



The Specialty Pharmacy Approach to Tackling Hepatitis C

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Introduction

Hepatitis C is a liver disease that results from infection with the Hepatitis C virus (HCV), which is spread primarily through contact with the blood of an infected person.¹ The virus attacks hepatocytes and leads to inflammation. The hepatitis C virus was discovered in 1989 as the principal cause of post-transfusion non-A/non-B hepatitis. However, screening of blood products for HCV has virtually eliminated this mode of transmission. Currently, the most important risk factor for HCV infection is IV drug abuse, but in up to 40% of cases, the exact mode of HCV transmission remains undefined.² High risk populations and behaviors that may lead to hepatitis C infection as identified by the CDC are included in Table 1. Although vaccines are available for hepatitis A and hepatitis B, a vaccine for hepatitis C is not available.

Table 1. Risk factors for hepatitis C infection

- Current or former injection drug user, even if only one time or many years ago.
- Treated for a blood clotting problem before 1987.
- Blood transfusion or organ transplant before July 1992.
- Long-term hemodialysis treatment.
- Abnormal liver tests or liver disease.
- Exposed to blood through a needle stick or other sharp object injury.
- Co-infection with HIV.

Adapted from CDC at <http://www.cdc.gov/hepatitis/HCV/HCVfaq.htm#section1>

The incidence (new cases) of acute HCV infection in the U.S. has decreased dramatically over the past 25 years, falling from 7 to 0.7 cases per 100,000 people, according to a CDC study published in the *Archives of Internal Medicine, February 2011*.³ It is estimated that each year about 17,000 Americans become infected with hepatitis C⁴ and current prevalence is estimated to be 3.2 million infected adults. As chronic hepatitis C is a progressive disease, over time the number of patients who require liver transplant secondary to hepatitis C has grown, highlighting the continuing unmet antiviral needs for these patients.

Hepatitis C infection usually produces no signs or symptoms during its earliest stages and is most often diagnosed in the setting of post-exposure surveillance, or seroconversion in high-risk individuals (e.g. health-care professionals or injecting drug users) previously known to be seronegative.⁵ There is some data to suggest that people who develop symptoms after being exposed to the virus are more likely to experience spontaneous viral clearance. In contrast, those who remain asymptomatic are more likely to require antiviral therapy or to progress to a chronic infection.² This is problematic as most people don't know they have been harboring a hepatitis C virus until liver damage is identified, decades later, during routine medical tests.⁶ It is estimated that up to 85% of those who become infected with the hepatitis C virus develop chronic HCV infection.²

Chronic hepatitis C infection can cause significant complications. Chronic infection with HCV is one of the most

important causes of chronic liver disease and is the most common indication for orthotopic liver transplantation (OLT) in the United States. Hepatitis C is also responsible for an estimated 12,000 deaths annually in the U.S., due to cirrhosis or liver cancer.⁴

This newsletter discusses treatments for chronic hepatitis C, highlighting the challenges of using antiviral therapies, and outlining why choosing a pharmacy with proactive programs tailored to support the specific needs of this patient population is vital to obtaining optimal outcomes from these costly hepatitis therapies.



Goal of Therapy

The goal of HCV treatment is to achieve a sustained virologic response (SVR) defined as the absence of HCV RNA in serum at least 6 months (24 weeks) after therapy is completed. An SVR is associated with a 99% chance of remaining HCV RNA negative during long-term follow-up. Achievement of an SVR is associated with long-term clearance of HCV infection, which is regarded as a virologic “cure,” as well as with improved morbidity and mortality.⁷ Response to antiviral therapy may be classified as response, relapse or breakthrough, and non response. In patients with non response, HCV-RNA levels never become undetectable during treatment.⁸ In patients with breakthrough, HCV RNA levels initially become undetectable but reappear during therapy.



Chronic Hepatitis C - Good News

There are 6 main genotypes of the hepatitis C virus that cause human infection. Genotype is an important factor in determining the likelihood of response, selection of medications, and the duration of therapy. The three main genotypes within the United States are Type 1, 2 and 3. Type 2 and type 3 collectively occur in about 16% of infected individuals and both respond favorably to dual ribavirin-pegylated interferon (PegIFN) therapy, demonstrating an SVR of 70-80%. Genotype 1, however, occurs in about 80% of individuals, but is much harder to treat, demonstrating an SVR of 40-50% with dual antiviral therapy. The good news is that with the recently approved hepatitis-specific protease inhibitors, triple antiviral therapy produces an SVR of up to 70%.⁹⁻¹⁵

Treatment

Patients who test positive for HCV should be referred to a specialist to assess treatment options. Drug therapy is complicated, and involves a commitment from the patient to continue with therapy through unpleasant side effects and long treatment duration, as well as willingness to return to clinic frequently for lab tests and viral load monitoring. The complex decision to initiate antiviral therapy needs to be based on factors such as the patient’s interest, identified barriers to adherence, clinical and laboratory findings, probability of disease progression without therapy, odds of treatment success, likelihood of adverse effects, and absolute and relative contraindications to therapy.¹⁶

The standard of care for patients with chronic hepatitis C virus infection has been PegIFN and ribavirin used concomitantly. These drugs are generally administered for either 48 weeks (HCV genotypes 1, 4, 5, and 6) or for 24 weeks (HCV genotypes 2 and 3). Although PegIFN and ribavirin remain vital components of therapy, the emergence of hepatitis C protease inhibitors has led to a substantial improvement in SVR rates and introduced the option of abbreviated therapy in many patients with genotype 1 chronic HCV infection.⁷ In the spring of 2011, the U.S. Food and Drug Administration (FDA) approved two agents in this new class of drugs for hepatitis C: boceprevir (Victrelis[®]) and telaprevir (Incivek[®]).

Each of the agents used in hepatitis C protocols has the potential to cause significant adverse events and requires intense patient monitoring. The pegylated interferons (Pegasys[®], PegIntron[®]) are known for causing flu-like symptoms, fatigue, injection site reactions and depression. Ribavirin can cause anemia and body rash. Key adverse effects associated with the new protease inhibitors include anemia (boceprevir), and mild to severe body rash (telaprevir).^{17,18} Because the treatment course for HCV is long, (up to 48 weeks), guiding patients through side effect management and encouraging them to continue taking their therapy, is an important role for the specialty pharmacy.

Effect of Adherence and Dose Maintenance on SVR

The importance of adherence to antiviral therapy cannot be overstated. Studies of dual antiviral therapy have shown that when patients take 80% of the medications for 80% of the duration, 63% of patients obtain an SVR. When adherence drops below 80%, only 52% of patients obtain an SVR. Adherence to antiviral therapy is even more important with the addition of the protease inhibitors for both achieving SVR and reducing the risk of developing viral resistance. Yet, with the addition of the protease inhibitors, the difficulty of remaining adherent with therapy has become even more challenging due to complicated dosing regimens, significant adverse events, and other factors as outlined in Table 2.

Table 2. Factors of increased drug therapy complexity with HCV protease inhibitors

1. Triple therapy that includes both injectable and oral dose formulations (pegylated interferon, ribavirin, protease inhibitor)
2. Three times daily dosing, multiple pills per dose, food requirements
3. Varying duration of therapy based on patient response, antiviral used, response to previous treatment, presence of cirrhosis
4. Potential for significant adverse events that must be proactively managed
5. Extensive drug-drug interactions
6. Patient population that may have concomitant comorbidities including transplant, HIV, mood disorders, and drug addiction support medications
7. Sophisticated payer prior authorization criteria
8. High cost for drug therapy
9. Importance of compliance with therapy because of the risk of developing resistance
10. Multiple lab test follow-up appointments, during therapy and at end of therapy

Fairview Specialty Pharmacy Approach

We take great pride in the personal service and quality of care that each patient who interacts with Fairview Specialty Pharmacy receives. The hepatitis C program highlights Fairview's high touch approach to helping patients safely and effectively use complex and costly medications. With the introduction of protease inhibitors for hepatitis C, we have observed A) a great increase in the cost to treat, B) an increase in number of patients seeking treatment and C) an increase in the complexity of treatment. Because of this increased complexity, all patients who are receiving hepatitis C products are enrolled in our Hepatitis C Therapy Management Program. Fairview pharmacists and nurses utilize our proprietary patient management and documentation system to support patients in safely and successfully completing a course of therapy.

At Fairview Specialty Pharmacy, we ensure that patients are set up for success with therapy. Every new patient receives extensive education regarding the hepatitis C agents. Patients are instructed on what to expect, and coached on the benefits of completing therapy, even when this becomes difficult. Each patient's comprehension is assessed and documented, and additional follow-up is planned when necessary. After a patient leaves the doctor's office, and is at home with one drug to inject and two oral therapies that require multiple tablets per dose, reviewing the directions on how to use each drug helps

clarify and reinforce what was discussed in clinic. We continue to provide ongoing management that keeps patients safely on track and compliant with this complicated therapy. The pharmacy plays an essential role after therapy has started to assess for the emergence of side effects. Targeted questions are asked to identify side effects as early as possible in an effort to keep patients on therapy. Patients can be coached through many of the minor or self limiting adverse effects, but for more serious reactions, we contact the provider, or refer the patient back to the provider for follow-up.

When a new order is received, we proactively screen for drug-drug interactions. The prescriber is contacted when a risky drug interaction is identified and we work with the prescriber to find solutions. We tap into our experience in managing these drug interactions, especially those involving protease inhibitors, to help enable more patients to benefit from these therapies. For example, our clinical pharmacists have provided recommendations to facilitate triple therapy for patients who were also on HIV medications and phenytoin, both of which have significant drug interactions with protease inhibitors.

We also ask patients if they are keeping laboratory and physician appointments. We review viral loads, and other laboratory values, at key time points (weeks 2, 4, 12, 24, 48, and at 6 months after therapy completion) to ensure patients are responding to antiviral therapy and doses are modified appropriately based on laboratory values.

We monitor and measure adherence based on patients' self report, pill counts, medication possession ratio (MPR), persistency, and attrition rate. We also record time points of therapy discontinuation, reason for discontinuation, and assess the amount

of unused medication. The results are reported to our payers and used to help collaborate with them to design effective waste minimization strategies.

Since the availability of the new protease inhibitors, Fairview Specialty Pharmacy staff has made important interventions to ensure efficacy, patient safety, and drug waste reduction. Our patients have reported tremendous appreciation for interventions made on their behalf. Some examples are listed below.

- Preventing an ordered, but unneeded refill of telaprevir beyond the standard duration of 12 weeks. By preventing this 28-day refill, \$19,000 per month in wasted medication was avoided.
- Keeping patients on track by providing accurate information about the right dose and right duration of each medication. In one case, our nurse corrected a patient who thought that he should discontinue all three medications at 12 weeks (instead of just the telaprevir) because his viral load was undetectable at week 4.
- Alerting prescribers to significant drug interactions with protease inhibitors, which were then addressed and resulted in modified therapy. This becomes even more vital as prescribers begin to treat more complicated patients (e.g., liver transplant and HIV-HCV coinfecting patients).
- Referring patients to prescribers when significant adverse events (such as depression or rashes) are reported.
- Contacting prescribers to obtain refill orders for the protease inhibitor to ensure that the patient completes the appropriate duration of therapy. Understanding how critical patient adherence is to virologic success, in many cases, we have expedited orders to avoid missed doses.
- Coaching patients to safely remain on therapy when they are experiencing mild to moderate adverse events in a condition where patient self-discontinuation is costly to the payer and society.

Conclusion

While the new therapies for hepatitis C offer patients a greater chance of achieving virologic success, hepatitis C remains very difficult to treat. Most patients with genotype 1 hepatitis C will require a three drug regimen, which includes one of the newly approved protease inhibitors. These protease inhibitors add both complexity and cost to the hepatitis C drug regimen. Thus, it is important to help patients remain on therapy. Fairview Specialty Pharmacy partners with patients, providers, and payers to ensure that the complicated and costly drug regimen for hepatitis C is successful, and used efficiently and effectively. In providing knowledgeable outreach to patients, our pharmacists and nurses help patients safely stay on track with hepatitis C drug regimens to achieve optimal clinical outcomes. ■

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Fairview Specialty Pharmacy provides comprehensive specialty pharmacy services. As part of Fairview Health Services, a nonprofit healthcare system which includes the University of Minnesota Medical Center, we have expertise across the full spectrum of specialty diseases and provide a personalized approach that builds trust with our patients. We leverage our relationships with clinical experts and key opinion leaders at the University of Minnesota Medical Center and other specialist providers to provide comprehensive and cohesive care for patients who require specialty medications.



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