, HIV longer if younger)

6-20% develop cirrhosis (severe scarring of liver).

Over subsequent 10 yrs approx.  
 50% (1-5%/yr.) develop complications of cirrhosis; esophageal (throat) variceal bleeding, abdomen swelling (ascites) peripheral edema (leg swelling), liver failure; require liver transplant  
 3% per year rate of liver cancer

### Possible Benefits of Treatment

-Cure of infection “sustained viral response”  
 Type 1: 45% (12 mo Rx) (70% if EVR)  
 Type 2 or 3: 60-80% (with 6 mo Rx)

Predictors of good response;

- Non- type 1 genotype
  - <5 yrs of infection
  - no cirrhosis
  - <1,000,000 IU RNA/ml
  - <45 yrs old
  - low iron liver stores
  - negative or 2 log reduction in viral titers at 3 months of Rx

- Decrease risk of cirrhosis and associated complications.
- Decrease risk of liver cancer.
- Improve quality of life

### Possible Drawbacks of Treatment

- flu-like symptoms (common)
- anemia
- depression/psychiatric problems
- thyroid problems
- flare of autoimmune disease
- relapse of substance abuse
- birth defects (see treatment risks/benefit sheet for additional information)

## Side Effects of Interferon and Ribavirin in the Treatment of Hepatitis C

Appendix 3

### Interferon:

- Fatigue, malaise
- Muscle aches, Flu symptoms Fevers/chills
- Headaches
- Nausea/vomiting/loss of appetite
- Injection site tenderness
- Diarrhea
- Weight loss, up to 10% body weight
- Insomnia
- Dizziness
- Depression
- Personality change; forgetfulness, decreased concentration, cognitive changes, irritability, anxiety, emotional lability
- Mild bone marrow suppression: decreased platelets, white blood cells
- Retinal changes (esp. diabetic and hypertensive patients)
- Dry, itchy skin
- Hair loss (reversible)
- Worsening diabetes control
- Increased triglycerides

### Ribavirin:

- Anemia and fatigue
- Itching
- Skin rash
- Respiratory symptoms; mild shortness of breath, nasal congestion, cough, sinus congestion
- Birth defects

### Uncommon, Serious:

- Bacterial infections (pneumonia, abscess, skin infections)
- Autoimmune disease flare (rheumatoid arthritis, lupus, psoriasis, sarcoidosis, graft rejection)
- Severe depression, psychosis, disorientation, suicide
- Substance abuse relapse
- Seizures
- Vision loss (retinal vein thrombosis or ischemia)
- Damage to the back of the eye (retinopathy)
- Renal failure (interstitial nephritis)
- Heart attack, weakened heart muscle
- Birth defects
- Hyperthyroidism, hypothyroidism
- Severe reduction in blood cell counts (WBC, PLT, RBC)
- Isolated loss of nerve function “nerve palsy” (facial, oculomotor)
- Pancreatitis (inflammation of the pancreas)

**By system:**

## **Interferon including Pegylated Interferon side-effects**

## **Interferon including Pegylated Interferon side-effects**

### **General and miscellaneous**

Fever, chills, headache, muscle aches, joint pain, and fatigue, seizures, trouble sleeping, hair thinning, weight loss, weight gain, dizziness, inflammation in the joints, excessive sweating, numbness or tingling, viral and bacterial infections, nerve damage, hearing loss, thyroid problems (high and low activity), and muscle contractions/cramps. Hypercalcemia from hyperparathyroidism.

### **Gastrointestinal**

Nausea, vomiting, abdominal pain, changes in taste, diarrhea, loss of appetite and dry mouth, celiac disease, initiation or worsening of inflammatory bowel disease.

### **Cardiovascular Disorders**

Chest pain, heart attack, congestive heart failure, stroke, low-blood-pressure, and shortness of breath including the possibility of death from a heart related event.

### **Skin reactions**

Rashes, lichen planus, dry or itchy skin, lupus erythematosus [skin inflammation], and psoriasis [skin disorder causing red patches covered with white scales] Stevens Johnson Syndrome [lesions and redness of the skin produced by congestion/broken capillaries], injection site reactions or redness, injection site infections. Transient erythema (redness), eczema, depilation) skin necrosis, vasculitis, initiation or worsening of vitiligo.

### **Drug addiction**

May fall back into drug addiction or drug overdose including the use of IV drugs. Alcohol abuse or dependence may also relapse

### **Blood problems**

Thrombocytopenia (low-platelet), thrombotic thrombocytopenic purpura, low red blood cell counts or anemia, decreased blood clotting and low white cell counts. Also thrombotic disorders with blood clot formation has been reported. This could include embolic disease or blood clots to the lungs

### **Lung Disorders**

Difficulty breathing, asthma, pneumonia, lung inflammation, lung infiltrates, bronchiolitis obliterans, interstitial pneumonitis, pulmonary-emphysema, and pulmonary sarcoidosis [wide-spread lesion forming on lungs]

### **Renal function**

Decrease in kidney function and failure when protein is present in urine. Patients have developed complete renal failure while taking interferon and been dialysis dependent.

### **Liver toxicity**

Jaundice, elevated liver enzymes, liver pain, and decrease liver function

### **Auto immune disorders**

Initiation or exacerbation of lupus, rheumatoid arthritis, psoriasis, and other autoimmune disease has been clearly documented. These effects may be long lasting and may not reverse with interferon discontinuation. Worsening of Sjogrens disease, a disease of dry eyes and dry mouth.

### **Vision disorders**

Some eye problems occur especially in patients with diabetes mellitus or high-blood pressure

### **Brain**

cerebral atrophy (brain size changes) and aseptic meningitis (inflammation of the lining of the brain without evidence of infection.) Bell's Palsy or facial palsy (partial paralysis involving the eyelid and cheek), cognitive (thinking) defects may worsen or be new while taking interferon, these effects may not be reversible upon discontinuation of therapy.

### **Psychiatric, psychological, mood and behavioral problems**

Depression, anxiety, irritability, lack of concentration, insomnia, mental confusion, hallucinations, mania and bipolar disorders. Suicidal thoughts and attempts, homicidal thoughts, and psychosis. There are known cases of completed suicide and homicide while taking this medication. Irritability, neurosis, disorders of psychomotor activity, vegetative symptoms. Organic personality syndrome characterized by irritability and short temper; an organic affective syndrome marked by extreme emotional lability, depression, and tearfulness; and a delirium marked by clouding of consciousness, agitation, paranoia, and suicidal potential. Paranoid psychoses and confusional states.

### **Woman only**

Menstrual disorders, inability to have children, and spontaneous abortions.

Some of these side effects may be severe enough to cause death.

Some of these side effects may be irreversible

Most side effects (with the possible exception of altered thyroid function) will generally reverse upon stopping treatment.

**I have reviewed and understand the above side effects and my questions have been answered:**

Patient signature \_\_\_\_\_

## Hep C Center Baseline Patient Database (confidential)

Patient name (last, first) \_\_\_\_\_ date \_\_\_\_/\_\_\_\_/\_\_\_\_  
 referring PCP \_\_\_\_\_  
 DOB: \_\_\_\_/\_\_\_\_/\_\_\_\_ sex \_\_\_\_\_

How long have you known about your infection with hepatitis C? \_\_\_\_\_

**Which of the following risk factors for becoming infected with Hepatitis C have you had? (check all that apply):**

- Transfusion of blood products prior to 1992? if yes, year; \_\_\_\_\_
- Injection of illicit drugs (subcutaneously or intravenously) – even only once?  
 if yes, year started; \_\_\_\_\_ stopped; \_\_\_\_\_
- Blood exposure on or through skin (or in mouth) while working in a health care profession or in the military (e.g.: needle stick injury, military combat)? if yes, year; \_\_\_\_\_
- Hemodialysis?
- Tattoo or body piercing by non-professional or with unsterile needle?
- snorting cocaine? if yes, year started; \_\_\_\_\_ year stopped; \_\_\_\_\_

**Although hepatitis C is not felt to be spread sexually very easily, have you:**

- Had a sexual partner who was infected with hepatitis C?  Yes  No
- Had multiple sexual partners (>5), past or present?  Yes  No
- if yes: any same sex partners?  Yes  No

**The following questions are important in planning your treatment;**

- Do you currently drink alcoholic beverages?  Yes  No
- If yes, indicate: Number of years daily (or nearly daily): \_\_\_\_\_
- Average number of drinks per day: \_\_\_\_\_
- Last day you drank alcoholic beverage: \_\_\_\_/\_\_\_\_/\_\_\_\_
- Any history of binge drinking (>6 drinks per sitting)  Yes  No

Have you been educated regarding the importance of avoiding alcohol?  Yes  No

**To your knowledge, have you ever:**

- Had hepatitis B?  Y  N      Been vaccinated against hepatitis B?  Y  N
- Had hepatitis A?  Y  N      Been vaccinated against hepatitis A?  Y  N
- Been tested for HIV (the AIDS virus)?  Y  N (if yes, when? \_\_\_\_/\_\_\_\_/\_\_\_\_)
- Been diagnosed with kidney disease?  Y  N
- Been diagnosed with heart disease (angina or heart attack)?  Y  N
- Been depressed or been diagnosed and/or treated for psychiatric illness?  Y  N
- Been diagnosed with lung disease?  Y  N
- Been diagnosed with thyroid disease?  Y  N
- Been diagnosed with anemia?  Y  N

Been diagnosed with an autoimmune disorder (see below for specific names)?  Y  N  
(if yes, circle any diagnosis that applies: rheumatoid arthritis, lupus, myasthenia gravis, scleroderma,  
polymyositis, juvenile onset diabetes, pernicious anemia, psoriasis, bullous pemphigoid,  
other: \_\_\_\_\_)

Do you feel you currently have good social support from friends, family, etc?  Y  N  
If no, describe your current social situation; \_\_\_\_\_

Do you feel you would consider therapy for hepatitis C infection now/soon?  Y  N

---

**Thank you for your answers.**  
**All identifying information will be kept strictly confidential.**



## Hepatitis C Center - Initial H&P Template

*Physical Exam*

Patient name \_\_\_\_\_

Date of exam \_\_\_/\_\_\_/\_\_\_

**Check normal box if without abnormality, indicate specific pathology if present:**

BP \_\_\_/\_\_\_ Pulse \_\_\_ weight \_\_\_ lbs kg (circle one) height \_\_\_ RR \_\_\_ temp(F) \_\_\_

HEENT  nml  icteric sclera  eyeground changes (last eye exam: \_\_\_/\_\_\_/\_\_\_)  
 other \_\_\_\_\_

NECK  nml  JVD  bruit  thyroid (\_\_\_\_\_)  
 other \_\_\_\_\_

PULMO  nml  crackles  wheezes  
 other \_\_\_\_\_

CV  nml  murmur  gallop  
 other \_\_\_\_\_

ABD  nml  shift dullness  bulge flanks  hepatomegaly  
 splenomegaly  bruit  
 other \_\_\_\_\_

RECTAL  nml  hemorrhoids  heme + stool  
 deferred  other \_\_\_\_\_

EXTREM  nml  edema  rheumatoid changes  clubbing  
 other \_\_\_\_\_

NEURO  nml  confusion  tremor  asterixis  
 other \_\_\_\_\_

SKIN  nml  jaundice  spiders  psoriasis  track marks  petechiae  
 rash (\_\_\_\_\_)  tattoo  
 palmar erythema  other \_\_\_\_\_

OTHER ABNML \_\_\_\_\_  
 \_\_\_\_\_  
 \_\_\_\_\_

**Impression:** \_\_\_\_\_ **Plan:**  old records: \_\_\_\_\_  
 \_\_\_\_\_  abd U/S  CBC  Comp  P7  Liver Panel  cerruloplasmin (<50)  
 \_\_\_\_\_  HCVAb  HCV GT  Quant  Qual  AFP  U preg  AMA  
 \_\_\_\_\_  HBsAg  HBsAb  HbcAb  HAVAb  T chol  ANA  
 \_\_\_\_\_  Coags  HIV  TSH  U/A  Ferrat  Fe/TIBC  
 \_\_\_\_\_  support group  herbal sheet  Hep A Vac  Hep B Vac  Twinrix  
 \_\_\_\_\_  Liver Bx sheet  HCV Rx SE sheet

**RTC** \_\_\_\_\_

Exam by (signature): \_\_\_\_\_

## Liver Biopsy in the Pretreatment Evaluation of Hepatitis C

In order to more clearly understand the degree to which your hepatitis C infection has affected your liver, as well as to rule out any other possible causes of liver inflammation, a *liver biopsy* has been recommended. The biopsy will be taken with a needle and will be done as an outpatient by a gastroenterologist, interventional radiologist or other qualified provider under ultrasound guidance. You will likely stay in the procedure ward 3 hours. Your blood pressure and pulse will be monitored, and your blood may be checked before you go to be sure there is no signs of bleeding. The results of the biopsy are usually available in a week.

### Risks:

- Pain 1:5
- Puncture of lung, gallbladder, kidney 1:3,000
- Bleeding and need for blood transfusion 1:2,000
- Surgery <1:1,000
- Death 1:9,000-12,000

### Benefits:

- Allows a more accurate assessment of liver status, necessity and timing of treatment.
- Helps rule out other liver disease; autoimmune hepatitis, hemochromatosis, ETOH hepatitis, fatty liver, Wilson's disease, Alpha-1 antitrypsin deficiency

### Instructions:

- You will need to **stop taking any aspirin or aspirin-like products** (ibuprofen, Advil, Motrin, Aleve, etc.) **for 10 days prior to biopsy.**
- You will need to have someone pick you up after your biopsy as you will receive medication that will make you sleepy. It is uncommon to need any pain medication after the procedure, but the Hepatitis C Center can arrange for an appropriate prescription if needed.
- The procedure takes less than 30 minutes, but you will be watched for approx. 3 hours afterwards.

## Clinical Exclusion Criteria for Primary Care Hep C Treatment

### May be treated in Clinic if improvement occurs (minor contraindications):

- Alcohol/drug use (6 months abstinence required for treatment). Stable methadone is OK.
- Mild to moderate depression (BDI score 14-20, 0 to 13 being normal), Advised to delay interferon start until depression controlled with antidepressant treatment (4-6weeks minimum delay).
- Documented noncompliance with treatment (e.g. medications, clinic visits).

### May possibly be treated with subspecialist involvement (relative contraindications):

- Age 65 years or older; requires GI approval prior to treatment.
- **Ultrasonographic evidence of cirrhosis or liver mass**
- Severe depression (e.g. suicidal attempt or concrete ideation), history of hospitalization for moderate to severe psychiatric disease or unstable psychiatric disease. BDI-II (Beck depression index) > 20. Psychiatric evaluation, clearance and follow-along required.
- Anemia: Etiologic workup (possibly treatment) required prior to possible treatment (examples of unsuitability for treatment include sickle cell disease or thalassemia).
- Known bleeding disorder; requires hematologic consultation prior to liver biopsy.
- **Autoimmune disorder; requires rheumatologist approval and follow along for treatment**
  - Non-organ specific, e.g. rheumatoid arthritis, SLE, Sjögren's syndrome, scleroderma, polymyositis, rheumatic fever.
  - Organ specific, e.g. Myasthenia gravis, Grave's disease, thyroid disease, insulin-resistant diabetes, pernicious anemia, psoriasis, bullous pemphigoid, autoimmune hemolytic anemia, ITP.
- Any medical condition requiring, or likely to require, chronic administration of systemic corticosteroids; requires GI approval prior to treatment.
- Moderate to severe pulmonary disease (e.g. COPD, asthma); requires pulmonary consult for pulmonary clearance
- Mild to moderate cardiac disease; requires cardiology consult for cardiology clearance.
- CPT Score  $\geq 6$  (Child's B or C) (see session 4, page 10 of protocol); requires GI consultation.
- Patients with diabetes and/or hypertension history require baseline ophthalmologic exam within 6 months prior to start of treatment to rule out pre-existing retinopathy (interferon has been associated with retinopathy).
- Laboratory exclusion criteria for HCV treatment at primary care level; requires GI consultation:
  - Neutrophils < 1500 prior to therapy, WBC < 2,500/mm<sup>3</sup>
  - Hgb < 12 g% in men and <11 g% in females
  - Platelets < 100,000
  - Bilirubin >1.5 (except documented Gilbert's)
  - Positive autoimmune test: ANA, SMA, or AMA
  - Creatinine > ULN; obtain nephrology consult
  - TSH outside normal limits for local lab
  - Albumin <3.0 g/dl

### Absolute contraindications to treatment:

- Short life expectancy/severe comorbidities. (less than 10 years)
- Known advanced cirrhosis with clinical decompensation (e.g. ascites, encephalopathy, variceal bleeding or SBP) unless under treatment at a transplant center.
- Pregnancy in females or failure/inability by male or female to reliably use adequate birth control.
- Inadequate social support, including inability to comply with parenteral medication.
- Severe cardiac disease.

## Depression Instrument CES-D Scale

(Department of Health and Human Services, National Institute of Mental Health)

**Circle the number for each statement that best describes how often you felt or behaved this way *during the past week***

During the Past Week	Rarely or None of the Time (Less than 1 day)	Some or a little of the time (1-2 days)	Occasionally or a moderate amount of time (3-4 days)	Most or all of the time (5-7 days)
1. I was bothered by things that usually don't bother me.	0	1	2	3
2. I did not feel like eating; my appetite was poor.	0	1	2	3
3. I felt that I could not shake off the blues even with help from my family or friends.	0	1	2	3
4. I felt that I was just as good as other people.	0	1	2	3
5. I had trouble keeping my mind on what I was doing.	0	1	2	3
6. I felt depressed.	0	1	2	3
7. I felt that everything I did was an effort.	0	1	2	3
8. I felt hopeful about the future.	0	1	2	3
9. I thought my life had been a failure.	0	1	2	3
10. I felt fearful.	0	1	2	3
11. My sleep was restless.	0	1	2	3
12. I was happy.	0	1	2	3
13. I talked less than usual.	0	1	2	3
14. I felt lonely.	0	1	2	3
15. People were unfriendly.	0	1	2	3
16. I enjoyed life.	0	1	2	3
17. I had crying spells.	0	1	2	3
18. I felt sad.	0	1	2	3
19. I felt that people dislike me.	0	1	2	3
20. I could not get "going."	0	1	2	3

## Side Effects Module for the Patient

Common Side Effects	Things To Do
<b>Flu-like symptoms, muscle aches, fever, chills, headache:</b>	<ul style="list-style-type: none"> <li>• Take pain relievers as prescribed by your doctor</li> <li>• Drink a lot of clear fluids each day</li> <li>• Keep extra blankets and clothes near bed to manage the chills</li> <li>• Give your Interferon injections at bedtime to sleep through symptoms</li> <li>• Consider which day of the week would work best to administer your medicine</li> <li>• <i>You may take Tylenol 325 mg 1-2 tabs every 4-6 hours (do not take more than 8 tabs/day) for the first 1-2 weeks of Interferon therapy only:</i> <ul style="list-style-type: none"> <li>-Tylenol 325-650 mg one hour before <b>first</b> injection,</li> <li>-Tylenol 325-650 mg one hour before <b>second</b> injection,</li> <li>-Tylenol 325-650 mg one hour before each subsequent dose <b>for the first two weeks</b></li> </ul> </li> <li>• -You may take Tylenol Extra-strength (500mg tab) 1-2 tabs for headache. Talk with your doctor if headaches continue.</li> <li>• <i>NSAIDS (nonsteroidal anti-inflammatory drugs) can also be useful.</i> Examples include aspirin (or aspirin-containing medicines), naproxen (Aleve, Anaprox, Naprosyn, Naprelan), ibuprofen (Advil, Motrin), indomethacin (Indocin), ketoprofen (Orudis).</li> <li>• Ask the Hep C Center staff if you would like a referral to a recommended complementary medicine provider (herbalist, acupuncturist) to help manage side effects</li> </ul>
<b>Tiredness/fatigue:</b>	<ul style="list-style-type: none"> <li>• Rest as much as possible</li> <li>• Drink plenty of water and other nutritional fluids (10-16 glasses a day)</li> <li>• Get light exercise (walking and stretching)</li> <li>• Change work schedule, if possible</li> <li>• Get plenty of rest</li> <li>• Eat a healthy, balanced diet</li> <li>• You may take diphenhydramine (Benadryl) 25-50 mg at bedtime for sleep</li> </ul>
<b>Irritability, depression, anxiety:</b>	<ul style="list-style-type: none"> <li>• Seek help from support groups – ask the Hep C Center staff for information</li> <li>• Try relaxation techniques.</li> <li>• Find ways to laugh.</li> <li>• Call your doctor for feelings of depression most of the day that last longer than 1-2 days, especially if our feelings are interfering with your life and/or you have thoughts of death/suicide.</li> </ul>
<b>Loss of appetite/weight loss:</b>	<ul style="list-style-type: none"> <li>• Eat small frequent meals even if you have no appetite.</li> <li>• Treat food as medicine you must take to get healthy.</li> <li>• Monitor your weight - report more than 5 lbs loss to the Hep C Center staff.</li> <li>• In addition to water, drink clear juices.</li> <li>• Brush teeth often to help eliminate metallic taste in your mouth.</li> <li>• You may take Ensure or Boost (available at pharmacies without a prescription) as a food supplement.</li> </ul>
<b>Nausea and diarrhea:</b>	<ul style="list-style-type: none"> <li>• Take over-the-counter medication for nausea/diarrhea.</li> <li>• Avoid trigger foods and odors.</li> <li>• Keep water and crackers near bedside for nausea and dry mouth.</li> </ul>

<b>Nausea and diarrhea: (cont.)</b>	<ul style="list-style-type: none"> <li>• Try popsicles, dry toast or crackers.</li> <li>• Eat small frequent meals.</li> <li>• You may take Kaopectate 1-2 tablespoons after each loose stool or every 2 hours (up to 8 times a day).</li> <li>• Let the Hep C Center staff know if nausea and/or diarrhea persists.</li> </ul>
<b>Mild hair loss:</b>	<ul style="list-style-type: none"> <li>• Style hair in a fashion to make it fuller (hair will grow back after therapy finishes).</li> <li>• Use scarves; wear hats and/or hair extensions.</li> <li>• Do not over-wash or over-dry hair.</li> <li>• Avoid sun exposure and hair dye.</li> <li>• You may use Nioxin shampoo (ask Hep C Center staff) before you start the injections if hair loss is a major concern for you.</li> </ul>
<b>Dizziness:</b>	<ul style="list-style-type: none"> <li>• Stand up slowly</li> <li>• Drink plenty of water every day.</li> </ul>
<b>Skin problems, injection site reactions, rash, itching and dry skin:</b>	<ul style="list-style-type: none"> <li>• Use lotions immediately after bathing.</li> <li>• Rotate injection sites.</li> <li>• Apply ice pack to injection site for a few minutes prior to injection</li> <li>• Use sunscreen lotion.</li> <li>• Drink 10 or more glasses of water a day.</li> </ul>

**Call your doctor immediately if you have any of these side effects:**

- |  |   |
|--|---|
| <ul style="list-style-type: none"> <li>• Very slow or fast heartbeat</li> <li>• Shortness of breath</li> <li>• Sore throat</li> <li>• Blurred vision, loss of vision, eye pain, or light sensitivity</li> <li>• Symptoms of bladder infection: burning, urgency, Or increased urinary frequency</li> </ul> | <ul style="list-style-type: none"> <li>• Chest pain</li> <li>• Blue fingernails or lips</li> <li>• Fever</li> <li>• Depression</li> <li>• Numbness or tingling of hands or feet</li> <li>• Extreme fatigue</li> </ul> |
|--|---|

## Hep C Center Pretreatment Checklist

**Patient name** \_\_\_\_\_

*Initial Education Session (after + hep C Ab test)*

**Group format?** Y N (If not group format, indicate reason: \_\_\_\_\_)

Hepatitis C natural history, treatment risks/benefits reviewed. (appendices 2, 3)

Patient "Baseline database" form completed?

Patient considering treatment/desires further workup? Y N

**If no:** document reason: \_\_\_\_\_

### Initial Clinical Review

"Initial Hep C Workup" completed

Initial H&P template completed

If indicated, initiate vaccine series vs. Hep A \_\_\_/\_\_\_/\_\_\_ \_\_\_/\_\_\_/\_\_\_ (highest priority)

Hep B \_\_\_/\_\_\_/\_\_\_ \_\_\_/\_\_\_/\_\_\_ \_\_\_/\_\_\_/\_\_\_

Patient without Rx contraindications and interested in treatment? Y N

**If no:** document reason \_\_\_\_\_

Discussed of liver biopsy risks and benefits.

Patient agrees to biopsy? Y (arranged) N (skip to session 5; "Initial Injection Education Session")

**If no, document reason:** \_\_\_\_\_

### Post Liver Biopsy Case Review

Biopsy results reviewed? (entered into database)

Treatment still indicated? (fibrosis score >1)

Contraindications to Hep C Center Treatment (see appendix 7)? Y N

**If yes, document reason/action:** \_\_\_\_\_

**Referral to GI indicated? Y N if yes: Done? Y N**

Interferon/Ribavirin prescription written (\_\_\_/\_\_\_/\_\_\_) and drug approved?

**If no, reason:** \_\_\_\_\_

Schedule "Initial Injection Education Session"

Subspecialty evaluation indicated? (note: pts. With DM or HTN need baseline optho exam w/in 6 mo prior to

Rx start) Y N NI type(s): \_\_\_\_\_

**If yes;** subspecialty eval(s) completed? Y N **if no, reason:** \_\_\_\_\_

Document Child's Class \_\_\_\_\_

### Child-Turcotte-Pugh Classification

	1 point	2 points	3 points
Bilirubin (mg/dL)	<2	2-3	>3
Albumin (g/dL)	>3.5	2.8-3.5	<2.8
PT (sec prolonged) [INR]	1-3 [<1.7]	4-6 [1.8-2.3]	>6 [>2.3]
Ascites	none	slight	moderate
Encephalopathy	none	1-2	3-4

Child-Turcotte-Pugh Class: A = 5-6 points B = 7-9 points C = 10-15 points

**Note: No Primary Care treatment without GI consultation if score = 6 or above**

### Primary Care Hepatitis C Center – Treatment Protocol Schedule

	Week of Rx	Contact Person	Default Contact Type	Action
<input type="checkbox"/>	2	MD	Clinic	Labs, Side effect scale (SES)
<input type="checkbox"/>	4	MD/NCM	Clinic	Labs, SES, compliance
<input type="checkbox"/>	8	MD/NCM	Clinic	Labs, SES, compliance
<input type="checkbox"/>	12	MD	Clinic	Labs, SES, compliance <i>(less than 2 log drop stop Rx at this point &gt;&gt;&gt; discontinue Rx and letter to PCP)</i>
<input type="checkbox"/>	16	NCM	Remote	Labs, SES, compliance
<input type="checkbox"/>	20	MD/NCM	Clinic	Labs, SES, compliance
<input type="checkbox"/>	24	NCM	Remote	Labs, SES, compliance <i>(genotype 2, 3 stop Rx at this point &gt;&gt;&gt; letter to PCP)</i>
<input type="checkbox"/>	28	MD/NCM	Clinic	Labs, SES, compliance
<input type="checkbox"/>	32	NCM	Remote	Labs, SES, compliance
<input type="checkbox"/>	36	MD/NCM	Clinic	Labs, SES, compliance
<input type="checkbox"/>	40	NCM	Remote	Labs, SES, compliance
<input type="checkbox"/>	44	NCM	Remote	Labs, SES, compliance
<input type="checkbox"/>	48	MD/NCM	Clinic	Labs, SES, compliance
<input type="checkbox"/>	2-4 months post Rx	NCM	Remote	Labs, SES
<input type="checkbox"/>	6 months post Rx	MD/NCM	Clinic	Labs, SES <i>(clinical summary letter sent to PCP)</i>

\* Face-to-face contact with M.D. if needed/requested, at any time. Remote contact may be either by phone or email.

**NCM = nurse case manager, DS = depression score, PCP = primary care provider**

## Hep C Center Treatment contact sheet

**Patient name** \_\_\_\_\_ contact type;  scheduled  unscheduled  
 (check all  MD  MA  PA/NP  
 that apply)  in person  phone  
**Date** \_\_\_/\_\_\_/\_\_\_  
**Labs obtained?**  yes  no

# wks into Rx; \_\_\_\_\_ injection day: *M Tu W Th F Sa Su* daily water intake \_\_\_\_\_ oz  
 (goal is 8 oz/hr)

**clinical issues:**(comments on side effects by # - see reverse)

---

**How many missed doses since last contact?** INTERFERON: \_\_\_\_\_ doses out of \_\_\_\_\_ total doses  
 RIBAVIRIN: \_\_\_\_\_ doses out of \_\_\_\_\_ total doses

Reinforced need for double birth control (  not indicated due to : \_\_\_\_\_ )

EXAM: BP \_\_\_/\_\_\_ P\_\_\_ T\_\_\_ RR\_\_\_ Wt\_\_\_\_\_

no exam

**A/P:**

Estimated time spent in contact:  0-15 min.  15-30 min  30-45min  45-60 min  >60 min

signature \_\_\_\_\_

## Hepatitis C Treatment Side Effect Rating Scale\*

Side effects from interferon and ribavirin vary from day to day, week to week. Please indicate the level of severity that best characterizes your experience of each symptom (if any) over the past week.

(\*Adapted from the Neurotoxicity Rating Scale)

	<i>Absent</i>	<i>Mild</i>	<i>Moderate</i>	<i>Severe</i>	<i>Very Severe</i>
1. anxiety					
2. cough or nasal congestion					
3. sadness/depression					
4. restlessness					
5. no interest in activities					
6. difficulty making decisions					
7. strange thoughts					
8. all-over sick feeling					
9. difficulty getting to sleep					
10. difficulty staying asleep					
11. sleeping too much					
12. nausea					
13. vomiting					
14. loss of appetite					
15. tiredness/fatigue					
16. distractibility					
17. body aches					
18. joint pain					
19. chest pain					
20. other pain (_____)					
21. episodes of confusion					
22. word finding problem					
23. memory problem					
24. irritability					
25. decreased motivation					
26. hallucinations					
27. lack of emotions					
28. mood swings					
29. slowed movement					
30. tremor/shakiness					
31. walking problems					
32. vision problems					
33. bladder problems					
34. loss of interest in sex					
35. fever					
36. headaches					
37. nightmares/dreams					
38. shortness of breath					
39. rash/skin change/itching					
40. change in hair					
41. dizziness					

## Adjunct Therapy for the Clinician

<u>Condition</u>	<u>Therapy Options</u>
Myalgia and flu-like symptoms (common with initial Interferon)	Acetaminophen) 325-650 mg one hour before <b>first</b> injection, 325-650 mg one hour before <b>second</b> injection, 325-650 mg one hour before therapy for each subsequent dose for <b>the first four weeks, then as needed only.</b> <b>MAXIMUM 2,000 mg/day</b> Neurontin (gabapentin) start at 100 mg qhs and gradually increase up to 1200 mg (400 TID) (consider neurologist consult if high dose needed) NSAIDs or Cox 2 inhibitors (e.g.: Vioxx, Celebrex) are also effective
Headache	Same as above If not relieved, Tylenol #3, If still not relieved, Neurontin (gabapentin) start at 100 mg qhs up to 1600 mg (400mg QID) (consider neurologist consult if high dose needed)
Fever	Tylenol (acetaminophen) 325-650 mg q6-8h prn – no more than 2.5 grams per day. Ibuprofen 600 mg po TID if no cirrhosis.
Anemia/Leukopenia	1. Consider Epoetin alfa, Aranesp and/or Filgrastim for anemia/leukopenia (see appendix 15). 2. Consider dose reduction. (Appendix 15)
Fatigue (HCV or therapy-induced)	Ritalin (methylphenidate) 5 mg am and 5 mg noon; can use up to 10 mg am and 10 mg noon (Caution: substance abuse relapse) [Schedule II]. Provigil 100-200mg Q am po (\$\$\$) **first check CBC and/or TSH.
Alopecia	Nioxin shampoo (Must be started BEFORE initiating combination therapy if patient is concerned about possible hair loss). Reassurance that hair will re-grow post Rx.
Insomnia	Trazodone 50 mg qhs, Benadryl 50mg, Sonata 5 or 10 mg, Doxepin 50 mg, or Ambien (zolpidem) 5-10mg at bedtime.
Irritability/anxiety, Confusion, and/or MILD depression	Zoloft (sertraline)/Paxil (paroxetine)/Prozac (fluoxetine) or Wellbutrin (bupropion), or Lexapro (escitalopram ). Start low dose a month BEFORE initiating anti-HCV therapy and confirm efficacy via spouse or partner

[Effects seen usually after 2-4 weeks of therapy, if no response evident by week 2, increase dose]. Continue 6 months post Rx.  
Zyprexa, Abilify, Seroquel can also be used here, but in conjunction with the aid of a psychiatric consultation  
Note: Confusion may be a manifestation of occult infection and/or hepatic encephalopathy and therefore needs further prompt assessment.

MODERATE psychiatric  
Disease (with Psychiatrist)

Buspar (buspirone) or Lexapro (escitalopram) for anxious depression  
Effexor XR (venlafaxine) for flat depression  
Elavil (amitriptyline), Desyrel (trazodone) for sleep.  
Wellbutrin (bupropion) is especially flat depression (take in a.m., stimulatory).  
Mania symptoms (rare) should trigger hold of treatment and urgent psych consult.

Impotence

Discuss with physician. Trial of Viagra 50-100mg .

Diarrhea

Kaopectate (attapulgate) 15-30 ml after each loose stool or every 2 hours (up to 8 times a day); Imodium (loperamide) 2 mg capsules – 4 mg initially, then one after each loose stool (up to 16 mg per day); Lomotil (atropine/diphenoxylate) 1-2 tablets after each loose stool (up to 8 per day).

Nausea/vomiting

Compazine (prochlorperazine) 25 mg supp. 1 per rectum q12h prn; Phenergan (promethazine) inj. 12.5-25 mg IM/IV q4-6h prn or 25 mg tab 1-2 tabs po q4h. If vertiginous component evident, consider scopolamine patch to skin Q 3 days.

Oral sores

Combination of 50 cc's Mylanta with 30 cc's viscous lidocaine, and 30 cc's Benadryl solution, swish, gargle, and spit Q 6 hrs prn.  
Consider a trial of TNF-inhibitor such as thalidomide 100 mg/day.

## Use of Growth Factors in the Treatment of HCV

### Objectives :

- Avoid serious adverse events associated with significant anemia (MI, stroke, etc.) or neutropenia (infection)
- Maintain patients on the therapeutic doses of interferon and ribavirin. to maximize sustained viral response (SVR)
- Improve side effects, e.g. fatigue, dyspnea (Improve quality of life on treatment).

Note: consider more aggressive use of growth factors in patients with advanced fibrosis (stages 3, 4), given their higher risk of progression to cirrhosis. Use of growth factors in these, and any patients is especially worth considering in the first 3 months of treatment until it is know whether the patient is an early viral responder (EVR). EVR is strongly associated with SVR. In patients who are not EVR, the benefit of continued anti-HCV treatment is less clear, and the added resource utilization of growth factor use may not be appropriate.

### Guidelines for Consideration of Growth Factor Use (note—non-FDA approved indications):

Recombinant human erythropoietin (Procrit®, Epogen®):

- If Hb <10.0 g/dL in women, or 11g/dL in men
- Hgb decrease greater than 2g/dl in a 4 week period in persons with history of CAD.
- Hgb decreases greater than 3g/dL from start of treatment and patient experiencing severe fatigue.

Granulocyte colony stimulating factor (Neupogen®):

- ANC <500 in patients with cirrhosis and < 250 if no evidence of cirrhosis

Note: experts point to lack of data correlating infectious complications with WBC nadirs in HCV patients on interferon therapy, and thus would utilize neupogen only if ANC drops below 500 unless patient had additional immuno-compromise (cirrhosis, dialysis, HIV co-infected, post-transplant).

### Initial Labs:

- Repeat CBC (with reticulocyte count if anemic). For neutropenic patients, best to draw blood just prior to weekly interferon injection. In patients with significant anemia, consider obtaining LDH, haptoglobin, and repeat CBC with reticulocyte count to evaluate for underlying physiopathology: bone marrow suppression = low reticulocyte count (usual cause; interferon) vs. hemolysis = elevated LDH, decreased haptoglobin (usual cause = ribavirin) or both.
- Consider ribavirin dose reduction (see appendix 11: Treatment Flow Sheet) strongly indicated in patients with evidence of hemolysis (elevated LDH and reduced haptoglobin), as ribavirin is usually the cause of hemolysis, with interferon causing bone marrow suppression, making it difficult for the body to respond with increased erythropoiesis.
- If treatment with rEPO being considered, transferrin saturation should be at least 20%, and ferritin should be at least 100ng/ml to assure adequate iron stores.

### Medications Used:

#### 1) **Procrit® or Epogen® (Epoetin Alfa recombinant ) or Aranesp®:**

In addition to Epoetin initiation, consideration of ribavirin dose advised by pharmaceuticals (Schering; reduction of Rebetron by 200mg/day, Roche; reduction of Copegus directly to 600mg/day). Dose reduction appears to stabilize Hgb decline, but doesn't result in consistent Hgb increases. (Some data to support early use of Vit E, 800U/day, and Vit C 1-2gm/day – may delay

onset of anemia by a few months – this could buy enough time on full RIB dose to assess EVR). For patients with history of CAD, reduction of interferon dose by 25-50% in addition to decreasing ribavirin by 200 mg/day (Roche advises reduction of Copegus directly to 600mg/day, regardless of initial dose).

**Initial dose:** 40,000 units SQ once a week. Maximum dose 60,000 per week  
Write prescription: “Procrit (or Epogen) 40,000units/ml single dose vial  
disp: #4 (Procrit comes in carton of four single dose vials)  
e.g.: 40,000 units (1ml) SC Q week      refill x4

Folate 1 mg/day Disp: 30, refill x4

Prior authorization procedures may be time consuming, so anticipate potential need for rEPO (rapidly falling Hgb within first few weeks) and initiate paperwork early. Writing indication as “chemotherapy induced anemia” can be helpful in obtaining approval.

Monitor blood pressure, as rEPO can cause/exacerbate HTN. Monitor CBC weekly until stable EPO dose and Hgb reached.. Watch for DVT and other thrombotic events. Watch for migraine or other headaches.

Lab response usually takes 2-3 weeks. Dose is then adjusted (reduced by 25% weekly) until reaching maintenance dose required to maintain Hb >12 g/dL. If Hgb increases to >13.3g/dL (women or men) hold rEPO and check CBC weekly - when Hgb subsequently decreases to 12g/dL (women or men) resume at reduced dose of 20,000 units/week. CBC checked weekly until stable dose obtained. Full dose ribavirin may be started again when Hgb above 10g/dl for women, 11g/dL for men. For patients with cardiac history, full dose ribavirin and interferon may be restarted when weekly CBC demonstrates Hgb >12. If not laboratory response or falling Hgb, consider possibility of pure RBC aplasia; if evidence for PRA, stop interferon stop ribavirin, ask for hematology consult.

*Discontinue both ribavirin and interferon until Hgb recovers if:*

- Patients without CAD history Hgb drops below 8.5g/dl despite rEPO and ribavirin dose reduction.
- History CAD and Hgb remains <10 g/dl despite 4 wks of rEPO and reduced ribavirin and interferon.

Aranesp: can also be used to treat ribavirin induced anemia, see package insert

AE from erythropoietin: thrombotic disorders, pure red cell aplasia, polycythemia,

2) **Neupogen®: Filgrastim (G-CSF)**

Dose reduction of peg interferon by 25-50% advised until effect of Neupogen seen (usually rapid). Time to WBC recovery with dose reduction alone usually 4 weeks.

**Initial dose:** 300 mcg SQ 1-3 times per week (5mcg/kg)  
Write prescription : “Neupogen 300mcg/ml ; 1 ml vial  
disp: # 4 vials  
sig: 300mcg (1ml) SC Q wk (or as directed by MD) refill x 4

Monitor for side effects: rash, vasculitis, bone pain, myalgias, thrombocytopenia, splenomegaly, leukemoid reaction, exacerbation of psoriasis, but overall safety appears to be excellent.

Check CBC weekly (mid-way between doses to assess need for >Q wk dosing), and adjust dose by increasing or decreasing frequency (from Q week to TIW, the latter usually needed only in cirrhotic patients) to achieve maintain WBC >1.5 and ANC > 0.75.

**Peg interferon dose should be increased back to baseline if after WBC/ANC reaches goal.**

**Appendix 16**

## Hep C Center – Treatment Monitoring Standing Order Verification Form

Ordering physician (check one): \_\_\_\_\_ (LabCorp or Quest #)  
 \_\_\_\_\_ (\_\_\_\_\_)   
 \_\_\_\_\_ (\_\_\_\_\_)

c.c. results to: \_\_\_\_\_ **time period:**  
 Start date \_\_\_/\_\_\_/\_\_\_

Patient's name: \_\_\_\_\_ Stop date \_\_\_/\_\_\_/\_\_\_  
 Patient's D.O.B.: \_\_\_/\_\_\_/\_\_\_

**Diagnosis (ICD9 code); Chronic Hepatitis C (070.54)**

<b>Test (Unilab #)</b>	<b>Maximum # tests during time period:</b>
<input type="checkbox"/> CBC with plts (5200)	20
<input type="checkbox"/> ALT (9410)	8
<input type="checkbox"/> T. bilirubin (82247)	8
<input type="checkbox"/> Basic metab panel (80048)	8
<input type="checkbox"/> TSH (84443)	8
<input type="checkbox"/> Urine pregnancy (11230)*	15

**\*for women of childbearing age only**

**MD Signature:** \_\_\_\_\_

**24hr Primary Care Hepatitis C contact cell phone for critical values: (408) 314-9338**

## Organization of Hep C Center Patient Hardcopy Chart

### Inside cover:

- Treatment Flow Sheet
  - lab monitoring page followed by
  - medication choice/dosing sheet
- Baseline Clinical Evaluation Summary Sheet
- Pretreatment Checklist
- Prescriptions/med authorizations
- Copies of disability paperwork (if any)
- Protocol informed consents (if any)
- Insurance card information
- Office patient demographic sheet

### Front of back cover:

- Contact Datasheets: filed with most recent at front
  - Treatment contact sheets followed by
  - Pretreatment contact sheets
  - Consult notes placed as appropriate when obtained
  - Initial Injection Teaching Sheet
  - Side Effect Surveys/Depression Scales
- Dictated H&P
- H&P template forms
- Baseline patient data survey
- Referral form from PCP (if any)
- Outside PNs, with most recent note at front

### Behind first divider (marked “labs”):

- Labs, including pathology reports (chronologically with most recent at front) including outside labs

### Behind second divider (marked “x-rays”):

- X-ray reports (most recent in front) including outside studies

## Primary Care Hepatitis C Center Patient Teaching Documentation Tool

**Patient Name:** \_\_\_\_\_ **date:** \_\_\_/\_\_\_/\_\_\_  
**present during teaching:** patient spouse family sig other friend other  
**type of teaching provided:** individual group video only

**TOPIC (check off when covered):**

- Premedication regimen:
- Treatment regimen
  - Peg-intron
  - Pegasys
  - Rebetrol
  - Copegus
  - Consensus Interferon
  - Gamma interferon
- Medication storage
- Needed equipment provided (circle all that apply)
  - needles/syringes
  - vial
  - alcohol pads
  - sharps container
  - multidose pen
- Determining and preparing the correct dose
- Selecting and rotating injection sites
- Site preparation
- Needle insertion/injection
- Sharps disposal
- Follow-up labs and appointments; schedule and importance
- Side effect management (see appendix # 9; "Side Effects Module for the Patient")
- Patient education material and support information provided as desired.
- Pregnancy and contraception guidelines reviewed/reinforced.
- Need to avoid alcohol use reviewed.

Other issues:

I understand the instructions regarding the storage, preparation, and administration of my medication, side effects and management, the importance of ongoing blood testing and contact with the Hep C Center Staff during treatment, and when to call the Center staff

*patient signature and date*

*Hep C Center Staff signature and date*

## Hep C Center Pre-treatment Contact Sheet

Date \_\_\_/\_\_\_/\_\_\_

Patient name \_\_\_\_\_ contact type:  scheduled  unscheduled  
 MD  MA  PA/NP  
 in person  phone

**Reason for contact:**

- review labwork
- review liver biopsy
- education/counseling
- treatment initiation
- other: \_\_\_\_\_

History/issues:

---

EXAM: BP \_\_\_/\_\_\_ P \_\_\_ T \_\_\_ RR \_\_\_ Wt \_\_\_\_\_  
 no exam

A/P:

Estimated time spent in contact:  0-15 min.  15-30 min  30-45min  45-60 min  >60 min

Signature \_\_\_\_\_

Patient name \_\_\_\_\_

### Baseline Clinical Evaluation Summary Sheet

(all baseline labs except genotype and hepatitis serologies should be done w/in 3 months of Rx start date)

HCV genotype \_\_\_\_\_ Viral load (test type) \_\_\_\_\_ \_/\_/\_

**Hematology:**

PTT \_\_\_\_\_ PT (INR) \_\_\_\_\_ sec ( \_\_\_\_\_)

Hgb \_\_\_\_\_ HCT \_\_\_\_\_% PLT \_\_\_\_\_ WBC \_\_\_\_\_ %neutro: \_\_\_\_\_ (ANC= \_\_\_\_\_)

**Chemistry:**

Na \_\_\_\_\_ K \_\_\_\_\_ HCO3 \_\_\_\_\_ BUN \_\_\_\_\_ Cr \_\_\_\_\_ glucose \_\_\_\_\_

**Liver testing:**

Alb \_\_\_\_\_ tbili \_\_\_\_\_ Alk Phos \_\_\_\_\_ AST \_\_\_\_\_ ALT \_\_\_\_\_

**Iron studies:**

Iron \_\_\_\_\_ TIBC \_\_\_\_\_ % trans \_\_\_\_\_ Ferretin \_\_\_\_\_

**Urinalysis:**

protein \_\_\_\_\_ RBC \_\_\_\_\_ other \_\_\_\_\_

**Hepatitis serologies:**

HBsAg \_\_\_\_\_ HBsAb \_\_\_\_\_ HBcAb \_\_\_\_\_ HAVab \_\_\_\_\_

**Miscellaneous:**

T.Chol \_\_\_\_\_ HIV \_\_\_\_\_ urine preg \_\_\_\_\_ (\_/\_/\_)

TSH \_\_\_\_\_ AFP \_\_\_\_\_

Other significant lab results: \_\_\_\_\_

**Radiology:**

**Abd U/S**

(\_/\_/\_): \_\_\_\_\_

Other: \_\_\_\_\_

**Pathology:**

Liver biopsy results (\_/\_/\_): \_\_\_\_\_  biopsy declined

**COMMENTS:**

\_\_\_\_\_  
\_\_\_\_\_  
\_\_\_\_\_

\_\_\_\_/\_\_\_\_/\_\_\_\_

## Hep C Center Dear Doctor Letter

Dear Dr. \_\_\_\_\_,

Your patient, \_\_\_\_\_ has completed the pretreatment evaluation (see enclosed "Baseline Clinical Evaluation Summary Sheet") of their hepatitis C infection and has decided to initiate anti-viral treatment as follows:

**Interferon** (PEG-Intron Pegasys Consensus ): \_\_\_\_\_

**Ribavirin** (Rebetrol Copegus Generic) : \_\_\_\_\_

Start date \_\_/\_\_/\_\_                      Anticipated stop date \_\_/\_\_/\_\_

For your information, we have enclosed a copy of the Center's reference handout "Side Effects of Interferon and Ribavirin in the Treatment of Hep C." Your patient has been educated regarding these possible side effects and has been instructed to contact the Center should the need arise. If you have any questions or concerns regarding your patient's HCV treatment, please don't hesitate to call me on my cell phone at (XXX) \_\_\_\_\_.

Sincerely,

\_\_\_\_\_, MD

encl: append 3, 20