

YOUR GUIDE TO HEPATITIS

Hepatitis C Treatment

The goal of hepatitis C virus (HCV) treatment is to cure the virus, which can be done by using a combination of drugs.

The current standard-of-care involves taking ribavirin plus one of two newly approved therapies, Sovaldi (sofosbuvir) or Olysio (simeprevir), and in many cases pegylated interferon as well. The length of treatment, which can range from 12 to 48 weeks, depends on the person's HCV genotype (genetic structure of the virus), whether the person is eligible to take interferon and whether he or she is waiting for a liver transplant.

Many other hepatitis C drugs are in the late stages of development. These meds are called "direct-

acting antivirals," or DAAs, because they are designed specifically to attack the virus. As more DAAs become available, many people may be able to combine these highly effective medications without the need for either pegylated interferon or ribavirin, which is hopeful news because those two drugs, especially interferon, can cause serious side effects.

Here's more specific information about each type, or class, of approved HCV treatment along with drugs in the late stages of development:

Pegylated Interferon Alfa

Brand Name	Generic Name	Status	Pharmaceutical Company
PegIntron	peginterferon alfa-2b	Approved	Merck
Pegasys	peginterferon alfa-2a	Approved	Genentech

What are they?

Interferon is a protein made by the immune system, named because it interferes with viral reproduction. In addition, interferon signals the immune system to recognize and respond to microorganisms, including viral and bacterial infections. Infected cells release interferon to trigger the immune response. There are three types of interferon: alfa, beta and gamma. Interferon alfa is used to treat viral hepatitis and some types of cancer.

Nucleoside Analog

Brand Name	Generic Name	Status	Pharmaceutical Company
Copegus, Rebetol, Ribasphere	ribavirin	Approved	Genentech, Merck, Kadmon
and Moderiba			

What are they?

Although it is not effective against hepatitis C when used alone, ribavirin plays an important role in HCV combination treatment. Scientists have not determined exactly how it works. However, it is clear that combining ribavirin with pegylated interferon boosts cure rates and reduces the risk of relapse.

NS3/4A Protease Inhibitors (PIs)

Brand Name	Generic Name	Status	Pharmaceutical Company
Victrelis	boceprevir	Approved	Merck
Olysio	simeprevir (TMC435)	Approved	Janssen and Medivir AB
Sunvepra	asunaprevir (BMS-650032)	Phase III (not pursuing approval in U.S.)	Bristol-Myers Squibb
n/a	vaniprevir (MK-7009)	Phase III	Merck
n/a	paritaprevir (ABT-450)	Phase III	AbbVie
n/a	grazoprevir (MK-5172)	Phase III	Merck
Incivek	telaprevir	Discontinued as of 10/16/2014	Vertex

What are they?

Protease inhibitors (PIs) block a protein that plays a critical role in HCV replication: They bind to the viral protease, which is responsible for processing viral proteins. Olysio is used to treat HCV genotype 1 and is taken once a day. The first generation of HCV protease inhibitors, Incivek and Victrelis, are also only used to treat HCV genotype 1 but must be taken three times a day. Future protease inhibitors may be potentially effective against other HCV genotypes.

Nucleoside and Nucleotide NS5B Polymerase Inhibitors

Brand Name	Generic Name	Status	Pharmaceutical Company
Sovaldi	sofosbuvir (GS-7977)	Approved	Gilead Sciences
n/a	mericitabine (RG7128)	Phase III	Roche

What are they?

These drugs block the NS5B protein, which plays a role in the replication of HCV and is involved in creating copies of the viral RNA genome. Sovaldi is used to treat HCV genotypes 1, 2, 3 and 4 and is currently being researched as part of a once-a-day combination pill with the NS5A inhibitor ledipasvir for the treatment of genotype 1; Phase III studies have been very promising. If approved, the combination pill should be available by late 2014.

NS5A Inhibitors

Brand Name	Generic Name	Status	Pharmaceutical Company
Daklinza	daclatasvir (BMS-790052)	Phase III	Bristol-Myers Squibb
n/a	ledipasvir (GS-5885)	Phase III	Gilead Sciences
n/a	ombitasvir (ABT-267)	Phase III	AbbVie
n/a	GS-5816	Phase III	Gilead Sciences
n/a	elbasvir (MK-8742)	Phase III	Merck

What are they?

NS5A is an HCV protein, a part of the HCV replication complex (replicase), with multiple functions in the virus's life cycle. These inhibitors are currently being studied in combination with agents in other drug classes and show potential for use as a component of interferonand ribavirin-free regimens.

Non-Nucleoside NS5B Polymerase Inhibitors

Brand Name	Generic Name	Status	Pharmaceutical Company
Exviera	dasabuvir (ABT-333)	Phase III	AbbVie
n/a	beclabuvir (BMS-791325)	Phase III	Bristol-Myers Squibb
n/a	ABT-072	Phase II	AbbVie

What are they?

These drugs are active against NS5B but through a different mechanism than the nucleoside/nucleotide NS5B polymerase inhibitors described above.

Multi-Class Combination Drugs

Brand Name	Generic Name	Status	Pharmaceutical Company
Harvoni	sofosbuvir + ledipasvir (GS-7977 + GS-5885)	Approved	Gilead Sciences
Viekira Pak	(ombitasvir + paritaprevir + ritonavir) + dasabuvir	Approved	AbbVie
Viekirax	ombitasvir (ABT-267) + paritaprevir (ABT-450) + ritonavir	Phase III	AbbVie
n/a	asunaprevir + daclatasvir + BMS-791325	Phase III	Bristol-Myers Squibb
n/a	grazoprevir + elbasvir (MK-8742 + MK-5172)	Phase III	Merck

last revised 1/5/15