



INLAND EMPIRE HEALTH PLAN

MEMORANDUM

Report Title: Clinical Practice Guideline- Hepatitis C
Report Presented To: Pharmacy and Therapeutics Subcommittee
Report Presented On: Subcommittee Date May 2009

In April 2009, the American Association For The Study Of Liver Diseases published the latest guideline on “Diagnosis, Management, and Treatment of Hepatitis C: An Update”. The following is a summary of the recommendations:

Recommendation

1. As part of a comprehensive health evaluation, all persons should be screened for behaviors that place them at high risk for HCV infection
2. Persons who are at risk should be tested for the presence of HCV infection
 1. Persons for Whom HCV Screening is Recommended
 2. Persons who have injected illicit drugs in the recent and remote past, including those who injected only once and do not consider themselves to be drug users.
 3. Persons with conditions associated with a high prevalence of HCV infection including:
 4. Persons with HIV infection
 5. Persons with hemophilia who received clotting factor concentrates prior to 1987
 6. Persons who have ever been on hemodialysis
 7. Persons with unexplained abnormal aminotransferase levels
 8. Prior recipients of transfusions or organ transplants prior to July 1992 including:
 9. Persons who were notified that they had received blood from a donor who later tested positive for HCV infection
 10. Persons who received a transfusion of blood or blood products
 11. Persons who received an organ transplant

12. Children born to HCV-infected mothers
 13. Health care, emergency medical and public safety workers after a needle stick injury or mucosal exposure to HCV-positive blood
 14. Current sexual partners of HCV-infected persons
3. Persons infected with HCV should be counseled on how to avoid HCV transmission to others
 4. Patients suspected of having acute or chronic HCV infection should first be tested for anti-HCV
 5. HCV RNA testing should be performed in:
 - a) Patients with a positive anti-HCV test
 - b) Patients for whom antiviral treatment is being considered, using a sensitive quantitative assay
 - c) Patients with unexplained liver disease whose anti-HCV test is negative and who are immunocompromised or suspected of having acute HCV infection
 6. HCV genotyping should be performed in all HCV-infected persons prior to interferon-based treatment in order to plan for the dose and duration of therapy and to estimate the likelihood of response
 7. A liver biopsy should be considered in patients with chronic hepatitis C infection if the patient and health care provider wish information regarding fibrosis stage for prognostic purposes or to make a decision regarding treatment
 8. Currently available noninvasive tests may be useful in defining the presence or absence of advanced fibrosis in persons with chronic hepatitis C infection, but should not replace the liver biopsy in routine clinical practice
 9. Treatment decisions should be individualized based on the severity of liver disease, the potential for serious side effects, the likelihood of treatment response, the presence of comorbid conditions, and the patient's readiness for treatment
 10. For patients in whom liver histology is available, treatment is indicated in those with bridging fibrosis or compensated cirrhosis provided they do not have contraindications to therapy
 11. **The optimal therapy for chronic HCV infection is the combination of peginterferon alfa and ribavirin**
 12. **HCV RNA should be tested by a highly sensitive quantitative assay at the initiation of or shortly before treatment and at week 12 of therapy**

Genotypes 1 and 4 HCV Infection

- 13. Treatment with peginterferon plus ribavirin should be planned for 48 weeks; the dose for peginterferon alfa-2a is 180 µg subcutaneously per week together with ribavirin using doses of 1,000 mg for those 75 kg in weight and 1,200 mg for those >75 kg; the dose for peginterferon alfa-2b is 1.5 µg/kg subcutaneously per week together with ribavirin using doses of 800 mg for those weighing <65 kg; 1,000 mg for those weighing >65 kg to 85 kg, 1,200 mg for >85 kg to 105 kg, and 1,400 mg for >105 kg**
- 14. Treatment may be discontinued in patients who do not achieve an early virological response (EVR; 2 log reduction in HCV RNA at week 12 of treatment)**
- 15. Patients who do not achieve a complete EVR (undetectable HCV RNA at week 12 of treatment) should be re-tested at week 24, and if HCV RNA remains positive, treatment should be discontinued**
- 16. For patients with genotype 1 infection who have delayed virus clearance (HCV RNA test becomes negative between weeks 12 and 24), consideration should be given to extending therapy to 72 weeks**
- 17. Patients with genotype 1 infection whose treatment continues through 48 to 72 weeks and whose measurement of HCV RNA with a highly sensitive assay is negative at the end of treatment should be retested for HCV RNA 24 weeks later to evaluate for a sustained virological response (SVR; HCV RNA negative 24 weeks after cessation of treatment)**

Genotype 2 or Genotype 3 HCV Infection

- 18. Treatment with peginterferon plus ribavirin should be administered for 24 weeks, using a ribavirin dose of 800 mg**
- 19. Patients whose treatment continues through 24 weeks and whose measurement of HCV RNA with a highly sensitive assay is negative should be retested for HCV RNA 24 weeks later to evaluate for an SVR**
- 20. Patients with HCV-related cirrhosis who achieve an SVR, regardless of the genotype, should continue to be monitored at 6 to 12 month intervals for the development of HCC**
- 21. Retreatment with peginterferon plus ribavirin in patients who did not achieve an SVR after a prior full course of peginterferon plus ribavirin**

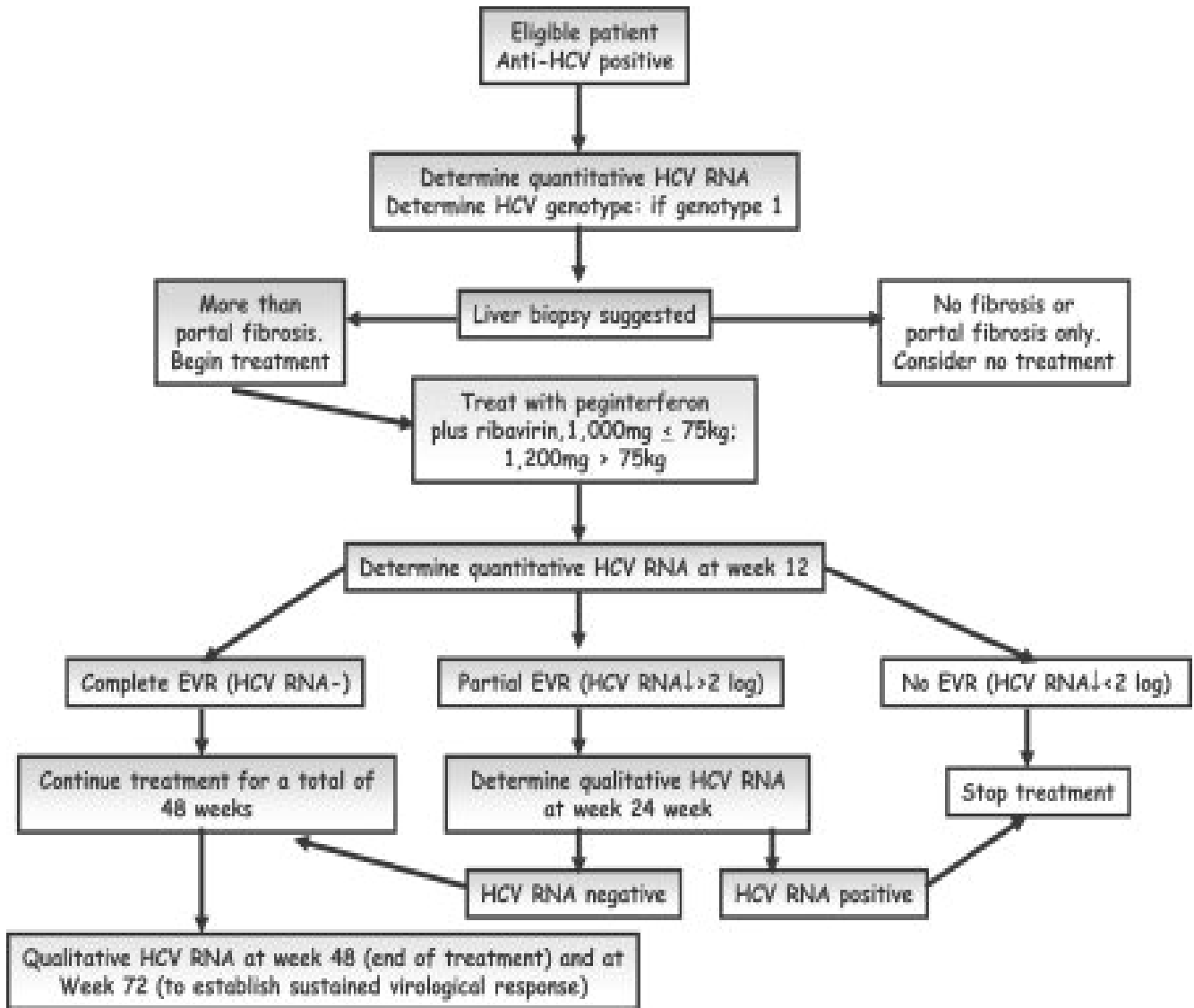
- is not recommended, even if a different type of peginterferon is administered
22. Retreatment with peginterferon plus ribavirin can be considered for non-responders or relapsers who have previously been treated with non-pegylated interferon with or without ribavirin, or with peginterferon monotherapy, particularly if they have bridging fibrosis or cirrhosis
 23. Maintenance therapy is not recommended for patients with bridging fibrosis or cirrhosis who have failed a prior course of peginterferon and ribavirin
 24. Regardless of the serum alanine aminotransferase level, the decision to initiate therapy with pegylated interferon and ribavirin should be individualized based on the severity of liver disease by liver biopsy, the potential for serious side effects, the likelihood of response, and the presence of comorbid conditions
 25. The treatment regimen for HCV-infected persons with normal aminotransferase levels should be the same as that used for persons with elevated serum aminotransferase levels
 26. The diagnosis and testing of children suspected of being infected with HCV should proceed as for adults
 27. Routine testing for anti-HCV at birth of children born to HCV-infected mothers is not recommended because of the high rate of positive antibody due to passive transfer from the mother. Testing for anti-HCV may be performed at 18 months of age or older
 28. Testing for HCV RNA may be considered at 1-2 months of age in infants born to HCV-infected mothers if early diagnosis is desired
 29. Children aged 2-17 years who are infected with HCV should be considered appropriate candidates for treatment using the same criteria as that used for adults.
 30. Children should be treated with pegylated interferon alfa-2b, 60 $\mu\text{g}/\text{m}^2$ weekly in combination with ribavirin, 15 mg/kg daily for a duration of 48 weeks
 31. Anti-HCV testing should be performed in all HIV-infected persons

32. HCV RNA testing should be performed to confirm HCV infection in HIV-infected persons who are positive for anti-HCV, as well as in those who are negative and have evidence of unexplained liver disease
33. Hepatitis C should be treated in the HIV/HCV co-infected patient in whom the likelihood of serious liver disease and a treatment response are judged to outweigh the risk of morbidity from the adverse effects of therapy
34. Initial treatment of hepatitis C in most HIV-infected patients should be peginterferon alfa plus ribavirin for 48 weeks at doses recommended for HCV mono-infected patients
35. When possible, patients receiving zidovudine (AZT) and especially didanosine (ddI) should be switched to an equivalent antiretroviral agent before beginning therapy with ribavirin
36. HIV-infected patients with decompensated liver disease should not be treated with peginterferon alfa and ribavirin and may be candidates for liver transplantation
37. All persons with chronic kidney disease awaiting renal replacement therapy, namely hemodialysis or kidney transplantation, should be screened for hepatitis C in order to plan for management and treatment
38. The decision to perform a liver biopsy in patients with kidney disease should be individualized, based upon the clinical assessment for the need for therapy and the need to establish the severity of the liver disease
39. Persons with chronic HCV infection and mild kidney disease (GFR >60 mL/minute) can be treated with the same combination antiviral therapy as that used in persons without kidney disease
40. Persons with chronic HCV infection and severe kidney disease not undergoing hemodialysis can be treated with reduced doses of both peginterferon (alpha-2a, 135 ug/week; alpha-2b, 1 µg/kg/week) and ribavirin (200-800 mg/day) with careful monitoring for adverse effects
41. Treatment of HCV in patients on dialysis may be considered with either standard interferon (2a or 2b) in a dose of 3 mU t.i.w. or reduced dose pegylated interferon 2a, 135 µg/week or 2b 1 µg/kg/week. (Class IIa, level C). Ribavirin can be used in combination with interferon in a markedly reduced daily dose with careful monitoring for anemia and other adverse effects
42. Treatment is not recommended for patients with chronic HCV infection who have undergone kidney transplantation, unless they develop

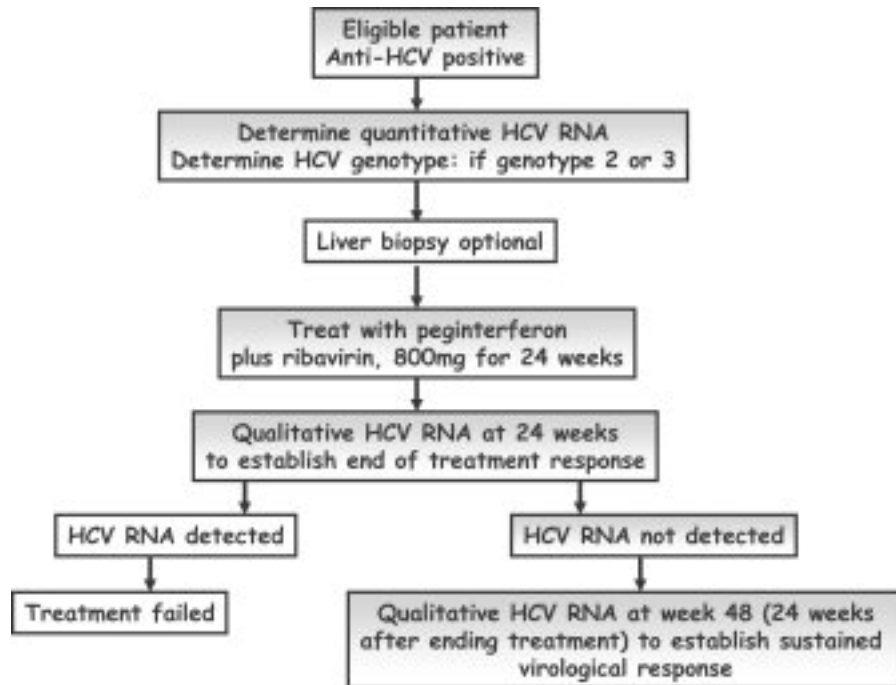
fibrosingcholestatic hepatitis

43. Patients with cryoglobulinemia and mild to moderate proteinuria and slowly progressive kidney disease can be treated with either standard interferon or reduced doses of pegylated interferon alfa and ribavirin
44. Patients with cryoglobulinemia and marked proteinuria with evidence of progressive kidney disease or an acute flare of cryoglobulinemia can be treated with rituximab, cyclophosphamide plus methylprednisolone, or plasma exchange followed by interferon-based treatment once the acute process has subsided
45. African Americans infected with HCV who are appropriate treatment candidates should be treated with the current optimal regimen consisting of pegylated interferon and ribavirin
46. African Americans with baseline neutropenia (ANC 1500 mm³) should not be excluded from hepatitis C treatment
47. Patients with HCV-related compensated cirrhosis, can be treated with the standard regimen of pegylated interferon and ribavirin but will require close monitoring for adverse events
48. Patients with HCV-related decompensated cirrhosis should be referred for consideration of liver transplantation
49. Interferon-based therapy may be initiated at a lower dose in patients with decompensated cirrhosis (CTP class B and C), as long as treatment is administered by experienced clinicians with vigilant monitoring for adverse events preferably in patients who have already been accepted as candidates for liver transplantation
50. Growth factors can be used for treatment-associated anemia and leukopenia to improve quality of life and may limit the need for antiviral dose reductions in patients with decompensated cirrhosis
51. Treatment of HCV-related disease following liver transplantation should be initiated in appropriate candidates after demonstration of recurrent histologic disease but should be undertaken with caution and under the supervision of a physician experienced in transplantation
52. Peginterferon alfa either with or without ribavirin should be the preferred regimen when treating patients with hepatitis C after liver transplantation
53. Interferon-based therapy should not be used in recipients of heart, lung, and kidney grafts, except for patients who develop fibrosing cholestatic hepatitis

54. Patients with acute HCV infection should be considered for interferon-based anti-viral therapy
55. Treatment can be delayed for 8 to 12 weeks after acute onset of hepatitis to allow for spontaneous resolution
56. Although excellent results were achieved using standard interferon monotherapy, it is appropriate to consider the use of peginterferon because of its greater ease of administration
57. Until more information becomes available, no definitive recommendation can be made about the optimal duration needed for treatment of acute hepatitis C; however, it is reasonable to treat for at least 12 weeks, and 24 weeks may be considered
58. No recommendation can be made for or against the addition of ribavirin and the decision will therefore need to be considered on a case-by-case basis
59. Treatment of HCV infection can be considered for persons even if they currently use illicit drugs or who are on a methadone maintenance program, provided they wish to take HCV treatment and are able and willing to maintain close monitoring and practice contraception
60. Persons who use illicit drugs should receive continued support from drug abuse and psychiatric counseling services as an important adjunct to treatment of HCV infection
61. Patients with HCV infection and concomitant mental and psychiatric disorders can be considered for treatment using the currently approved regimens.
62. Treatment of hepatitis C infection in patients with psychiatric disorders should be undertaken only with the support of a multi-disciplinary team that should include psychiatric counseling services
63. All persons with chronic HCV infection who lack antibodies to hepatitis A and B should be offered vaccination against these two viral infections
64. Persons with chronic HCV infection should be advised to abstain from alcohol consumption
65. No recommendation can be made for the use of herbal products. There is no current evidence that herbal products have a role in the treatment of patients with acute or chronic HCV infection



Treatment Algorithm for managing and treating patients with chronic HCV infection, genotype 1. SVR, sustained virologic response; EVR, early virologic response. RVR is omitted from this treatment algorithm because it has not yet been adequately evaluated. HCV RNA should be quantitated using a sensitive assay (10-50 IU/mL).



Treatment algorithm for managing and treating patients with chronic HCV infection, genotype 2 or 3. EVR, early virologic response; ETR, end of treatment response; SVR, sustained virologic response. RVR is omitted from this treatment algorithm because it has not yet been adequately evaluated. HCV RNA should be quantitated using a sensitive assay (10-50 IU/mL).