Establishing a Hepatitis C Treatment Program in a Free Clinic

Resources, Tools and Guidelines

Good News Clinics | Gainesville, Ga. | 770.297.5040 | www.goodnewsclinics.org

Table of Contents:

Good News Clinics

Background and History

Good News Clinics is a volunteer based ministry with humble beginnings, starting with one volunteer doctor and nurse seeing patients a few hours each week in a bathroom at Good News at Noon, a local mission. Over the years, Good News Clinics has grown to meet the community need, providing a wide range of services including primary care, dispensary, laboratory, dental exams, fillings and extractions and specialty referrals to 320 local specialty physicians who agree to see our patients in their offices free of charge.

Great need for our services exists among the poor and uninsured in our county who do not qualify for coverage under the Affordable Care Act. Last year, Good News Clinics provided over 17,000 patient visits as well as 39,000 prescriptions free of charge to uninsured Hall County residents who have incomes within 150% of the federal poverty level. Good News Clinics will begin its 25th year of operation in October of this year and now occupies an 11,000 sq. ft. clinic space. GNC now employs a staff of 25, including 2 nurse practitioners, and is served by 46 volunteer doctors and 43 volunteer dentists who, along with many other clinical and community volunteers, allow us to meet the need.

With a budget of $1.3 million, GNC provided over $20.3 million in care and services last year. By providing these services in the least expensive setting rather than the most expensive (emergency room), GNC saves tax dollars that would normally be spent on healthcare. GNC is a community-funded organization. We depend on our community as well as grants from private foundations for financial support. We receive support from Northeast Georgia Health System as well as individuals, businesses and organizations in our community.

Hepatitis C:
Disease and Treatment Overview

Hepatitis C is a liver disease caused by the hepatitis C virus (HCV). The virus can cause both acute and chronic hepatitis infection, ranging in severity from a mild illness lasting a few weeks to a serious, lifelong illness. HCV is a blood-borne virus and the most common modes of infection are through unsafe injection practices, inadequate sterilization of medical equipment, and the transfusion of unscreened blood and blood products. Globally, 130–150 million people have chronic HCV infection. A significant number of those who are chronically infected will develop liver cirrhosis or liver cancer. Approximately 700,000 people die each year from HCV-related liver diseases. Antiviral medicines can cure approximately 90% of persons with chronic HCV infection, thereby reducing the risk of death from liver cancer and cirrhosis, but access to diagnosis and treatment is low. There is currently no vaccine for HCV; however research in this area is ongoing.

The following individuals are at risk for contracting HCV:

- People who have injected illicit drugs, even if only one time, including those who have injected only once many years ago.
- Healthcare workers who have been exposed to infectious blood on the job or have been stuck by a needle infected with HCV.
- People who were notified that they received blood from a donor who tested positive after they had already donated their blood.
- People who received a blood transfusion or had a solid organ transplant before 1992.
- People who have HIV.
- People who received blood clotting factor products before 1987.
- People who are long-term hemodialysis patients.
- People who live in a household with an infected person.
- People who have/had unprotected sex with multiple partners, and/or between males, particularly where there is a history of a sexually transmitted disease.
- People who engage or have engaged in anal sex without a condom.
- People who have tattoos and body piercing.
- People who have ever worked or been housed in a prison.

The most common mode of infection for the patients seen in a volunteer clinic is through unsafe injection practices, primarily the sharing of needles and syringes. Rarely there are patients who have no history of intravenous drug use, but received transfusions before 1992. In 1992, the antibody titer evaluation for hepatitis became common practice. There are also rare patients denying a history of IV drug use, but may have one or more tattoos or body piercings, some applied while in prison. Patients at GNC are usually asymptomatic and are first detected to have abnormal liver function tests during a routine chemical profile while being evaluated for another illness at an outpatient clinic, emergency room, or in prison and thus are referred for follow-up evaluation.

Hepatitis C:
Continued

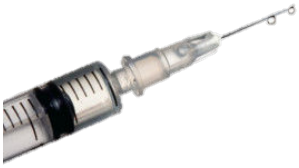
Many, in addition to history of IV drug use, also have a history of alcohol abuse. Chronic HCV and alcohol are common causes of chronic liver diseases in the United States, and both are recognized as major causes of liver disease worldwide. Each poses a major public and economic burden to society, and when the two coexist they appear to have a synergistic effect in the progression of chronic liver disease.

HCV is estimated to affect between 2.7 and 5.2 million citizens in the United States alone, HCV is a slowly progressing disease that over time increases a patient's risk for cirrhosis, liver failure, and hepatocellular carcinoma. HCV is the most common condition leading to liver transplantation. HCV also causes cirrhosis or liver cancer related death in 1%-5% of patients who have had the virus for 20-30 years. There are at least six distinct genotypes identified by a number, which are different sequences of the viral DNA. Each genotype represents slight variations in viral behavior medication susceptibility. In addition to genotypes, there are over 50 subtypes within those genotypes, which are identified by a lowercase letter.

The different "strains" of HCV result from the high chance of mutation in its genetic code during viral replication. Over the years very similar, but technically different types of HCV develop. Regardless of the HCV genotype, they all cause the same disease. In the United States, about 57% of people with HCV are genotype 1a, the most common type. Genotype 1b is found in about 17% of HCV positive individuals. Genotypes 2 and 3 are the next most common.

In 2014, the first complete treatment for HCV that requires once daily dosing was approved by the Food and Drug Administration. The drug, Harvoni from Gilead Sciences, shortened the duration of treatment and provided the first all-oral regimen for many patients. This drug reported cure rates approaching 96% for the most common genomes. Since its release, the FDA has approved many other therapeutic options. A major advantage of the new medications is the abbreviated duration, with most patients requiring only 12 weeks of therapy. A concerning limitation with the newest treatment options is the cost. Depending on a patient's other conditions, history of other HCV treatments, and severity of liver damage at start of treatment, some patients may require 24 weeks of therapy. The costs associated with these medications range from $94,500 to $147,000 for 12 weeks of therapy and double for patients requiring a longer duration of therapy. Additional costs associated with treatment of HCV are the costs of diagnostic testing and lab fees as well as the additional time for practitioners.

The obvious problem for volunteer clinics is that none of the patients can afford the drug costs or have insurance that will cover any of the expense. The ethical problem then arises: if the parent drug company will supply the medication free of charge to some but not all and the clinic is willing to cover most but not all the financial expenses of basic and follow-up laboratory data, who do you treat? At the Good News Clinics we have developed a protocol, which can be altered for each individual patient.

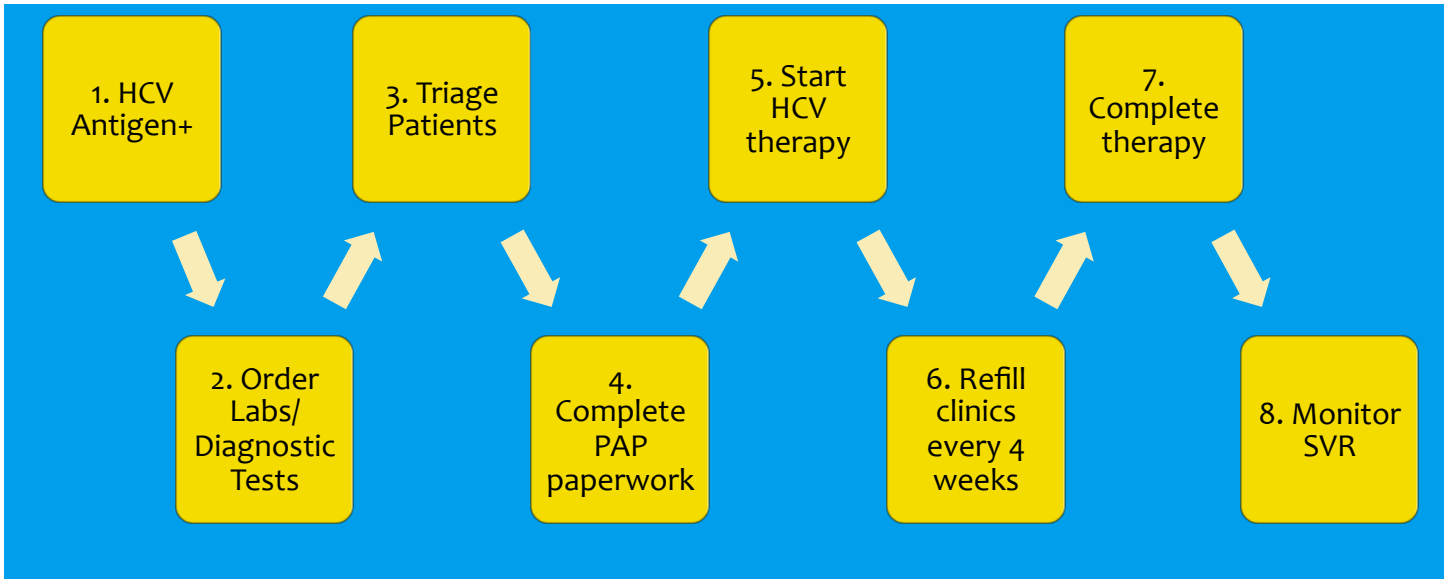


Program Overview

Effectively treating patients with cost consideration

Costs associated with treatment of HCV seem daunting for clinics with limited resources and may often be a source of hesitation to initiating treatment of HCV in eligible patients. There are at least six different genotypes of HCV. Different genotypes require different treatment plans. In an effort to treat as many of the eligible HCV positive patients at the Good News Clinics, a team of pharmacists and physicians have developed a streamlined approach to manage these patients while being mindful of resource allocation toward the project. The overall process involves non-invasive diagnostic testing, common laboratory values and a thorough physician evaluation to determine eligibility for treatment of each patient being considered for the program. The costs of the medications are covered completely by Gilead Sciences, Inc. and Bristol-Myers Squibb Company for patients meeting specific income and residence requirements. The dispensary staff at the clinic completes the applications for these prescription assistance programs. The staff also facilitates medication delivery directly to the clinic for dispensing and provides counseling for each patient beginning HCV treatment. Patients are started and maintained on therapy in cohorts to streamline the specific dates used for lab monitoring and maintain an organized approach to the treatment of multiple patients simultaneously.

The specific protocol implemented at the Good News Clinics (GNC) was adapted from a compilation of other HCV treatment programs with a concerted effort to stay within the available resources at the clinic, an important consideration for many charitable clinics. The protocol followed for treatment is within the guidelines developed by the Infectious Diseases Society of America and the American Association for the Study of Liver Diseases. The clinic uses diagnostic criteria supported within the guidelines for the staging of liver damage and the suggested treatments for the various genotypes of the virus.



GNC Treatment Protocol

1. Potential HCV positive patients are identified in an appointment with a GNC provider. Patients testing positive for HCV are then referred to the HCV protocol physician.

2. Patients are assessed for readiness to begin therapy and eligibility for the treatment program. (See further discussion on intent to treat). The following labs are ordered to aid in developing patient-specific treatment plans:
   a. HCV Genotype
   b. HCV Viral Load
   c. Complete Blood Count
   d. Comprehensive Metabolic Panel
   e. Additional diagnostic tests if indicated

3. Patients are triaged based on available resources and cohort patient load. Patients that are not eligible for treatment are reserved for future changes that may impact ability to initiate treatment.

4. Patients complete PAP paperwork along with dispensary staff to obtain medications from drug manufacturers. Patients are required to provide detailed financial information, proof of residence and proper identification. Dispensary staff complete the required diagnostic information based on physician evaluation.

5. The initial appointment for medication involves a one-on-one meeting with a pharmacist to discuss potential side effects and reinforce the importance of compliance to HCV therapy. Patients are scheduled for follow-up refill appointments at this time.

6. Patients return to clinic every 4 weeks for refill of medication. At this time the pharmacist discusses any side effects with patient and tries to troubleshoot any potential barriers to adherence. At the 1st refill appointment the clinic obtains a 4-week viral load to determine viral response to therapy.

7. Patients return to clinic upon completion of therapy to discuss follow-up monitoring. Patients are also counseled on abstinence from lifestyle behaviors that increase the risk of HCV reinfection. At this visit patients are scheduled for follow up labs at either 12 or 24 weeks following therapy completion based on length of therapy.

8. Patients return to clinic for final lab monitoring through HCV viral load. The sustained virologic response (SVR) of undetectable viral load indicates success of HCV therapy.

Diagnostic Evaluation:

HCV Diagnosis & Fibrosis Scoring Methods

Ultrasound

Some patients may require additional diagnostic information to determine an accurate level of fibrosis. Ultrasound interpretation is a non-invasive option for fibrosis staging if clinicians are unsure of a patient's level of liver damage. This diagnostic test requires additional resources or funding and may not be available to all charitable clinics. It is included as an option because laboratory tests may not provide enough information for all patients.

Laboratory Tests

HCV positive patients are identified during routine medical appointments at the clinic. Necessary laboratory values are obtained at baseline to determine a patient's genotype, viral load and severity of liver damage from HCV. In order to determine a patient's FIB-4 score (a scoring system for liver fibrosis), the clinic obtains a CBC and CMP for each patient. Patients are also monitored for the duration of treatment and after completion to determine success of therapy. The Fib-4 system ranges from 0 to 4 indicating no fibrosis to cirrhosis based on the interpretation of specific laboratory values. Clinicians may also utilize the Child-Pugh or Meld Scoring systems to determine a patient's prognosis or degree of cirrhosis in addition to the Fib-4 system. The Fib-4 score must be obtained to accurately complete the patient assistance program paperwork to obtain HCV medications.

$$\text{FIB-4 score} = \frac{[\text{age (years)}] \times \text{AST (U/L)}}{[\text{Platelets}(10^9/\text{L}) \times \text{ALT}^{1/2}\ (\text{U/L})]}$$

Fib – 4 Index	F Score	Fibrosis Level
< 1.45	F0	None
	F1	Minor Fibrosis
1.45-3.25	F2	Significant Fibrosis
> 3.25	F3	Severe Fibrosis
	F4	Cirrhosis

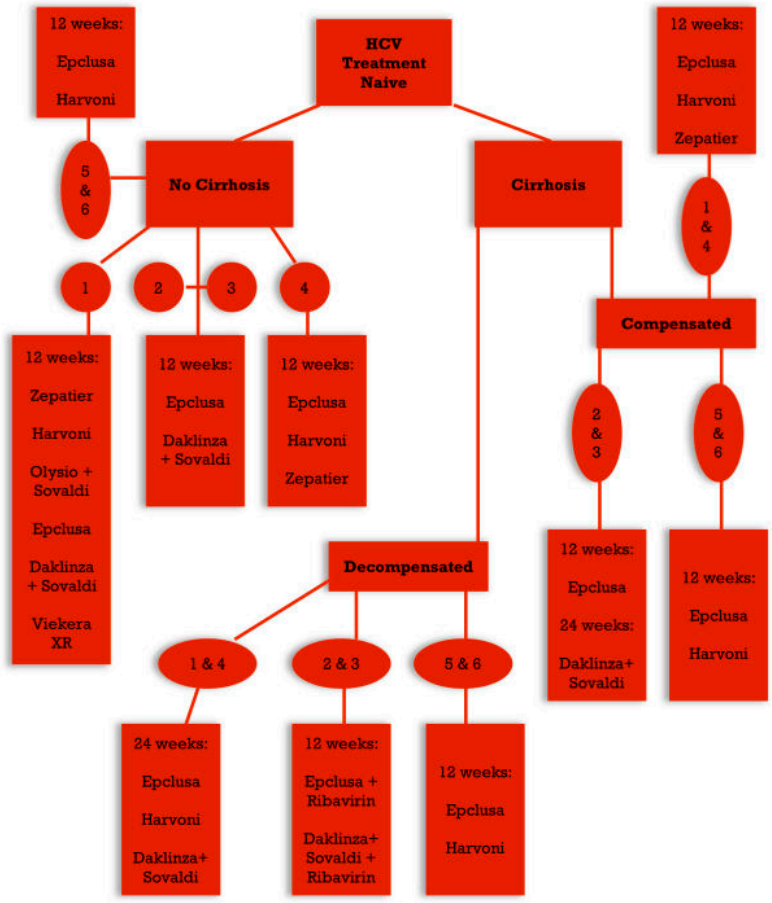
FibroScan & Biopsy

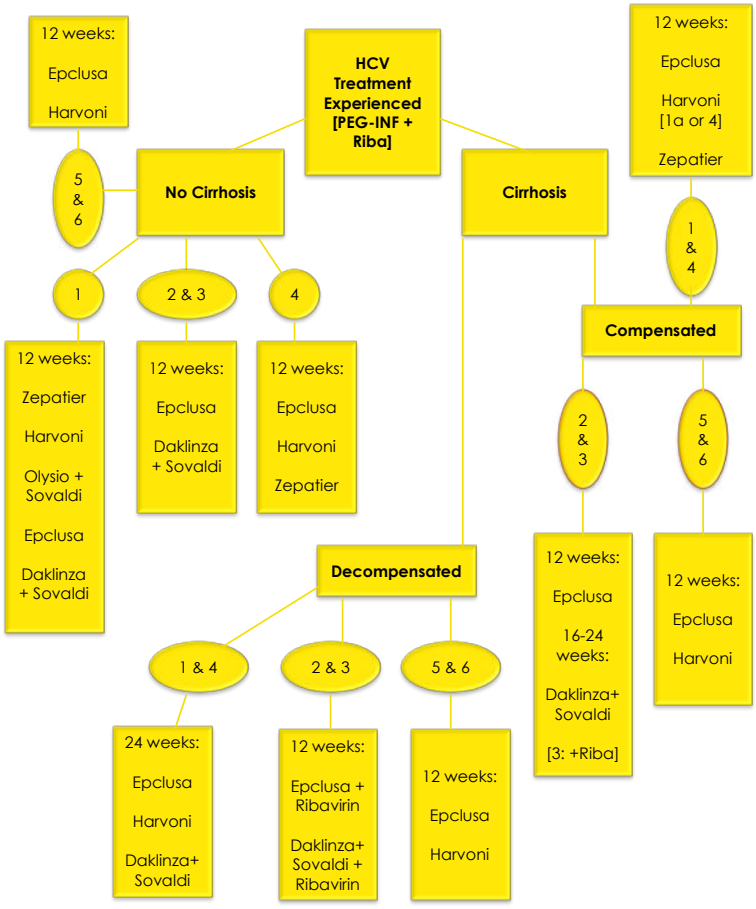
These procedures are the most accurate liver fibrosis staging tools. While these are considered the gold standard for liver staging in HCV treatment protocols, they may not be the most practical, especially for charitable clinics. These types of diagnostic exams are the most invasive and least cost effective for charitable clinics to implement on a routine basis for HCV patients. These diagnostic procedures are best reserved for final diagnostic clarification in extremely complicated patients or for clinics with ample resources.

Condensed Treatment Algorithms

These treatment algorithms have been adapted from the HCV Guidance: Recommendations for Testing, Managing, and Treating Hepatitis C Guidelines published by the Infectious Diseases Society of America and the American Association for the Study of Liver Diseases. These algorithms include the recommended treatments for each genotype of HCV along with the recommended duration of therapy based on the availability of medication through Patient Assistance Programs.

The HCV guidelines are a living document in that they are updated frequently due to many new developments in HCV treatment in the past decade. These charts should be used only as a quick reference and may require updates as new medications are released or as more information becomes available. Recommended regimens including medications not available through PAPs have been excluded but may be more appropriate for some patients. Please reference the HCV guidelines for the most comprehensive treatment recommendations.





Medication Considerations

There are many patient-specific factors that result in individualized treatment plans for each patient receiving HCV therapy. Some of the factors that may impact a patient's therapy are other medications, severity of liver damage, genotype and previous HCV treatment.

Drug Interactions and Dose Adjustments

Patients that are co infected with both HIV and HCV require special attention to drug interactions. Many HIV therapies interact with the available HCV medications. The general recommendation is to work with the HIV clinician to adjust each patient's HIV therapies to non-interacting options. Patients with severe renal impairment or that are on strong CYP3A inhibitors will likely require dosing adjustments of some of the available HCV therapies.

Previous HCV Treatment

Patients that were previously treated for HCV may have limitations for available therapies. The algorithm for previous treatment with PEG-Interferon + Ribavirin is included in this document. For patients previously treated with the newer direct acting antivirals, it is recommended to test for polymorphisms due to possible resistance. The best therapy will be selected based on these results and from review of the HCV Guidelines.

Length of Therapy

As portrayed in the treatment algorithms, most patients are eligible for 12 weeks of HCV treatment with a once daily medication. Some patients will require longer therapeutic duration if they have worsened liver function. In order to determine an accurate length of therapy, it is important to obtain all necessary laboratory values for the patient at baseline and to assess the patient's level of fibrosis.

Compliance

Compliance to HCV therapies is of utmost importance for therapeutic success. Patients that are non-compliant with medication experience much lower success rates, which may also lead to HCV therapy resistance. In order to determine a patient's ability to comply with therapy, they interact with a team of clinicians at GNC to determine their readiness to initiate and comply with HCV therapy.

Ethical Considerations

With limited resources, who gets treatment?

Roughly 70% of HCV infected patients will not develop advanced liver cirrhosis or liver cancer. So, the argument goes, why spend tens of billions of dollars for a drug that will not make much of a practical difference in the lives of these patients? What remains undisputed by people on all sides of this debate are the long-term risks posed by chronic HCV. Since there is no vaccine for HCV, prevention strategies currently rely on limiting exposure to the virus. One of the several ways to limit exposure is to eliminate the virus load from infected patients. The only way to do this is actively treat with effective drug programs those who carry a detectable viral load.

HCV is a contagious virus that is transmitted through contact with infected blood and blood products. Untreated patients with detectable viral loads remain a continued threat to infect contacts over a long period of time. One of the more pressing problems facing clinicians is dealing with the sheer volume of patients seeking these treatments.

To answer some of the questions and aid in ethical decisions, the Good News Clinics has developed an in-house protocol that can be altered depending on the clinical situation with each patient. If the patient is stable clinically regarding other organ systems (cardiovascular, pulmonary, renal, etc), is not currently on active chemotherapy for malignancy, is not currently a heavy consumer of alcohol, is not using IV or other illegal drugs, or is not living with someone who is a current IV drug user, then further attempts to secure HCV medication will be put in process. Patients are contacted at frequent intervals by pharmacy personnel and are followed at frequent intervals by physicians or certified clinical nurse practitioners to evaluate tolerance and possible side effects to medications.

Additional follow-up is completed after a patient finishes the 12 or 24-week course of therapy. This follow-up serves as reinforcement to abstain from behaviors that increase an individual's risk of HCV reinfection.

Appendix:
Additional Resources, Tools and Reproducible Documents

Hepatitis C Diagnosis Triage Summary

Patient Name: _____ Date of Birth: _____

Patient Chart #: _____

Genotype: _____

Viral Load: _____

Date of Lab Draw: _____

HIV Status: _____

Past treatments: _____

_____

Fib-4 Score: _____

Child Pugh Score: _____

Meld Score (optional): _____

Other pertinent labs: _____

Ultrasound: _____

FIB-4 score = $\frac{\text{[age (years)]} \times \text{AST (U/L)}}{\text{[Platelets}(10^9/\text{L}) \text{ X ALT}^{1/2} \text{ (U/L)]}}$

Fib – 4 Index	F Score	Fibrosis Level
< 1.45	F0	None
	F1	Minor Fibrosis
1.45-3.25	F2	Significant Fibrosis
> 3.25	F3	Severe Fibrosis
	F4	Cirrhosis

Hepatitis C Treatment Program

Lab Draw Order Form

Patient Name: _____ Date of Birth: _____

Patient Chart #: _____

Initial Labs:

- HCV Viral Load
- HCV Genotype
- CBC with Differential
- CMP

Week 4 of therapy:

- HCV Viral Load
- Other labs as indicated

12 or 24 weeks after completion of therapy:

- HCV Viral Load
- Other labs as indicated

Insert Clinic Name Here

Insert Clinic Address Here

Date:_____

PLEASE HAVE PERSON PROVIDING ASSITANCE COMPLETE FORM – FORM MUST BE NOTARIZED

I _____ certify and verify that _____,
(PRINT NAME OF PERSON ASSISTING WITH BILLS) (PRINT PATIENT NAME)

To the best of my knowledge has a monthly income of $_____ at this time, and has

been in this financial status for _____.
(LENGTH OF TIME)

Please indicate how the patient lives and any conditions that are imposed on that arrangement:

The patient lives with _____
(PRINT NAME)

at _____.
(STREET) (CITY) (ZIP)

Relationship to patient: _____

I pay for, or provide, the following items for the patient: _____

_____

Additional comments: _____

_____

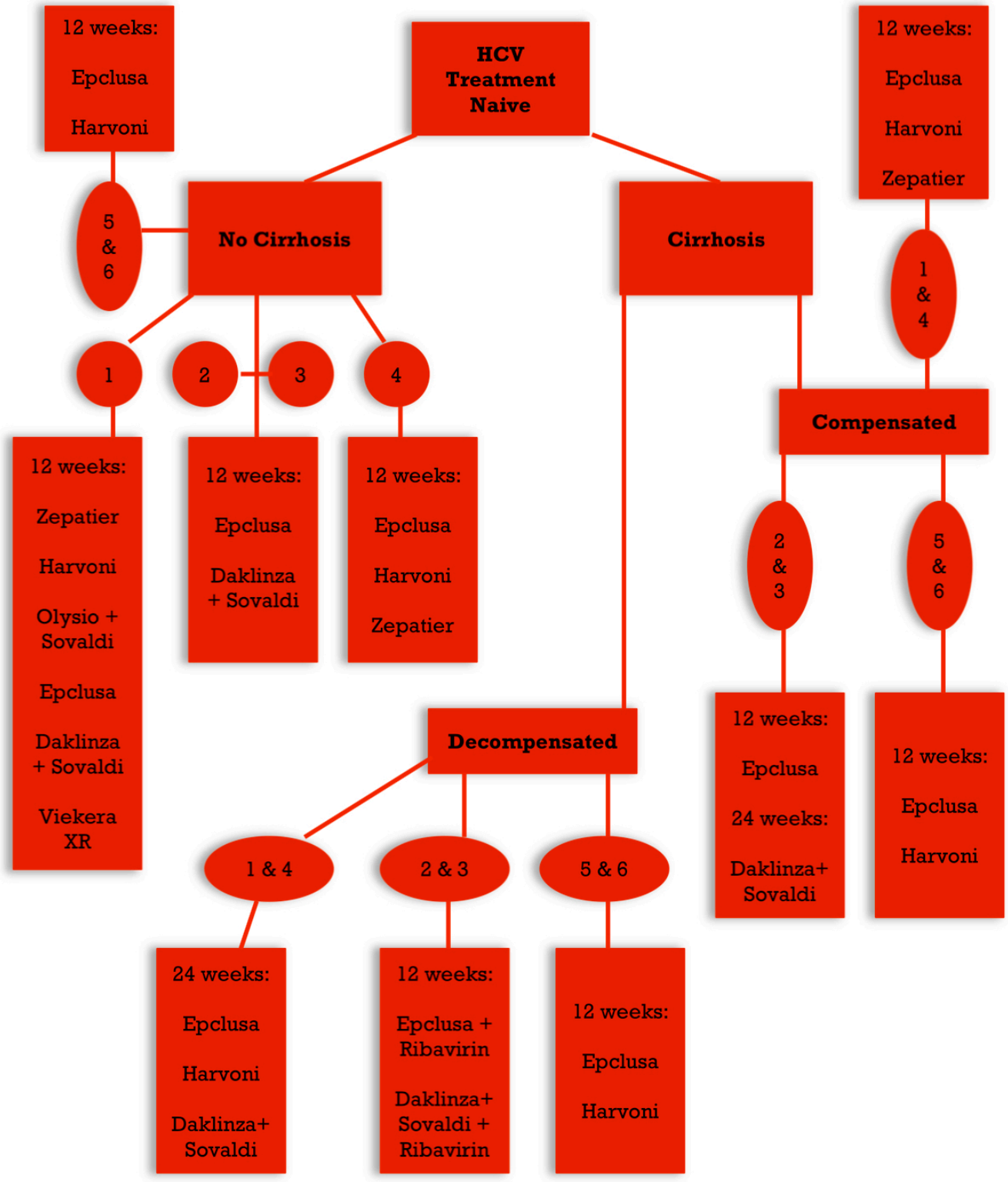
Signature: _____ Date: _____

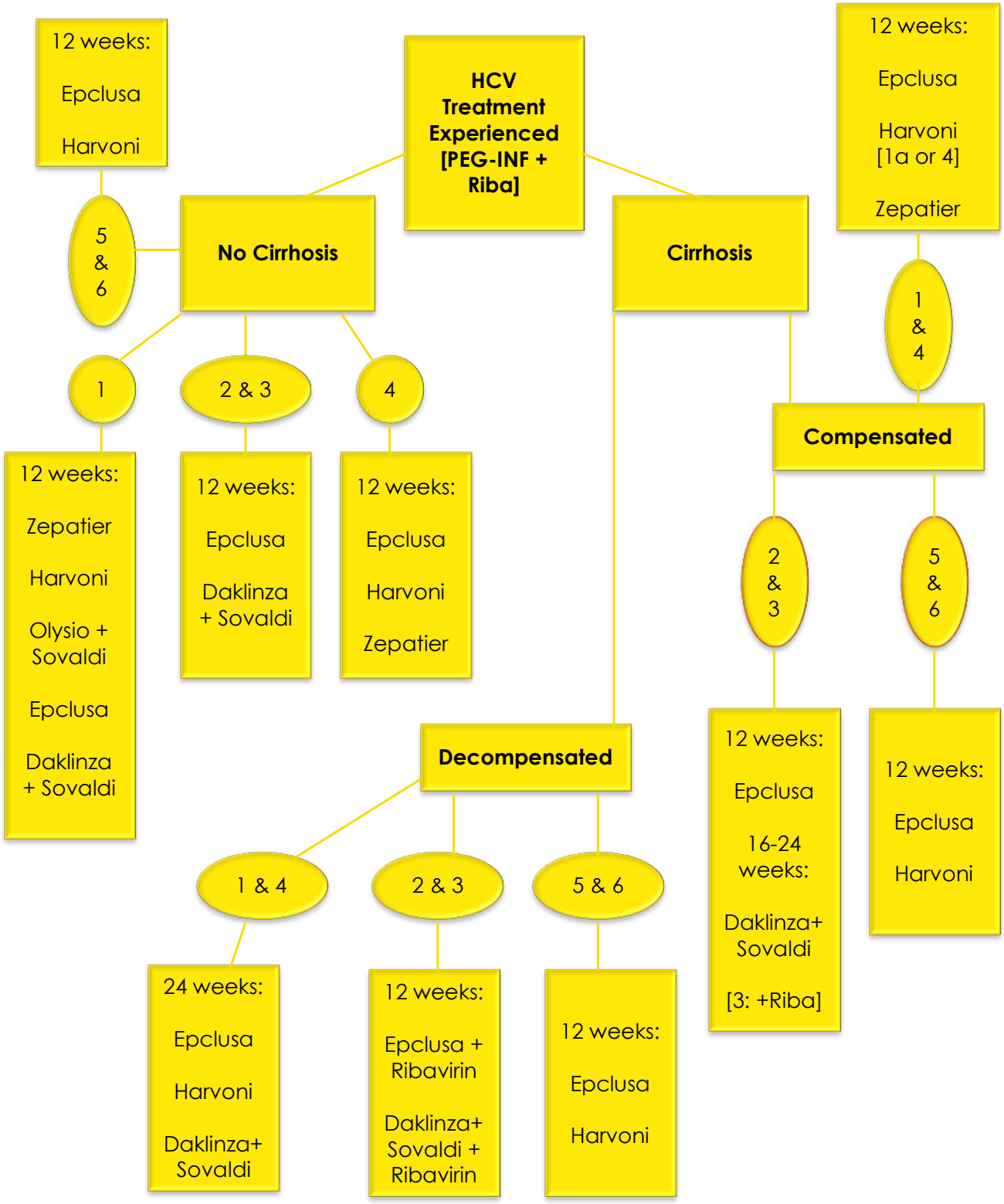
Home Phone Number: _____ Cell Phone Number: _____

Proof of address is required from person providing assistance and applicant, if living in same home

PLEASE PLACE NOTARY SEAL HERE

_____ _____
(NOTARY SIGNATURE) (DATE)


HCV Treatment Naive
No Cirrhosis
Cirrhosis
5 & 6
12 weeks: Epclusa Harvoni
1
2
3
4
12 weeks: Zepatier Harvoni Olysio + Sovaldi Epclusa Daklinza + Sovaldi Viekera XR
12 weeks: Epclusa Daklinza + Sovaldi
12 weeks: Epclusa Harvoni Zepatier
12 weeks: Epclusa Harvoni Zepatier
1 & 4
Compensated
2 & 3
5 & 6
12 weeks: Epclusa 24 weeks: Daklinza+ Sovaldi
12 weeks: Epclusa Harvoni
Decompensated
1 & 4
2 & 3
5 & 6
24 weeks: Epclusa Harvoni Daklinza+ Sovaldi
12 weeks: Epclusa + Ribavirin Daklinza+ Sovaldi + Ribavirin
12 weeks: Epclusa Harvoni


HCV Treatment Experienced [PEG-INF + Riba]
No Cirrhosis
Cirrhosis
5 & 6
12 weeks: Epclusa Harvoni
1
2 & 3
4
12 weeks: Zepatier Harvoni Olysio + Sovaldi Epclusa Daklinza + Sovaldi
12 weeks: Epclusa Daklinza + Sovaldi
12 weeks: Epclusa Harvoni Zepatier
12 weeks: Epclusa Harvoni [1a or 4] Zepatier
1 & 4
Compensated
2 & 3
5 & 6
12 weeks: Epclusa 16-24 weeks: Daklinza+ Sovaldi [3: +Riba]
12 weeks: Epclusa Harvoni
Decompensated
1 & 4
2 & 3
5 & 6
24 weeks: Epclusa Harvoni Daklinza+ Sovaldi
12 weeks: Epclusa + Ribavirin Daklinza+ Sovaldi + Ribavirin
12 weeks: Epclusa Harvoni