DAWN OF A NEW ERA

New guidelines, new treatments: Project Inform’s Andrew Reynolds takes a look at the standard of care for HCV in 2014

Welcome to the 2014 POSITIVELY AWARE HCV (hepatitis C virus) Drug Guide. Not long ago this guide would have consisted of only two drugs: interferon and ribavirin. In 2011, two new HCV protease inhibitors came on the scene: Incivek and Victrelis. These first generation HCV protease inhibitors marked a significant step forward in the HCV treatment landscape, but they required up to 48 weeks of therapy with several debilitating side effects.

Many patients and providers chose to wait for newer, less toxic, and potentially interferon-free regimens. At the end of 2013 two more drugs, Sovaldi and Olysio, were approved by the FDA, marking the beginning of what is called the “Direct Acting Antiviral” (DAA) era. There are several others that have been submitted to the FDA and are anticipated to be approved and available by the end of 2014, with even more expected to be approved in 2015. With these new medications, we now have a clear goal in HCV treatment: Cure!

NEW GUIDELINES

With new advances in HCV, we also have new recommendations to guide decisions for its testing, management, and treatment. The American Association for the Study of Liver Diseases (AASLD) and Infectious Diseases Society of America (IDSA) released the “Recommendations for Testing, Managing, and Treating Hepatitis C” to keep medical providers up to date with the rapidly changing treatment landscape. It is a very comprehensive document that provides guidance for doctors, physician’s assistants, and nurse practitioners (hereafter referred to as medical providers) who may not be as experienced with HCV as are liver specialists like hepatologists or gastroenterologists. Many HIV providers and infectious disease specialists can already manage HCV treatments, and as these regimens get simpler and easier to manage and the need for specialists decreases, primary care providers will become very important players in the treatment of HCV. And finally, although these guidelines are written for medical providers, it is a fairly accessible document for patients to use to inform themselves and be better advocates for their own personal health: The more informed you are, the better your care will be. Read the AASLD’s complete guidelines at hcvguidelines.org.

HCV SCREENING: WHO SHOULD BE TESTED?

To be perfectly candid, we have not done a very

Who should get tested for HCV?
What to consider when deciding if you should get tested

Anyone born between 1945 and 1965 should be tested for HCV at least once in their lifetime.

Anyone with risk factors for HCV should be tested at least once, or on an on-going basis at intervals to be determined.

The following risk behaviors or exposures call for HCV testing:

- Injection drug use, even if it was just once
- Intranasal drug use (from straws)
- Any incarceration
- Long-term hemodialysis
- Getting a tattoo in an unregulated setting
- Children born to an HCV-infected mother


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good job of testing people for HCV, with estimates of 50–75% of people living with HCV who are unaware they have the virus. The reasons for this are many, but include lack of funding, stigma (especially for people who inject or have injected drugs), and lack of access to health care. In addition, poor HCV treatment options with limited effectiveness were a common rationale for not testing: Why test someone to tell them they have a disease for which there is poor treatment? With new advances in HCV therapy and improved access to health care under the Affordable Care Act (ACA), many of the old barriers are disappearing. The U.S. Centers for Disease Control and Prevention (CDC) and United States Preventative Services Task Force (USPSTF) have recommended HCV screening in two distinct groups: (1) People born between 1945 and 1965, the so-called “baby-boomer” guidelines, and (2) people with risk factors for HCV (see box below and at right). The USPSTF recommendations are particularly important, as they have positive consequences for public and private health insurance coverage of screening.

**SEXUAL TRANSMISSION OF HCV: CONSIDERATIONS FOR HIV-POSITIVE INDIVIDUALS**

Overall, the risk of sexual transmission of HCV is quite low: Studies have shown very low rates of HCV in non-injecting, HIV-negative individuals, regardless of gender or sexual orientation. Although sexual transmission of HCV is not a universally accepted risk factor, there is a consensus that HIV-positive people, especially gay men, are at increased risk of infection through sex. HIV-positive gay men have higher rates of sexually transmitted HCV, and as such, they should be screened routinely. It is standard practice to screen for HCV upon entry to HIV primary care, but while there are no clear guidelines for routine screening, an annual HCV test for sexually active gay men should be considered.

**WHAT TO TAKE, AND WHEN?**

In addition to pegylated interferon (PEG) and ribavirin (RBV), there are four FDA approved DAAs available: Incivek, Victrelis, Olysio, and Sovaldi. While the ultimate goal of HCV treatment is to use non-interferon-based regimens for 12 weeks or less, we are not fully there yet. We do have some non-interferon-based treatments, but it won’t be until the end of 2014 that we will start to see a wide array of FDA-approved ones.

Incivek and Victrelis are no longer recommended for the treatment of HCV. It’s not that these drugs don’t work, but rather they just don’t match up in effectiveness, side effect profile, or length of treatment when compared to the newer DAAs. With these new drugs, HCV can be treated with a variety of different regimens depending upon variables like treatment experience, presence of other co-morbidities (such as HIV or renal disease), and genotype (GT). Genotype is especially important: There are several different types of HCV, numbered from 1–6, and there

- Blood exposures on the job, including needle sticks or blood splashes to mucous membranes
- An organ transplant or transfusion as follows:
  - Received a blood transfusion before July 1992
  - Received an organ transplant before July 1992
  - Any notification of having received blood from a donor who later tested positive for HCV
- Received clotting factors before 1987

Other medical conditions:
- HIV infection
- Unexplained chronic liver disease, hepatitis, and/or elevated liver enzymes

SOURCE: RECOMMENDATIONS FOR TESTING, MANAGING, AND TREATING HEPATITIS C, P. 8

- fisting
- sharing sex toys
- co-occurring STDs
- multiple sex partners
- group sex
- use of non-injection drugs (especially during sex)
are even subtypes that are designated by letters (1a, 1b, etc.). Different GTs respond to medications differently, and some require more drugs and/or a longer length of time for treatment. For people who are treatment naïve, Sovaldi (sofosbuvir) is the recommended DAA for GT 1 through 6, along with ribavirin. Pegylated interferon is still recommended for GT 1, 4, 5, and 6, but GT 2 and 3 are FDA approved to be treated without it. As new HCV drugs get approved by the FDA, the AASLD/IDSA guidelines will be updated to include new recommended and alternative treatment regimens for people to consider.

For those who cannot tolerate interferon, there are alternative interferon-free regimens. One worth noting is the off-label (non-FDA-approved, but scientifically validated) use of Sovaldi and Olysio (simeprevir) with or without ribavirin for the treatment of GT 1: This is the first DAA combination that has been used in this manner to treat HCV and serves as a harbinger of what’s to come.

The new AASLD/IDSA guidelines do not yet offer guidance on when to start HCV therapy (that will come in a later version), so deciding on treatment is a decision left to you and your medical provider (and in some cases, your insurance carrier, see below). Some people are choosing to treat now, even with interferon-based regimens, while others are still waiting for the easier to take, all-oral regimens at the end of this year and beyond. That said, people with fibrosis scores—a measure of the amount of scarring of the liver using a range of 0 (no scarring) to 4 (cirrhosis)—of F2 or F3 might not want to wait to start treatment. Similarly, HIV/HCV co-infected persons should be considered for treatment due to the risk of more rapidly advancing liver disease. There may be other factors in deciding to start treatment now, and HCV-infected people should start having that discussion with their medical provider and making a treatment plan.

A chart listing the recommended and alternative HCV treatments for treatment naïve, treatment experienced and HIV/HCV co-infected people can be found on page 36.

**HIV/HCV TREATMENT OPTIONS**

**HIV/HCV co-infection** is a very serious issue. In addition to the increased risk of sexual transmission discussed earlier, HIV often leads to a faster progression of HCV-related liver disease. Good HIV care and a healthy immune system may slow down HCV disease progression, but it is not a cure. Until recently, the only FDA-approved HCV treatments for HIV-positive people were pegylated interferon and ribavirin. The first generation PIs could be used off-label, but the drug-to-drug interactions and side effects of these medications made them very challenging for co-infected people to take. Sovaldi was approved for use in co-infected people, and has shown very promising cure results in this population. The AASLD/IDSA guidelines include recommendations for treatment of co-infection with both interferon-based and non-interferon-based treatments. The future of treatment for this population is also bright: Several of the new DAAs are either expected to be approved for treatment in HIV/HCV co-infection, or are under study. Many of these clinical trials have shown very promising results.

**A NOTE ON COST AND ACCESS TO HCV MEDICATIONS**

For all the excitement over the effectiveness of the most recent HCV drugs, as well as those soon to be approved, there is significant concern about the cost of these treatments. Sovaldi is listed at $1,000 per pill, or $84,000 for a 12-week course of treatment and $168,000 for a 24-week one. Olysio is less expensive, at $790 per pill, but that is still over $66,000 for 12 weeks, plus the cost of the additional weeks of pegylated interferon and ribavirin. The cost of these medications are putting significant pressure on both public and private insurers, and many of them are scrambling to see how they can afford to cover the cost of HCV treatment without bankrupting the system.

These are challenging issues that health economists, policy makers, and medical ethicists need to wrestle with, but for you the patient, the only thing that matters is achieving a cure. Do not let the high cost of these drugs prevent you from seeking treatment. There are programs that can help you cover some or all of the costs of the medications. We have a list of patient assistance programs, co-pay assistance programs, and other resources in this issue, found on page 37.

**A BRAVE NEW WORLD**

It is a very exciting time in the world of hepatitis C. Along with new HCV treatments, we have HCV screening guidelines to identify new infections, the ACA to improve access to medical care for those infected, and the AASLD/IDSA testing, management, and treatment guidelines to guide care and treatment. This HCV Drug Guide is designed to further educate and empower you in your care and treatment, and we hope you find it useful.
HOW TO USE THIS GUIDE

Here’s where you’ll find definitions and descriptions of things you’ll need to know about in order to make an informed decision about your HCV care and treatment.

The HCV Drug Guide will include medications that are FDA approved, expected to be approved this year, or are likely to be approved through June of 2015. The information provided on FDA-approved drugs comes from the package labels, as well as other data sources such as conference presentations and medical journal articles. For the non-FDA-approved drugs, the information comes from conference presentations and medical journals.

All current HCV drugs must be taken in combination with other drugs. Pegylated interferon is an injectable medication, but all other HCV medications are taken as pills. Although there are currently no fixed dose combination (FDC) pills for HCV like there are for HIV (Atripla, Combidir, etc.), there are several on the horizon that are likely to be approved by Fall 2014.

Each drug page will include:

**DRUG NAMES**
Drug names can be very confusing. We include the brand name, the generic name and often an abbreviation. For example, Sovaldi is the brand name of sofosbuvir. Sovaldi can be abbreviated as SOV, and sofosbuvir is abbreviated as SOF. Drugs that have been FDA-approved will have a brand name, while those that have not yet reached that stage will have a generic name. In some cases, it might not even have a name, but rather a series of letters and numbers (for example, ABT-450). For those drugs which have been FDA-approved, the brand name will appear first, at the top of the page, followed by the common name(s); for all other drugs the common or generic name will appear first.

**FDA STATUS**
We will indicate if a drug is approved, and any drug that has been submitted for FDA approval will have an estimate of its approval date. Drugs or drug combinations are listed in order of approval, or expected approval date.

**DRUG CLASS**
Just as HIV medications are divided into several different drug classes, the “DAA” (direct acting antiviral) era of HCV treatment has seen the development of several different classes as well. Currently, there are four classes of HCV drugs:

- Pegylated interferon alfa
- Nucleoside analogs
- NS3/4A protease inhibitors
- Nucleoside and nucleotide NS5B polymerase inhibitors

In the years to come, we will see more drugs from some of these classes, as well as two new classes:

- NSSA inhibitors
- Non-nucleoside NS5B polymerase inhibitors

Toward the end of 2014, we will begin to see FDCs of two drugs from different classes, with several more in the development pipeline.

**GENOTYPE**
Genotype (GT) refers to the strains or variations of HCV. Worldwide, there are probably 11 distinct
genotypes, but for this guide we will only refer to GT 1–6. In the United States, GT 1–4 are most prevalent, with GT 1 the most common overall. Within each genotype, there are several subtypes that are indicated by numbers and letters (GT 1a and GT 1b and so on). The different genotypes do not have a role in disease progression or severity, but they do respond differently to different HCV drugs so they impact treatment choices. Some genotypes can be treated for a shorter amount of time and without interferon. We will list the genotype(s) that the specific HCV medication works against. In the long run, the goal of treatment will be to create a “pan-genotypic” treatment regimen that works across all genotypes with equal effectiveness.

APPROVED FOR HIV/HCV CO-INFECTION
To date we have not had many options for treating HCV in HIV-positive people. Indeed, prior to Sovaldi, the only treatment that was FDA approved for HIV/HCV co-infected people was the dual therapy of pegylated interferon and ribavirin. It remains to be seen which of the forthcoming HCV medications will be approved for co-infection.

MANUFACTURER
This section includes the name of the company that makes the drug.

AVERAGE WHOLESALE PRICE (AWP)
The AWP is the measure used by insurance companies—both private and public—to determine the average cost of prescription drugs. HCV drugs are very expensive, and there is much concern over the burden these high costs are going to place on programs like Medicaid and Medicare, as well as the Veterans Administration and private insurance carriers. Patients should never have to pay for medications at this price, but it’s still important to know these costs when shopping for health insurance coverage. Each of the pharmaceutical companies has a Patient Assistance Program (PAP) to help uninsured and underinsured people cover all or part of the costs. There are also pharmaceutical co-pay programs and non-profit organizations that can help with some additional support for co-pays. We provide a list of HCV drug patient assistance and co-pay programs on page 37.

DOSAGE
HCV drugs are taken in a variety of ways, at different times, and with differing food restrictions. Sometimes, the same drug is taken differently depending upon a variety of factors like genotype or liver health. This section will describe the dosage requirements for the drug, as well as provide details about restrictions and other relevant information.

POTENTIAL SIDE EFFECTS AND ADVERSE EVENTS
This section offers information about side effects (including adverse events) associated with the HCV drugs. It’s not an exhaustive list, but rather a selection of the most commonly reported side effects. The information comes from the package insert and study data for the FDA-approved drugs, and clinical trial and study data for the ones that have yet to receive FDA approval. Since HCV medications are never taken alone, we’ll cover potential side effects that are associated with the entire regimen, as opposed to a single drug. It would be hard to separate one cause of a side effect from another, and in the end, it doesn’t really matter what the cause is but only that you are experiencing it. Everyone experiences side effects differently: Just because it’s listed doesn’t mean you will automatically have it. Talk to your medical provider about side effects before starting treatment, communicate with him or her about any you may have during treatment, and get blood tests as directed to look for side effects such as anemia (low red blood cell count) or neutropenia (low white blood cell count).

POTENTIAL DRUG INTERACTIONS
This section provides information about the variety of known and potential drug interactions. Like the side effects section, it’s not an exhaustive list of interactions, but rather the most important ones for drugs that are commonly used by people living with HCV. You can find a complete list in the package insert, but you should also talk to your medical provider and/or pharmacist about any medications you are taking so you can minimize drug interactions. The information comes from the package insert and study data for the FDA-approved drugs, and clinical trial and study data for the ones that have yet to receive FDA approval.

MORE INFORMATION
This section contains information that does not fit in any of the above sections, but is still important for you to know.
## HCV medications by class

<table>
<thead>
<tr>
<th>CLASS</th>
<th>BRAND NAME</th>
<th>GENERIC/COMMON NAME</th>
<th>STATUS</th>
<th>GENOTYPE (FDA AND OFF-LABEL)</th>
<th>IFN-FREE?</th>
<th>APPROVED FOR HIV/HCV CO-INFECTION?</th>
<th>MANUFACTURER</th>
<th>FIND IT ON PAGE</th>
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</thead>
<tbody>
<tr>
<td>Pegylated interferon</td>
<td>PegIntron</td>
<td>Peginterferon alfa-2b PEG; IFN</td>
<td>Approved</td>
<td>1,2,3,4,5,6</td>
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<td>Yes</td>
<td>Merck</td>
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<td>Pegasys</td>
<td>Peginterferon alfa-2a PEG; IFN</td>
<td>Approved</td>
<td>1,2,3,4,5,6</td>
<td>N/A</td>
<td>Yes</td>
<td>Genentech</td>
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<td>Nucleoside analog</td>
<td>Ribosphere</td>
<td>ribavirin RBV</td>
<td>Approved</td>
<td>1,2,3,4,5,6</td>
<td>Yes, with several other HCV drugs only</td>
<td>Yes</td>
<td>Kadmon</td>
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<tr>
<td>Nucleoside analog</td>
<td>Copegus</td>
<td>ribavirin RBV</td>
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<td>1,2,3,4,5,6</td>
<td>Yes, with several other HCV drugs only</td>
<td>Yes</td>
<td>Genentech</td>
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<td>Rebetol</td>
<td>ribavirin RBV</td>
<td>Approved</td>
<td>1,2,3,4,5,6</td>
<td>Yes, with several other HCV drugs only</td>
<td>Yes</td>
<td>Merck</td>
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<td>NS3/4A protease inhibitor</td>
<td>Incivek</td>
<td>telaprevir TVR</td>
<td>Approved</td>
<td>1</td>
<td>No</td>
<td>No</td>
<td>Vertex</td>
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<td>NS3/4A protease inhibitor</td>
<td>Vicrelis</td>
<td>boceprevir BOC</td>
<td>Approved</td>
<td>1</td>
<td>No</td>
<td>No</td>
<td>Merck</td>
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<tr>
<td>NS3/4A protease inhibitor</td>
<td>Olysio</td>
<td>simeprevir, SMV</td>
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<td>1</td>
<td>No</td>
<td>No</td>
<td>Janssen</td>
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<td>NS3/4A protease inhibitor</td>
<td>N/A</td>
<td>asunaprevir ASV</td>
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<td>Bristol-Myers Squibb</td>
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<td>NS3/4A protease inhibitor</td>
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<td>ABT-450/r</td>
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<td>Yes</td>
<td>TBD</td>
<td>AbbVie</td>
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<tr>
<td>Nucleoside and Nucleotide NS5B polymerase inhibitor</td>
<td>Sovaldi</td>
<td>sofosbuvir SOF, SOV</td>
<td>Approved</td>
<td>1,2,3,4,5,6</td>
<td>Yes, for GT 2 and 3; in limited cases for GT 1</td>
<td>Yes</td>
<td>Gilead Sciences</td>
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<tr>
<td>NS5A inhibitor</td>
<td>N/A</td>
<td>ledipasvir LDV</td>
<td>Submitted for approval</td>
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<td>TBD</td>
<td>Gilead Sciences</td>
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<tr>
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<td>daclatasvir DCV</td>
<td>Submitted for approval</td>
<td>1,2,3,4</td>
<td>Yes</td>
<td>TBD</td>
<td>Bristol-Myers Squibb</td>
<td>49</td>
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<tr>
<td>NS5A inhibitor</td>
<td>N/A</td>
<td>ombitasvir (ABT-267)</td>
<td>Submitted for approval</td>
<td>1</td>
<td>Yes</td>
<td>TBD</td>
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<td>Non-nucleoside NS5B polymerase inhibitors</td>
<td>N/A</td>
<td>dasabuvir (ABT-333)</td>
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<td>Yes</td>
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<td>Yes</td>
<td>TBD</td>
<td>Bristol-Myers Squibb</td>
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</table>
**AASLD/IDSA recommendations**

*(SEE PAGE 31 FOR DRUG ABBREVIATIONS)*

### RECOMMENDATIONS FOR TREATMENT-NAÏVE PATIENTS OR THOSE WHO HAD A VIRAL RELAPSE AFTER PRIOR PEGYLATED INTERFERON/RIBAVIRIN THERAPY

<table>
<thead>
<tr>
<th>HEPATITIS C GENOTYPE</th>
<th>RECOMMENDED REGIMENS</th>
<th>ALTERNATIVE REGIMENS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>GT 1</strong></td>
<td>(1) IFN eligible: SOF + PEG + RBV for 12 weeks</td>
<td>(1) IFN eligible: SMV for 12 weeks + PEG + RBV for 24 weeks</td>
</tr>
<tr>
<td></td>
<td>(2) IFN ineligible: SOF + SMV + RBV for 12 weeks</td>
<td>(2) IFN ineligible: SOF + RBV for 24 weeks</td>
</tr>
<tr>
<td><strong>GT 2</strong></td>
<td>SOF + RBV for 12 weeks</td>
<td>None</td>
</tr>
<tr>
<td><strong>GT 3</strong></td>
<td>SOF + RBV for 24 weeks</td>
<td>SOF + PEG + RBV for 12 weeks</td>
</tr>
<tr>
<td><strong>GT 4</strong></td>
<td>(1) IFN eligible: SOF + PEG + RBV for 12 weeks</td>
<td>SMV for 12 weeks + PEG + RBV for 24-48 weeks</td>
</tr>
<tr>
<td></td>
<td>(2) SOF + RBV for 24 weeks</td>
<td></td>
</tr>
<tr>
<td><strong>GT 5</strong></td>
<td>SOF + PEG + RBV for 12 weeks</td>
<td>Peg + RBV for 48 weeks</td>
</tr>
<tr>
<td><strong>GT 6</strong></td>
<td>SOF + PEG + RBV for 12 weeks</td>
<td>Peg + RBV for 48 weeks</td>
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</table>

### RECOMMENDATIONS FOR PATIENTS IN WHOM PREVIOUS PEG/RBV TREATMENT HAS FAILED

<table>
<thead>
<tr>
<th>HEPATITIS C GENOTYPE</th>
<th>RECOMMENDED REGIMENS</th>
<th>ALTERNATIVE REGIMENS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>GT 1</strong></td>
<td>SOF + PEG + RBV for 12 weeks</td>
<td>SOF + PEG + RBV for 12 weeks</td>
</tr>
<tr>
<td></td>
<td>SMV for 12 weeks + PEG + RBV for additional 24 weeks</td>
<td></td>
</tr>
<tr>
<td><strong>GT 2</strong></td>
<td>SOF + RBV for 12 weeks</td>
<td>SOF + PEG + RBV for 12 weeks</td>
</tr>
<tr>
<td><strong>GT 3</strong></td>
<td>SOF + RBV for 24 weeks</td>
<td>SOF + PEG + RBV for 12 weeks</td>
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<td><strong>GT 4</strong></td>
<td>SOF + PEG + RBV for 12 weeks</td>
<td>SMV for 12 weeks + PEG + RBV for 24-48 weeks</td>
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<td></td>
<td>SOF + RBV for 24 weeks</td>
<td></td>
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<tr>
<td><strong>GT 5</strong></td>
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<td>SOF + RBV for 24 weeks</td>
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<td><strong>GT 6</strong></td>
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<td>SOF + RBV for 24 weeks</td>
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### RECOMMENDATIONS FOR HCV TREATMENT IN PATIENTS WHO ARE CO-INFECTED WITH HIV/HCV

<table>
<thead>
<tr>
<th>HEPATITIS C GENOTYPE</th>
<th>RECOMMENDED REGIMENS</th>
<th>ALTERNATIVE REGIMENS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>GT 1, treatment-naïve and those with viral relapse after prior PEG/RBV treatment</strong></td>
<td>(1) IFN eligible: SOF + PEG + RBV for 12 weeks</td>
<td>SMV + PEG + RBV for 12 weeks, followed by PEG + RBV for additional 24 weeks</td>
</tr>
<tr>
<td></td>
<td>(2) IFN ineligible: SOF + RBV for 24 weeks</td>
<td>IFN ineligible: None</td>
</tr>
<tr>
<td></td>
<td>SOF + SMV + RBV for 12 weeks</td>
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<tr>
<td><strong>GT 1, treatment-experienced</strong></td>
<td>SOF + SMV + RBV for 12 weeks</td>
<td>(1) IFN eligible: SOF + PEG + RBV for 12 weeks</td>
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<td>(2) IFN ineligible: SOF + RBV for 24 weeks</td>
<td>(2) IFN ineligible: SOF + RBV for 24 weeks</td>
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<td><strong>GT 2, regardless of treatment history</strong></td>
<td>SOF + RBV for 12 weeks</td>
<td>SOF + PEG + RBV for 12 weeks</td>
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<tr>
<td><strong>GT 3, regardless of treatment history</strong></td>
<td>SOF + RBV for 24 weeks</td>
<td>SOF + PEG + RBV for 12 weeks</td>
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<td><strong>GT 4, regardless of treatment history</strong></td>
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<td>(2) IFN ineligible: SOF + RBV for 24 weeks</td>
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<tr>
<td><strong>GT 5 or GT 6</strong></td>
<td>SOF + PEG + RBV for 12 weeks</td>
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</table>
Hepatitis C Co-Pay and Patient Assistance Programs (PAPs)

Like HIV, treatment for HCV is expensive, but the good news is that help is out there. Many of the pharmaceutical companies have a patient assistance program (PAP) to help uninsured and underinsured people cover all or part of the costs of their drug. There are also pharmaceutical co-pay programs and non-profit organizations that can help with some additional support for co-pays. Check with each program for details.

<table>
<thead>
<tr>
<th>DRUG</th>
<th>COMPANY</th>
<th>CONTACT INFO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Copegus</td>
<td>Genentech</td>
<td>(888) 941-3331; pegaysaccesssolutions.com</td>
</tr>
<tr>
<td>Incivek</td>
<td>Vertex Pharmaceuticals</td>
<td>(855) 837-8394; incivek.com</td>
</tr>
<tr>
<td>Olysio</td>
<td>Janssen Pharmaceuticals</td>
<td>(855) 565-9746; janssenprescriptionassistance.com/olysio-cost-assistance; olysio.com</td>
</tr>
<tr>
<td>Pegasys</td>
<td>Genentech</td>
<td>(888) 941-3331; pegaysaccesssolutions.com; pegasys.com</td>
</tr>
<tr>
<td>PegIntron</td>
<td>Merck</td>
<td>(866) 939-4372; merckhelps.com; pegintron.com</td>
</tr>
<tr>
<td>Sovaldi</td>
<td>Gilead</td>
<td>(855) 769-7284; mysupportpath.com; sovaldi.com</td>
</tr>
<tr>
<td>Victrelis</td>
<td>Merck</td>
<td>(866) 939-4372; merckhelps.com; victrelis.com</td>
</tr>
</tbody>
</table>

ADDITIONAL PROGRAMS

**Harbor Path**
harborpath.org
Provides a single site for all patient assistance programs for both HIV and HCV medications.

**Needy Meds**
needymeds.com
Provides a one-stop site for patient assistance programs and other discount opportunities for a variety of pharmaceuticals; also has a very useful database to find free and low-cost medical clinics.

**Patient Access Network Foundation**
(866) 316-7263
panfoundation.org
Has an HCV-specific program, and can offer up to $7,000 in financial assistance for eligible individuals.

**Patient Advocate Foundation**
www.copays.org/diseases/hepatitis-c
Has an HCV-specific program, and can offer up to $7,500 in co-pay assistance for eligible individuals.
**PegIntron; Pegasys**

**COMMON NAMES:** PEG; IFN; pegylated interferon; interferon

**FDA STATUS:** Approved

**CLASS:** Interferon (interferon alfa-2a, interferon alfa-2b)

**GENOTYPE:** 1, 2, 3, 4, 5, 6

**Approved for HIV/HCV co-infection.**

**DOSAGE:** Administer one injection once a week with or without food; must be taken in combination with ribavirin and other HCV drugs (see below for more details). Interferon should never be taken by itself. Take your missed dose as soon as possible on the same day or the next day and then continue on your regular dosing schedule; if multiple days are missed, check with your medical provider about what to do; never double dose or take doses too close together.

**MANUFACTURER:** PegIntron: **Merck**; Pegasys: **Genentech** (Roche)

**AWP:** $800 per week for four 180 mcg syringes

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**Potential side effects and adverse events**

Interferon has a large number of side effects associated with it: fatigue, headaches, nausea, chills, insomnia, anemia, pyrexia (fever), injection site reactions, loss of appetite, rash, myalgia (muscle pain), neutropenia, irritability, depression, alopecia (hair loss), dyspnea (shortness of breath), arthralgia (joint pain), pruritus (itching), flu-like feelings, dizziness, diarrhea, cough, weight loss, vomiting, unspecified pain, dry skin, anxiety, abdominal pain, leukopenia and thrombocytopenia. In the case of the psychiatric/emotional side effects: interferon has been associated with depression, anxiety and in rare cases, suicidal thoughts. If you have a history of any of these conditions, talk to your provider before starting HCV treatment (it does not mean you can’t take HCV treatment, you just want to watch for signs and be able to take preventative actions ahead of time). As an injectable, injection site reactions (redness, swelling, and/or itching) and inflammation are common. If you have autoimmune hepatitis, or are allergic to any of the ingredients in interferon, you should not take it.

**Potential drug interactions**

There are few drug interactions with interferon: Be sure to tell your medical provider or pharmacist about all the medications and herbs you take, whether prescribed, over the counter, or illicit, before starting this drug. Caution is advised when taken with warfarin, phenytoin, or methadone. Methadone levels may increase due to interferon, so methadone levels and signs and symptoms of a stronger narcotic effect should be monitored.

**More information**

Interferon is the oldest HCV drug we have, and quite frankly it’s the one most people can’t wait to get rid of. Most of the severe side effects that people experience while on HCV treatment are caused by interferon, and the fact that it is an injectable drug makes it even less desirable to people. The DAA era will likely make this drug obsolete, but there may still be a role for select patients. In the meantime, interferon is still used and recommended in many treatment regimens for GT 1 and 4.
**Generic available**

**FDA STATUS:** Approved

**CLASS:** Nucleoside analog

**GENOTYPE:** 1, 2, 3, 4, 5, 6

**Approved for HIV/HCV co-infection.**

**DOSAGE:** Ribavirin dosage depends upon the brand, and is given in either fixed doses or in doses related to weight (“weight-based”). The dose range is 800 mg to 1,400 mg per day taken in two divided doses. Must be taken with food. Ribavirin should never be taken by itself. Take your missed dose as soon as possible, unless it’s too close to your next dose. Never double dose.

**MANUFACTURER:**
- Genentech (Copegus)
- Merck (Rebetol)
- Kadmon (Ribasphere)

**AWP:** $325 per week, based on 1,200 mg/day

**Potential side effects and adverse events**

There are two very serious potential side effects associated with ribavirin: Anemia, and birth defects or fetal death. The anemia can be very severe and can happen very quickly, usually within the first 1–2 weeks of starting treatment. The anemia can cause severe fatigue, dizziness, headaches, and shortness of breath; routine blood testing to look for anemia, neutropenia, and other blood conditions is recommended. The anemia may also cause or worsen cardiac conditions. The other major side effect is birth defects or fetal death in pregnant women. Pregnant women or women who are trying to become pregnant cannot take ribavirin; women of childbearing age and their male sexual partners must use two forms of birth control throughout treatment and for six months post-treatment. It is unknown if ribavirin passes through breast milk or the impact it could have on breastfeeding babies. Other side effects that have been reported with ribavirin include rash and itching, and there is a small risk of pancreatitis. If you experience any symptoms related to pancreatitis (severe stomach pain that radiates to your back, nausea, vomiting, and/or diarrhea) you should call your advice nurse (when applicable) or go to an emergency department for evaluation.

**Potential drug interactions**

Ribavirin cannot be used with didanosine (Videx-EC, Videx, ddI) as this combination can lead to potentially fatal levels of ddI; similarly, azathioprine (an immunosuppressive) cannot be used; ribavirin is okay to take with other HIV antivirals, but check closely for anemia.

**More information**

It’s not entirely understood how ribavirin works against HCV, but along with interferon, it’s been a major part of HCV treatment for years, and will continue to play an important role in the future. The side effects can be challenging, even without interferon. Consequently, just as interferon-free treatment is the goal of the new standard of care, there is a move for ribavirin-free ones as well.

### Important labs for monitoring your hematological levels

Ribavirin (and some other HCV medications), can affect your body’s production of red blood cells, white blood cells and platelets. Follow your medical provider’s directions for regular screening to check for these conditions. Be sure to keep copies of your lab results and track them over time. NOTE: Whenever a lab test is out of range, there is usually an indication (such as a star or other way to highlight it).

<table>
<thead>
<tr>
<th>CONDITION</th>
<th>LAB TEST</th>
<th>NORMAL RANGE</th>
<th>SYMPTOMS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anemia</td>
<td>Hemoglobin</td>
<td>Male: 13.5-17.5; Female: 12.0-16.0</td>
<td>Fatigue, shortness of breath, chills, rapid heart rate, depression</td>
</tr>
<tr>
<td></td>
<td>Hematocrit</td>
<td>Male: 42-54; Female: 37-47</td>
<td></td>
</tr>
<tr>
<td>Neutropenia</td>
<td>Neutrophils</td>
<td>45–75% of white blood cells (WBC)</td>
<td>None</td>
</tr>
<tr>
<td>Leukopenia</td>
<td>Leukocytes</td>
<td>4.5-11.0 (x10^3/mm³)</td>
<td>Usually none, but regular or unusual infections may indicate this condition</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>Platelets</td>
<td>150–399 (x10^3/mm³)</td>
<td>Easy or excessive bleeding, spontaneous nosebleeds or bleeding gums, unusually heavy menstrual flows, and/or blood in urine or stools</td>
</tr>
</tbody>
</table>
**VICTRELIS**

**COMMON NAMES:** boceprevir, BOC

**FDA STATUS:** Approved

**CLASS:** NS3/4A protease inhibitor

**GENOTYPE:** 1

**Not approved for HIV/HCV co-infection.** (Off-label treatment is possible, but there are many drug interactions to monitor.)

**DOSAGE:**
Take four 200 mg capsules three times daily—every 7–9 hours—with food; must be taken in combination with pegylated interferon and ribavirin. VICTRELIS should never be taken by itself. Take your missed dose as soon as possible, unless it is closer to the time of your next dose. Never double your dose. A four-week lead-in period of pegylated interferon and ribavirin is necessary, followed by the introduction of VICTRELIS (continuing with PEG/RBV) for a length of time that is determined by treatment response. The chart at the bottom of this page summarizes the various treatment durations.

**MANUFACTURER:** Merck

**AWP:** $1,750 per week

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**Potential side effects and adverse events**

The most commonly reported side effects are fatigue, anemia, nausea, taste changes, chills, insomnia, diarrhea, decreased appetite, and neutropenia (low white blood cell count). VICTRELIS is taken with pegylated interferon and ribavirin, and the most common side effects reported by people taking this regimen related to those two medications are: fatigue, headaches, nausea, fever, chills, and joint pain. For more information see their respective drug pages. Pegylated interferon has been associated with depression, anxiety, and in rare cases, suicidal thoughts. If you have a history of any of these conditions, talk to your provider before starting HCV treatment (it does not mean you can’t take HCV treatment, you just want to watch for signs and take preventative actions). When VICTRELIS is used with ribavirin, pregnant women or women who are trying to become pregnant cannot take it; women of child-bearing age and their male sexual partners must use two forms of birth control throughout treatment and for six months after treatment. Changes in hematological (blood) values are common, and routine blood testing to look for anemia (low red blood cell count), neutropenia, and other blood conditions is recommended.

**Potential drug interactions**

Before starting treatment, talk with your medical provider or pharmacist about any medications, supplements, or herbs you are taking, including prescribed, over-the-counter, or illicit substances. VICTRELIS interacts with many other drugs; for a complete listing refer to the package insert. Do not take with St. John’s wort. Do not take with Sustiva (efavirenz) and avoid Kaletra (lopinavir/ritonivir), Prezista (darunavir), and Reyataz (atazanavir). Can be taken with nucleoside reverse transcriptase inhibitors (including Truvada), Isentress (raltegravir), Tivicay (dolutegravir), Edurant (rilpivirine); dose adjustments needed if taken with Selzentry (maraviroc). VICTRELIS increases the levels of erectile dysfunction drugs (Viagra, Cialis, and Levitra), so these doses should not exceed 10 mg Cialis or 2.5 mg of Levitra per 72 hours, or 25 mg of Viagra per 48 hours. Do not take with rifampin, lovastatin, simvastatin, nor with sedatives/hypnotics such as midazolam or triazolam; can be taken with methadone and buprenorphine, but monitoring of methadone levels and patient discomfort is recommended as some may need a dose increase due to reduced concentrations of methadone.

**More information**

VICTRELIS is not likely to be used any longer due to its limited effectiveness, high pill burden, and long length of treatment duration. The AASLD/IDSA no longer recommend its use. High levels of drug resistance in people who don’t achieve an SVR is another problem with this drug. Merck is developing other HCV drugs that look more promising than VICTRELIS, including some excellent early results for treating HIV/HCV co-infected people, likely to be submitted for approval in late 2015.

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**Approved treatment durations for VICTRELIS**

<table>
<thead>
<tr>
<th>PATIENT’S TREATMENT HISTORY</th>
<th>HCV RNA LEVELS AT WEEK 8</th>
<th>HCV RNA LEVELS AT WEEK 24</th>
<th>TREATMENT RECOMMENDATIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment-naive</td>
<td>Undetectable</td>
<td>Undetectable</td>
<td>Continue 3-drug regimen through week 28</td>
</tr>
<tr>
<td>Treatment-naive</td>
<td>Detectable</td>
<td>Undetectable</td>
<td>Continue 3-drug regimen through week 36 and then take PEG/RBV through week 48</td>
</tr>
<tr>
<td>Partial responders or viral relapers</td>
<td>Undetectable</td>
<td>Undetectable</td>
<td>Continue 3-drug regimen through week 36</td>
</tr>
<tr>
<td>Partial responders or viral relapers</td>
<td>Detectable</td>
<td>Undetectable</td>
<td>Continue 3-drug regimen through week 36 and then take PEG/RBV through week 48</td>
</tr>
</tbody>
</table>

**OTHER CONSIDERATIONS FOR TREATMENT CONTINUATION:**
- If a patient has a detectable viral load of above 100 IU/mL at week 12, discontinue treatment.
- If a patient has a detectable viral load of any level at week 24, discontinue treatment.
Potential side effects and adverse events

The most serious side effect of Incivek is a severe rash that may require treatment in a hospital, and in extreme cases can possibly be fatal. Any rash, blisters, or skin lesions, mouth sores, red or inflamed eyes, swelling and/or fever should be reported to your medical provider; you may not have to stop treatment, but only a medical provider can make that call. Other side effects include fatigue, pruritis (itching), anal pruritis and discomfort (burning sensation), nausea, diarrhea, vomiting, and hemorrhoids. Incivek increases anemia severity. Incivek is taken with pegylated interferon and ribavirin; the most common side effects related to those two medications are: fatigue, headaches, nausea, fever, chills, and arthralgia (joint pain). For more information, see individual drug pages. Pegylated interferon has been associated with depression, anxiety, and in rare cases, suicidal thoughts. If you have a history of any of these conditions, talk to your provider before starting HCV treatment (it does not mean you can’t do HCV treatment, you just want to watch for signs and take preventative actions). When Incivek is used with ribavirin, pregnant women or women who are trying to become pregnant cannot take it; women of childbearing age and their male sexual partners must use two forms of birth control throughout treatment and for six months after treatment.

Potential drug interactions

Before starting treatment, talk with your medical provider or pharmacist about any medications, supplements, and herbs you are taking, including prescribed, over-the-counter, or illicit substances. Incivek interacts with many other drugs; for a complete listing refer to the package insert. Do not take Incivek with St. John’s wort. Avoid Kaletra (lopinavir/ritonavir), Lexiva (fosamprenavir), and Prezista (darunavir); can be taken with Norvir-boosted Reyataz (atazanavir), as well as the nucleoside reverse transcriptase inhibitors (NRTIs or nukes), including Truvada; non-nukes (NNRTIs) Edurant (rilpivirine) and Intellence (etravirine); INSTIs Isentress (raltegravir) and Tivicay (dolutegravir). Dose adjustments needed if taken with Sustiva (efavirenz) or Selzentry (maraviroc). Incivek increases the levels of erectile dysfunction drugs (Viagra, Cialis, and Levitra), doses should not exceed 10 mg Cialis or 2.5 mg of Levitra per 72 hours, or 25 mg of Viagra per 48 hours. Do not take with carbamazepine, phenobarbital, phenytoin, rifampin, lovastatin, simvastatin, nor with sedatives/hypnotics such as midazolam or triazolam. Caution is advised when taken with warfarin, clarithromycin, or erythromycin. Okay to take with methadone, but monitoring of methadone levels and patient discomfort is recommended as some may need a dose increase due to reduced concentrations of methadone.

More information

There’s not a whole lot to say about this drug, as it’s not going to be prescribed any longer and the AASLD/IDSA no longer recommend its use. It was great when it came on the scene, especially when compared to the effectiveness of pegylated interferon and ribavirin dual therapy for the treatment of GT 1, but it just doesn’t stand up to the new and forthcoming HCV drugs in terms of pill burden and dosing, as well as SVR rates and side effects.

Incivek is “response-guided therapy”: Treatment should be stopped if one has a detectable HCV viral load greater than 1000 IU/mL at week 4 or 12, or a detectable viral load of any level at week 24.

Approved treatment durations for Incivek

<table>
<thead>
<tr>
<th>HCV RNA LEVELS DURING TREATMENT</th>
<th>INCIVEK, PEGYLATED INTERFERON, AND RIBAVIRIN</th>
<th>PEGYLATED INTERFERON AND RIBAVIRIN</th>
<th>TOTAL TREATMENT DURATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Undetected at weeks 4 and 12</td>
<td>Take for 12 weeks</td>
<td>Additional 12 weeks</td>
<td>24 weeks</td>
</tr>
<tr>
<td>Detectable at weeks 4 and 12</td>
<td>Take for 12 weeks</td>
<td>Additional 36 weeks</td>
<td>48 weeks</td>
</tr>
</tbody>
</table>

Prior partial and null responder patients

<table>
<thead>
<tr>
<th></th>
<th>INCIVEK, PEGYLATED INTERFERON, AND RIBAVIRIN</th>
<th>PEGYLATED INTERFERON AND RIBAVIRIN</th>
<th>TOTAL TREATMENT DURATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients</td>
<td>Take for 12 weeks</td>
<td>Additional 36 weeks</td>
<td>48 weeks</td>
</tr>
</tbody>
</table>
Olysio

COMMON NAMES: simeprevir, SMV

FDA STATUS: Approved

CLASS: NS3/4A protease inhibitor

GENOTYPE: 1

Not approved for HIV/HCV co-infection. (Off-label usage may occur)

DOSSAGE:
Take one 150 mg capsule once daily with food; must be taken in combination with pegylated interferon/ribavirin (see below for more details). Do not crush or dissolve the capsule. Olysio should never be taken by itself. Take your missed dose as soon as possible, unless it is closer to the time of your next dose. Never double your dose. The chart on this page summarizes the various treatment regimens and durations.

MANUFACTURER:
Janssen Therapeutics

AWP:
$6,250 per week

Potential side effects and adverse events
Olysio is associated with a rash and photosensitivity. The rash was generally mild, with very few people experiencing a severe rash. The photosensitivity is considered mild to moderate, and anyone taking Olysio should wear sunscreen and take other protective measures. Other side effects include pruritus (itching), nausea, myalgia (muscle pain) and shortness of breath. Since Olysio is taken with pegylated interferon and ribavirin, additional side effects related to those medications include fatigue, headaches, nausea, fever, chills, and joint pain. For more information on the side effects of each of these medications, see their respective drug pages. Pegylated interferon has been associated with depression, anxiety, and in rare cases, suicidal thoughts. If you have a history of any of these conditions, talk to your provider before starting HCV treatment. Since Olysio is used with ribavirin, pregnant women or women who are trying to become pregnant cannot take it; women of child-bearing age and their male sexual partners must use two forms of birth control throughout treatment and for six months after treatment. Changes in hematological (blood) values are common, and routine blood testing to look for anemia, neutropenia, and other blood conditions is recommended.

Potential drug interactions
Talk to your medical provider and/or pharmacist about any and all medications you are taking whether they’re prescribed, over-the-counter, or illicit. Olysio interacts with many other medications, and this is not a complete list. For a more detailed review of drug interactions, see the package insert. Olysio should not be taken with any HIV protease inhibitors (PIs), the non-nucleoside reverse transcriptase inhibitors (NNRTIs) Sustiva (efavirenz, also in Atripla) or Viramune (nevirapine) or Intellence (etravirine), or with cobicistat-boosted regimens (Stribild). Olysio can be taken with Edurant (rilpivirine), Isentress (raltegravir), Tivicay (dolutegravir), and the nucleoside reverse transcriptase inhibitors including Truvada, Ziagen (abacavir), Emtriva (emtricitabine), Epivir (lamivudine), Epzicom, and Viread (tenofovir). Olysio boosts the levels of erectile dysfunction drugs (Viagra, Cialis, and Levitra). Start with the lowest dose possible and increase as needed. Do not use with the herbs milk thistle (silymarin) or St. John’s wort. Anticonvulsants such as phenobarbital, carbamazepine, phenytoin, and oxcarbazepine should not be used as they reduce the concentrations of Olysio, thus reducing its effectiveness. Rifampin, rifabutin, and rifapentine should not be taken. Antibiotics erythromycin, clarithromycin, and telithromycin increase levels of Olysio so they should be avoided, as should the antifungals fluconazole, voriconazole, itraconazole, ketoconazole, and posaconazole. Antiarrhythmics such as Tambocor and Cordarone should not be taken; no interactions with methadone and buprenorphine.

More information
GT 1 can be treated with Sovaldi and Olysio with or without ribavirin in what is called “off-label” (not FDA-approved) use based on the results of the “COSMOS” study, which saw high SVR (cure) rates and minimal side effects for both treatment-naïve and prior non-responders. For individuals who need treatment now, but cannot tolerate interferon, this is an excellent option. In May 2014, Janssen submitted this combination for FDA approval.

TWO IMPORTANT COMPONENTS OF OLYSIO TREATMENT
1. People with genotype 1a need a blood test called a “Q80K polymorphism”, for a resistant strain of HCV. This polymorphism reduces treatment effectiveness and other medications should be considered.
2. Olysio is “response-guided therapy”: Treatment should be stopped if one has a detectable HCV viral load of any level at weeks 4, 12, or 24.

Approved treatment durations for Olysio

<table>
<thead>
<tr>
<th>PATIENT TREATMENT HISTORY</th>
<th>OLYSIO, PEGYLATED INTERFERON AND RIBAVIRIN</th>
<th>PEGYLATED INTERFERON AND RIBAVIRIN</th>
<th>TOTAL TREATMENT DURATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment-naïve; or viral relapers (including those with cirrhosis)</td>
<td>Take for 12 weeks</td>
<td>Additional 12 weeks</td>
<td>24 weeks</td>
</tr>
<tr>
<td>Prior non-responder (including partial and null responders)</td>
<td>Take for 12 weeks</td>
<td>Additional 36 weeks</td>
<td>48 weeks</td>
</tr>
</tbody>
</table>
FDA STATUS: Approved

CLASS: Nucleotide analog NS5B polymerase inhibitor

GENOTYPE: 1, 2, 3, 4, 5, 6

Approved for HIV/HCV co-infection.

DOSAGE: Take one 400 mg tablet once daily with or without food; must be taken in combination with either ribavirin or pegylated interferon and ribavirin (see below for more details). Sovaldi should never be taken by itself. Take your missed dose as soon as possible, unless it is closer to the time of your next dose. Never double your dose. The chart on this page summarizes the various treatment regimens.

MANUFACTURER: Gilead Sciences, Inc.

AWP: $7,250 per week

Potential side effects and adverse events
Since Sovaldi is taken with pegylated interferon and ribavirin or ribavirin alone, the most common side effects reported by people taking this regimen are related to those two medications: fatigue, headaches, nausea, fever, chills, and arthralgia (joint pain). For more information on the side effects of each of these medications, see their respective drug pages. Pegylated interferon has been associated with depression, anxiety, and in rare cases, suicidal thoughts. If you have a history of any of these conditions, talk to your provider before starting HCV treatment (it does not mean you can’t take HCV treatment, you just want to watch for signs and be able to take preventative actions ahead of time). When Sovaldi is used with ribavirin, pregnant women or women who are trying to become pregnant cannot take it; women of childbearing age and their male partners must use two forms of birth control throughout treatment and for six months after treatment. Changes in hematological (blood) values are also common, and routine blood testing to look for anemia, neutropenia, and other blood conditions is recommended.

Potential drug interactions
Sovaldi may interact with other drugs: Be sure to tell your medical provider or pharmacist about all the medications, supplements, and herbs you take, whether prescribed, over-the-counter, or illicit, before starting this regimen, and inform them of any changes as they happen. Sovaldi is safe to take with HIV antivirals except Aptivus/Norvir (tipranavir/ritonavir), with no clinically relevant changes or dose adjustments necessary. Sovaldi has no interactions with methadone.

The following cannot be taken with Sovaldi: St. John’s wort, rifabutin, or rifapentine. Anticonvulsants such as phenobarbital, carbamazepine, phenytoin, and oxcarbazepine should not be used as they reduce the concentrations of Sovaldi, thus reducing its therapeutic effectiveness.

More information
Sovaldi has a lot of “firsts”: first drug of its class; first drug to receive FDA approval for use without interferon, and first DAA to receive FDA approval for use in HIV/HCV co-infected patients. It immediately became the most popular HCV medicine, achieving the status of preferred treatment regimen in the AASLD/IDSA guidelines and is becoming one of the fastest prescribed medicines ever. Given the history of HCV treatment and the desire for regimens that are easier to take, along with its treatment effectiveness and the fact that it can be used without interferon for GT 2 and 3 (and in some cases, even 1), and its use and effectiveness in co-infected people, it’s no wonder it has become so widely used. Sovaldi has also been approved for use with ribavirin in people who have hepatocellular carcinoma (liver cancer) and are awaiting a liver transplant. It’s also becoming common to see medical providers treat GT 1 with Sovaldi and Olysio with or without ribavirin in “off-label” (not FDA-approved) use based on the results of a clinical trial called “COSMOS.” The results were very promising, with high SVR rates and minimal side effects for both treatment-naive and prior non-responders. In April 2014, AASLD recommended this regimen for HIV/HCV co-infected patients who were previous non-responders or ineligible for interferon treatment. For individuals who need treatment now, but cannot tolerate the side effects of interferon, this is an excellent option. By the end of 2014, we are likely to see other potential combinations: Upon FDA approval, Gilead will release a fixed dose combination of Sovaldi and ledipasvir (see drug page for more information on this combination). The approval of the BMS drug, daclatasvir (see page 49), a drug that has also been shown to be highly effective when used with Sovaldi, will also create new treatment opportunities.

Approved treatment durations for Sovaldi

<table>
<thead>
<tr>
<th>HCV MONO-INFECTED AND HIV/HCV CO-INFECTED</th>
<th>TREATMENT</th>
<th>DURATION OF TREATMENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genotype 1 and 4</td>
<td>Sovaldi + pegylated interferon + ribavirin</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Genotype 2</td>
<td>Sovaldi + ribavirin</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Genotype 3</td>
<td>Sovaldi + ribavirin</td>
<td>24 weeks</td>
</tr>
</tbody>
</table>
FDA STATUS:
A fixed dose combination submitted for approval; ruling expected Fall 2014

CLASS:
ledipasvir: NS5A inhibitor; sofosbuvir: Nucleotide analog NS5B polymerase inhibitor

GENOTYPE: 1 (possibly 3)
Being studied in HIV/HCV co-infection; has shown promising results in clinical studies

DOSAGE:
Still investigational. A fixed dose combination (FDC) of ledipasvir 90 mg/sofosbuvir 400 mg. Take one tablet once daily with or without food; may or may not be taken in combination with ribavirin (see chart for more details). Take your missed dose as soon as possible, unless it is closer to the time of your next dose. Never double your dose. Duration of therapy not yet determined, but the submission for approval to the FDA was based on the following clinical trial data, which gives a sense of what the final approval will look like. The chart summarizes the various treatment regimens for these studies.

MANUFACTURER:
Gilead Sciences

Potential side effects and adverse events
In the ledipasvir/sofosbuvir regimens taken without ribavirin, the most commonly reported side effects are fatigue, headache, nausea, and diarrhea; less frequently reported side effects include insomnia, rash, and pruritis (itching). In all cases, the side effects were considered mild and no one in the ION studies had to stop treatment because of them. It is also notable that there were no cases of anemia in any ribavirin-free group, and only two people experienced any hematologic (blood) abnormalities. In the regimens containing ribavirin, the side effects were similar, with higher rates of fatigue, insomnia, and anemia. There were more cases of hematologic abnormalities, and routine blood testing to look for anemia, neutropenia, and other blood conditions is recommended. No one in this group had to stop the treatment due to side effects. When this combination is used with ribavirin, pregnant women or women who are trying to become pregnant cannot take it; women of childbearing age and their male sexual partners must use two forms of birth control throughout treatment and for six months after treatment.

Potential drug interactions
Ledipasvir does not appear to have any significant drug interactions. Sofosbuvir may interact with other drugs: Be sure to tell your medical provider or pharmacist about all the medications, supplements, and herbs you take, whether they are prescribed, over-the-counter, or illicit, before starting this regimen, and inform them of any changes as they happen. It is safe to take with HIV antivirals except Aptivus/Norvir (tipranavir/ritonavir), with no clinically relevant changes or dose adjustments necessary; there are no interactions with methadone. The following cannot be taken with Sovaldi (sofosbuvir): St. John’s wort, tipranavir/ritonavir, rifampin, rifabutin, and rifapentine. Anticonvulsants such as phenobarbital, carbamazepine, phenytoin, and oxcarbazepine should not be used as they reduce the concentrations of Sovaldi, thus reducing its therapeutic effectiveness.

More information
This combination may be a real game-changer for treating HCV GT 1: One pill, once daily potentially curing HCV in eight weeks is an astounding achievement. It is also worth noting that the combination of sofosbuvir with another NS5A inhibitor, BMS’ daclatasvir, also cures people at very high rates with minimal side effects. We will get a better sense of its indications and dosing once it gets FDA approval, but in addition to treating GT 1, this combination has shown very promising results for people with the more difficult to treat GT 3, as well as in HIV/HCV co-infected individuals. Sofosbuvir alone is already approved, as Sovaldi.

Phase III clinical trial results for ledipasvir/sofosbuvir

<table>
<thead>
<tr>
<th>STUDY</th>
<th>PATIENT GROUP</th>
<th>TREATMENT</th>
<th>DURATION</th>
<th>SVR 12</th>
</tr>
</thead>
<tbody>
<tr>
<td>ION-1</td>
<td>GT 1 treatment-naive (including 15.7% with cirrhosis)</td>
<td>SOF/LDV</td>
<td>12 weeks</td>
<td>97.7%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>SOF/LDV + RBV</td>
<td>12 weeks</td>
<td>97.2%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>SOF/LDV</td>
<td>24 weeks</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td></td>
<td>SOF/LDV + RBV</td>
<td>24 weeks</td>
<td>N/A</td>
</tr>
<tr>
<td>ION-2</td>
<td>GT 1 treatment-experienced (including 20% with cirrhosis)</td>
<td>SOF/LDV</td>
<td>12 weeks</td>
<td>93.6%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>SOF/LDV + RBV</td>
<td>12 weeks</td>
<td>96.4%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>SOF/LDV</td>
<td>24 weeks</td>
<td>99.1%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>SOF/LDV + RBV</td>
<td>24 weeks</td>
<td>99.1%</td>
</tr>
<tr>
<td>ION-3</td>
<td>GT 1 treatment-naive, no cirrhosis</td>
<td>SOF/LDV</td>
<td>8 weeks</td>
<td>94%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>SOF/LDV + RBV</td>
<td>8 weeks</td>
<td>93.1%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>SOF/LDV</td>
<td>12 weeks</td>
<td>95.4%</td>
</tr>
</tbody>
</table>

COMMON NAMES:
ledipasvir/sofosbuvir, LDV/SOF
FDA STATUS: 
daclatasvir and asunaprevir: Submitted for approval; ruling expected Fall 2014 
BMS-791325: Not yet submitted for approval

CLASS: 
daclatasvir: NS5A replication complex inhibitor 
asunaprevir: NS3/4A protease inhibitor 
BMS-791325: Non-nucleoside NS5B polymerase inhibitor

GENOTYPE: 1, 2, 3, 4 (depending upon regimen)

Potential side effects and adverse events
As this drug has not yet been FDA-approved, side effects data come from conference presentations and peer-reviewed scientific papers published in medical journals. A complete listing of side effects will be included in the package insert. The most commonly reported side effects from the daclatasvir/sofosbuvir combination are fatigue, headache, and nausea, but all were considered to be mild to moderate in intensity; when ribavirin is included, there is an increased risk of these side effects. For more information on the side effects of ribavirin, refer to its drug page. When this regimen is used with ribavirin, pregnant women or women who are trying to become pregnant cannot take it; women of childbearing age and their male sexual partners must use two forms of birth control throughout treatment and for six months post-treatment. Changes in hematological (blood) values were also seen in the clinical trials, and routine blood testing to look for anemia, neutropenia, and other blood conditions are recommended; the side effects associated with the daclatasvir/asunaprevir combination include nasopharyngitis, elevated liver enzymes, headaches, diarrhea, and pyrexia (fever); the side effects reported in the daclatasvir/asunaprevir/BMS-791325 combination include headache, diarrhea, fatigue, and nausea.

Potential drug interactions
There is limited data on the drug interactions with either daclatasvir or asunaprevir. More detailed information will be available upon FDA approval, and you can then refer to the package insert for more information. Daclatasvir is thought to have a low potential for drug interactions overall; it has no known interactions and is safe to use with other HCV DAAs, including asunaprevir, BMS-791325, Sovaldi (sofosbuvir), and MK-5172 (NS3/4A PI from Merck). Limited data has shown that there are no dose adjustments necessary with some HIV medications. There are no available data on drug interactions between asunaprevir and other drugs at the time of writing as the studies are ongoing, but as it is a protease inhibitor, it is likely to interact with the HIV PIs as well, but be suitable for use with the NRTIs, rilpivirine, integrase inhibitors, and maraviroc. There are no available data on the interactions of BMS-791325, but studies are underway.

More information
Before Gilead bought sofosbuvir (Sovaldi) from Pharmasset and decided to pursue the combination of ledipasvir/sofosbuvir, the combination of daclatasvir/sofosbuvir had generated quite a buzz in the HCV community due to its high level of cure rates. Gilead suspended working with BMS, much to the criticism, from many advocates and people with HCV, but the potential for this combination remains high. The combination of daclatasvir/sofosbuvir has shown excellent treatment response rates in this population, but also in the more difficult to treat GT 3 patients. It remains to be seen if the FDA will approve this use, or if clinicians will have to use them off-label. Similarly, the daclatasvir/asunaprevir combination has been shown to be effective against GT 1b, which is the most common strain of HCV world-wide. Daclatasvir is also being investigated for its use in HIV/HCV co-infected people.

| Phase II clinical trial results for daclatasvir + asunaprevir + BMS-791325 |
|-----------------------------|-----------------|-----------------|----------------|-----------------|
| STUDY NAME | DRUG REGIMEN | GENOTYPE | NUMBER OF PARTICIPANTS | SVR 12 |
| AI443-014 | Daclatasvir + asunaprevir + BMS-791325 75 mg | 1a and 1b (included some people with cirrhosis) | 77 | 92.2% (71/77) |
| AI443-014 | Daclatasvir + asunaprevir + BMS-791325 150 mg | 1a and 1b (included some people with cirrhosis) | 84 | 91.7% (77/84) |

COMMON NAMES:
daclatasvir, DCV; asunaprevir, ASV; BMS-791325

MANUFACTURER:
Bristol-Myers Squibb
FDA STATUS:
Submitted for approval; ruling expected Fall 2014

CLASS:
**ABT-450/r:** NS3/4A protease inhibitor, boosted with ritonavir;**ombitasvir:** NS5A inhibitor**dasabuvir:** Non-nucleoside NS5B polymerase inhibitor

GENOTYPE: 1

Not approved for HIV/HCV co-infection, but currently under study

DOSEAGE:
Still investigational. ABT 450/r (150 mg/100 mg) is co-formulated with ombitasvir (25 mg); take one tablet once daily with or without food. Must be taken in combination with one 200 mg tablet of dasabuvir, twice daily; none should ever be taken by itself. If ribavirin is prescribed, take a weight-based dose, two times daily with food. Take your missed dose as soon as possible, unless it’s too close to your next dose. Never double dose.

MANUFACTURER: AbbVie

Potential side effects and adverse events
As this drug has not yet been FDA-approved, side effects data come from conference presentations and peer-reviewed scientific papers published in medical journals. A complete listing of side effects will be included in the package insert. The most commonly experienced were headaches, fatigue, nausea, asthenia (loss of strength), insomnia, pruritus (itching), diarrhea, dyspnea (difficulty breathing), cough, and myalgia (muscle pain); all side effects were considered mild. When taken with ribavirin, there is an increased risk of fatigue, nausea, headaches, and pruritus. For more information on the side effects of ribavirin, refer to its drug page. When this regimen is used with ribavirin, pregnant women or women who are trying to become pregnant cannot take it; women of childbearing age and their male sexual partners must use two forms of birth control throughout treatment and for six months post-treatment. Changes in hematological (blood) values were also seen in the clinical trials, and routine blood testing to look for anemia, neutropenia, and other blood conditions are recommended.

Potential drug interactions
There is limited data on the drug interactions with this regimen; more detailed information will be available upon FDA approval, and you can then refer to the package insert for more information. There is a small sample of people who were on methadone or buprenorphine, and there were no clinically relevant drug interactions. As ABT-450/r is a protease inhibitor (boosted with ritonavir), there may be other drug interactions that you will need to be aware of, especially when used with HIV medicines.

More information
The results from the clinical trials of this regimen are very promising for both GT 1a and 1b. FDA approval is pending, but it looks like this regimen has higher SVR (cure) rates for GT 1a when ribavirin is used. GT 1b does not look like it will need ribavirin, which is good news for the rest of the world as GT 1b is the most common genotype across the globe. Research studies are underway to see how this regimen works for people co-infected with HIV/HCV and in people with post-liver transplants.

### Phase III clinical trial results for ABT-450/r; ombitasvir + dasabuvir

<table>
<thead>
<tr>
<th>STUDY</th>
<th>GENOTYPE, PATIENT TYPE</th>
<th>NUMBER</th>
<th>TREATMENT</th>
<th>SVR 12</th>
</tr>
</thead>
<tbody>
<tr>
<td>PEARL-II</td>
<td>GT 1b, treatment experienced</td>
<td>179</td>
<td>ABT-450/r-ombitasvir+dasabuvir + RBV</td>
<td>97% (85/88)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>ABT-450/r-ombitasvir + dasabuvir</td>
<td>100% (91/91)</td>
</tr>
<tr>
<td>PEARL-II</td>
<td>GT 1b, treatment naive</td>
<td>419</td>
<td>ABT-450/r-ombitasvir+dasabuvir + RBV</td>
<td>99% (209/210)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>ABT-450/r-ombitasvir + dasabuvir</td>
<td>99% (207/209)</td>
</tr>
<tr>
<td>PEARL-IV</td>
<td>GT 1a, treatment naive</td>
<td>305</td>
<td>ABT-450/r-ombitasvir+dasabuvir + RBV</td>
<td>97% (97/100)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>ABT-450/r-ombitasvir + dasabuvir</td>
<td>90% (185/205)</td>
</tr>
<tr>
<td>TURQUOISE-II 12 &amp; 24 weeks</td>
<td>GT 1 treatment naive and treatment experienced with compensated cirrhosis</td>
<td>380</td>
<td>ABT-450/r-ombitasvir+dasabuvir + RBV for 12 weeks</td>
<td>92% (191/208)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>ABT-450/r-ombitasvir+dasabuvir + RBV for 24 weeks</td>
<td>96% (165/172)</td>
</tr>
<tr>
<td>SAPPHIRE-I</td>
<td>GT 1, treatment naive</td>
<td>631</td>
<td>ABT-450/r-ombitasvir+dasabuvir + RBV</td>
<td>96% (455/473)</td>
</tr>
<tr>
<td>SAPPHIRE-II</td>
<td>GT 1, treatment experienced</td>
<td>394</td>
<td>ABT-450/r-ombitasvir+dasabuvir + RBV</td>
<td>96% (286/297)</td>
</tr>
</tbody>
</table>
Hepatitis C.

Who can you talk to about it?

Talk with a real person, one-to-one.

Call now: 877-HELP-4-HEP

You can talk to us.
We’re Help-4-Hep, and one of our phone counselors is ready to help you meet the challenges of hepatitis C head-on...where to get tested, how to get treatment, or help paying for lab work and medicines. All from someone who’s had hepatitis C touch their own life.
HCV resources, services, and information

HELP-4-HEP
877-435-7443 toll-free
National hepatitis C support line staffed by trained peer counselors. Health education, resources, referrals for testing and treatment, and emotional support. Monday–Friday, 9 am–7pm EST.

HIV Health InfoLine
800-822-7422 toll-free
Staffed by trained Project Inform operators and staff, many of whom also live with or are impacted by HIV. Call-back service Monday–Friday, 10 am–4 pm PST.

AIDS/HIV Nightline
800-628-9240 toll-free
Operates 5 pm–5 am and is run by the San Francisco Suicide Prevention hotline. Very strong on offering emotional support and health education.

The HCV Advocate
hcvadvocate.org

Hep C Association
hepcassoc.org
An excellent source for HCV news and information.

Hep C Connection
hepc-connection.org
Array of services for people throughout Colorado. Excellent site for news and information.

Caring Ambassadors
hepcchallenge.org
Array of services and advocacy around HCV. They also publish Hepatitis C Choices.

Project Inform
projectinform.org
Advocates for issues related to HIV, HCV and health care access. Up-to-date information on HIV and HCV care and health care reform.

Treatment Action Group
treatmentactiongroup.org
National advocacy, research, and policy think tank on HIV, hepatitis C and tuberculosis. Fact sheets, policy papers and annual Pipeline Report.

Test Positive Aware Network
tpan.com
Offers an array of services for people in the Chicago area, including HIV and HCV testing. Publishes bi-monthly POSITIVELY AWARE magazine as well as annual HIV drug and HCV drug guides.

National AIDS Treatment Advocacy Project
natap.org
Excellent website for scientific results from HIV and HCV conferences and academic articles.

HIVandHepatitis.com
Presents high quality and accurate news coverage on the prevention and treatment of HIV, HCV, and HIV/HCV co-infection.

AN ESTIMATED 25% OF THE 1.1 MILLION HIV-POSITIVE PEOPLE IN THE U.S. ARE CO-INFECTED WITH HCV.

3X MORE THAN Triples THE Risk FOR LIVER DISEASE, LIVER FAILURE, AND LIVER-RELATED DEATH FROM HCV.

SOURCE: CDC