Hepatitis C Treatment
What do I use?

Bruce Burkett

Executive Director

Hep C Alliance

- Financial Disclosures
- I do receive unrestricted educational grants from Janssen, Genentech, Gilead, BMS, AbbVie, and Vertex

- History of Treatment
- Interferon mono therapy
- Schering-Plough, Amgen and Roche
- Interferon and Ribavirin
- Pegalyted Interferon and Ribavirin
- Peg/Riba Incivek (Telaprevir)
- Peg/Riba Victrelis (Boceprevir)

Infectious Disease Society of America Guidelines for treatment

Genotype	Recommended	Alternative	NOT Recommended
1	IFN eligible: SOF + PEG/RBV x 12 weeks	IFN eligible: SMV x 12 weeks + PEG/RBV x 24 weeks*	Monotherapy with PEG, RBV, or a DAA Do not treat decompensated cirrhosis with PEG or SMV
	IFN ineligible: SOF + SMV ± RBV x 12 weeks	IFN ineligible: SOF + RBV x 24 weeks	
2	SOF + RBV x 12 weeks	None	
3	SOF + RBV x 24 weeks	SOF + PEG/RBV x 12 weeks	
4	IFN eligible: SOF + PEG/RBV x 12 weeks	SMV x 12 weeks + PEG/RBV x 24-48 weeks	
	IFN ineligible: SOF + RBV x 24 weeks		
5 or 6	SOF + PEG/RBV x 12 weeks	PEG/RBV x 48 weeks	

Sofosbuvir

- **Approval Status**: FDA approved December 6, 2013
- **Indication for HCV Monoinfection and HCV-HIV Coinfection**
  - GT 1,4: Sofosbuvir + peginterferon + ribavirin (12 weeks)
  - GT 2: Sofosbuvir + ribavirin (12 weeks)
  - GT 3: Sofosbuvir + ribavirin (24 weeks)
- **Additional Indication for HCV Monoinfection**
  - GT 1 (interferon ineligible): Sofosbuvir + ribavirin (24 weeks)
  - HCC and awaiting transplant: Sofosbuvir + ribavirin (up to 48 weeks)
- **Class & Mechanism**
  - Nucleotide analog inhibitor of NS5B polymerase enzyme
- **Dosing:** 400 mg PO once daily with or without food
- **Adverse Effects (AE) attributable to Sofosbuvir**
  - Fatigue, headache
- **Wholesaler Acquisition Cost in United States**
  - 28 tablet bottle = $28,000; estimated 12-week cost = $84,000

Sofosbuvir + Ribavirin
Adverse Effects

Event	Sofosbuvir + RBV (n=256)	SOF + PEG + RBV (n=327)
Discontinuation due to adverse event	3 (1%)	5 (2%)
Fatigue	92 (36%)	192 (59%)
Headache	64 (25%)	118 (36%)
Nausea	46 (18%)	112 (34%)
Pruritus	19 (7%)	59 (18%)
Hemoglobin < 10 g/dl	23 (9%)	74 (23%)
Neutropenia	0	54 (17%)
Influenza-like illness	7 (3%)	51 (16%)
Depression	14 (5.5%)	31 (9.5%)
Insomnia	31 (12%)	81 (41%)

Source: Lawitz E, et al. N Engl J Med. 2013;368:1878-87.

Recommended regimen for treatment-naive patients with HCV genotype 1 who are eligible to receive IFN.
Daily sofosbuvir (400 mg) and weight-based RBV (1000 mg [<75 kg] to 1200 mg [≥75 kg]) plus weekly PEG for 12 weeks, regardless of subtype.

Sofosbuvir
Drug-Drug Interactions

Sofosbuvir not recommended for coadministration with*:

- **Anticonvulsants**
  - Carbamazepine
  - Oxcarbazepine
  - Phenobarbital
  - Phenytoin
- **Antimycobacterials**
  - Rifabutin
  - Rifampin
  - Rifapentine
- **Herbal Supplements**
  - St. John's wort
- **HIV Protease Inhibitors**
  - Tipranavir/ritonavir

*Not recommended because of potential marked decrease in sofosbuvir levels

Source: Sofosbuvir (*Sovaldi*) Prescribing Information. Gilead Sciences.

Recommended regimen for treatment-naive patients with HCV genotype 1 who are not eligible to receive IFN.

Daily sofosbuvir (400 mg) plus simeprevir (150 mg), with or without weight-based RBV (1000 mg [<75 kg] to 1200 mg [≥75 kg] for 12 weeks

Who is Intolerance to IFN?

Autoimmune hepatitis and other autoimmune disorders

Hypersensitivity to PEG or any of its components

Decompensated hepatic disease

History of depression, or clinical features consistent with depression

A baseline neutrophil count below 1500/µL, a baseline platelet count below 90,000/µL or baseline hemoglobin below 10 g/dL

A history of preexisting cardiac disease

Alternative regimens for treatment-naive patients with HCV genotype 1 who are not eligible to receive IFN.

Daily sofosbuvir (400 mg) and weight-based RBV (1000 mg [<75 kg] to 1200 mg [>75 kg]) for 24 weeks regardless of subtype; however, this regimen may be less effective than daily sofosbuvir (400 mg) plus simeprevir (150 mg), particularly among patients with cirrhosis.

Alternative regimens for treatment-naive patients with HCV genotype 1 who are eligible to receive IFN.

Daily simeprevir (150 mg) for 12 weeks and weight-based RBV (1000 mg [<75 kg] to 1200 mg [>75 kg]) plus weekly PEG for 24 weeks is an acceptable regimen for IFN-eligible persons with either HCV genotype 1b or

HCV genotype 1a infection in whom the Q80K polymorphism is not detected prior to treatment.

Alternative regimen for PEG/RBV (without an HCV protease inhibitor) nonresponder patients with HCV genotype 1 who are eligible to receive IFN.
Daily simeprevir (150 mg) for 12 weeks plus weight-based RBV (1000 mg [<75 kg] to 1200 mg [>75 kg]) and weekly PEG for 48 weeks is an alternative for **IFN-eligible** persons. (All patients with cirrhosis who are receiving simeprevir should have well compensated liver disease.)

Recommended regimen for genotype 2 PEG/RBV nonresponders.
Daily sofosbuvir (400 mg) and weight-based RBV (1000 mg [<75 kg] to 1200 mg [>75 kg]) for 12 weeks.
(Patients with cirrhosis may benefit by extension of treatment to 16 weeks.)

Recommended regimen for HCV genotype 3 PEG/RBV nonresponders.
Daily sofosbuvir (400 mg) and weight-based RBV (1000 mg [<75 kg] to 1200 mg [>75 kg]) for 24 infection.

Alternate regimen for HCV genotype 3 PEG/RBV nonresponder patients who are eligible to receive IFN.
Retreatment with daily sofosbuvir (400 mg) and weight-based RBV (1000 mg [<75 kg] to 1200 mg [>75 kg]) plus weekly PEG for 12 weeks is an alternative for IFN-eligible persons

Recommended regimen for HCV genotype 4, PEG/RBV nonresponder patients.
Daily sofosbuvir (400 mg) for 12 weeks and daily weight-based RBV (1000 mg [<75 kg] to 1200 mg [>75 kg]) plus weekly PEG for 12 weeks is recommended for retreatment of IFN-eligible persons

The following regimens are NOT recommended for treatment-naive patients with HCV genotype 4. PEG/RBV for 48 weeks Monotherapy with PEG, RBV, or a DAA
(Telaprevir- or boceprevir-based regimens)

Alternate regimen for HCV genotype 4, PEG/RBV nonresponder patients. Daily sofosbuvir (400 mg) and weight-based RBV (1000 mg [<75 kg] to 1200 mg [>75 kg]) for 24 weeks is recommended for

Alternative regimens for treatment-naive patients with HCV genotype 5 or 6.
Daily weight-based RBV (1000 mg [<75 kg] to 1200 mg [>75 kg]) plus weekly PEG for 48 weeks is an acceptable regimen for persons.

Recommended regimen for HCV genotype 5 or 6, PEG/RBV nonresponder patients. Daily sofosbuvir (400 mg) for 12 weeks and daily weight-based RBV (1000 mg [<75 kg] to 1200 mg [>75 kg]) plus weekly PEG for 12 weeks is recommended for retreatment of IFN-eligible persons

Recommended regimen for treatment-naive patients with HCV genotype 5 or 6.
Daily sofosbuvir (400 mg) and weight-based RBV (1000 mg [<75 kg] to 1200 mg [>75 kg]) plus weekly PEG for 12 weeks is recommended for IFN-eligible persons.

Simeprevir (*Olysio*) Summary

- **Approval Status: FDA approved December 6, 2013**
- **Indication for HCV Monoinfection**
  - **GT 1: Simeprevir (12 weeks) + peginterferon + ribavirin (12 or 36 weeks)**
  - **Poor response to Simeprevir + Peginteferon + Ribavirin with GT1a and NS3 Q80K polymorphism at baseline**
- **Class & Mechanism**
  - **NS3/4A protease inhibitor**
  - **Activity against GT 1,2,4,5,6 (strongest activity against GT 1a, 1b)**
- **Simeprevir Dosing**
  - **150 mg PO once daily with food**
  - **In combination with peginterferon + ribavirin (triple therapy)**
- **Adverse Effects (AE) attributable to Simeprevir**
  - **Rash (including a photosensitivity reaction), pruritus, and nausea**
- **Wholesaler Acquisition Cost in United States**
  - **28 tablet bottle = $22,120; estimated 12-week cost = $66,360**

Simeprevir + PEG + Ribavirin for Treatment-Naïve HCV GT1
QUEST-1 Trial: Adverse Effects

QUEST 1: Event	Simeprevir + PEG + RBV (n=264)	Placebo + PEG + RBV (n=130)
Discontinuation due to adverse event	3%	3%
Grade 3/4 adverse event	23%	29%
Fatigue	40%	38%
Headache	31%	37%
Pruritus	21%	11%
Rash (any type)	27%	25%
Anemia	19%	11%
Neutropenia	16%	11%
Bilirubin increase	9%	4%
Photosensitivity condition	3%	1%

Source: Jacobson I, et al. 48th Annual Meeting of EASL. Abstract 1425.

Recommended regimen for HCV genotype 1 PEG/RBV (with an HCV protease inhibitor) nonresponder patients:
Daily sofosbuvir (400 mg) for 12 weeks plus weight-based RBV (1000 mg [<75 kg] to 1200 mg [>75 kg]) and weekly PEG for 12 to 24 weeks, regardless of subtype or IFN eligibility.

GT 1 Patients in whom previous treatment with PEG/RBV plus either telaprevir or boceprevir has failed

SOF x 12 weeks + PEG/RBV x 12-24 weeks OR
SOF + RBV x 24 weeks, OR
SOF + PEG/RBV x 24 weeks

NOT RECOMMENDED:

PEG/RBV ± telaprevir or boceprevir or SMV
Monotherapy with PEG, RBV, or a DAA Do not treat decompensated cirrhosis with PEG or SMV

Recommended regimen for HCV genotype 1 PEG/RBV (without an HCV protease inhibitor) nonresponder patients:
Daily sofosbuvir (400 mg) plus simeprevir (150 mg), with or without weight-based RBV (1000 mg [<75 kg] to 1200 mg [>75 kg]) for 12 weeks is recommended for retreatment of HCV genotype 1 infection, regardless of subtype or IFN eligibility.

How much is too much?

Sovaldi Wholesale accusation cost (WAC) is $87,000 for 12 weeks treatment
Total cost for 12 weeks **$97,389**

Olysis WAC is $66,000 for 12 weeks
Total cost for 12 weeks **$76,389**
Peg Interferon $9,852 and Ribavirin is $537 12 weeks $10,389

Sovaldi and Olysis together 12 weeks **$153,000**

How Do I Pay For Treatment?

Co Payments and Deducatable

My Insurance copay $210 and $3,000 deductible

Many plans 20% to 30% copay and up $5,000 deductible

$19,477 copayment???

Patient Access Network Foundation (PANF)
P.O. Box 221858
Charlotte, NC 28222-1858
Toll Free: 1-866-316-PANF (7263)
www.panfoundation.org

OLYSIO™ Savings Program

OLYSIO™ Savings Program may provide instant savings on your out-of-pocket medication costs for OLYSIO™. Once eligible patients qualify and activate their OLYSIO™ Savings Card, patients pay only $25 per fill, with a maximum annual benefit of $25,000, 12 months after activation or 3 fills (12-week supply), whichever comes first. Not valid for patients enrolled in Medicare, such as Medicare Part D, or Medicaid. Other restrictions apply.

You may be eligible if:

You have been prescribed OLYSIO™

You currently have commercial/private insurance that covers prescription costs for OLYSIO™

Additional restrictions apply

Johnson & Johnson Patient Assistance Foundation

Johnson & Johnson Patient Assistance Foundation, Inc. (JJPAF) is committed to providing access to medicines for uninsured individuals who lack the financial resources to pay for them. If you are uninsured and unable to pay for your medicine, please contact a JJPAF program specialist at 1-800-652-6227 or visit the Foundation website at **JJPAF.org** to see if you might qualify for assistance.

You may be eligible if:
Single Person
$58,350 or less

Family Size of 2
$78,650 or less

Larger Families
Income levels are adjusted accordingly

To be eligible for a PEGASYS Co-pay Card, your patient must meet these criteria:

- Be prescribed PEGASYS to treat chronic hepatitis B or C
- Be 18 years of age or older
- Not reside or receive treatment in Vermont
- Not participate in charitable fund sources (eg, Genentech® Access to Care Foundation)
- Not participate in any federal- or state-funded health care program (eg, Medicare, Medicaid or TRICARE)

HEPATITIS C INFORMATION AND RESOURCES

FUND STATUS AND ELIGIBILITY

Open - We are accepting applications for new and renewal patients. If your application for assistance is approved you can begin receiving funding immediately.

Maximum Award Level: $7,500 Per Year

Eligibility Criteria

Patient should be insured and insurance must cover the medication for which patient seeks assistance.

Patient must have a confirmed diagnosis of Hepatitis C.

Patient must reside and receive treatment in the United States.

Patient's income must fall below 400% of the **Federal Poverty Guideline** (FPG) with consideration of the **Cost of Living Index**(COLI) and the number in the household.

1-866-512-3861 **cpr@patientadvocate.org**

http://www.copays.org/

Special Groups

Cirrhosis

Treatment-naive patients with compensated cirrhosis, including those with hepatocellular carcinoma, should receive the same treatment as recommended for patients without cirrhosis.
Patients with decompensated cirrhosis (moderate or severe hepatic impairment; CTP class B or C) should be referred to a medical practitioner with expertise in that condition (ideally in a liver transplant center).

*The recommended regimen for patients with any HCV genotype who have decompensated cirrhosis (moderate or severe hepatic impairment; **CTP class B or C**) who may or may not be candidates for liver transplantation, including those with hepatocellular carcinoma. This regimen should be used only by highly experienced HCV providers*

Daily sofosbuvir (400 mg) plus weight-based RBV (with consideration of the patient's creatinine clearance and hemoglobin level) for up to 48 weeks

*The following regimens are NOT recommended for patients with decompensated cirrhosis (moderate or severe hepatic impairment; **CTP class B or C**):*

Any IFN-based therapy

Monotherapy with PEG, RBV, or a DAA

Telaprevir-, boceprevir-, or simeprevir-based regimens

Alternative regimen for PEG/RBV (with or without an HCV protease inhibitor) nonresponder patients with HCV genotype 1, regardless of subtype.
Eligible to receive IFN:
Daily sofosbuvir (400 mg) for 12 weeks and weight-based RBV (1000 mg [<75 kg] to 1200 mg [>75 kg]) plus weekly PEG for 12 to 24 weeks

HIV/HCV Coinfected

Genotype 1

Recommended TX

Treatment-naive and prior PEG/RBV relapsers
IFN eligible: SOF + PEG/RBV x 12 weeks

IFN ineligible: SOF + RBV x 24 weeks
SOF + SMV ± RBV x 12 weeks

Treatment experienced (prior PEG/RBV nonresponders) regardless of IFN eligibility:
SOF + SMV ± RBV x 12 weeks

Alternative TX

Treatment naive and prior PEG/RBV relapsers
IFN eligible: SMV x 12 weeks + PEG/RBV x 24 weeks*

IFN ineligible: None

Treatment experienced (prior PEG/RBV nonresponders)
IFN eligible:
SOF +PEG/RBV x 12 Weeks
IFN ineligible: SOF + RBV x 24 Weeks

HIV/HCV Coinfected Patients

Genotype 2 and 3

SOF + RBV x 12 weeks

Genotype 4, 5, and 6

SOF + PEG/RBV x 12 weeks

There are a few drug-drug interactions with HIV Medications to watch out for. These drug have been found to be compatible with the new treatments.

For SOF use:
ALL except didanosine, zidovudine, or tipranavir
For SMV use:
LIMITED to raltegravir, rilpivirine, maraviroc, enfuvirtide, tenofovir, emtricitabine, lamivudine, abacavir

Patients who had previous treatment with PEG/RBV plus either telaprevir or boceprevir that failed

1a SOF x 12 weeks + PEG/RBV x 24 weeks

SOF + RBV x 24 weeks

1b SOF x 12 weeks + PEG/RBV x 12-24 weeks

SOF + RBV x 24 weeks

What's next?

Phase 3 DAA Combinations (without Interferon)			
Drug Name/ Category	**Drug Name/ Category**	**Company**	**Verified**
ABT-450/r (Protease Inhibitor) Ombitasvir (ABT-267) (NS5A Inhibitor) Dasabuvir (ABT-333) (Polymerase Inhibitor) Note: Phase 3 studies completed. Has some results in blog.		Abbott / Enanta	April 16, 2014
Daclatasvir (BMS-790052) (NS5A Inhibitor)	Asunaprevir (BMS-650032) (Protease inhibitor) BMS-791325 (Polymerase Inhibitor) Note: Phase 3 studies completed. Has some results in blog.	Bristol-Myers Squibb	April 16, 2014
Daclatasvir (BMS-790052) (NS5A Inhibitor)	Sovaldi (Sofosbuvir) (Polymerase Inhibitor) Note: has some Phase 2 results in blog.	Bristol-Myers Squibb /Gilead	April 16, 2014
Faldaprevir (Protease Inhibitor)	Deleobuvir (BI207127) (Polymerase Inhibitor) Note: Studies cancelled.	Boehringer Ingelheim Pharma	April 16, 2014
MK-5172 (Protease Inhibitor)	MK-8742 Inhibitor (NS5A Inhibitor) Has Phase 2 results in blog.	Merck	April 16, 2014
Olysio (Simeprevir) (Protease Inhibitor)	Sovaldi (Sofosbuvir) (Polymerase Inhibitor) Has Phase 2 results in blog.	Janssen	April 16, 2014
Sovaldi (Sofosbuvir) (Polymerase Inhibitor)	Ledipasvir (GS-5885) (NS5A) Note: Phase 3 studies completed. Has results in blog.	Gilead	April 16, 2014

Sofosbuvir-Ledipasvir Fixed-Dose Combination +/- RBV
ION-1, ION-2, and ION-3

Study	Population	Treatment	Duration	SVR 12 Rates
ION-1 (n= 865)	GT-1 Treatment-naïve (15.7% with cirrhosis)	SOF/LDV	12 weeks	97.7% (209/214)
		SOF/LDV + RBV	12 weeks	97.2% (211/217)
		SOF/LDV	24 weeks	NA (n = 217)
		SOF/LDV + RBV	24 weeks	NA (n = 217)
ION-2 (n= 440)	GT-1 Treatment-experienced (20.0% with cirrhosis)	SOF/LDV	12 weeks	93.6% (102/109)
		SOF/LDV + RBV	12 weeks	96.4% (107/111)
		SOF/LDV	24 weeks	99.1% (108/109)
		SOF/LDV + RBV	24 weeks	99.1% (110/111)
ION-3 (n= 647)	GT-1 Treatment-naïve (0.0% with cirrhosis)	SOF/LDV	8 weeks	94.0% (202/215)
		SOF/LDV + RBV	8 weeks	93.1% (201/216)
		SOF/LDV	12 weeks	95.4% (206/216)

Source: Gilead Sciences, Inc.

Free CME Course Helps Physicians Identify and Care for Patients with Liver Disease

Primary care providers are on the front lines of implementing the CDC's recommendation to screen all baby boomers—people born from 1945 to1965—for hepatitis C. In addition, the U.S. Preventative Services Task Force recently upgraded to B its recommendation for hepatitis B (HBV) screening of persons at high risk of infection. To help improve primary care physicians' knowledge of these diseases, the American Association for the Study of Liver Diseases (AASLD), in collaboration with ECHO, the American College of Physicians (ACP), CDC, and Department of Veterans Affairs, has developed ACT-First, a free, online CME course. After completing the course, physicians will know which patients to screen for liver diseases, how to screen, what to do in the patient with positive serologies, what to tell the patient, and how to decide who is a candidate for therapy.

aasld.org/ACTFirst

This slide deck is from the University of Washington's *Hepatitis C Online* and *Hepatitis Web Study* projects.

Hepatitis C Online

www.hepatitisc.uw.edu

Hepatitis Web Study

http://depts.washington.edu/hepstudy/

Funded by a grant from the Centers for Disease Control and Prevention.

Hepatitis web study