HCV FACT SHEETS

TAG
Treatment Action Group

December 15, 2015

Dear Colleagues,

Treatment Action Group has just released hepatitis C fact sheets in English and Spanish. We have enclosed copies of our fact sheets on

- adherence,
- diagnostics, and
- treatment (Sovaldi, Olysio, Viekira Pak, Harvoni, Daklinza, and ribavirin).

PDFs of our fact sheets are available at: http://www.treatmentactiongroup.org/hcv/factsheets.

We are also happy to send you hard copies at no charge. You can order these online at: http://www.treatmentactiongroup.org/pub-request.

As usual, we welcome any suggestions for improving our materials.

Estimados/as colegas,

La organización Treatment Action Group (TAG) acaba de publicar unas hojas informativas sobre la hepatitis C en inglés y español. Hemos adjuntado copias de nuestras hojas informativas sobre

- adherencia,
- diagnóstico, y
- tratamiento (Sovaldi, Olysio, Viekira Pak, Daklinza, y ribavirina).

Todos estos materiales están disponibles como PDF en: http://www.treatmentactiongroup.org/hcv/factsheets.

Por supuesto, también estaremos encantados de haceros llegar copias impresas de forma gratuita. Podéis solicitarlas en: http://www.treatmentactiongroup.org/pub-request.

Como siempre, agradecemos cualquier sugerencia para mejorar nuestros materiales.

Sincerely, atentamente,

Tracy Swan
Hepatitis/HIV Project Director, Treatment Action Group
Directora del Proyecto de Hepatitis/VIH de Treatment Action Group

ADHERENCE

What is adherence? Adherence means sticking to something. It is often used to describe taking medicine without missing doses for as long as needed. Good adherence helps to maintain—or improve—your health.

This fact sheet is about adherence to hepatitis C treatment. It may be helpful for other medications, whether you are taking them for a short time, or for the rest of your life.

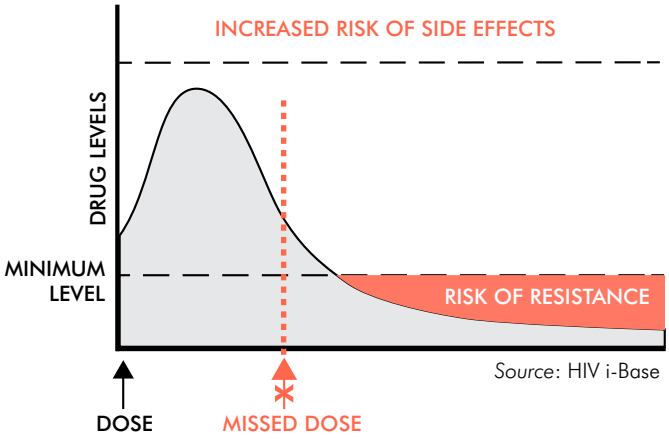
With hepatitis C treatment, the most important thing a person can do to be cured is not to miss taking any of their medication—and to finish all of it.

Knowing how hepatitis C treatment works—instead of just being told to take all of your medication—makes it easier to understand why adherence matters so much.

How does hepatitis C virus (HCV) treatment work? Just like people, viruses do not live forever; they are constantly reproducing. Hepatitis C drugs work by blocking different steps in the virus life cycle; this prevents HCV from making more of itself. Once the virus stops reproducing, it dies off. After both of these things happen, a person is cured.

People need to stay on HCV treatment for a certain amount of time to make sure that drugs can get the job done. Hepatitis C treatment lasts from eight to 24 weeks. (Researchers are looking at even shorter treatment.)

Why is adherence important? For drugs to work, there have to be enough of them in a person's body. If drug levels get too low, the drugs won't work; if they get too high, side effects can be worse.



What is drug resistance? Each day, HCV makes billions of copies of itself. Some of these copies are not the same as the original virus. They have changes, called *mutations*. Some mutations are harmless, but others can stop hepatitis C drugs from working (called *drug resistance*).

When people miss doses of their hepatitis C treatment, the virus gets a chance to reproduce. Some of the copies it makes might have mutations that cause drug resistance. Drugs can stop working if changes in the hepatitis C virus make it resistant to the drugs.

Some people have drug resistance even though they have never been on hepatitis C treatment. Many of them have been cured anyway. But most people who are not cured will have resistance to one or more of the hepatitis C drugs they took. Resistance to certain hepatitis C drugs can disappear within months. But resistance to other drugs can last for years and might prevent re-treatment from working.

Why does dosing matter? Some drugs linger in a person's body for weeks, while others pass through it in a few hours. Researchers can see how long drugs stay in a person's body and whether food changes this. They use this information to figure out how often drugs need to be taken. Some drugs need to be taken on an empty stomach. Other drugs need to be taken with food to work. It's a good idea to ask whether this means with a snack or a full meal.

Some HCV drugs need to be taken only once a day. It is important to take them around the same time each day to keep enough of the drug in your system. For HCV drugs that need to be taken twice a day, it is best to take them every 12 hours—or as close to it as possible.

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Drug interactions: Some medications should not be used together. Combining them can change drug levels (called *drug-drug interactions*). Higher drug levels can worsen side effects. When drug levels are too low, drugs cannot do their job. Low drug levels put people at risk for drug resistance or not being cured.

Before you start hepatitis C treatment, talk with your health care provider about starting, using, or stopping any medications, supplements, or herbal remedies to avoid drug-drug interactions.

How is adherence measured? In clinical trials, adherence is checked often, usually in more than one way. Methods used in research include:

- taking a blood sample to check medication levels;
- keeping a written record of when medication is taken;
- bringing pill bottles or blister packs to clinic visits for pill counts;
- using pill bottles with caps that track each time bottles were opened (called MEMS);
- using blister packs that track each time a pill is removed—this information can be sent to a smart phone;
- using new pill bottles that light up, buzz, and send text and voice mail messages. These can also track how many times a pill bottle has been opened and shut, and how many pills are left; and
- using edible "smart pills" to see when medication was taken.

"Smart pills" work with a patch that is worn on a person's torso. Each smart pill has a sensor that becomes activated after it enters the stomach. When the smart pill is activated, it sends a wireless signal to the patch. Then the patch sends information (including when the pill was taken, heart rate, and how active you are) to a mobile app. The smart pills come in regular packaging or in blister packs. Depending on the pharmacy and type of medication a person uses, it may be possible to combine a smart pill with a person's regular medication. In the future, the technology that goes with smart pills will change.

There are other, less complicated ways to support adherence. Some people leave their medication in a familiar spot (such as the bathroom or by the coffee pot). Others use pillboxes to make sure that they are taking medication at the right time. People also use alarms on their smart phones or mobile applications to support adherence.

What makes adherence difficult? Adherence can be difficult for many reasons. Often people simply forget to take medication or refill their prescriptions. Sometimes people have other reasons for missing their medication, including:

- having side effects from medication—especially if you don't feel sick;
- feeling better, even though you haven't finished treatment;
- not wanting to think about why you need to take medication;
- being tired of taking medication every day;
- not wanting other people to know why you are taking medication;
- having to take several different medications, at different times, with or without food;
- loss of or change in employment and insurance;
- difficulty getting prescriptions refilled or delivered;
- money problems;
- responsibilities, including work and childcare;
- being arrested;
- having a busy or chaotic life;
- moving;
- traveling, especially when time zones are different;
- becoming homeless; and
- untreated mental illness.

It's important not to be too hard on yourself if you forget a dose of your medication—nobody is perfect! Sometimes talking to another person who is going through a similar experience, a health care provider, or a pharmacist can help you with adherence tips and support.

Hepatitis C Virus (HCV) Diagnostics

What is screening? Screening looks to see whether someone might have a disease. For hepatitis C virus (HCV), screening means looking for *antibodies* instead of the virus.

What are antibodies? Antibodies are Y-shaped proteins made by a person's immune system. They are part of the immune system's response to viruses, bacteria, and other harmful substances (called *antigens*).

Antibodies attach themselves to antigens or infected cells and tag them so that other immune cells can find and disable them. Antibodies stay in a person's body long after the antigen that triggered them disappears (this is called *immunological memory*). If the same antigen enters a person's body again, even years later, the immune system will remember it—and send antibodies to destroy it.

When HCV enters a person's bloodstream, it triggers an immune response. The immune system makes HCV-fighting antibodies. Sometimes, the immune system gets rid of hepatitis C virus by itself (this is called *spontaneous viral clearance*). About a quarter of people with hepatitis C will spontaneously clear the virus. This is more likely in young people (especially women), people who do not have HIV, and people with the IL28B CC genotype (refer to TAG's Hepatitis C and the IL28B Gene fact sheet).

Even when a person has cleared HCV or been cured by treatment, HCV antibodies remain in a person's blood for years.

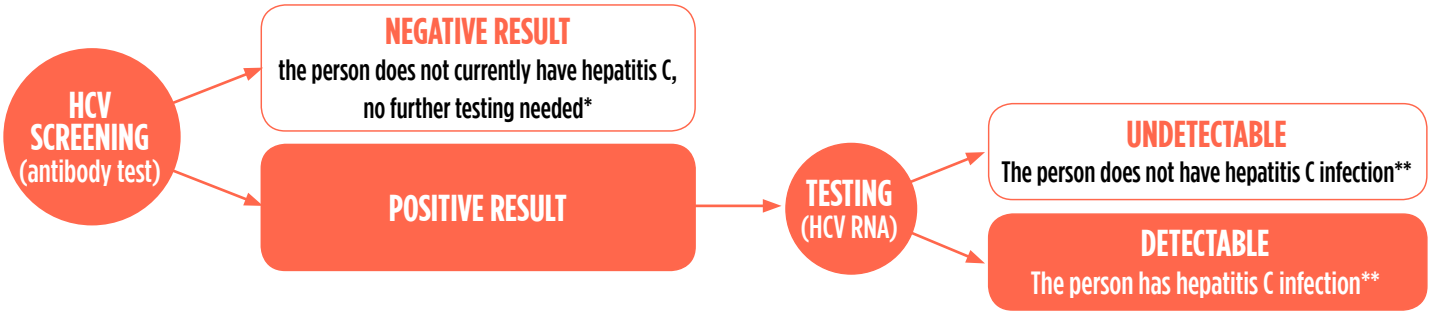
What does a negative HCV antibody test result mean? A negative antibody test result usually means that the person has not been infected with hepatitis C (unless they were infected very recently or have a weakened immune system).

The body needs at least two months (and sometimes up to nine months) to make antibodies. People with weakened immune systems (from an illness or certain medications) are not always able to produce antibodies. This might happen in people with autoimmune disorders (when a person's immune system attacks his or her own organs or tissues), HIV-positive people with a CD4 cell count below <200 cells/mm^3, and people taking immunosuppressants.

What does a positive HCV antibody test result mean? A positive antibody test result means that a person has been infected with hepatitis C. It does not mean that the person still has hepatitis C. A different test, to look for the actual hepatitis C virus, is needed to make a diagnosis.

What is testing? Testing will confirm—or rule out—whether someone has a disease.

How is a person tested for hepatitis C? A viral-load test (called *HCV RNA*) is used to check for hepatitis C in the bloodstream. Usually, hepatitis C virus can be found in a person's bloodstream two weeks after he or she becomes infected.



*Except in case of recent risk (within six months) or in people with a weakened immune system

**During the first six months after HCV infection, a person may spontaneously clear the virus; if there was a recent risk, repeat viral-load testing to confirm chronic hepatitis C infection

There are two types of **viral-load tests:** *qualitative* and *quantitative*.

Qualitative testing checks whether there is hepatitis C virus in the bloodstream (detectable or undetectable). *Quantitative* testing measures the amount of hepatitis C virus in the bloodstream. These tests are used during and after HCV treatment to see if it is working and whether a person is cured.

HCV Qualitative Testing

WHAT THE RESULT SAYS	**Undetectable, the lower limit of detection (LLOD) varies;** it can be as low as <5 IU/mL	**Detectable, below the lower limit of quantification (LLOQ);** the lowest amount of hepatitis C virus that the test can measure	**Detectable**
WHAT THE RESULT MEANS	No hepatitis C virus was found in the bloodstream (this means that a person either spontaneously cleared HCV or that they were cured)	Hepatitis C was found in the bloodstream, but the amount of the virus was too small for the test to measure	Hepatitis C was found in the bloodstream; the amount of virus is reported in international units per milliliter (IU/mL). A person with a positive antibody test result and detectable HCV RNA has chronic hepatitis C (unless they were recently infected)

HCV Core Antigen Testing

The hepatitis C core antigen is a viral protein. Since the core antigen is part of hepatitis C virus, it can usually be found in the bloodstream two weeks after infection.

Since HCV core antigen testing is simpler and less expensive than viral-load testing, some experts suggest using it in resource-limited settings. Core antigen testing can be used—often with HCV antibody testing—to detect acute HCV or to confirm chronic HCV infection. HCV core antigen testing can also be used to measure treatment outcome. Although it does not detect low levels of HCV (<1,000 IU/mL), usually the hepatitis C viral load is much higher in people who relapse after HCV treatment.

HCV Genotyping

There are at least six known hepatitis C genotypes, numbered in the order that they were discovered. Each genotype has many subtypes, each given a letter in the order that they were discovered. People can be infected with more than one HCV genotype (called *mixed infection*). This is most likely to happen to people who got blood products or blood transfusions many years ago or in a place where the blood supply is not checked for HCV; people on kidney dialysis; or people who inject drugs with shared, unsterilized equipment.

Currently, the type and length of HCV treatment depend on which genotype a person has. Soon, it might be possible to use one HCV regimen for everyone (called *pangenotypic*), making HCV genotyping unnecessary.

Liver Disease Staging

The type and length of HCV treatment sometimes depend on how much liver damage a person has (for example, people with cirrhosis are often given ribavirin and treated longer than people who have less liver damage).

There are different methods to determine how much liver damage a person has (called *staging*). Although noninvasive tests are not always as precise as a liver biopsy, they are safer, less expensive, and easier to perform and undergo. It is becoming more common to use routine blood tests or ultrasound imaging to see whether a person has cirrhosis.

New HCV Diagnostics

Now that HCV treatment is simpler, safer, and more effective, diagnostics need to become simpler and less expensive.

Ideally, HCV will soon be diagnosed with a single rapid point-of-care test and cured with a pangenotypic regimen.

SOVALDI

The goal of hepatitis C virus (HCV) treatment is a cure (when there is no HCV in a person's bloodstream at least 12 weeks after treatment is finished).

What is Sovaldi? Sovaldi (sofosbuvir) is an HCV-fighting drug that must be used with other drugs. In the United States, Sovaldi is approved for people with hepatitis C genotypes 1, 2, 3, or 4 who are over 18 years old.

How is Sovaldi used? Sovaldi is taken once daily, with or without food, for 12 to 24 weeks. Some people will use Sovaldi with a drug called **ribavirin (RBV)**, which is taken twice daily with food. The type and length of treatment depends on HCV genotype, treatment history, whether a person has cirrhosis, and the other drugs used with it.

Harvoni is a combination of Sovaldi and ledipasvir (see TAG's **Harvoni** fact sheet for more information).

Sovaldi and Olysio—another HCV-fighting drug—have been approved for use in people over 18 years old who have HCV genotype 1 (see TAG's **Olysio** fact sheet for more information).

Sovaldi and Daklinza—another HCV-fighting drug—have been approved for use in people over 18 years old who have HCV genotype 3 (see TAG's **Daklinza** fact sheet for more information).

Hepatitis C treatment is changing quickly. Sovaldi is being studied with, and used in, interferon-free combinations that have not been approved yet.

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Sovaldi-Based Treatment Regimens and Cure Rates in HCV Clinical Trials and Real-World Settings*

(Sovaldi has been used with pegylated interferon and ribavirin—or ribavirin alone—but these regimens are no longer recommended for genotype 1)

Genotype 1, never treated for HCV, no cirrhosis	+ Cirrhosis
Sovaldi + Olysio (with or without RBV), 12 weeks: **95%** to **97%** (in a small trial; real-world: 88% to 92%)	Sovaldi + Olysio (with or without RBV), 24 weeks: **100%** (real-world: 75% to 87%) Sovaldi + Olysio, 12 weeks: **88%**
Genotype 1, treatment-experienced, no cirrhosis	**+ Cirrhosis**
Sovaldi + Olysio (with or without RBV), 12 weeks: **95%** (real-world: 81% to 87%)	Olysio + Sovaldi, 12 weeks: **79%** Sovaldi + Olysio (with or without RBV), 24 weeks: **95%** (real-world: 76% to 79%)
Genotype 2, never treated or treatment-experienced (includes people with cirrhosis)	
Sovaldi + RBV, 12 weeks: **88%** to **100%** (real-world: in people with cirrhosis, 65% [never-treated] and 75% [treatment-experienced]) Sovaldi + RBV, 16 weeks: **87%** Sovaldi + RBV, 24 weeks: **100%**	
Genotype 3, never treated for HCV, no cirrhosis	**+ Cirrhosis**
Sovaldi + Daklinza, 12 weeks: **98%** Sovaldi + PEG-IFN and RBV, 12 weeks: **96%** Sovaldi + RBV, 16 weeks: **83%** Sovaldi + RBV, 24 weeks: **90%** to **94%**	Sovaldi + Daklinza, 12 weeks: **58%** Sovaldi + PEG-IFN and RBV, 12 weeks: **91%** Sovaldi + RBV, 24 weeks: **82%** to **92%**
Genotype 3, treatment-experienced, no cirrhosis	**+ Cirrhosis**
Sovaldi + Daklinza, 12 weeks: **92%** Sovaldi + PEG-IFN and RBV, 12 weeks: **94%** Sovaldi + RBV, 24 weeks: **87%**	Sovaldi + Daklinza, 12 weeks: **69%** Sovaldi + PEG-IFN and RBV, 12 weeks: **86%** Sovaldi + RBV, 24 weeks: **60%** to **77%**
Genotype 4, never treated for HCV, no cirrhosis (all information in genotype 4 is from small trials)	**+ Cirrhosis**
Sovaldi + PEG-IFN and RBV, 12 weeks: **96%** Sovaldi + RBV, 24 weeks: **100%**	Sovaldi + RBV, 24 weeks: **100%**
Genotype 4, treatment-experienced, no cirrhosis	**+ Cirrhosis**
Sovaldi + RBV, 24 weeks: **87%**	Sovaldi + RBV, 24 weeks: **67%**

*Cure rates in clinical trials are higher than in real life since people in them are usually healthier and get extra monitoring and support. Some trials were small (fewer than 200 people).

The most important thing a person can do to be cured is not to miss taking doses of HCV treatment—called *adherence*. Adherence lowers the risk for drug resistance.

What is drug resistance? Each day, HCV makes billions of copies of itself. Some of these copies are not the same as the original virus. They may have changes (called *mutations*) that can stop hepatitis C drugs from working. If people miss doses of their treatment, the virus gets a chance to reproduce—and some of these copies can be resistant to HCV treatment.

Some people have drug resistance even though they have never been on hepatitis C treatment—but many can be cured anyway. Most people who are not cured have resistance to one or more of the HCV drugs they've taken. Resistance to certain hepatitis C drugs can disappear within months. But resistance to other drugs can last for years and might prevent re-treatment from working. Some people who were treated with—but not cured by—Sovaldi have been re-treated with—and cured by—a combination of drugs including Sovaldi.

Sovaldi and age, gender, and race/ethnicity: In clinical trials, there was no difference in cure rates by age (over 65 vs. under 65). Women were slightly more likely to be cured than men. There is not much information about cure rates by race or ethnicity because most people in the trials were white. Sovaldi and RBV are slightly less effective for black and Hispanic people versus nonblack and non-Hispanic people.

Side effects from Sovaldi: Talk with your health care provider about possible side effects and how they will be managed. In clinical trials of Sovaldi and RBV, headache and fatigue were most common. At least 15 percent of trial participants had one or more of these side effects: nausea, insomnia, itching, anemia, weakness, rash, diarrhea, and irritability; usually, these were mild.

Does Sovaldi work for HIV-positive people? Yes. In clinical trials, cure rates were the same for HIV-positive people.

Sovaldi and other medications: Combining medications can increase or lower drug levels (called *drug-drug interactions*). Increasing drug levels can make side effects from each drug worse. If drug levels get too low, a drug can stop working, putting people at risk for drug resistance or not being cured.

Sovaldi should not be used with a medication called amiodarone because it can cause life-threatening heart problems.

Talk with your health care provider before starting or stopping medications, supplements, or herbal remedies.

There are other drugs that should be switched, stopped, or avoided while using Sovaldi. More information is available in Sovaldi's prescribing information (https://www.gilead.com/~/media/Files/pdfs/medicines/liver-disease/sovaldi/sovaldi_pi.pdf) and at: www.hep-druginteractions.org.

Sovaldi and HIV antiretrovirals: Sovaldi can be used with all HIV drugs ***except*** boosted Aptivus.

Storing Sovaldi: Keep Sovaldi below room temperature (86°F).

Sovaldi in people with kidney disease: Sovaldi can be used in people with mild or moderate kidney damage. People with severe kidney disease (eGFR<30 mL/min/1.73 m^2) and people on dialysis should consult a specialist.

Sovaldi in people with cirrhosis: HCV treatment guidelines recommend that people with serious liver damage (Child-Pugh Class B or C) be treated by a specialist. In clinical trials, Sovaldi and RBV have been used in people with Child-Pugh Class B or Class C cirrhosis or liver cancer.

Sovaldi during pregnancy, nursing, and in children: It is not known whether Sovaldi causes harm to unborn babies. If you are pregnant or planning pregnancy, talk with your health care provider about the risks and benefits of HCV treatment. It is not known whether Sovaldi passes into breast milk.

RBV causes birth defects and miscarriage. RBV should not be used by pregnant women or by male partners of pregnant women. RBV stays in a person's body for months, so women and their male partners should avoid pregnancy until six months ***after*** stopping RBV (for more information, see TAG's ribavirin fact sheet).

Sovaldi and RBV are under study in children (ages 3 to 17) with HCV genotypes 2 and 3. Harvoni (Sovaldi and another drug in one pill) is under study in children (ages 3 to 18).

Access to Sovaldi may be restricted by public and private payers. The criteria differ depending on the type of coverage and the state it is issued in. Support Path is Gilead's patient assistance program for Sovaldi. People with private insurance may be eligible for assistance with copayments. Uninsured people may be eligible for medication at no charge. Information about Support Path is available by phone at 1.855.769.7284, Monday through Friday between 9:00 a.m. and 8:00 p.m. (Eastern Time), or online at: http://www.gilead.com/responsibility/us-patient-access/support%20path%20for%20sovaldi%20and%20harvoni.

This fact sheet is current as of November 2015. Always check for updated information.

The goal of hepatitis C virus (HCV) treatment is a cure (when there is no hepatitis C virus in a person's bloodstream at least 12 weeks after treatment is finished).

What is Olysio? Olysio (simeprevir) is an HCV-fighting drug. It must be used with other drugs to treat hepatitis C. In the United States, Olysio is approved for people with hepatitis C genotype 1 who are over 18 years old.

How is Olysio used? Olysio is taken once daily, with food, for 12 or 24 weeks. The type and length of treatment depends on HCV treatment history, whether a person has cirrhosis, and the other HCV drugs used with Olysio.

Hepatitis C treatment is changing quickly. Although Olysio was approved for use with pegylated interferon (PEG-IFN) and ribavirin (RBV), it is being studied and used with other drugs in interferon-free combinations.

U.S. HCV treatment guidelines list Olysio and PEG-IFN, or Olysio and Sovaldi, with or without RBV, as alternative treatments for genotype 4 in people being treated for the first time.

Olysio: Treatment Length and Cure Rates from Clinical Trials and Real-World Settings*

Genotype 1, never treated for HCV, no cirrhosis	+ Cirrhosis
Olysio + Sovaldi (with or without RBV), 12 weeks: **95%** (in a small trial; real-world: 88% to 92%)	Olysio + Sovaldi (with or without RBV), 24 weeks: **100%** (real-world: 75% to 87%)
Genotype 1, treatment-experienced, no cirrhosis	**+ Cirrhosis**
Olysio + Sovaldi (with or without RBV), 12 weeks: **95%** (real-world: 81% to 87%)	Olysio + Sovaldi (with or without RBV), 24 weeks: **95%** (real-world: 76% to 79%)

*Cure rates in clinical trials are higher than in real life since the people in them are usually healthier and get extra monitoring and support. These results came from a small trial (fewer than 200 people); Olysio and Sovaldi are being studied in larger trials.

The most important thing a person can do to be cured is not to miss taking doses of HCV treatment—called *adherence*. Adherence lowers the risk for drug resistance.

What is drug resistance? Each day, HCV makes billions of copies of itself. Some of these copies are not the same as the original virus. They may have changes that can stop hepatitis C drugs from working (called *drug resistance*). If people miss doses of their treatment, the virus gets a chance to reproduce—and some of these copies can be resistant to HCV treatment.

Some people have drug resistance even though they have never been on hepatitis C treatment—but many can be cured anyway.

Most people who are not cured have resistance to one or more of the HCV drugs they've taken. Sometimes, resistance disappears within months. Resistance may pop back up if hepatitis C is re-treated with the same drug—or another drug from the same family. No one is sure how long HCV drug resistance lasts, or whether it will make it harder to re-treat hepatitis C.

Olysio and age, gender, and race/ethnicity: In real-world settings, cure rates did not differ by age (over 65 vs. under 65) in people treated with Olysio and Sovaldi (with or without RBV). Real-world cure rates were slightly higher in women than men. There is not much information from clinical trials of Olysio and Sovaldi by race or ethnicity because most people in the trials were white. In real-world reports, there was no difference in cure rates between black people and nonblack people. Drug levels of Olysio are higher in people of Asian ancestry; this may worsen their side effects.

Side effects from Olysio: Olysio can cause photosensitivity (severe sunburn, blistering). Limit exposure to sunlight, tanning beds, and sunlamps while using Olysio, and wear a hat, sunglasses, sunscreen, and protective clothing. If sunburn or rash occur, consult your health care provider immediately. In a clinical trial of Olysio and Sovaldi, the most common side effects were fatigue, headache, nausea, dizziness, diarrhea, insomnia, rash, and sensitivity to light. **Olysio can cause rash**, especially during the first four weeks of treatment. Consult your health care provider immediately if you have mouth sores or red and swollen eyes.

Does Olysio work for HIV-positive people? With PEG-IFN and RBV, Olysio was just as effective for people with HIV. There are no clinical trials of Olysio and Sovaldi (with or without RBV) in HIV/HCV, but cure rates have been the same among coinfected people treated in real-world settings.

Olysio can be used with these HIV drugs: Isentress (raltegravir), Selzentry (maraviroc), Fuzeon (enfuvirtide), Edurant (rilpivirine), Epivir (lamivudine), Ziagen (abacavir), Viread (tenofovir), Emtriva (emtricitabine), and Truvada (emtricitabine and tenofovir disoproxil fumarate).

Olysio and other medications: drug-drug interactions: Olysio should not be used with certain drugs. Combining medications can increase or lower drug levels (called *drug-drug interactions*). Increasing drug levels can make side effects from each drug worse. If drug levels get too low, a drug can stop working, putting people at risk for drug resistance or not being cured. **Talk with your health care provider about starting or stopping any medications, supplements, or herbal remedies.**

Some drugs should be switched, stopped, or avoided while using Olysio. More information is available in Olysio's prescribing information (https://www.olysio.com/shared/product/olysio/prescribing-information.pdf) and at: www.hep-druginteractions.org.

Storing Olysio: Store Olysio at room temperature (under 86°F). Keep Olysio in the same bottle it came in to protect it from light.

Olysio in people with kidney disease: Olysio can be used by people with mild or moderate kidney disease. People with severe kidney disease should consult with a specialist before using Olysio. It has not been studied in people on dialysis.

Olysio in people with cirrhosis: Hepatitis C treatment guidelines recommend that people with serious liver damage (Child-Pugh Class B or C cirrhosis) be treated by a specialist. Olysio is ***not recommended*** for people with Child-Pugh Class C cirrhosis.

Olysio during pregnancy, nursing, and in children: In animal studies, high doses of Olysio caused birth defects. Since it is not known whether Olysio will harm unborn babies, it should be used during pregnancy only if the potential benefits of HCV treatment outweigh the risks.

In animal studies, Olysio was found in breast milk—and it harmed breast-fed baby rats. It is not known whether Olysio passes into human breast milk, but nursing mothers should decide whether to stop breast-feeding or discontinue treatment with Olysio to avoid potential risk to their infants.

RBV causes birth defects and miscarriage. RBV should not be used by pregnant women or by male partners of pregnant women. RBV stays in a person's body for months, so women and their male partners should avoid pregnancy until six months ***after*** stopping it. Using two forms of birth control to prevent pregnancy while taking RBV—and for six months afterward—is recommended (for more information, see TAG's ribavirin fact sheet).

It is not clear whether RBV passes into breast milk. Nursing is not recommended while taking RBV.

Olysio has not been studied in children, and it is not approved for people under 18 years old.

Access to Olysio may be restricted by public and private payers. The criteria differ depending on the type of coverage and the state it is issued in. People with private insurance may be eligible for assistance with copayments. Uninsured people may be eligible for medication at no charge.

Janssen's patient assistance program is called Olysio Support. Information is available by phone, at 1.855.565.9746, Monday through Friday between 8:00 a.m. and 8:00 p.m. (Eastern Time), or online at: http://www.janssenprescriptionassistance.com/olysio-cost-assistance.

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The goal of hepatitis C virus (HCV) treatment is a cure (when there is no HCV in a person's bloodstream at least 12 weeks after treatment is finished).

What is Viekira Pak? Viekira Pak is a combination of hepatitis C virus–fighting drugs (paritaprevir/ritonavir/ombitasvir and dasabuvir) that block different steps of the virus life cycle. In the United States, Viekira Pak is approved for people with hepatitis C genotype 1 who are over 18 years old.

What is Technivie? Technivie is a combination of paritaprevir/ritonavir and ombitasvir. Technivie is approved for people over 18 years of age who have hepatitis C genotype 4 without cirrhosis.

How is Viekira Pak used? Viekira Pak is taken twice daily, with food, for 12 or 24 weeks. Viekira Pak comes in a box of 28 daily-dose packs (each has two pink tablets and two beige tablets). Both pink tablets are taken in the morning. One beige tablet is taken in the morning and one in the evening. Some people will need to take another drug, called ribavirin (RBV), twice daily with Viekira Pak.

How is Technivie used? Technivie is taken once daily, with food, for 12 weeks. Technivie comes in a box of 28 daily-dose packs with two pink tablets. Both pink tablets are taken in the morning. It should be used with another drug, called ribavirin (RBV), which is taken twice daily. Using Technivie by itself can be considered for people who cannot take RBV if they are being treated for the first time.

It is important to make sure that you have gotten the right treatment (with or without RBV) for the recommended length of time (12 or 24 weeks).

Viekira Pak and Technivie with Cure Rates*

Genotype 1a (including mixed or unknown subtypes), never treated or treatment-experienced, no cirrhosis	+ Cirrhosis
Viekira Pak + RBV, 12 weeks: **94%** to **97%**	Viekira Pak + RBV, 24 weeks: **95%** Viekira Pak + RBV, 12 weeks: **89%** (consider 12 weeks of treatment according to HCV treatment history)
Genotype 1b, never treated or treatment-experienced, no cirrhosis	**+ Cirrhosis**
Viekira Pak, 12 weeks: **100%**	Viekira Pak + RBV, 12 weeks: **99%**
Genotype 4, never treated, no cirrhosis	**+ Cirrhosis**
Technivie + RBV, 12 weeks: **100%** (**90.9%** without RBV)	N/A
Genotype 4, treatment-experienced, no cirrhosis	**+ Cirrhosis**
Technivie + RBV, 12 weeks: **100%**	N/A

*Cure rates in clinical trials are higher than in real life since the people in them are usually healthier and get extra monitoring and support.

The most important thing a person can do to be cured is not to miss taking doses of HCV treatment—called ***adherence***. Adherence lowers the risk for drug resistance.

What is drug resistance? Each day, HCV makes billions of copies of itself. Some of these copies are not the same as the original virus. They may have changes (called ***mutations***) that can stop hepatitis C drugs from working. If people miss doses of their treatment, the virus gets a chance to reproduce—and some of these copies can be resistant to HCV treatment. Some people have drug resistance even though they have never been on hepatitis C treatment—but many can be cured anyway.

Most people who are not cured have resistance to one or more of the HCV drugs they've taken. Resistance to certain hepatitis C drugs can disappear within months. But resistance to other drugs can last for years and might prevent re-treatment from working.

Viekira Pak or Technivie and age, gender, and race/ethnicity: In clinical trials, cure rates did not differ by age (over 65 vs. under 65). Cure rates were the same for women and men. There is not much information about how well Viekira Pak or Technivie work by race or ethnicity because most people in the trials were white. But researchers noticed two things: adding RBV to Viekira Pak increased cure rates for African Americans with HCV genotype 1a (100% vs. 84%), and people with a common genetic factor among African Americans (called the IL28B TT genotype) were less likely to be cured by Viekira Pak (see TAG's Hepatitis C and the IL28B Gene fact sheet).

Side effects from Viekira Pak and Technivie: Talk with your health care provider about possible side effects and how they will be managed. In clinical trials, the most common side effects from Viekira Pak or Technivie were nausea, itching, and insomnia. People taking RBV also experienced fatigue, weakness, rash, and other skin reactions (see TAG's RBV fact sheet for more information). Most of these side effects were mild.

Liver enzyme levels may increase while taking Viekira Pak or Technivie. Your health care provider should check your liver with blood tests during the first four weeks of treatment—and afterward as needed.

Do Viekira Pak and Technivie work for HIV-positive people? Yes, but Viekira Pak or Technivie should not be used by coinfected people unless they are also being treated for HIV. This is because one of the drugs in Viekira Pak and Technivie can cause resistance to some HIV drugs. In a clinical trial of 63 people with HIV and hepatitis C genotype 1, 93.5% were cured after 12 weeks of Viekira Pak plus RBV. Technivie has not been studied in people coinfected with HIV and hepatitis C genotype 4.

Viekira Pak or Technivie can be used with these HIV drugs: Isentress or Reyataz (300 mg), which should be taken in the morning, ***without ritonavir (Norvir)***, plus Truvada or Viread with Epivir or Emtriva.

Viekira Pak or Technivie and other medications: Viekira Pak or Technivie should not be used with certain drugs. Combining medications can increase or lower drug levels (called *drug-drug interactions*). Increasing drug levels can make side effects from each drug worse. If drug levels get too low, a drug can stop working, putting a person at risk for drug resistance or not being cured. **Talk with your health care provider about starting or stopping any medications, supplements, or herbal remedies.**

Some drugs should be switched, stopped, or avoided while using Viekira Pak or Technivie. More information is available in the prescribing information for Viekira Pak and Technivie (http://www.rxabbvie.com/pdf/viekirapak_pi.pdf and http://www.rxabbvie.com/htm/technivie/technivie_pi.htm) and at: www.hep-druginteractions.org.

Viekira Pak or Technivie and hormonal contraception (birth control): Viekira Pak and Technivie cannot be used with medications containing ethinyl estradiol (women can use progestin-only birth control). Medications containing ethinyl estradiol can be restarted two weeks after stopping Viekira Pak or Technivie.

Viekira Pak or Technivie during pregnancy, nursing, and in children: It is not known whether Viekira Pak or Technivie cause harm to unborn babies. If you are pregnant or planning pregnancy, talk with your health care provider about the risks and benefits of HCV treatment. It is not known whether Viekira Pak or Technivie pass into breast milk.

Viekira Pak and Technivie have not been studied in children and are not approved for people under 18 years old.

Ribavirin causes birth defects and miscarriage. Ribavirin should not be used by pregnant women or by male partners of pregnant women. Ribavirin stays in a person's body for months. Women and their male partners should avoid pregnancy for six months ***after*** they have stopped taking ribavirin. Using two forms of birth control to prevent pregnancy while taking ribavirin—and for six months afterward—is recommended. Nursing during treatment with ribavirin is not recommended. There is a ribavirin pregnancy registry at: http://www.ribavirinpregnancyregistry.com.

Storing Viekira Pak: Keep Viekira Pak or Technivie at room temperature (below 86°F).

Viekira Pak or Technivie in people with kidney disease: Viekira Pak or Technivie can be used by people with mild or moderate kidney disease. People with severe kidney disease should consult with a specialist before using Viekira Pak or Technivie. They have not been studied in people on dialysis.

Viekira Pak or Technivie in people with cirrhosis: Hepatitis C treatment guidelines recommend that people with serious liver damage (Child-Pugh Class B or C cirrhosis) be treated by a specialist. Technivie has not been studied in people with HCV genotype 4 and cirrhosis. Viekira Pak and Technivie should ***not*** be used in people with Child-Pugh Class B or Class C cirrhosis.

Access to Viekira Pak and Technivie may be restricted by public and private payers. The criteria differ by type of coverage and the state it is issued in. ProCeed is AbbVie's Viekira Pak patient assistance program. ProCeed may help people with private insurance with copayments. Uninsured people may be eligible for free medication through proCeed.

Information about proCeed is available by phone at 1.844.2PROCEED (1.844.277.6233), seven days a week between 7:00 a.m. and midnight (Eastern Time), or online at: https://www.viekira.com/proceed-support/proceed-benefit.

Information about the Technivie patient assistance program is also available by phone at 1.844.2PROCEED (1.844.277.6233), seven days a week between 7:00 a.m. and midnight (Eastern Time), or online at: www.Technivie.com.

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HARVONI

TAG
Treatment Action Group

The goal of hepatitis C virus (HCV) treatment is a cure (when there is no hepatitis C virus in a person's bloodstream at least 12 weeks after treatment is finished).

What is Harvoni? Harvoni is two HCV-fighting drugs (sofosbuvir and ledipasvir) in one pill. In the United States, Harvoni is approved for HIV-negative and HIV-positive people with hepatitis C genotypes 1, 4, 5, and 6 who are over 18 years old.

How is Harvoni used? Harvoni is taken once daily, with or without food, for 8 to 24 weeks. Treatment length depends on HCV treatment history, whether a person has cirrhosis, and the amount of hepatitis C virus in a person's bloodstream (called *HCV RNA* or *viral load*).

FDA Recommended Treatment Length and Cure Rates in Clinical Trials*

Genotype 1, never treated for HCV, no cirrhosis	+ Cirrhosis
12 weeks: **96%** to **99%** (if HCV RNA is less than 6 million copies IU/mL, consider 8 weeks) 8 weeks: **94%** (97% if HCV RNA is less than 6 million copies IU/mL)	12 weeks: **94%**
Genotype 1, treatment-experienced, no cirrhosis	**+ Cirrhosis**
12 weeks: **95%**	24 weeks: **100%** (if ribavirin is added, consider shortening treatment to 12 weeks)
Genotype 4, 5, and 6, never treated or treatment-experienced, with or without cirrhosis	
12 weeks. **Genotype 4: 93%; Genotype 5: 93%; Genotype 6: 96%**	

*Cure rates in clinical trials are higher than in real life since the people in them are usually healthier and get extra monitoring and support.

The most important thing a person can do to be cured is not to miss taking doses of HCV treatment—this is called *adherence*. Adherence lowers the risk for drug resistance.

What is drug resistance? Each day, HCV makes billions of copies of itself. Some of these copies are not exactly the same as the original virus. They may have changes (called *mutations*) that can stop hepatitis C drugs from working. If people miss doses of their treatment, HCV gets a chance to reproduce—and some of the copies it makes may not respond to HCV treatment.

Some people have drug resistance even though they have never been on hepatitis C treatment—but many can be cured anyway.

Most people who are not cured have resistance to one or more of the HCV drugs they've taken. Resistance to certain hepatitis C drugs can disappear within months. But resistance to certain drugs, including Harvoni, can last for years and may limit re-treatment options.

Harvoni and age, gender, and race/ethnicity: In clinical trials, cure rates did not differ by age (over 65 vs. under 65). Cure rates have been the same for women and men. There is not much information about how well Harvoni works by race or ethnicity because most of the people in the trials were white. With HCV alone, black (99%, or 89/90) versus nonblack (96%, or 431/448) people were just as likely to be cured by 12 weeks of Harvoni. In ION-4, a trial in HIV/HCV coinfection, the overall cure rate was higher (96%, or 321/335) than among black participants (90%, or 105/115).

Side effects from Harvoni: Talk with your health care provider about possible side effects and how they will be managed. In clinical trials of Harvoni, the most common side effects were fatigue, headache, nausea, diarrhea, and insomnia; usually, these were mild.

Does Harvoni work for HIV-positive people? Yes. In clinical trial of 335 HIV/HCV-coinfected people, 321 (96%) were cured after 12 weeks of Harvoni. Harvoni cannot be used with certain HIV drugs (see Harvoni and other medications, below).

Harvoni and other medications: Harvoni should not be used with certain drugs. Combining medications can increase or lower drug levels (called *drug-drug interactions*). Increasing drug levels can make side effects from each drug worse. If drug levels get too low, a drug can stop working, putting people at risk for drug resistance or not being cured.

Harvoni should not be used with a medication called amiodarone because sofosbuvir can cause life-threatening heart problems.

Talk with your health care provider before starting or stopping any medications, supplements, or herbal remedies.

Some drugs should be switched, stopped or avoided while using Harvoni. More information is available in Harvoni's prescribing information (http://www.accessdata.fda.gov/drugsatfda_docs/label/2014/205834s000lbl.pdf) and at: www.hep-druginteractions.org.

Harvoni and HIV Antiretrovirals

HIV Integrase Inhibitors	
Stribild (elvitegravir/cobicistat/emtricitabine/tenofovir DF)	Do not use Stribild with Harvoni
HIV Non-Nucleoside Reverse Transcriptase Inhibitors	
Atripla (efavirenz/emtricitabine/tenofovir DF)	Harvoni can increase tenofovir concentration; renal monitoring for tenofovir-associated adverse events is recommended; efavirenz may lower the level of ledipasvir—one of the drugs in Harvoni
HIV Protease Inhibitors	
Boosted **Aptivus** (ritonavir/tipranavir)	Do not use boosted Aptivus with Harvoni
Kaletra (ritonavir/lopinavir), boosted **Prezista** (ritonavir/darunavir), boosted **Reyataz** (ritonavir/atazanavir), with **Viread** (tenofovir DF) or **Truvada** (emtricitabine/tenofovir DF)	Consider a different HCV or HIV regimen to avoid increased tenofovir concentration; renal monitoring for tenofovir-associated adverse events is recommended

Storing Harvoni: Keep Harvoni at room temperature (below 86°F).

Harvoni in people with kidney disease: Harvoni can be used in people with mild or moderate kidney disease. It is not recommended for people with severe kidney disease (eGFR<30 mL/min/1.73 m^2) or for people on dialysis.

Harvoni in people with cirrhosis: HCV treatment guidelines recommend that people with serious liver damage (Child-Pugh Class B or C) be treated by a specialist. In clinical trials, people with Child-Pugh Class B or C cirrhosis have been treated with Harvoni and ribavirin.

Harvoni during pregnancy, nursing, and in children: It is not known whether Harvoni causes harm to unborn babies. If you are pregnant or planning pregnancy, talk with your health care provider about the risks and benefits of HCV treatment. It is not known whether Harvoni passes into breast milk. Harvoni is under study in children (ages 3 to 18).

Access to Harvoni may be restricted by public and private payers. The criteria differ depending on the type of coverage and the state it is issued in. Support Path is Gilead's patient assistance program for Harvoni. People with private insurance may be eligible for assistance with copayments. Uninsured people may be eligible for medication at no charge. Information about Support Path is available online at: http://www.gilead.com/responsibility/us-patient-access/support%20path%20for%20sovaldi%20and%20harvoni. Information about Support Path is also available by phone at 1.855.769.7284, Monday through Friday between 9:00 a.m. and 8:00 p.m. (Eastern Time), or online at: https://www.harvoni.com/support.

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The goal of hepatitis C virus (HCV) treatment is a cure (when there is no HCV in a person's bloodstream at least 12 weeks after treatment is finished).

What is Daklinza? Daklinza (daclatasvir) is an HCV-fighting drug that blocks different steps of the virus life cycle. In the United States, Daklinza is approved for people over 18 years old who have HCV genotype 3 (although it has been used in other genotypes).

How is Daklinza used? Daklinza is taken once daily with another drug, Sovaldi (also once daily), with or without food, for 12 weeks. Daklinza and Sovaldi have also been used to treat HCV genotypes 1, 2, and 4 (including in people with HIV/HCV) and before and after liver transplantation.

People with cirrhosis may need longer treatment with Daklinza and Sovaldi, or a third drug called ribavirin (RBV), which is taken twice daily with food.

Daklinza is FDA-approved for use in genotype 3. Treatment guidelines from the American Association for the Study of Liver Diseases (AASLD) and the Infectious Diseases Society of America (IDSA) include recommendations for Daklinza and Sovaldi.

Daklinza: Recommendations from the FDA and the AASLD/IDSA, and Cure Rates*

Genotype 1, never treated for HCV, no cirrhosis	+ Cirrhosis
AASLD/IDSA: Daklinza + Sovaldi, 12 weeks. HCV: **100%;** HIV/HCV: G1a: **96.7%**; G1b: **100%**	**AASLD/IDSA:** Daklinza + Sovaldi, ±RBV, 24 weeks. HIV/HCV: G1a: **97%**; G1b: **100%**
Genotype 2, never treated for HCV, no cirrhosis	**+ Cirrhosis**
AASLD/IDSA: Daklinza + Sovaldi, 12 weeks. HIV/HCV: **100%**** (for people who cannot tolerate RBV)	**AASLD/IDSA:** Consider 24 weeks of Daklinza + Sovaldi. **No data** (for people who cannot tolerate RBV)
Genotype 2, treatment-experienced (with Sovaldi + RBV), with or without cirrhosis	
AASLD/IDSA: Individualize treatment decisions; consider Daklinza + Sovaldi + RBV for 24 weeks (especially for people with cirrhosis). HIV/HCV: **100%****	
Genotype 3, never treated for HCV, no cirrhosis	**+ Cirrhosis**
AASLD/IDSA: Daklinza + Sovaldi, 12 weeks. HCV: **98%**; HIV/HCV: **100%****	**AASLD/IDSA:** Daklinza + Sovaldi, ±RBV, 24 weeks. HCV: **58%**
FDA: Daklinza + Sovaldi, 12 weeks	**FDA:** Daklinza + Sovaldi (ideal treatment length has not been established)
Genotype 3, treatment-experienced, no cirrhosis	**+ Cirrhosis**
AASLD/IDSA & FDA: Daklinza + Sovaldi, 12 weeks. HCV: **92%**; HIV/HCV: **100%****	**AASLD/IDSA:** Daklinza + Sovaldi, + RBV, 24 weeks. HCV: **69%;** HIV/HCV: **100%**** (for people who are ineligible for PEG-IFN)
FDA: Daklinza + Sovaldi, 12 weeks	**FDA:** Daklinza + Sovaldi (ideal treatment length has not been established)

*Cure rates in clinical trials are higher than in real life since the people in them are usually healthier and get extra monitoring and support.
**Studied in fewer than 10 people

The most important thing a person can do to be cured is to not miss taking doses of HCV treatment—this is called *adherence*. Adherence lowers the risk for drug resistance.

What is drug resistance? Each day, HCV makes billions of copies of itself. Some copies are not exactly the same as the original virus. They may have changes (called *mutations*) that can stop hepatitis C drugs from working. If people miss doses of their treatment, hepatitis C gets a chance to reproduce—and some of the copies it makes may be resistant to HCV treatment.

Some people have drug resistance even though they have never been on hepatitis C treatment—but many can be cured anyway. Certain mutations make Daklinza less effective, including one called Y93H.

Daklinza and Sovaldi in Genotype 3, with and without the Y93H Mutation

Cure Rate (12 weeks of Daklinza + Sovaldi)	With Y93H	Without Y93H
Overall	54%	92%
No cirrhosis	67%	98%
Cirrhosis	25%	68%

Most people who are not cured by HCV treatment have resistance to one or more of the drugs they've taken. Resistance to certain hepatitis C drugs can disappear within months. But resistance to certain drugs, including Daklinza, can last for years—and might limit re-treatment options.

Daklinza and age, gender, and race/ethnicity: In clinical trials, cure rates did not differ by age (over 65 vs. under 65). Cure rates have been the same for women and men. In ALLY-2, a trial of Daklinza and Sovaldi in people with HIV/HCV, the overall cure rate was the same regardless of race/ethnicity. Information about how well Daklinza works by race or ethnicity is limited since most people in the clinical trials were white.

Side effects from Daklinza: **Talk with your health care provider about possible side effects and how they will be managed.** In clinical trials of Daklinza and Sovaldi, the most common side effects were fatigue and headache; usually, these were mild.

Does Daklinza work for HIV-positive people? Yes. In ALLY-2, a clinical trial in 153 HIV/HCV-coinfected people, 149 (97%) were cured after 12 weeks of Daklinza and Sovaldi.

Daklinza and other medications: drug-drug interactions: Daklinza should not be used with certain drugs. Combining medications can increase or lower drug levels (called *drug-drug interactions*). Increasing drug levels can make side effects from each drug worse. If drug levels get too low, a drug can stop working, putting people at risk for drug resistance or not being cured.

Talk with your health care provider before starting or stopping any medications, supplements, or herbal remedies.

Some drugs should be switched, stopped, or avoided while using Daklinza.

Sovaldi—which is used with Daklinza—should not be used with a medication called amiodarone because it can cause life-threatening heart problems.

More information is available in Daklinza's prescribing information (http://www.accessdata.fda.gov/drugsatfda_docs/label/2015/206843Orig1s000lbl.pdf) and at: www.hep-druginteractions.org.

Daklinza and HIV antiretrovirals: Daklinza can be used with most HIV drugs. A lower or higher dose of Daklinza may be needed when it is used with certain antiretrovirals.

HIV Integrase Inhibitors	
Stribild (elvitegravir/cobicistat/emtricitabine/tenofovir DF)	Lower Daklinza dose from 60 mg to 30 mg
HIV Non-Nucleoside Reverse Transcriptase Inhibitors	
Atripla (efavirenz/emtricitabine/tenofovir DF)	Increase Daklinza dose from 60 mg to 90 mg
Intelence (etravirine)	Do not use Daklinza with Intelence
Viramune (nevirapine)	Do not use Daklinza with Viramune
HIV Protease Inhibitors	
Boosted **Reyataz** (ritonavir/atazanavir)	Lower dose of Daklinza from 60 mg to 30 mg

Storing Daklinza: Keep Daklinza at room temperature (between 59°F and 86°F).

Daklinza in people with kidney disease: Daklinza can be used without dose adjustment in people with mild, moderate, or severe kidney disease.

Daklinza in people with cirrhosis: HCV treatment guidelines recommend that people with serious liver damage (Child-Pugh Class B or C) be treated by a specialist. Daklinza can be used in mild, moderate, or severe hepatic impairment without dose adjustment. In clinical trials, people with Child-Pugh Class B or Class C cirrhosis have been treated with Daklinza and Sovaldi, with or without RBV. Daklinza-based treatment is less effective for people with Child-Pugh Class C cirrhosis.

Daklinza and Sovaldi have also been used to treat people for hepatitis C after liver transplantation.

Daklinza during pregnancy, nursing, and in children: It is not known whether Daklinza causes harm to unborn babies. In animal studies of pregnant rats and rabbits, very high doses of Daklinza caused birth defects, miscarriage, and maternal death. No harm was seen at lower doses.

If you are pregnant or planning pregnancy, talk with your health care provider about the risks and benefits of HCV treatment. It is not known whether Daklinza passes into human breast milk (in animal studies using much higher doses, it was found in the breast milk of rats).

Daklinza has not been studied in children, and it is not approved for people under 18 years old.

Access to Daklinza may be restricted by public and private payers. The criteria differ depending on the type of coverage and the state it is issued in. Patient Support Connect is BMS's patient assistance program for Daklinza. People with private insurance may be eligible for assistance with copayments. Uninsured people may be eligible for medication at no charge. Information and enrollment forms are available online at: https://bmsdm.secure.force.com/patientsupportconnect/patient and http://www.bmspaf.org/documents/bmspaf-enrollment-form.pdf or by phone at 1.800.736.0003.

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RIBAVIRIN

The goal of hepatitis C virus (HCV) treatment is a cure (when there is no hepatitis C virus in a person's bloodstream at least 12 weeks after treatment is finished).

What is ribavirin? Ribavirin (RBV) is an HCV-fighting drug. RBV does not work by itself. Adding RBV to other drugs can increase the chance of being cured from HCV. In the United States, ribavirin is approved for children (3 to 18 years of age) and adults.

RBV is made by Merck (sold as Rebetol), Genentech (sold as Copegus), and Kadmon Pharmaceuticals (sold as Ribasphere).

How is ribavirin used? RBV is taken twice a day with food; the dose is based on weight.

Is there anyone who cannot use ribavirin? People with sickle cell disease or thalassemia cannot use RBV. People who have serious heart disease cannot use RBV since it increases the risk for heart attacks.

Ribavirin and pregnancy: RBV causes birth defects and miscarriage. RBV should not be used by pregnant women or by male partners of pregnant women. RBV stays in a person's body for months, so women and their male partners should avoid pregnancy until six months ***after*** stopping it. Using two forms of birth control to prevent pregnancy while taking RBV—and for six months afterward—is recommended. There is an RBV pregnancy registry at: http://www.ribavirinpregnancyregistry.com.

Ribavirin and nursing: It is not clear whether RBV passes into breast milk. Nursing is not recommended while taking RBV.

Side effects from RBV: Talk with your health care provider about possible side effects and how they will be managed. Some people develop ***anemia*** (low red blood cell count) from RBV, usually within the first few weeks of treatment. It is important to have blood tests before and during RBV treatment to check for anemia and other side effects. Anemia is usually treated by lowering RBV dose.

When RBV was used without interferon in clinical trials, side effects included: aching muscles, anxiety, back pain, colds, constipation, coughing, diarrhea, dizziness, fever, headaches, insomnia, irregular periods, irritability, itchy skin, nausea, night sweats, rash, stomach pain and swelling, stuffy nose, tiredness, vomiting, and weakness.

Ribavirin and bilirubin levels: *Bilirubin* is left over from the breakdown of red blood cells. RBV can increase the amount of bilirubin in the bloodstream. ***Jaundice*** (yellow skin and eyes), dark urine, and pale stool are common signs of increased bilirubin.

TAG
Treatment Action Group

RIBAVIRIN

Does ribavirin work for HIV-positive people? Yes. RBV can temporarily lower CD4 cell count (but not the percentage of CD4 cells)—even for people on HIV drugs. This usually returns to normal after finishing HCV treatment.

HIV-positive people should not use RBV with Retrovir, Videx, or Zerit. Using Reyataz and RBV may cause jaundice.

Ribavirin and other medications: RBV should not be used with certain drugs. Combining medications can increase or lower drug levels (called ***drug-drug interactions***). Increasing drug levels can worsen side effects. Decreasing drug levels may cause a drug to stop working; this can lead to drug resistance or treatment failure.

Talk with your health care provider about starting or stopping any new medications, supplements, or herbal remedies.

More information about drug-drug interactions is available in ribavirin's prescribing information (http://www.accessdata.fda.gov/drugsatfda_docs/label/2011/021511s023lbl.pdf or http://kadmon.com/files/ribasphere-tablets-pi.pdf or http://www.merck.com/product/usa/pi_circulars/r/rebetol/rebetol_pi.pdf) and at: www.hep-druginteractions.org.

Storing ribavirin: Keep RBV at room temperature (between 59°F and 86°F).

Ribavirin and age, gender, and race/ethnicity: RBV is always used with other drugs, so it is not known whether there are differences in how well it works by age, gender, or race/ethnicity. The risk for anemia from RBV is higher for people over 65 and women. There is no information on ribavirin side effects according to race/ethnicity.

Ribavirin and kidney disease: RBV is filtered out through the kidneys. People with moderate or severe kidney disease, and people on dialysis, are treated with lower RBV doses. People with severe kidney disease should consult with a specialist before using RBV.

Ribavirin and advanced liver disease: Hepatitis C treatment guidelines recommend that people with serious liver damage (Child-Pugh Class B or C cirrhosis) be treated by a specialist.

Access to ribavirin: Kadmon's Keys Program provides patient assistance. People with private insurance may be eligible for assistance with copayments. Uninsured people may be eligible for medication at no charge. Information about the Keys Program is available by phone, at 1.888.668.3393, Monday through Friday between 9:00 a.m. and 5:00 p.m. (Eastern Time), or online at: https://www.pparx.org/prescription_assistance_programs/kadmon_patient_assistance_program.

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