Cost and Access to Direct-Acting Antiviral Agents

This is a PDF version of the following document:
Module 4: Evaluation and Preparation for Hepatitis C Treatment
Lesson 3: Cost and Access to Direct-Acting Antiviral Agents

You can always find the most up to date version of this document at https://www.hepatitisc.uw.edu/go/evaluation-treatment/cost-access-medications/core-concept/all.

Background

Since 2014, the United States Food and Drug Administration (FDA) approval of a new generation of direct-acting antiviral (DAA) oral medications has revolutionized the landscape for hepatitis C virus (HCV) treatment. Therapy with DAAs has been markedly more effective than older therapies, easier to tolerate, and highly effective, even in traditionally more difficult-to-treat patients, such as those with treatment experience, cirrhosis, or HIV coinfection. Enthusiasm for these therapies, however, has been tempered by the high price of these medications and the challenges patients and clinicians face with respect to drug access. For medical providers, the process of obtaining insurance approval for new HCV treatment regimens can be daunting, complicated, and time-consuming. In addition, even when drug approval occurs, it may occur only after a substantial delay, potentially resulting in loss to follow-up. The purpose of this core concept is to describe some of the financial barriers to obtaining medication, to review some cost-effectiveness data on these therapies, and to provide practical guidance on how medical providers can navigate the system to increase access to HCV treatment for their patients.
Price of Direct-Acting Antiviral Agents

List "Sticker" Price

The price of the drug typically discussed in the public arena is the wholesale acquisition cost, which is the published list or "sticker" price of the medication set by the pharmaceutical company. The DAA medications are among of the most expensive oral medications in history, with daily wholesale acquisition prices ranging from $650 to $1125 (Figure 1). The wholesale acquisition costs are substantially higher than the estimated production costs for the medications (Figure 2).[1] For example, the wholesale acquisition cost of a 12-week course of sofosbuvir is $84,000 and the estimated production cost is $68 to 136. The ultimate "price for cure" of a recommended HCV treatment course depends on the HCV genotype, liver disease severity, and the combination of medications used (Figure 3). For example, the cost of recommended therapy for a treatment-naive patient with genotype 1a ranges from $54,600 to $150,000. This is further increased when patients require a longer (24-week) duration of therapy, as can occur in patients with decompensated cirrhosis.

Actual Medication Cost

The actual cost paid for the medications, however, may be significantly less than the wholesale acquisition cost, due to contracts, rebates, and discounts negotiated between payers and pharmaceutical companies.[2] Although the wholesale acquisition cost is general public knowledge, information on the actual cost paid is not available to the public. Negotiations for pricing can vary considerably and depend in large part of the nature of the payer.[2] In many settings, these negotiations are often conducted on behalf of insurance plans by pharmacy benefit management (PBM), a third-party generally for-profit intermediary in the pharmacy supply chain, which can greatly influence the actual drug cost and potential reimbursement rates. When insurance companies are allied with specific PBMs, the agreements may facilitate medication access by lowering drug cost but often do so in exchange for exclusivity (restrictions that dictate which medication can be prescribed) and thereby may reduce choice for the medical provider and patient. These negotiations of drug pricing between pharmaceutical companies and payers or PBMs are for all intents and purposes confidential business dealings and can obscure the price transparency that is otherwise part of a truly free market.[3] Even with such negotiated discounts, the cost of these drugs can prohibit widespread access. One study that examined the published discount prices of sofosbuvir and ledipasvir-sofosbuvir in countries where such data were available suggested that paying for widespread treatment in national health systems would still consume large proportions of their entire pharmaceutical budget.[4] The exorbitant pricing of these DAAs has garnered considerable public scrutiny and outcry from the press and medical community.[5] Despite these objections, there has been little change to the pricing of these regimens.
Cost-Effectiveness of Direct-Acting Antiviral Agents

Definitions Related to Cost-Effectiveness Analysis

A cost-effectiveness analysis is a formal method to compare the costs and clinical outcomes associated with one intervention with another “standard” comparator and can be used to help set funding priorities. The unit used for this comparison is the incremental cost-effectiveness ratio (ICER), which is a statistic used to summarize the effectiveness of a health care intervention; the ICER is a ratio defined as the difference between the cost of two possible interventions divided by the difference in health effects of the two interventions (Figure 4). The most common application of ICER related to hepatitis C therapy is a cost-effectiveness analysis and the ICER is typically measured as cost per quality-adjusted life years (QALY) gained between two strategies. For example, a typical hepatitis C treatment ICER uses the costs of different therapies as the intervention comparison (cost of new therapy minus the old therapy) divided by the QALY comparison (QALY with new therapy minus QALY of old therapy) (Figure 5). The ICER is then determined as the cost in dollars per quality of life year (QALY) gained. Once the ICER is calculated, it is examined against a benchmark, generally $50,000 to $100,000 per QALY gained, which is considered in the United States to be our society’s “willingness to pay” threshold, although this value is clearly debatable.[6]

Issues to Consider with Cost-Effectiveness Studies

There are some caveats to consider in cost-effectiveness analyses. First, these statistical models are based on multiple assumptions regarding treatment strategies and the natural history of disease (largely based on prior literature) that should be noted carefully before interpreting results. Second, the cost-effectiveness analysis assumes the main objective is to maximize net health benefits for a target population under constrained resources, a primary goal that may not be shared by clinicians who are more focused on the welfare of the individual patients they serve. Third, these analyses comprise only one of many criteria, including political, societal, and ethical priorities, that need consideration when making decisions related to resource allocation. This last consideration is important when considering HCV therapy with DAAs. Most published cost-effectiveness analysis studies have reported that new treatments for hepatitis C appear to be cost-effective compared with older comparators, but note that the benefit to society (and payers) would not occur until at least 10 years after the initial treatment.[7] It is clear that while HCV DAAs may be cost-effective, the projected cost of widespread medication coverage of all HCV-infected patients in the United States would exceed $300 billion and is neither affordable nor feasible.[8,9]

Cost-Effectiveness Studies with DAAs

Several cost-effectiveness studies have been published on the DAAs, with summary points listed below. Notably, many of these studies did not include the potential treatment benefits accrued with reduction of non-liver-related morbidity and mortality, or the prevention of secondary HCV infection, which may confer significant downstream cost savings.

- Several cost-effectiveness analysis studies have examined ledipasvir-sofosbuvir in genotype 1 infection and most demonstrated this combination was cost-effective in selected groups compared with older standard of care (some version of interferon-based therapy), with most ICERs in the “willing to pay” range of less than $100,000 per QALY gained (Figure 6).[10]
- In the cost-effectiveness analyses performed by Chhatwal and Najafzadeh, in addition to the cost of the drug, patient age, and severity of fibrosis had substantial influence on the ICERs. In the ledipasvir-sofosbuvir analysis, there was a lower ICER observed in treatment-naive patients with cirrhosis compared to those without cirrhosis.[9] In contrast, treatment-experienced patients with genotype 1 infection and cirrhosis had a higher ICER than those without cirrhosis, mainly due to the greater cost of the ledipasvir-sofosbuvir treatment course for treatment-experienced patients with cirrhosis (24 weeks used in the analysis) versus the
12-week course for treatment-experienced patients without cirrhosis (Figure 7).[9]

- Studies by Linas and Najafzadeh concluded that genotype 2 or 3 is notably less cost-effective to treat than genotype 1 with sofosbuvir-based therapy in treatment-naïve non-cirrhotic patients.[11,12] This is not surprising when one considers that a reasonable majority of non-cirrhotic patients with genotype 2 or 3 infection can be cured with less expensive peginterferon-based therapy.
Process to Acquire HCV Treatment Medications

Insurance and Medicaid Approval

Because of the very high cost of new HCV regimens, many insurance companies and Medicaid programs require a prior authorization in order for the patient to receive the medications.[13,14] To date, insurance carriers do not have a uniform policy as to who qualifies for hepatitis C treatment, which adds complexity and challenges for patients and providers seeking DAA coverage. In addition, each state has its own Medicaid policies related to HCV therapy, and there is no uniform national policy as to who qualifies for the treatment under Medicaid. Many payers have adopted guidelines that involve rationing treatment to patients with advanced liver fibrosis (Metavir F3 or F4 fibrosis) or those patients deemed to have higher medical priority based on a variety of clinical features (Figure 8). Clinicians who care for Medicaid patients with hepatitis C should attempt to find state-specific policies on prior authorization for hepatitis C treatment by contacting their state Medicaid board. The National Viral Hepatitis Roundtable and Harvard Center for Health Law and Policy Innovation have provided national summary of state Medicaid policies on HCV drug access in November 2016.[15]

Requirements to Acquire DAAs for Patients

Insurance companies and Medicaid programs often have multiple requirements that must be met before DAAs are authorized. These restrictive criteria may dictate who can prescribe DAAs and what clinical documentation and laboratory testing are necessary. They may stipulate the type of methods and criteria used for fibrosis staging. After the prescription for medication has been submitted, the patient should be counseled that it may take months before they receive a decision from their insurance company. The following list outlines some of the potential requirements that providers may encounter and note these vary by insurance and state:

- **Provider Experience**: Some policies stipulate that only certain medical providers that have adequate expertise in treating hepatic C can prescribe DAAs. Typically, hepatologists, gastroenterologists, and infectious diseases specialists have been granted permission to prescribe DAAs without any further requirements. General medical providers may need documentation of consultation support by experts, such as through the Extension for Community Health Outcome (ECHO) programs.[16,17]

- **Fibrosis Staging**: In most circumstances, insurers will require proof of fibrosis staging. Degree of fibrosis can be established by (a) liver biopsy OR (b) a combination of non-invasive measures, including AST-to-platelet ratio index (APRI), FibroSURE, and transient elastography.

- **Baseline Laboratory Studies**: Most insurance plans will require a thorough evaluation with laboratory studies prior to receiving approval for medications to treat HCV. Typical required baseline laboratory studies are listed below. In addition, except for the HCV genotype, a window of time may be required for these laboratory studies to be accepted as pretreatment studies.
  - HCV Genotype
  - HCV RNA
  - Complete blood count (CBC)
  - Serum creatinine and calculated glomerular filtration rate
  - Prothrombin Time (PT)/International Normalized Ratio (INR)
  - Hepatic function panel: albumin, total and direct bilirubin, alanine aminotransferase (ALT), aspartate aminotransferase (AST), and alkaline phosphatase

- **Clinic Note Documentation**: Some or all of the following patient-specific information may be required in order to qualify for treatment coverage:
  - Alcohol sobriety for at least 6 months
  - CAGE or AUDIT-C alcohol use survey if the patient is not 100% abstinent to alcohol
  - No injection drug use for at least 6 months
○ Drug or alcohol screening tests
○ Pregnancy status if female of child-bearing age
○ Evaluation of psychosocial readiness for treatment
○ Justification of choice of regimen and duration of treatment
○ Documentation of hepatitis A and B status

**Medicaid Guidance**

Effective November 5, 2015, the Centers for Medicare and Medicaid Services (CMS) released a guidance document ([Assuring Medicaid Beneficiaries Access to Hepatitis C Drugs](#)) for states with regard to access restrictions on DAA treatments for hepatitis C in state Medicaid programs. In this guidance, they note that although states have the discretion to establish limitations on coverage—for example, through preferred drug lists and use of prior authorization—these practices must ensure access to clinically appropriate treatment. Further, this CMS document states that limiting access to treatment to individuals with a fibrosis score of F3 or F4, requiring a period of abstinence from drug and alcohol use, or significantly limiting the types of providers able to prescribe hepatitis C drugs are examples of unreasonable restrictions on access to treatment. It remains to be seen whether this CMS guidance document will change Medicaid restrictions.

**Insurance Denials**

The insurance companies may block treatment with an outright denial, or they may deny a specific medication selection or duration of therapy. If the insurance company denies a medication for the patient, the medical provider should resubmit the application for the medication, with a specific appeal letter qualifying the request as a reapplication. Given the complexity of this process, assistance from a pharmacist or pharmacy technician, or someone experienced with the process, can prove crucial to ensure a streamlined process for the patient medication approval. In general, if a patient’s medication request is rejected twice they can apply for a patient assistance program with the pharmaceutical manufacturer, if that pharmaceutical has an active patient assistance program and the patient’s financial circumstances meet the program’s requirements.

**Pharmaceutical Patient Assistance Programs**

If an insurance company denies a patient’s HCV medication prescription twice, providers should consider contacting the pharmaceutical company Patient Assistance Programs. Unfortunately, not all medications have pharmaceutical company Patient Assistance Programs. Of note, the Gilead Support Path Program for ledipasvir-sofosbuvir and sofosbuvir now provides free medication only for eligible uninsured patients. In general, for most of the other patient assistance programs, patients are considered for Patient Assistance if their application has been rejected by their insurance company twice, the application resubmitted to their insurance company and rejected a second time (must be within 60 days), and patients have an income less than $100,000 per year. Patients should be counseled that the pharmaceutical company assistance program will likely require tax information, social security benefits, and other documents that reflect a patient’s income. The following is a list of active hepatitis C treatment pharmaceutical sponsored patient assistance programs for patients living in the United States.
Patient Advocacy Groups

Several groups have emerged that can act as advocates for patients struggling to deal with the diagnosis, symptoms and complications from Hepatitis C as well as act as advocates and resources for patients struggling through the insurance approval and drug assistance process. Such groups include:

- **Patient Advocate Foundation**: The Patient Advocate Foundation's [Hepatitis C CareLine](#) is a hotline (800-532-5274) for both patients and medical providers and this service non-profit organization that provides assistance, including case management services, to patients diagnosed with hepatitis C. The Hepatitis C CareLine has case managers that will assist patients in efforts to try and access new medications to treat hepatitis C.
- **HCV Advocate**: The [HCV Advocate](#) is a nonprofit organization founded in 1997 geared to providing education, support, and services to patients with HCV infection and coinfection with HCV and HIV, including medical providers. The website includes Educational material about HCV appropriate for patients, Information about HCV and disability services, Information about the Hepatitis C Support Project (HCSP), Updates on clinical trials for HCV treatments, and Current news updates on HCV news and HCV treatment.
Summary Points

- New DAAs have been highly effective in treating chronic HCV infection, but the extremely high cost of these medications has served as a major barrier to more widespread treatment access.
- The wholesale acquisition cost for the newer DAAs ranges from $417 to $1125 per day. The actual price paid for the medication may be significantly lower because of contracts, rebates, and discounts.
- Most new regimens for hepatitis C treatment have been shown to be cost-effective, but given the large numbers of persons infected with hepatitis C in the United States, universal treatment is neither feasible nor affordable at the current prices of these medications.
- The process of acquiring prior authorization approval for DAAs for patients with hepatitis C can be confusing and time-consuming, particularly with respect to staying up to date with the restrictions and requirements of various insurance plans.
- Many insurance and state Medicaid programs are only approving DAAs for hepatitis C treatment for patients with F3 or F4 fibrosis.
Citations

   [PubMed Abstract]

   [PubMed Abstract]

   [PubMed Abstract]

   [PubMed Abstract]

   [PubMed Abstract]

   [PubMed Abstract]

7. AASLD-IDSA. Recommendations for testing, management, and treating hepatitis C. Overview of cost, reimbursement, and cost-effectiveness considerations for hepatitis C treatment regimens.
   [AASLD-IDSA Hepatitis C Guidance]

   [PubMed Abstract]

   [PubMed Abstract]

    [PubMed Abstract]

    [PubMed Abstract]

    [PubMed Abstract]


References


### Figures

**Figure 1 Wholesale Acquisition Cost of Direct Acting Antiviral Agents**

<table>
<thead>
<tr>
<th>Medication</th>
<th>Trade Name</th>
<th>Manufacturer</th>
<th>WAC for 1 Day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daclatasvir</td>
<td>Daklinza</td>
<td>Bristol-Myers Squibb</td>
<td>$750</td>
</tr>
<tr>
<td>Elbasvir-Grazoprevir</td>
<td>Zepatier</td>
<td>Merck &amp; Co., Inc.</td>
<td>$650</td>
</tr>
<tr>
<td>Ledipasvir-Sofosbuvir</td>
<td>Harvoni</td>
<td>Gilead Sciences</td>
<td>$1125</td>
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<tr>
<td>Glecaprevir-Pibreintasvir</td>
<td>Mavyret</td>
<td>AbbVie</td>
<td>$417</td>
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<tr>
<td>Ombitasvir-Paritaprevir-Ritonavir</td>
<td>Technivie</td>
<td>AbbVie</td>
<td>$912</td>
</tr>
<tr>
<td>Ombitasvir-Paritaprevir-Ritonavir and Dasabuvir</td>
<td>Viekira Pak</td>
<td>AbbVie</td>
<td>$992</td>
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<tr>
<td>Simeprevir</td>
<td>Olysio</td>
<td>Janssen</td>
<td>$790</td>
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<tr>
<td>Sofosbuvir</td>
<td>Sovaldi</td>
<td>Gilead Sciences</td>
<td>$1000</td>
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<td>Sofosbuvir-Velpatasvir</td>
<td>Epclusa</td>
<td>Gilead Sciences</td>
<td>$890</td>
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<tr>
<td>Sofosbuvir-Velpatasvir-Voxilaprevir</td>
<td>Vosevi</td>
<td>Gilead Sciences</td>
<td>$890</td>
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</table>
Figure 2 Wholesale Acquisition Cost versus Estimated Production Cost for DAAs and 12-Week Treatment Course

### Estimated Cost* for Initial Recommend Treatment of Genotype 1a HCV

<table>
<thead>
<tr>
<th>Regimen and Duration of Therapy</th>
<th>Cost of Regimen*</th>
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<tbody>
<tr>
<td>Elbasvir-Grazoprevir for 12 weeks</td>
<td>$54,600</td>
</tr>
<tr>
<td>Elbasvir-Grazoprevir for 16 weeks</td>
<td>$72,800</td>
</tr>
<tr>
<td>Ledipasvir-Sofosbuvir for 12 weeks</td>
<td>$94,500</td>
</tr>
<tr>
<td>Ombitasvir-Paritaprevir-Ritonavir + Dasabuvir + Ribavirin for 12 weeks</td>
<td>$83,819</td>
</tr>
<tr>
<td>Sofosbuvir + Simeprevir for 12 weeks</td>
<td>$150,000</td>
</tr>
<tr>
<td>Sofosbuvir-Velpatasvir for 12 weeks</td>
<td>$74,760</td>
</tr>
<tr>
<td>Sofosbuvir + Daclatasvir x 12 weeks</td>
<td>$147,000</td>
</tr>
</tbody>
</table>

*Regimen and Duration of therapy for Initial treatment of patients with Genotype 1a without cirrhosis  
*Cost of regimen estimated based on Wholesale Acquisition Cost (WAC)
## Estimated Cost* for Initial Recommend Treatment of Genotype 1b HCV

<table>
<thead>
<tr>
<th>Regimen and Duration of Therapy^</th>
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<tr>
<td>Elbasvir-Grazoprevir for 12 weeks</td>
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<td>Ledipasvir-Sofosbuvir for 12 weeks</td>
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<td>Ombitasvir-Paritaprevir-Ritonavir + Dasabuvir for 12 weeks</td>
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<td>Sofosbuvir + Simeprevir for 12 weeks</td>
<td>$150,000</td>
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<tr>
<td>Sofosbuvir + Daclatasvir x 12 weeks</td>
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^Regimen and Duration of therapy for Initial treatment of patients with Genotype 1b without cirrhosis

*Cost of regimen estimated based on Wholesale Acquisition Cost (WAC)
**Figure 3 (Image Series) - Wholesale Acquisition Cost (WAC) for Treatment of HCV Genotypes 1 to 6**

**Image 3C: Genotype 2**

<table>
<thead>
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<th>Regimen and Duration of Therapy</th>
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<tr>
<td>GT 2 HCV without Cirrhosis</td>
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<tr>
<td>Sofosbuvir-Velpatasvir x 12 weeks</td>
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<td>Daclatasvir + Sofosbuvir x 12 weeks</td>
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<tr>
<td>GT 2 HCV with Compensated Cirrhosis</td>
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<td>Sofosbuvir-Velpatasvir x 12 weeks</td>
<td>$74,760</td>
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<tr>
<td>Daclatasvir + Sofosbuvir x 16 weeks</td>
<td>$196,000</td>
</tr>
<tr>
<td>Daclatasvir + Sofosbuvir x 24 weeks</td>
<td>$294,000</td>
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*Cost estimates based on Wholesale Acquisition Cost (WAC)*
### Estimated Cost of Regimens for Treatment HCV GT 3 HCV

<table>
<thead>
<tr>
<th>Regimen and Duration of Therapy</th>
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</thead>
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<tr>
<td><strong>GT 3 HCV without Cirrhosis</strong></td>
<td></td>
</tr>
<tr>
<td>Daclatasvir + Sofosbuvir x 12 weeks</td>
<td>$147,000</td>
</tr>
<tr>
<td>Sofosbuvir-Velpatasvir x 12 weeks</td>
<td>$74,760</td>
</tr>
<tr>
<td><strong>GT 3 HCV with Compensated Cirrhosis</strong></td>
<td></td>
</tr>
<tr>
<td>Sofosbuvir-Velpatasvir x 12 weeks +/- Ribavirin</td>
<td>$74,760</td>
</tr>
<tr>
<td>Daclatasvir + Sofosbuvir x 24 weeks +/- Ribavirin</td>
<td>$294,000</td>
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*Cost estimates based on Wholesale Acquisition Cost (WAC)*
### Estimated Medication Cost* for Treatment of Genotype 4 Chronic HCV

<table>
<thead>
<tr>
<th>Regimen and Duration</th>
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<tbody>
<tr>
<td>Ombitasvir-Paritaprevir-Ritonavir + Ribavirin x 12 weeks</td>
<td>$77,000</td>
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<tr>
<td>Sofosbuvir-Velpatasvir x 12 weeks</td>
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<tr>
<td>Elbasvir-Grazoprevir x 12 weeks</td>
<td>$54,600</td>
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<tr>
<td>Ledipasvir-Sofosbuvir x 12 weeks</td>
<td>$94,500</td>
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*Regimen and Duration of therapy for Initial treatment of patients with Genotype 4 without cirrhosis and with compensated cirrhosis

*Cost of regimen estimated based on Wholesale Acquisition Cost (WAC)
**Figure 3 (Image Series) - Wholesale Acquisition Cost (WAC) for Treatment of HCV Genotypes 1 to 6**

**Image 3F: Genotypes 5 or 6**

<table>
<thead>
<tr>
<th>Regimen and Duration</th>
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</thead>
<tbody>
<tr>
<td>Sofosbuvir-Velpatasvir x 12 weeks</td>
<td>$74,760</td>
</tr>
<tr>
<td>Ledipasvir-Sofosbuvir x 12 weeks</td>
<td>$94,500</td>
</tr>
</tbody>
</table>

*Cost estimates based on Wholesale Acquisition Cost (WAC)*
Figure 4 General Principle of Incremental Cost-Effectiveness Ratio (ICER)

<table>
<thead>
<tr>
<th>Incremental Cost-Effectiveness Ratio (ICER)</th>
</tr>
</thead>
</table>
| \[
| \text{ICER} = \frac{(C_1 - C_0)}{(E_1 - E_0)}
|\]

- $C_1$ = cost in intervention group
- $C_0$ = cost in control group
- $E_1$ = effect in intervention group
- $E_0$ = effect in control group
### Incremental Cost-Effectiveness Ratio (ICER) with Hepatitis C Treatments

The formula for calculating the Incremental Cost-Effectiveness Ratio (ICER) is:

\[
\text{ICER} = \frac{(C_n - C_0)}{(\text{QALY}_n - \text{QALY}_0)}
\]

- \( C_n \) = cost of new hepatitis C therapy
- \( C_0 \) = cost of old hepatitis C therapy
- \( \text{QALY}_n \) = quality adjusted life years with new hepatitis C therapy
- \( \text{QALY}_0 \) = quality adjusted life years with old hepatitis C therapy
Figure 6 Cost Effectiveness Analysis Studies Involving Ledipasvir-Sofosbuvir


| Wholesale Acquisition Cost (WAC) of Direct Acting Antiviral Agents used to Treat HCV |
|---------------------------------|---------------------------------|---------------------------------|---------------------------------|
| **Author** | **Target Population** | **Intervention versus Standard of Care** | **Incremental Cost-Effectiveness Ratio (ICER)** |
| Chhatwal | Treatment-naive and Treatment-experienced GT 1-4 | For GT1: LDV-SOF versus PR + TPV or BOC | Naive non-cirrhotic: $31,452
Naive cirrhotic: $9,703
Experienced non-cirrhotic: $35,853
Experienced cirrhotic: $79,238 |
| Younossi | Treatment-naive and Treatment-experienced GT 1 | LDV-SOF versus [no treatment, SOF + PR, SMV + PR, SOF + SMV, SOF + RBV, or PR + BOC] | LDV-SOF cost-saving (less costly and more effective) compared with older comparators with ICERs ~$29,000 versus PR + SOF under variety of scenarios |
| Najafzadeh | Treatment-naive GT 1, 2, or 3 | For GT1: SOF + RBV, LDV-SOF, SOF + DCV versus PR + SOF versus PR + BOC | LDV-SOF was cost-saving for GT1 when compared to PR + BOC with an estimated ICER of $14,432 |

**Abbreviations:** GT = genotype; LDV-SOF = ledipasvir-sofosbuvir; PR = peginterferon plus ribavirin; BOC = boceprevir; SOF = sofosbuvir; SMV = simeprevir; RBV = ribavirin; DCV = daclatasvir
The numbers shown on the bar graph represent the incremental cost-effectiveness ratio (ICER) in dollars per quality of life year (QALY) for treatment-naive and treatment experienced patients with genotype 1 chronic HCV, including those with and without cirrhosis.

**Figure 8 Highest Priority for Initiating HCV Treatment Based on Highest Risk for Severe Complications**

Source: American Association for the Study of Liver Disease, the Infectious Diseases Society of America. When and whom to initiate HCV therapy. Recommendations for testing, management, and treating hepatitis C.

<table>
<thead>
<tr>
<th>2015 AASLD/IDSA: HCV Guidance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Settings of Liver-Related Complications and Extrahepatic Disease in Which HCV Treatment is Most Likely to Provide the Most Immediate and Impactful Benefits</td>
</tr>
</tbody>
</table>

**Highest Priority for Treatment Owing to Highest Risk for Severe Complications**

- **Advanced fibrosis (Metavir F3) or compensated cirrhosis (Metavir F4)**
  - Rating: Class I, Level A

- **Organ transplant**
  - Rating: Class I, Level B

- **Type 2 or 3 essential mixed cryoglobulinemia with end-organ manifestations**
  - Rating: Class I, Level B

- **Proteinuria, nephrotic syndrome, or membranous glomerulonephritis**
  - Rating: Class I, Level B