

HCV Medications

OVERVIEW

<u>Hepatitis C virus (HCV)</u> infection causes liver inflammation that can lead to liver problems, including cancer. People who have chronic HCV need medication to treat it. HCV drugs can help clear the virus from the body and ease symptoms.

Even if an HCV infection hasn't caused symptoms yet, it's still important to treat it. This is because drugs can also lower the risk of complications from HCV, such as dangerous liver problems.

HCV has different genetic variations (<u>genotypes</u>). The medication prescribed for HCV depends on the genotype a person has. Genotype 1 is the most common type in the U.S.

Here are the medications available to treat HCV, plus some helpful information about what to expect with their treatment. <u>Read more about U.S HCV therapy guidelines, including simplified treatment regimens that cover all genotypes.</u>

DIRECT ACTING ANTIVIRALS (DAAs)

Direct-acting antivirals (DAAs) are currently the <u>standard of care</u> for chronic HCV infection. These drugs work by attacking HCV directly, which means they're more targeted than older treatments such as interferons (see below). Additionally, they don't affect as many systems in the body as interferons, so they may not cause as many side effects. All DAAs are oral drugs.

Side effects of DAAs can include:

- <u>anemia</u>
- diarrhea
- <u>fatigue</u>
- $\circ \ \text{headaches}$
- ∘ nausea
- vomiting
- slow heartbeat

grazoprevir

Grazoprevir is an HCV protease inhibitor. Protease inhibitors work by stopping viruses from multiplying. Grazoprevir has good activity against a range of HCV genotypes, including some that are resistant to most currently used DAAs. It's only available in combination with elbasvir and sold as grazoprevir/elbasvir (Zepatier) [see below].

ledipasvir

Ledipasvir is another type of HCV protease inhibitor called an NS5A inhibitor. The action of these drugs isn't fully understood. They may work by stopping the virus from copying itself or may help prevent drug resistance (when a drug no longer works to treat a condition). Ledipasvir is only available in combination with sofusbuvir and sold as ledipasvir/sofosbuvir (Harvoni) [see below].

elbasvir

Elbasvir is another NS5A inhibitor. Elbasvir is available in combination with grazoprevir and sold as grazoprevir/elbasvir (Zepatier) [see below].

sofosbuvir (Sovaldi)

Sofosbuvir (Sovaldi) is a nucleotide analog NS5B polymerase inhibitor. It works by blocking a protein called NS5B, which HCV needs to replicate itself and survive. See Step 7 of the <u>HCV life cycle</u>. Sofosbuvir must be used in combination with other HCV medications. The combination of medications depends on the genotype.

Sofosbuvir is indicated for the treatment of:

- $\circ\,$ Adults with genotype 1, 2, 3 or 4 without cirrhosis or with compensated cirrhosis as a component of a combination DAA regimen
- $\circ\,$ Children 3 years of age and older with genotype 2 or 3 without cirrhosis or with compensated cirrhosis in combination with ribavirin

Recommended adult treatment regimen and duration:

Genotype	Adult Patient Population	Regimen and Duration
1 or 4	Treatment-naïve without cirrhosis or with compensated cirrhosis (Child-Pugh A)	sofosbuvir + peginterferon alfa + ribavirin 12 weeks
2	Treatment-naïve and treatment experienced without cirrhosis or with compensated cirrhosis (Child-Pugh A)	sofosbuvir + ribavirin 12 weeks
3	Treatment-naïve and treatment experienced without cirrhosis or with compensated cirrhosis (Child-Pugh A)	sofosbuvir + ribavirin 24 weeks

Recommended dosage in adults: One 400 mg tablet taken orally once daily with or without food.

Recommended dosage in children: The recommended dosage in children varies based on the child's weight. Your child's healthcare provider will determine the correct dosage. The most common side effects of sofosbuvir include:

- when taken with ribavirin: fatigue and headache
- $\circ\,$ when taken with ribavirin and peginterferon alfa: fatigue, headache, nausea, insomnia, and anemia

Because sofosbuvir is always taken in combination with ribavirin, which can cause serious birth defects, do not take sofosbuvir if you or your sexual partner is pregnant or wants to become pregnant. Do not become pregnant for 6 months after you or your partner stop taking sofosbuvir.

ledipasvir/sofosbuvir (Harvoni)

Harvoni, which contains ledipasvir and sofosbuvir, is used to treat several HCV genotypes. The FDA approved Harvoni in 2014.

Harvoni is indicated for the treatment of chronic HCV in adults and children 3 years of age and older:

- Genotype 1, 4, 5, or 6 infection without cirrhosis or with compensated cirrhosis
- Genotype 1 infection with decompensated cirrhosis, in combination with ribavirin
- $\circ\,$ Genotype 1 or 4 infection who are liver transplant recipients without cirrhosis or with compensated cirrhosis, in combination with ribavirin

Recommended treatment regimen and duration in people 3 years of age and older:

Genotype	Patient Population	Regimen and Duration
	Treatment-naïve without cirrhosis or with compensated cirrhosis (Child-Pugh A)	Harvoni 12 weeks
	Treatment-experienced without cirrhosis	Harvoni 12 weeks
1	Treatment-experienced with compensated cirrhosis (Child-Pugh A)	Harvoni 24 weeks
	Treatment-naïve and treatment experienced with decompensated cirrhosis (Child-Pugh B or C) $% \left({\left({\frac{{{\left({\frac{{{\left({\frac{{{\left({\frac{{{\left({\frac{{{\left({\frac{{{\left({\frac{{{\left({\frac{{{\left({\frac{{{\left({\frac{{{}}}}{{\left({\frac{{}}} \right)}}}}\right(r + ringation }} \right)} \\ {\left({\frac{{{\left({\frac{{{}}} \right)}}{ringation }} \right)} \right)} } \right)} } \right)$	Harvoni + ribavirin 12 weeks
1 or 4	Treatment-naïve and treatment experienced liver transplant recipients without cirrhosis, or with compensated cirrhosis (Child-Pugh A)	Harvoni + ribavirin 12 weeks
4, 5, or 6	Treatment-naı̈ve and treatment experienced without cirrhosis or with compensated cirrhosis (Child-Pugh A) $% \left(A^{\prime}\right) =0$	Harvoni 12 weeks

Recommended dosage in adults: One tablet (90 mg ledipasvir + 400 mg sofosbuvir) taken orally once daily with or without food.

Recommended dosage in children: The recommended dosage in children varies based on the child's weight. Your child's healthcare provider will determine the correct dosage.

The most common side effects of Harvoni are fatigue, headache, and weakness.

If used in combination with ribavirin: do not take Harvoni if you or your sexual partner is pregnant or wants to become pregnant. Do not become pregnant for 6 months after you or your partner stop taking Harvoni + ribavirin.

elbasvir/grazoprevir (Zepatier)

Zepatier, which contains elbasvir and grazoprevir, is used to treat HCV genotypes 1 and 4. The FDA approved

Zepatier in 2016.

Zepatier is indicated for the treatment of chronic HCV genotype 1 or 4 infection in adults. Zepatier is indicated for use with ribavirin in certain patient populations.

Recommended adult treatment regimen and duration:

Genotype	Adult Patient Population	Regimen and Duration
	Treatment-naïve or PegIFN/RBV experienced* without baseline NS5A polymorphisms [†]	Zepatier 12 weeks
1a	Treatment-naïve or PegIFN/RBV experienced* with baseline NS5A polymorphisms [†]	Zepatier + ribavirin 16 weeks
1b	Treatment-naïve or PegIFN/RBV experienced*	Zepatier 12 weeks
la or 1b	PegIFN/RBV/PI experienced [‡]	Zepatier + ribavirin 12 weeks
4	Treatment-naïve	Zepatier 12 weeks
	PegIFN/RBV experienced*	Zepatier + ribavirin 16 weeks

*Peginterferon alfa + ribavirin

†Polymorphisms at amino acid positions 28, 30, 31, or 93‡Peginterferon alfa + ribavirin + HCV NS3/4A protease inhibitor

Recommended dosage: One tablet (50 mg elbasvir + 100 mg grazoprevir) taken orally once daily with or without food.

The most common side effects of Zepatier include:

- $\,\circ\,$ when taken alone for 12 weeks: fatigue, headache, and nausea
- $\circ~$ when taken with ribavirin for 16 weeks: anemia and headache

If used in combination with ribavirin: do not take Zepatier if you or your sexual partner is pregnant or wants to become pregnant. Do not become pregnant for 6 months after you or your partner stop taking Zepatier + ribavirin.

sofosbuvir/velpatasvir (Epclusa)

Epclusa, which contains sofosbuvir and velpatasvir, is used to treat all 6 HCV genotypes. The FDA approved Epclusa in 2016. It can be used in combination with ribavirin in people with moderate to severe cirrhosis.

Epclusa is indicated for the treatment of adults and children 6 years of age and older or weighing at least 17 kg with chronic HCV genotype 1, 2, 3, 4, 5, or 6 infection:

- without cirrhosis or with compensated cirrhosis
- $\circ~$ with decompensated cirrhosis for use in combination with ribavirin

Recommended adult treatment regimen and duration:

Pati	ient Population	Regimen and Duration
	atment-naïve and treatment experienced, without cirrhosis and with compensated nosis (Child-Pugh A)	Epclusa 12 weeks
	atment-naïve and treatment experienced, with decompensated cirrhosis (Child- h B and C)	Epclusa + ribavirin 12 weeks

Recommended dosage in adults: One tablet (400 mg sofosbuvir + 100 mg velpatasvir) taken orally once daily with or without food.

Recommended dosage in children: The recommended dosage in children varies based on the child's weight. Your child's healthcare provider will determine the correct dosage.

The most common side effects of Epclusa include:

- \circ when taken alone for 12 weeks: headache and fatigue
- $\circ\,$ when taken with ribavirin for 12 weeks: fatigue, anemia, nausea, headache, insomnia, and diarrhea

If used in combination with ribavirin: do not take Epclusa if you or your sexual partner is pregnant or wants to become pregnant. Do not become pregnant for 6 months after you or your partner stop taking Epclusa + ribavirin.

sofosbuvir/velpatasvir/voxilaprevir (Vosevi)

Vosevi, which contains sofosbuvir, velpatasvir, and voxilaprevir, is used to treat all 6 HCV genotypes. The FDA approved Vosevi in 2017.

Vosevi is indicated for the treatment of adults with chronic HCV infection without cirrhosis or with compensated cirrhosis (Child-Pugh A) who have:

- $\circ\,$ Genotype 1, 2, 3, 4, 5, or 6 infection and have previously been treated with an HCV regimen containing an NS5A inhibitor
- $^{\circ}$ Genotype 1a or 3 infection and have previously been treated with an HCV regimen containing

sofosbuvir without an NS5A inhibitor

Recommended adult treatment regimen and duration:

Genotype	Patients Previously Treated with an HCV Regimen Containing:	Regimen and Duration
1, 2, 3, 4, 5, or 6	An NS5A inhibitor ^a	Vosevi 12 weeks
1a or 3	Sofosbuvir without an NS5A inhibitor ^b	Vosevi 12 weeks

a. Prior NS5A inhibitor experience includes daclatasvir, elbasvir, ledipasvir, ombitasvir, or velpatasvir
b. Prior treatment experience includes sofosbuvir with or without any of the following: peginterferon alfa/ribavirin, ribavirin, HCV NS3/4A protease inhibitor (boceprevir, simeprevir, or telaprevir)

Recommended dosage in adults: One tablet (400 mg sofosbuvir + 100 mg velpatasvir + 100 mg voxilaprevir) taken orally once daily with food.

The most common side effects of Vosevi are headache, fatigue, diarrhea, and nausea.

glecaprevir/pibrentasvir (Mavyret)

Mavyret, which contains glecaprevir and pibrentasvir, is used to treat all 6 HCV genotypes. The FDA approved Mavyret in 2017. Mavyret is the first treatment that can be administered for only 8 weeks in people without cirrhosis. Most of the other combination drugs must be administered for a minimum of 12 weeks.

Mavyret is indicated for the treatment of:

- Adults and children 12 years and older or weighing at least 45 kg with chronic HCV genotype 1, 2, 3, 4, 5 or 6 infection without cirrhosis or with compensated cirrhosis (Child-Pugh A)
- Adults and children 12 years and older or weighing at least 45 kg with HCV genotype 1 infection, who previously have been treated with a regimen containing an HCV NS5A inhibitor or an NS3/4A protease inhibitor, but not both.

Recommended treatment regimen and duration:

Genotype	Patient Population	Regimen and Duration
1, 2, 3, 4, 5, or 6	Treatment-naïve without cirrhosis or with compensated cirrhosis (Child-Pugh A)	Mavyret 8 weeks
1	Patients previously treated with an HCV regimen containing an NS5A inhibitor ¹ without prior treatment with an NS3/4A protease inhibitor	Mavyret 16 weeks
1	Patients previously treated with an HCV regimen containing an NS3/4A inhibitor ² without prior treatment with an NS5A inhibitor	Mavyret 12 weeks
	Prior treatment experience with regimens containing (peg) interferon, ribavirin, and/or sofosbuvir, but no prior treatment experience with an HCV NS3/4A or NS5A inhibitor	No cirrhosis: Mavyret 8 weeks
1, 2, 4, 5, or 6		Compensated cirrhosis (Child-Pugh A): Mavyret 12 weeks

1. Treated with prior regimens containing ledipasvir and sofosbuvir or daclatasvir with (peg) interferon and

ribavirin

2. Treated with prior regimens containing simeprevir and sofosbuvir, or simeprevir, boceprevir, or telaprevir with (peg) interferon and ribavirin

Recommended dosage in adults and children 12 years and older or weighing at least 45 kg: Three tablets (each tablet: 100 mg glecaprevir + 40 mg pibrentasvir) taken at the same time orally once daily with food.

The most common side effects of Mavyret are headache and fatigue.

INTERFERONS

Interferons played a role in the treatment of chronic HCV prior to the availability of DAAs. Interferons no longer recommended for the treatment of HCV they can cause a lot of side effects, and they're not as effective for treating chronic HCV infection.

Interferon is a protein that your body makes. It helps your immune system develop an immune response to viruses, including HCV. A common brand-name interferon is peginterferon alfa-2a (PegIFN, Pegasys). Interferons were part of combination treatments for genotype 1, but they could also be used for genotypes 2 and 3. The more common side effects of interferons include:

- \circ anxiety
- dry mouth
- excessive fatigue
- headache
- $\circ\,$ mood changes or depression
- weight loss
- worsening hepatitis symptoms

Other more serious side effects can happen over time. These side effects may include:

- autoimmune diseases (when your body attacks itself)
- reduced red blood cell levels (can lead to anemia)
- reduced white blood cell levels (can lead to infections)
- $\circ~$ high blood pressure (can lead to a stroke or heart attack)
- $\circ~$ reduced thyroid function
- $\circ\$ changes in vision
- liver disease
- lung disease
- inflammation of your bowel or pancreas
- allergic reaction
- slowed growth in children

DISCONTINUED MEDICATIONS

The following medications have been discontinued and are no longer used in HCV treatment regimens.

- boceprevir (Victrelis)
- daclatasvir (Daklinza)
- ombitasvir/paritaprevir/ritonavir (Technivie)
- ombitasvir/paritaprevir/ritonavir/dasabuvir (Viekira Pak)

- simeprevir (Olysio)
- telaprevir (Incivek)

TALK WITH YOUR HEALTHCARE PROVIDER

HCV infection can cause unpleasant symptoms and lead to serious health complications. Your treatment for the condition will depend on:

- your health
- $\circ\,$ the HCV genotype you have
- $\circ~$ other factors

Different types of drugs used to treat HCV work in different ways and can cause unique side effects. Ask your healthcare provider which medication might be a good fit for you. Together, you can find the most effective drug to treat your HCV infection with the fewest side effects.

MORE INFORMATION

Ribavirin

- Hepatitis C Online: Ribavirin (Copegus, Rebetol, Ribasphere)
- MedlinePlus: <u>Ribavirin</u>

sofosbuvir (Sovaldi)

- Download the full Prescribing Information
- Hepatitis C Online: Sofosbuvir (Sovaldi)

ledipasvir/sofosbuvir (Harvoni)

- Visit the Harvoni website
- Download the full Prescribing Information
- Hepatitis C Online: Ledipasvir-Sofosbuvir (Harvoni)

elbasvir/grazoprevir (Zepatier)

- Download the full Prescribing Information
- Download the Patient Information leaflet
- Hepatitis C Online: Elbasvir-Grazoprevir (Zepatier)

sofosbuvir/velpatasvir (Epclusa)

- Visit the Epclusa website
- Download the full Prescribing Information
- Read important safety information
- Hepatitis C Online: Sofosbuvir-Velpatasvir (Epclusa)

sofosbuvir/velpatasvir/voxilaprevir (Vosevi)

- Visit the <u>Vosevi website</u>
- Download the full <u>Prescribing Information</u>
- Read important safety information

• Hepatitis C Online: <u>Sofosbuvir-Velpatasvir-Voxilaprevir (Vosevi)</u>

glecaprevir/pibrentasvir (Mavyret)

- Visit the <u>Mavyret website</u>
- Download the full <u>Prescribing Information</u>
- Hepatitis C Online: <u>Glecaprevir-Pibrentasvir (Mavyret)</u>

Interferon

Hepatitis C Online: <u>Peginterferon alfa-2a (Pegasys)</u>

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