CAPITALIZING ON HCV ADVANCEMENTS:

Treatment Management and Benefit Design Strategies for Managed Care
<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
</tr>
</thead>
</table>
| 6:20-6:55 AM | • Evolving Guidelines and Evidence-Based HCV Treatments  
                • Therapeutic Recommendations for Various HCV Patient Types  
                
                *Nancy S. Reau, MD* |
| 6:55–7:30 AM | • Pharmacy Benefit Design Innovations for a New Era of HCV Management  
                • HCV Specialty Pharmacy Services and Disease Management Strategies for Managed Care Pharmacy  
                
                *Jeffrey D. Dunn, PharmD, MBA* |
| 7:30–7:45 AM | Faculty Discussion Session                                               |
After completing this activity, the participant should be better able to:

- Apply evidence-based treatment strategies to optimize outcomes for patients with HCV within a managed care setting
- Cite recently updated American Association for the Study of Liver Disease (AASLD), Infectious Diseases Society of America (IDSA), and the American College of Gastroenterology (ACG) treatment guidelines on current and emerging treatment options for HCV, including efficacy, safety, and tolerability
- Recommend benefit design that takes into account patient out-of-pocket expenses (OOP) to remove barriers and improve adherence and overall value for the management of HCV
- Evaluate pharmacy management strategies, including specialty pharmacy services and disease management, that MCOs can implement to improve overall patient outcomes for HCV patients
- Provide accurate and appropriate counsel as part of the managed care treatment team
CAPITALIZING ON HCV ADVANCEMENTS:

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Capitalizing on HCV Advancements: Treatment Management and Benefit Design Strategies for Managed Care

Jeffrey D. Dunn, PharmD, MBA
Senior Vice President
VRx Pharmacy Services, LLC
Faculty Disclosure

• The **faculty** reported the following financial relationships or relationships to products or devices they or their spouse/life partner have with commercial interests related to the content of this CME activity:

  Jeffrey D. Dunn, PharmD, MBA

  – *Consulting Fees*: Vertex Pharmaceuticals, Janssen Pharmaceuticals, Gilead Sciences, Inc., and AbbVie, Inc.
Clinical Burden of Hepatitis C Continues to Grow

Prevalence in the US ~1.6% of the population (4.1 million)\(^1\)

<table>
<thead>
<tr>
<th>Increase in prevalence is projected over the next 3 decades(^2)</th>
<th>Majority of currently infected individuals have not yet been diagnosed(^2)</th>
</tr>
</thead>
</table>

Principal cause of death from liver disease and the leading indication for liver transplantation in the US\(^1,2\)

<table>
<thead>
<tr>
<th>40% of deaths from liver disease can be attributed to HCV(^3)</th>
<th>HCV-related cirrhosis accounts for ~40% of liver transplants(^4)</th>
</tr>
</thead>
</table>

Prevalence of HCV in the US and Patient Engagement in HCV Care

<table>
<thead>
<tr>
<th>Number of People in Millions</th>
<th>Chronic HCV Infection</th>
<th>Tested for HCV</th>
<th>Referred to Care</th>
<th>Received HCV RNA Test</th>
<th>Received Liver Biopsy</th>
<th>Treated for HCV Infection</th>
<th>Achieved Sustained Virologic Response</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>3.2</td>
<td>1.6</td>
<td>1.0-1.2</td>
<td>0.63-0.75</td>
<td>0.38-0.56</td>
<td>0.22-0.36</td>
<td>0.17-0.2</td>
</tr>
</tbody>
</table>

HCV=hepatitis C virus; RNA=ribonucleic acid.

Economic Burden of HCV is Projected to Increase

- Total health care cost due to HCV infection
  - 2011: ~$6.5 billion
  - 2024: ~$9.1 billion
- Increasing costs due to more advanced liver diseases including
  - Decompensated cirrhosis (46%)
  - Compensated cirrhosis (20%)
  - Hepatocellular carcinoma (16%)

Chronic HCV Infection Presents a Significant Challenge to Managed Care

“The Silent Epidemic”
Disease with a long, indolent course

Aging of a large pool of enrollees
Many patients are undiagnosed or not on therapy
Many patients are asymptomatic

Cornerstone therapies have high costs

Challenges Presented to Managed Care by HCV

Improved methods to enhance identification and treatment of affected patients are needed
  • Role of active screening?

Patient adherence to therapy is suboptimal
  • Regimens are complex

Long-term monitoring of patients necessary to enhance outcomes

Associated with significant comorbidities, ie, HIV, etc

Current therapies have limitations
  • Adverse events
  • Convenience

Unanswered Questions in the Management of HCV

Will the initial expense of therapy be offset by cost savings from the prevention of future disease burden?
• If so, how can MCOs assure patients are receiving the best care with the most efficient use of health care resources?

What can be done to ensure diagnosis and appropriate treatment of infected patients, which will reduce future health burden?

What methods can be used during treatment to further reduce total HCV costs?

HCV=hepatitis C virus; MCO=managed care organization.

Treating HCV

Goal of treatment is to prevent complications and death from HCV infection by achieving virologic cure.

**Recommended regimens:**
- sofosbuvir and ribavirin + pegylated interferon alpha
- sofosbuvir and simeprevir + ribavirin;
- simeprevir + RBV + PEGIFN is an alternative for some genotype 1 and 4 infections;
- Specific combinations, treatment duration, and alternative regimens depend on HCV genotype, and interferon eligibility

Combination therapy has been shown to be superior to peginterferon monotherapy

Several Novel HCV Therapies are in the Pipeline

- Interferon-free double, triple, and quadruple therapy combinations
- Greater efficacy
- Increased complexity

Protease Inhibitors (>5)

- Polymerase inhibitors
  - Nucleoside and non-nucleoside
- NS5A inhibitors
- Entry inhibitors
- Cyclophilin inhibitors
- MicroRNA inhibitors
- Vaccines

Others

- Decreased total cost?
- Improved long-term outcomes?

Increased pharmacy cost

HCV Is Evolving Rapidly with a New Standard of Care Emerging


HCV=hepatitis C virus; PEGIFN=peg interferon; RBV=ribavirin; GT=genotype.


1991

Standard Interferon

1998

Peginterferon/ Ribavirin

2001

Interferon + Ribavirin

Boceprevir or Telaprevir + PEGIFN/RBV

Simeprevir or Sofosbuvir + RBV +/- PEGIFN

Sofosbuvir + PEGIFN/RBV or Sofosbuvir + Simeprevir +/- RBV

GT1

2011

GT2/3

2013

GT 4-6

2014

2014

Sofosbuvir + RBV

Sofosbuvir + RBV

Sofosbuvir + PEGIFN + RBV

Sofosbuvir + RBV

Sofosbuvir + PEGIFN + RBV

Sofosbuvir + RBV

Sofosbuvir + PEGIFN + RBV
HCV Therapies in Development: 2014*

**On Market**
- IFN & PEG IFN
- Ribavirin
- Boceprevir
- Telaprevir (to be discontinued)
- Simeprevir
- Sofosbuvir

**Phase III**
- ABT-450/r
- Mericitabine
- Ledipasvir
- BMS-791325
- Daclatasvir
- BI-207127
- ABT-333
- Narlaprevir
- MK-8742
- Asunaprevir
- Vaniprevir
- ABT-267

**Phase II**
- Sovaprevir
- Miravirsen
- IDX719
- GS-9451
- MK-5172
- GS-9669
- GS-9620
- GS-5816
- VX-222
- Tegobuvir
- Silibinin
- SCY-635
- ACH-3102
- Danoprevir
- ABT-072
- Setrobuvir
- ACH-2684

**Phase I**
- TT-034
- VGX-6150

**Research/P reclinical**
- Many others, including immune stimulants and gene therapy

*Sample, not an exhaustive list.
<table>
<thead>
<tr>
<th>Regimens with one DAA + PEG-IFN alfa/RBV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ritonavir-boosted Danoprevir (PI)</td>
</tr>
<tr>
<td>GS-9451 (Vedroprevir; PI)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Regimens with 2-3 DAAs (± PEG-IFN alfa and/or RBV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>GS-9526 (PI) + Tegobuvir</td>
</tr>
<tr>
<td>GS-9451 + Tegobuvir (NNI)</td>
</tr>
<tr>
<td>Daclatasvir (NS5A) + Asunaprevir (PI)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>IFN-free regimens</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABT-450/r + ABT-267 + ABT-333 +/- RBV</td>
</tr>
<tr>
<td>Daclatasvir + Asunaprevir ± RBV</td>
</tr>
<tr>
<td>BI-201335 + BI-207127 ± RBV</td>
</tr>
<tr>
<td>Ledipasvir + Sofosbuvir ± RBV</td>
</tr>
<tr>
<td>Daclatasvir + Simeprevir + RBV</td>
</tr>
<tr>
<td>MK-5172 + MK-8742 ± RBV</td>
</tr>
<tr>
<td>Dataclasvir + Asunaprevir + BMS-79135</td>
</tr>
<tr>
<td>GS-5816 + Sofosbuvir</td>
</tr>
<tr>
<td>Daclatasvir + Sofosbuvir</td>
</tr>
<tr>
<td>ABT-493 + ABT-530 ± RBV</td>
</tr>
<tr>
<td>ABT-450/r/ABT-267 + ABT-333 + RBV</td>
</tr>
</tbody>
</table>

*Sample, not an exhaustive list.*

DAA=direct acting antiviral; PEG-IFN=pegylated interferon; RBV=ribavirin; NNI= non-nucleoside NS5B inhibitor; PI=protease inhibitor; NS5A=replication complex inhibitor; NI=nucleoside NS5B inhibitor; Cyp=cyclophilin inhibitor, IFN=interferon; r=ritonavir.
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  Nancy S. Reau, MD
  - *Consulting Fees*: AbbVie, Gilead, Idenix Pharmaceuticals, Janssen
  - *Contracted Research*: AbbVie, Gilead
Evolving Guidelines and Evidence-Based HCV Treatments
Recommendations for when and in whom to initiate treatment

Treatment is recommended for patients with chronic HCV infection

Rating: Class I, Level A

Treatment is assigned the highest priority for those patients with advanced fibrosis (Metavir F3), those with compensated cirrhosis (Metavir F4), liver transplant recipients, and patients with severe extrahepatic hepatitis C (Table 1).

Based on available resources, treatment should be prioritized as necessary so that patients at high risk for liver-related complications and severe extrahepatic hepatitis C complications are given high priority (Table 1).

Ratings: See tables
Who Requires HCV therapy?

1. High risk for liver-related complications
2. High risk for progression
3. High risk for transmission
4. Serious extra-hepatic complication
5. Other
SVR is Associated with Reduced Mortality Among HCV-infected Persons

- 530 adults with advanced fibrosis prospectively followed for median 8.4 years after HCV treatment
- 192 (36%) achieved SVR

Hepatocellular Carcinoma in HCV-infected Patients with Advanced Hepatic Fibrosis Following SVR

- 1000 patients followed for median 5.7 years
  - 85% cirrhosis
- Risk of HCC increased with:
  - Age >45 years
  - Platelet count <150 x 108/L
  - AST/ALT ratio > 0.90
  - Diabetes Mellitus

HCC Incidence According to Disease Stage

SVR=sustained virologic response; HCC=hepatocellular carcinoma; AST/ALT ratio=aspartate transaminase–alanine transaminase ratio

Van der Meer et al. The Liver Meeting 2013;Abstract 143.
Who Requires HCV therapy?

1. High risk for liver related complications
2. High risk for progression
3. High risk for transmission
4. Serious extra-hepatic complication
5. Other
Risk Factors Associated with Faster Fibrosis Progression in Chronic HCV

**Disease state factors**
- Fibrosis stage
- HCV onset after 40 years of age
- Persistently elevated ALT

**Host factors**
- Male gender
- Age >45 years
- Obesity/steatosis
- Diabetes
- HIV, HBV co-infection
- Immune system compromise
- Iron overload
- Life style (ETOH, smoking)

**Viral factors**
- Genotype 3


ALT=alanine aminotransferase
ETOH=alcohol
Progression is Not Linear: Importance of Duration and Aging


- ~50% cirrhosis at 40 years
- 10 – 15% cirrhosis at 20 years
- ~50% cirrhosis at 40 years
SVR and All-cause Mortality in CHC Patients with Advanced Fibrosis

530 patients followed for a median of 8.4 years

Baseline factors significantly associated with all-cause mortality
- Older age
- **Genotype 3** (2-fold increase in mortality and HCC)
- Higher Ishak fibrosis score
- Diabetes
- Severe alcohol use


SVR=sustained virologic response
CHC=chronic hepatitis C
HCC=hepatocellular carcinoma
HCV Genotype 3 in the VA HCV Clinical Case Registry 2000-2009: Cirrhosis and HCC

- 88,348 patients with genotype 1 (80%)
- 13,077 genotype 2 (12%)
- 8,337 genotype 3 (7.5%)
- Mean follow-up: 5.4 years
- After adjustment for demographic, clinical and antiviral treatment factors, comparison between genotypes 3 and 1:

<table>
<thead>
<tr>
<th></th>
<th>Hazard Ratio</th>
<th>Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cirrhosis</td>
<td>1.31</td>
<td>1.22-1.39</td>
</tr>
<tr>
<td>HCC</td>
<td>1.80</td>
<td>1.61-2.03</td>
</tr>
</tbody>
</table>

**Conclusion:** Genotype 3 associated with significantly higher risk of cirrhosis and HCC vs genotype 1, independent of age, diabetes, BMI, or antiviral treatment

Coinfected Patients Have Higher Rates of Hepatic Decompensation Despite ART


ART = antiretroviral treatment
Who Requires HCV therapy?

1. High risk for liver related complications
2. High risk for progression
3. High risk for transmission
   - MSM with high-risk sexual practices
   - Active injection-drug users
   - Incarcerated persons
   - Persons on long-term hemodialysis
     • Rating: Class IIA, Level C
4. Serious extra-hepatic complication
5. Other
Who Requires HCV therapy?

1. High risk for liver related complications
2. High risk for progression
3. High risk for transmission
4. Serious extra-hepatic complication
5. Other
Extrahepatic Manifestations of HCV

- **Hematologic Disorders**
  - Mixed Cryoglobulinemia
  - Lymphoproliferative Disorders
- **Renal**
  - Membranoproliferative glomerulonephritis (MPGN)
- **Dermatologic Diseases**
  - Porphyria Cutanea Tarda
  - Leukocytoclastic Vasculitis
  - Lichen Planus
  - Necrolytic Acral Erythema
- **Diabetes Mellitus**
- **Autoimmune Disorders**
  - Autoantibodies
  - Thyroid Disease
  - Autoimmune ITP
  - Sjogren’s Syndrome
  - Rheumatoid Arthritis
  - Sarcoidosis
  - Myasthenia Gravis
- **Ophthalmologic Features**
- **Neurologic**
  - Mononeuropathy multiplex
  - Acute inflammatory syndromes
  - Cerebral vasculitis
Extrahepatic Manifestations of HCV

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</tr>
<tr>
<td>• Renal</td>
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<tr>
<td>– Membranoproliferative</td>
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<tr>
<td>glomerulonephritis (MPGN)</td>
</tr>
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<td>• Dermatologic Diseases</td>
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<td>– Necrolytic Acral Erythema</td>
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</tr>
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<td>– Cerebral vasculitis</td>
</tr>
<tr>
<td>• Diabetes mellitus</td>
</tr>
<tr>
<td>• Fatigue</td>
</tr>
<tr>
<td>• Poor Quality of Life</td>
</tr>
</tbody>
</table>
SVR ↓ Complications of DM

Cumulative incidence of ESRD in three study cohorts, analyzed by the modified log rank test with death adjusted as a competing risk event

- Treated cohort
- Untreated cohort
- Uninfected cohort

Cumulative incidence of acute coronary event in three study cohorts, analyzed by the modified log rank test with death adjusted as a competing risk event

SVR=sustained virologic response; DM=disease management; ESRD=end stage renal disease
Who Requires HCV therapy?

1. High risk for liver related complications
2. High risk for progression
3. High risk for transmission
4. Serious extra-hepatic complication
5. Other
HCV Viral Replication Increases All Cause Mortality


**All Causes**

Cumulative mortality (%)

- Anti-HCV seropositives, HCV RNA detectable
- Anti-HCV seropositives, HCV RNA undetectable
- Anti-HCV seronegatives

Follow-up years

*P*<0.001 for comparison among three groups

*P*<0.001 for HCV RNA detectable vs. undetectable

Between 1995 and 2010, 41% of the 126,862 new primary registrants for liver transplants carried a diagnosis of HCV infection.1


DCC=decompensated cirrhosis
HCC=hepatocellular carcinoma
Liver Cancer Projected to be the 3rd Leading Cause of Cancer-related Death by 2030

“Projecting Cancer Incidence and Deaths to 2030: The Unexpected Burden of Thyroid, Liver and Pancreas Cancers in the United States.”

Cancer Research, published online on May 19, 2014

- Cancer incidence and deaths in the US projected for 2020 and 2030
- Breast, prostate, and lung cancers will remain the top cancer diagnoses
- Lung cancer is projected to remain the top cancer killer
  - Pancreas and liver cancers are projected to surpass breast, prostate, and colorectal cancers to become the second and third leading causes of cancer-related death by 2030

Cancer Res. 1–9. 2014 AACR
Summary

• Patients with the most immediate need should be prioritized for therapy
• SVR improves Quality of Life and extrahepatic manifestations of HCV
• SVR decreases the risk of HCC and improves liver and all-cause mortality rates

SVR=sustained virologic response
HCC=hepatocellular carcinoma
Therapeutic Recommendations for Various HCV Patient Types
Milestones in Therapy of HCV: Overall SVR Rates

Average SVR Rates from Clinical Trials

<table>
<thead>
<tr>
<th>Year</th>
<th>IFN 6m</th>
<th>IFN 12m</th>
<th>IFN/RBV 6m</th>
<th>IFN/RBV 12m</th>
<th>Peg-IFN 12m</th>
<th>Peg-IFN/RBV 12m</th>
<th>T12/PR24 P/R/B (48 wk) + lead-in</th>
<th>DAA+DAA</th>
<th>DAA+PR</th>
</tr>
</thead>
<tbody>
<tr>
<td>1991</td>
<td>6%</td>
<td>16%</td>
<td>34%</td>
<td>42%</td>
<td>39%</td>
<td>54-56%</td>
<td>79%*</td>
<td></td>
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<tr>
<td>1999</td>
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<td>68%*</td>
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<td>2002</td>
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<td>2010</td>
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<tr>
<td>2014</td>
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<td></td>
<td>90%*</td>
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</table>

For Most Patients, Where Are We Now?
## Currently Available Agents

### Protease Inhibitor (PI) Additional Regimen Components

<table>
<thead>
<tr>
<th>PI</th>
<th>Components</th>
<th>Considerations</th>
</tr>
</thead>
</table>
| Boceprevir (TID)    | PEGIFN alfa + weight-based RBV  | - Genotype  
- Naïve  
- Previous treatment failure  
- Compensated cirrhosis  
- Response guided therapy |
| Telaprevir (TID)    |                                 |                                                                                |
| Simeprevir (QD)     |                                 |                                                                                |

### Polymerase Inhibitor Additional Regimen Components

<table>
<thead>
<tr>
<th>PI</th>
<th>Components</th>
<th>Considerations</th>
</tr>
</thead>
</table>
| Sofosbuvir (QD)     | PEGIFN alfa + weight-based RBV  | SOF+RBV for genotype 2/3  
SOF+PEG/RBV G1     |
First Line Therapy

**G1 PATIENTS**

- SOF 400 mg QD + PEG-IFN + RBV
- f/u 24 wk
- SVR 90%

**G2/3: ALL ORAL THERAPY**

- G2
  - SOF 400mg QD + RBV
  - f/u 24 wk
  - SVR 97%
- G3
  - SOF 400mg QD + RBV
  - f/u 24 wk
  - SVR 77%

Mishra P. on behalf of the FDA Sofosbuvir Review Team. October 25, 2013
Currently Available BUT Off-Label: COSMOS
Sofosbuvir (NUC) and Simeprevir (PI)

Cohort 1 (F0-F2 Nulls): SVR12
(N = 80, all arms)

Cohort 2 (F3-F4 Naives/Nulls): SVR12

Sulkowski, et al.
Lancet. 2014

svr12 (%)

24-Wk Arms 12-Wk Arms

SMV + SOF + RBV

SMV + SOF

0 20 40 60 80 100

19/24 14/15 26/27 13/14

93.3 96.3 92.9

28/30 13/14 25/27

93 93 94

12 Weeks 24 Weeks Overall

## Initial HCV Treatment Recommendations

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Recommended</th>
<th>Alternative</th>
<th>NOT Recommended</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><strong>IFN eligible</strong>: SOF + PEG/RBV x 12 weeks</td>
<td><strong>IFN eligible</strong>: SMV x 12 weeks + PEG/RBV x 24 weeks</td>
<td>TVR + PEG/RBV x 24 or 48 weeks (RGT) BOC + PEG/RBV x 28 or 48 weeks (RGT) PEG/RBV x 48 weeks Monotherapy with PEG, RBV, or a DAA. Do not treat decompensated cirrhosis with PEG or SMV</td>
</tr>
<tr>
<td></td>
<td><strong>IFN ineligible</strong>: SOF + SMV ± RBV x 12 weeks</td>
<td><strong>IFN ineligible</strong>: SOF + RBV x 24 weeks</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>SOF + RBV x 12 weeks</td>
<td>None</td>
<td>PEG/RBV x 24 weeks Monotherapy with PEG, RBV, or a DAA Any regimen with TVR, BOC, or SMV</td>
</tr>
<tr>
<td>3</td>
<td>SOF + RBV x 24 weeks</td>
<td>SOF + PEG/RBV x 12 weeks</td>
<td>PEG/RBV x 24-48 weeks Monotherapy with PEG, RBV, or a DAA Any regimen with TVR, BOC, or SMV</td>
</tr>
<tr>
<td>4</td>
<td><strong>IFN eligible</strong>: SOF + PEG/RBV x 12 weeks</td>
<td>SMV x 12 weeks + PEG/RBV x 24-48 weeks</td>
<td>PEG/RBV x 48 weeks Monotherapy with PEG, RBV, or a DAA Any regimen with TVR or BOC</td>
</tr>
<tr>
<td></td>
<td><strong>IFN ineligible</strong>: SOF + RBV x 24 weeks</td>
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</tr>
<tr>
<td>5 or 6</td>
<td>SOF + PEG/RBV x 12 weeks</td>
<td>PEG/RBV x 48 weeks</td>
<td>Monotherapy with PEG, RBV, or a DAA Any regimen with TVR or BOC</td>
</tr>
</tbody>
</table>

# HCV Treatment Recommendations for Patients in Whom Previous Treatment Has Failed

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Recommended</th>
<th>Alternative</th>
<th>NOT Recommended</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patients in whom previous PEG/RBV has failed</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>SOF + SMV ± RBV x 12 weeks</td>
<td>SOF x 12 weeks + PEG/RBV x <strong>12-24 weeks</strong>&lt;br&gt;<strong>SOF + RBV x 24 weeks</strong>&lt;br&gt;SMV x 12 weeks + PEG/RBV x <strong>48 weeks</strong></td>
<td>PEG/RBV ± telaprevir or boceprevir Monotherapy with PEG, RBV, or a DAA&lt;br&gt;Do not treat decompensated cirrhosis with PEG or SMV</td>
</tr>
<tr>
<td>2</td>
<td>SOF + RBV x 12 weeks</td>
<td>SOF + PEG/RBV x 12 weeks</td>
<td>PEG/RBV ± telaprevir or boceprevir Monotherapy with PEG, RBV, or a direct-acting antiviral agent&lt;br&gt;Do not treat decompensated cirrhosis with PEG</td>
</tr>
<tr>
<td>3</td>
<td>SOF + RBV x 24 weeks</td>
<td>SOF + PEG/RBV x 12 weeks</td>
<td>PEG/RBV ± any current protease inhibitor Monotherapy with PEG, RBV, or a DAA&lt;br&gt;Do not treat decompensated cirrhosis with PEG</td>
</tr>
<tr>
<td>4</td>
<td>SOF + PEG/RBV x 12 weeks</td>
<td><strong>SOF + RBV x 24 weeks</strong></td>
<td>PEG/RBV ± any current HCV protease inhibitor Monotherapy with PEG, RBV, or a DAA&lt;br&gt;Do not treat decompensated cirrhosis with PEG</td>
</tr>
<tr>
<td>5 or 6</td>
<td>SOF x 12 weeks + PEG/RBV 12 weeks</td>
<td></td>
<td>PEG/RBV ± any current HCV protease inhibitor Monotherapy with PEG, RBV, or a DAA&lt;br&gt;Do not treat decompensated cirrhosis with PEG</td>
</tr>
<tr>
<td><strong>Patients in whom previous treatment with PEG/RBV plus either telaprevir or boceprevir has failed</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>SOF x 12 weeks + PEG/RBV x <strong>12-24 weeks</strong>&lt;br&gt;<strong>SOF + RBV x 24 weeks</strong>&lt;br&gt;<strong>SOF + PEG/RBV x 24 weeks</strong></td>
<td></td>
<td>PEG/RBV ± telaprevir or boceprevir or SMV Monotherapy with PEG, RBV, or a DAA&lt;br&gt;Do not treat decompensated cirrhosis with PEG or SMV</td>
</tr>
</tbody>
</table>

1. All oral therapy is efficacious
2. Baseline characteristics are losing impact
3. Special populations are no longer special
ABT-450/r (PI) + ABT-267 (NS5A) + ABT-333 (NNI) + RBV: SAPPHIRE and TURQUOISE

SAPPHIRE-I
- Treatment Naïve
- No cirrhosis
- N=473
- ABT-450/r + ABT-267 + ABT-333 + RBV
- SVR 96%

SAPPHIRE-II
- Experienced
- No cirrhosis
- N=297
- ABT-450/r + ABT-267 + ABT-333 + RBV
- SVR 96%

TURQUOISE-II
- Treatment Naïve/Experienced
- 100% w/cirrhosis
- N=208
- ABT-450/r + ABT-267 + ABT-333 + RBV
- SVR 92%

- N=172
- ABT-450/r + ABT-267 + ABT-333 + RBV
- SVR 96%

Feld et al. NEJM 2014; Zeuzem et al. NEJM 2014; Poordad et al NEJM 2014
Sofosbuvir (NUC) + Ledipasvir (NS5A) +/- RBV in G1 97% (1886/1952) Overall SVR

ION-1 treatment naïve: N = 865
ION-2 treatment experienced: N = 440
ION-3 treatment naïve: N = 64

LDV/SOF Phase 3 Program (ION-1, ION-2, ION-3)

- ION-1 treatment naïve: N = 865
- ION-2 treatment experienced: N = 440
- ION-3 treatment naïve: N = 64

Afdhal et al NEJM 2014, Kowdley et al NEJM 2014
1. All oral therapy is efficacious
2. Baseline characteristics are losing impact
3. Special populations are no longer special
SAPPHIRE-I: ITT SVR12 Rates in Subpopulations

Adapted from the Jordan Feld presentation at ILC/EASL on April 11, 2014
SAPPHIRE-II Results: ITT SVR12 Rates
>95% in All Prior Peginterferon/Ribavirin Response Groups

<table>
<thead>
<tr>
<th>Prior Response</th>
<th>SVR12, % Patients</th>
<th>Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prior Relapse</td>
<td>95.3%</td>
<td>82/86</td>
</tr>
<tr>
<td>Prior Partial Response</td>
<td>100.0%</td>
<td>65/65</td>
</tr>
<tr>
<td>Prior Null Response</td>
<td>95.2%</td>
<td>139/146</td>
</tr>
</tbody>
</table>

Adapted from the Stefan Zeuzem presentation at ILC/EASL on April 10, 2014
SVR Rates of SOF-Based Regimens Across Genotypes and Among Patients with Multiple Negative Predictive Factors

- Retrospective multivariate analysis of Phase 2 and 3 SOF data identified 6 negative predictors associated with relapse:
  - Prior treatment failure, cirrhosis, IL28B non-CC, HCV RNA ≥ 800,000 IU/mL, body weight ≥ 75kg, male gender
  - 89% of patients in the Phase 3 program had up to 4 negative predictors

Foster G, EASL, 2014, O66
Expectations: Current Phase 2/3 Clinical Trials

1. All oral therapy is safe and efficacious
2. Baseline characteristics are losing impact
3. Special populations are no longer special
SVR12 by Presence of Cirrhosis

ION-1 (LDV/SOF±RBV x 12 or 24 weeks)

Error bars represent 95% confidence intervals
Mangia A, EASL, 2014, O164
TURQUOISE-II Results: ITT SVR12 Rates by Surrogates of Portal Hypertension and Hepatic Function

12-week arm | 24-week arm
--- | ---
Baseline Platelet Count (x10^9/L): <100 | 88.9% | 84.0%
Baseline Platelet Count (x10^9/L): ≥100 | 97.0% | 98.9%
Baseline Serum Albumin Count (g/L): <35 | 92.6% | 92.9%
Baseline Serum Albumin Count (g/L): ≥35 | 95.7% | 96.8%

Adapted from the Fred Poordad presentation at ILC/EASL on April 12, 2014
LDV/SOF STR for Treatment of HCV GT 1 Co-infected with HIV (Interim Analysis)

**ERADICATE Study (NIAID, LDV/SOF)**

- **ARV Untreated: LDV/SOF**
  - Week 4: 100/100
  - Week 8: 100/100
  - EOT: 100/100
  - SVR4: 100/100
  - SVR8: 100/100
  - SVR12: 100/100

- **ARV Treated*: LDV/SOF**
  - Week 4: 13/13
  - Week 8: 37/37
  - EOT: 37/37
  - SVR4: 30/30
  - SVR8: 22/22
  - SVR12: 10/10

- N = 50 GT 1, TN, stable HIV disease

- **Interim results**
  - SVR 12
  - SVR 4

- LDV/SOF STR was well tolerated with no discontinuations

Osinusi A, EASL, 2014, O14
50% of infected persons in the US are unaware of their status.

1. Referral to a specialist/someone who can treat (from a primary care doctor, HIV clinic, opiate substitution clinic, needle exchange program)

2. Attending an appointment
   1. Receive pre-treatment work-up
   2. Meet eligibility criteria
   3. Agree to initiate treatment

1. Efficacious regimen
2. Treatment adherence

SVR Improves Short and Long Term Outcomes

- Improves histology
- Decreases risk of cirrhosis, liver cancer, and transplantation
- Improves quality of life
- Improves insulin resistance
- Decreases all cause mortality

<table>
<thead>
<tr>
<th>Time, y</th>
<th>Without SVR</th>
<th>With SVR</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>405</td>
<td>192</td>
</tr>
<tr>
<td>1</td>
<td>393</td>
<td>181</td>
</tr>
<tr>
<td>2</td>
<td>382</td>
<td>168</td>
</tr>
<tr>
<td>3</td>
<td>363</td>
<td>162</td>
</tr>
<tr>
<td>4</td>
<td>344</td>
<td>156</td>
</tr>
<tr>
<td>5</td>
<td>317</td>
<td>144</td>
</tr>
<tr>
<td>6</td>
<td>295</td>
<td>125</td>
</tr>
<tr>
<td>7</td>
<td>250</td>
<td>88</td>
</tr>
<tr>
<td>8</td>
<td>207</td>
<td>56</td>
</tr>
<tr>
<td>9</td>
<td>164</td>
<td>40</td>
</tr>
<tr>
<td>10</td>
<td>135</td>
<td>28</td>
</tr>
</tbody>
</table>

All-cause mortality

\[ P \lt 0.001 \]

How Much Should Hepatitis C Treatment Cost?

By THE EDITORIAL BOARD  MARCH 15, 2014

A new pill to treat hepatitis C raises difficult questions about fair
Summary

• HCV is responsible for significant morbidity and mortality in the US
• Effective screening and early eradication are instrumental to decreasing disease burden
• Nearly all patients will achieve a cure with well tolerated all-oral therapy
• Multiple factors continue to make access to providers and therapy an issue
CAPITALIZING ON HCV ADVANCEMENTS: Treatment Management and Benefit Design Strategies for Managed Care
Pharmacy Benefit Design Innovations for a New Era of HCV Management

Jeffrey D. Dunn, PharmD, MBA
Senior Vice President
VRx
Salt Lake City, UT
HCV Is a Top 10 Specialty Category Under Pharmacy Benefit

PMPY (per member per year)

- Inflammatory conditions: $50.62
- Multiple sclerosis: $37.98
- Cancer: $31.98
- HIV: $20.78
- Hepatitis C: $7.82
- Growth Deficiency: $7.41
- Anticoagulant: $6.74
- Pulmonary Hypertension: $5.71
- Respiratory Conditions: $5.56
- Transplant: $4.92

PMPY=per member per year.

http://www.drugtrendreport.com/commercial/specialty-trend-by-therapy-class.
<table>
<thead>
<tr>
<th>Rank</th>
<th>Therapy Class</th>
<th>PMPY Spend</th>
<th>Trend</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Utilization</td>
<td>Unit Cost</td>
<td>Total</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>Inflammatory Conditions</td>
<td>$50.62</td>
<td>9.0%</td>
<td>14.0%</td>
<td>23.0%</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Multiple Sclerosis</td>
<td>$37.98</td>
<td>0.5%</td>
<td>17.3%</td>
<td>17.8%</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Cancer</td>
<td>$31.98</td>
<td>3.4%</td>
<td>22.3%</td>
<td>25.8%</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>HIV</td>
<td>$20.78</td>
<td>-2.1%</td>
<td>11.1%</td>
<td>9.0%</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Hepatitis C</td>
<td>$7.82</td>
<td>28.9%</td>
<td>4.8%</td>
<td>33.7%</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Growth Deficiency</td>
<td>$7.41</td>
<td>1.7%</td>
<td>7.7%</td>
<td>9.5%</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>Anticoagulant</td>
<td>$6.74</td>
<td>1.7%</td>
<td>0.3%</td>
<td>2.1%</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>Pulmonary Hypertension</td>
<td>$5.71</td>
<td>5.1%</td>
<td>6.2%</td>
<td>11.3%</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>Respiratory Conditions</td>
<td>$5.56</td>
<td>1.5%</td>
<td>25.7%</td>
<td>27.2%</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>Transplant</td>
<td>$4.92</td>
<td>2.2%</td>
<td>-6.9%</td>
<td>-4.7%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Other</td>
<td>$27.68</td>
<td>-24.9%</td>
<td>43.7%</td>
<td>18.8%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>TOTAL SPECIALTY</td>
<td>$207.19</td>
<td>-0.4%</td>
<td>18.7%</td>
<td>18.4%</td>
<td></td>
</tr>
</tbody>
</table>

PMPY=per member per year.

http://www.drugtrendreport.com/commercial/specialty-trend-by-therapy-class.
HCV Drug and Disease Cost Issues

Drug costs
- Drug acquisition
- Emerging agents
- Emergence of more high cost oral therapies

Clinical burden
- Appropriate diagnosis, adherence, and routine monitoring is difficult
- Patient education/health management programs
- Management of safety monitoring

Total costs need to be evaluated
- Direct and indirect
Finding a Balance Between Shifting Costs and Patient Nonadherence Can be a Challenge

- Member decision factors
  - Cost share
  - Compliance
  - Efficacy/tolerability

- Benefit design factors
  - Medical vs pharmacy
  - Copay vs coinsurance
  - Specialty tiers
Pharmacy Benefit Design: Basic Elements

Manage costs by restricting utilization of resources

Medical and pharmacy designs usually independent

Cost sharing used to influence utilization patterns

- Patient cost-share related to acquisition cost of service or product
- Assumes inelastic demand or willingness to pay

## HCV Benefit Design: Common Components

<table>
<thead>
<tr>
<th>Cost management</th>
<th>Utilization management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug discounts</td>
<td>Medical necessity review</td>
</tr>
<tr>
<td>Channel management</td>
<td>Clinical management via treatment algorithms/patient eligibility/duration of therapy</td>
</tr>
<tr>
<td>Rebates</td>
<td>Prior authorization</td>
</tr>
<tr>
<td>Benefit design options</td>
<td>Formulary management (tiers, utilization caps)</td>
</tr>
</tbody>
</table>

HCV Pharmacy Management Strategies

Incentive programs
- Member
- Physician: differential reimbursement, P4P

Specialty pharmacy integration

Coordination/collaboration
- Data management/widespread use of IT

Case management
- Needs to be more active and educated

Patient support programs
- Mandatory?
- Use of those provided by manufacturers?

P4P=pay for performance; IT=information technology.
Approaches to HCV Pharmacy Benefit Design

**Benefit Design**

- **Tiers**
  - Evaluating out-of-pocket expenses and distribution

- **Biosimilars**
  - The first follow-on biologics or biosimilars are in late stage development

**Application of guidelines/algorithms/disease management**

- Need information concerning retreatment
- What to do for patients intolerant to or having contraindications to peginterferon or ribavirin?
## Impact of Patient Behavior on Success of the HCV Pharmacy Benefit Design

<table>
<thead>
<tr>
<th>Disease and Treatment Variables</th>
<th>Healthcare Delivery Variables</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Complex therapy</td>
<td>• Patient awareness/education</td>
</tr>
<tr>
<td>• Treatment tolerability and</td>
<td>• Strengthening patient-provider relationships</td>
</tr>
<tr>
<td>efficacy issues</td>
<td>• Patient empowerment</td>
</tr>
<tr>
<td>• Asymptomatic disease</td>
<td>• Integrated communication channels</td>
</tr>
<tr>
<td></td>
<td>• Medication therapy management</td>
</tr>
<tr>
<td></td>
<td>• Telephonic counseling</td>
</tr>
<tr>
<td></td>
<td>• Medication reminders</td>
</tr>
</tbody>
</table>
Formulary Management

More Formulary Control

- Need for data: CER?
- Prior authorizations: levels of evidence
- Quantity limits
- Start/stop rules

Contracts

- Work with drug manufacturers; outcomes-based
- Net effective pricing

CER: comparative effectiveness research
Health Care Reform Is Encouraging a Move Towards Delivering Value, Not Volume

Payment/delivery paradigm emphasis is on rewarding value instead of volume

Value-based purchasing, shared savings, gain-sharing, bundled payments, capitation, etc

Incentives such as the CMS 5-Star Rating System are being implemented to coordinate care among/across providers

Beginning in January 2012, plans with $\geq 4$ stars receive bonuses along with higher rebates and plans with $\leq 3$ stars will be flagged as “low-quality” on the Medicare website

New structures are promoting actual and virtual integration

Accountable care organizations (ACOs), medical homes, home-based chronic care management, community health teams, health care innovation zones
New Models Based on Consistent Themes Are Being Implemented

<table>
<thead>
<tr>
<th>Models and Tactics Used by Accountable Care Organizations (ACO)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ACOs</strong> provide an organizational structure that supports health promotion, patient-centered care and clinical integration</td>
</tr>
<tr>
<td>- Patient-centered medical homes (Advanced Primary Care)</td>
</tr>
<tr>
<td><strong>Payment mechanisms focused on “fee for value” rather than “fee for volume”</strong></td>
</tr>
<tr>
<td>- Quality incentives for improved processes and outcomes</td>
</tr>
<tr>
<td>- Likely to take it in steps:</td>
</tr>
<tr>
<td>- Fee for service: per case/“at risk” quality payments – bundled – capitation</td>
</tr>
</tbody>
</table>
Payer Environment Must Continually Adapt as New HCV Therapies Emerge

Present
• Perverse incentives – volume over value
• Unsustainable health care cost trajectory
• Medicare and Medicaid will cut payment rates
• Will reach a point where we can no longer cost-shift to commercial payers to make up for declining government payment levels
• Efficiency gains will not be enough for success

Future
• Consequences of care outcomes shared between payers and providers
• Primary care is pivotal in managing health and utilization
• Proactively managing the health of individuals is rewarded
• Proactively managing the health of our communities is rewarded
• If we can perform better than others, we have more to gain financially in a capitation environment
<table>
<thead>
<tr>
<th>Program</th>
<th>Actions</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Specialty Pharmacy MTM</td>
<td>• Design program workflow and integration with Care Management</td>
</tr>
<tr>
<td>– Integration with Care Management</td>
<td>• Analyze drug utilization patterns to select targeted drugs/disease states</td>
</tr>
<tr>
<td>– Coordinate site of care</td>
<td>• Train personnel:</td>
</tr>
<tr>
<td>– Ensure appropriate dosing</td>
<td>– Specialty diseases</td>
</tr>
<tr>
<td>– Adherence</td>
<td>– Medications</td>
</tr>
<tr>
<td>– Education on use</td>
<td>– Site of care logistics</td>
</tr>
<tr>
<td>– Expectation management</td>
<td></td>
</tr>
</tbody>
</table>

MTM=medication therapy management.
Managed care will be required to develop novel solutions to meet the anticipated growth of the symptomatic HCV population.

Providers, patients, and payers are challenged to identify the most effective allocation of agents (especially for specialty).

Limited resources challenge patients, providers, and payers.

HCV pharmacy is a current and future concern for plan sponsors and patients.

Current plan designs based on older premises often do not apply to the needs of HCV pharmacy.

Newer approaches will be considered.

Primary stakeholders include patients, physicians, managed care organizations, industry, and payers.
HCV Specialty Pharmacy Services and Disease Management Strategies for Managed Care Pharmacy
Emergence of Direct-Acting Antiviral Agents (DAAs) is driving efforts to carefully manage HCV drug therapy.

Price and value of HCV therapies rarely questioned

Vigorous debate about the overall value* of treatments

Payers now actively apply payment reforms and quality measurement to HCV services

*clinical, pharmacoeconomic, humanistic, societal, etc.
Payers Want to Ensure Appropriate Utilization

**Right Drug**
- Is there another medication that may be more appropriate?
- Or may be less expensive yet equally effective?

**Right Patient**

**Right Time**
- Should therapy be discontinued?
- Have labs been performed at the right time to measure results?

*Is this the correct dose?*
*Is this the right time in the regimen?*
*Does the patient have enough meds? Too many?*
Evolving Payer Interventions to Manage HCV Treatment

• HCV has emerged as one of the most important categories to manage
• Payers are using multiple interventions to manage access and use of HCV drugs including
  – Prior authorization with criteria aligned closely with FDA-approved product labels and clinical guidelines
  – Close monitoring of patient response
  – Patient cost-sharing
• Growing cost pressures will influence plans to modify current approaches to managing HCV agents
• Many plans now manage patient access to preferred regimens through the use cost sharing and step edits

Partnership Between Specialty Pharmacy and Health Plans Can Improve Outcomes

• Health plans partner with specialty pharmacies to help improve patient outcomes while lowering overall costs

• As many as three-quarters of plans now mandate specialty pharmacy use to access HCV products
  – Specialty pharmacists are uniquely positioned close to HCV patients providing plans an ally in their attempts to manage HCV product use and ensure patient adherence to their treatment

<table>
<thead>
<tr>
<th>Cost</th>
<th>Utilization</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Network management</td>
<td>• Prior authorization</td>
</tr>
<tr>
<td>• Member cost share</td>
<td>• Step edits</td>
</tr>
<tr>
<td>• Quantity restrictions</td>
<td>• Therapy management</td>
</tr>
<tr>
<td>• Managed formularies</td>
<td>• Patient education</td>
</tr>
<tr>
<td>• Rebates</td>
<td>• Physician education</td>
</tr>
<tr>
<td></td>
<td>• Health care purchaser education</td>
</tr>
</tbody>
</table>
Benefits of Specialty Pharmacy Providers

• Improved outcomes
  – Greater collaboration between providers and adherence programs can improve clinical outcomes
  – Single points of patient contact and connections to related services may help improve the care experience

• Cost savings
  – Synchronized medical and pharmacy services can yield significant total cost savings

• Enhanced delivery of care
  • Utilization of patient registries and clinical pathways allow improved data capture which can be used to optimize the delivery of care

United Health Center for Health Reform and Modernization. April 2014.
When Does it Make Sense to Use a Specialty Pharmacy Provider?

• Prescription volume is limited
• Relatively small patient population
• Patients are likely to have co-pay issues
• Ongoing patient education necessary
• Prior authorizations are likely
• Side effects need to be managed
• Appeals will be necessary
• Quality data is needed
• Adherence is a challenge
Patient, Provider, and Payer Expectations of Specialty Pharmacy Providers

Access to a Clinical Pharmacist
- Pharmacy and medical benefit
- Engagement with patients
- Engagement with physicians and clinics
- Real time visibility to drug, disease, and patient variables

Patient Access and Empowerment
- Patient assistance programs
- Drug and disease education
- Persistence and compliance

Quality Clinical Programs
- Best practices in formulary and clinical management
- Patient and provider network satisfaction

Predictable Costs
- Value-based health care
- Bending the cost curve
- Documented comparative outcomes
Strategies for HCV Pharmacy Management

• Utilize fibrosis staging to prioritize the need for therapy\(^1\)
  – Accurate assessment of fibrosis is vital in assessing the urgency for treatment
  – Degree of hepatic fibrosis is a robust predictor of disease progression and clinical outcomes

• Identify and encourage use of preferred agents
  – May be different per line of business

• Utilize prior authorization
  – Ensures appropriate genotype, drug selection, and duration

• Encourage collaborative and coordinated care

• Coordinate with specialty pharmacy providers
  – Including disease education and adherence programs
  – Monitoring response to therapy

Use of Technology to Enhance Specialty Pharmacy Data Acquisition, Analysis, and Communication

• Robust and timely data acquisition allows monitoring of utilization and costs

• Application of proven, existing cost management programs
  – Pre-approvals
  – Step therapy
  – Quantity controls
  – Substitutions

• Ability to introduce new programs
  – Limits on point-of-service quantities
  – Tightened access criteria
  – Alternative administration channels

• Coordination with extended care team
Disease Management Strategies and Specialty Pharmacy Drugs
Disease Management Strategies in HCV

• Coordinated disease management is critical to promoting improved health outcomes and cost containment

• Challenges include
  – Managing patients with multiple comorbidities requiring complicated drug regimens
  – Need for ongoing dose adjustment
  – Monitoring for drug-related side effects and drug-drug interactions
  – Poor adherence to the treatment regimen

• “High touch” approach to care management may be required to motivate patients to remain adherent to their treatment plan
## HCV Disease Management Plan

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Timing</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>HCV Baseline Assessment</td>
<td>Week 0</td>
<td>Collect/verify labs (eg, weight, viral load, biopsy, Hb) and previous HCV therapy, duration, and outcome</td>
</tr>
<tr>
<td>Pharmacist Verification</td>
<td>New RXs</td>
<td>Evaluate therapy by genotype, treatment history, effectiveness, and safety; resolve actual or potential drug-related problems</td>
</tr>
<tr>
<td>Care Plan</td>
<td>Week 0, PRN</td>
<td>Identify treatment goals and document care plan</td>
</tr>
<tr>
<td>Medical Assessment</td>
<td>Week 0, Monthly</td>
<td>Collect/verify allergies, comorbidities, concomitant medications; clinician triage</td>
</tr>
<tr>
<td>Patient Education and Training</td>
<td>Week 0, PRN</td>
<td>Clinician initial consult (drug, disease, expectations, AE management; adherence); HCV educational packet; injection training</td>
</tr>
<tr>
<td>Support Program Referral</td>
<td>Week 0, PRN</td>
<td>Facilitate enrollment in manufacturer programs and other supportive organizations</td>
</tr>
<tr>
<td>Side Effect Management</td>
<td>Week 0, PRN</td>
<td>HCV Care Kits, side effect management guides, and clinician counseling</td>
</tr>
<tr>
<td>Adherence and Distribution Calls</td>
<td>At Least Monthly</td>
<td>Outbound call by patient care coordinator to arrange refills, evaluate side effects, education needs, and administration</td>
</tr>
<tr>
<td>Futility Rules and Treatment Outcomes</td>
<td>Varies by Regimen</td>
<td>Collect VL and provide recommendations for treatment plan; outreach to obtain SVR results</td>
</tr>
</tbody>
</table>

Use of Evidence-Based Treatment Algorithms to Minimize Variations in Care

- Ensure standards of HCV care are consistently followed
- Monitor therapy to detect and resolve problems
- Identify opportunities for referral to specialists to address specific issues or problems
- Proactively identify opportunities to maintain/improve adherence
- Provide education to empower patients and caregivers to take charge of their therapy

Specialty Pharmacy Initiative: Phase I Environmental Scan. FMCP. Nov 2009.
Patient Adherence is Critical to Improved Health Outcomes

Specialty HCV drugs improve outcomes

**but** ...

Patients do not take medications the way they should, or in the way it was studied to produce published results
# Adherence Counseling for Patients with HCV

<table>
<thead>
<tr>
<th>Initial</th>
<th>Ongoing</th>
<th>Follow Up</th>
</tr>
</thead>
</table>
| Therapy and disease state overview including:  
  - Disease state education  
  - Drug administration  
  - Treatment-related adverse events (AEs)  
  - Importance of adherence  
  - Depression screening |  
  - Discuss diagnosis and treatment  
  - Review dose, administration, duration of therapy  
  - Depression screening  
  - Address barriers to adherence  
  - Provide guidance for missed doses and AE management  
  - Laboratory reminders and importance of follow up testing |  
  - Adherence assessment including medication possession and refills  
  - Address barriers to adherence  
  - Enact dispensing and/or prescriber engagement to support adherence |

## Utilizing Technology to Improve Adherence

<table>
<thead>
<tr>
<th>Feature</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medication Reminders</td>
<td>Reminders pop up when it’s time to take a medication; user can mark as taken, snooze, or mark as skipped</td>
</tr>
<tr>
<td>Adherence graph</td>
<td>Users can view a graph that charts their adherence through the course of therapy</td>
</tr>
<tr>
<td>Viral load graph</td>
<td>Users can enter viral load following lab work and app graphs their data over time</td>
</tr>
<tr>
<td>E-mail</td>
<td>Medication regimen, adherence graph, and viral load graph can all be emailed to the doctor/nurse/caregiver</td>
</tr>
<tr>
<td>Online tracking</td>
<td>Users document their viral load, doctor visits, symptoms using an app or web-based system</td>
</tr>
</tbody>
</table>

Collaborative Care is Critical to Improving Adherence

- Collaboration between specialty pharmacists, nurses, and physicians allows the care team to
  - Verify the diagnosis and presence of comorbidities
  - Ensure treatment is aligned with the guidelines
  - Monitor and adjust therapy as required to optimize clinical response
  - Minimize treatment duplication and over/underdosing
  - Manage issues related to complexity of treatment
  - Identify and address barriers to adherence
  - Identify gaps in care
  - Provide patient and caregiver education

Summary

- HCV has emerged as one of the most important categories to manage
- Payers are using at multiple interventions to manage access and use of HCV drugs
- Health plan partnerships with specialty pharmacies can improve patient outcomes while lowering overall costs
- Coordinated disease management is vital to promoting improved health outcomes and cost containment
- Use of evidence-based treatment algorithms can minimize variations in HCV care
- Patient adherence is critical to improved outcomes
CAPITALIZING ON HCV ADVANCEMENTS:

Treatment Management and Benefit Design Strategies for Managed Care