Objectives

1. Assess appropriateness of HCV therapy in patients with HIV, renal insufficiency, decompensated liver disease or liver transplant.
2. Describe common resistance features in HCV.
3. Compare and contrast emerging HCV therapies.
4. Describe the role of specialty pharmacists in the management of special populations and collaborations with the healthcare team.
Outline

- HIV-HCV Coinfection
- Renal Insufficiency
- Decompensated Liver Disease and Post-Liver Transplant
- HCV Resistance
- Future Treatment Options
- Specialty Pharmacy Role in Treatment of Special Populations
- Healthcare Team Collaborations
- Insurance Issues
- Case study
HIV/HCV Coinfection: Impact

- High prevalence of HCV in HIV-infected adults
- Accelerates liver fibrosis progression
- Leading cause of death in D:A:D cohort

![Mortality Chart](chart.png)

![SVR Rates Chart](chart2.png)

References:
HIV/HCV Coinfection: Treatment Pearls

- Same regimens as used for HCV monoinfection
- Efficacy similar between HCV monoinfection and HIV/HCV coinfection populations
- HIV antiretroviral therapy (ART) should not be interrupted
- Special attention to drug-drug interactions
  - Avoid “double dosing” RTV when using RTV-boosted DAA therapy (i.e. paritaprevir)
  - Adjust DCV dose based on concomitant ART
  - Monitor impact of DAA and ART on TDF

Drug-Drug Interactions

- Major issue for HIV/HCV coinfection
- Watch Out:
  - Ritonavir (used for both HIV and HCV treatment regimens)
  - Daclatasvir (dose adjustment may be necessary)
  - Tenofovir disoproxil fumarate (TDF)
    - Boosted protease inhibitors, dolutegravir, efavirenz, rilpivirine
    - Additional renal function monitoring
  - Older ART not studied with DAA therapy
<table>
<thead>
<tr>
<th>Sofosbuvir</th>
<th>Ledipasvir</th>
<th>Velpatasvir</th>
<th>Simeprevir</th>
<th>Ombitasvir</th>
<th>Efavirenz</th>
<th>Paritaprevir, ritonavir, ombitasvir plus dasabuvir (POS)</th>
<th>Paritaprevir, ritonavir, ombitasvir (POD)</th>
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<td>Ritonavir-boosted tipranavir</td>
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<th>Ombitasvir</th>
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<th>Paritaprevir, ritonavir, ombitasvir (POD)</th>
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</tr>
</tbody>
</table>

www.hcvguidelines.com
Drug-Drug Interactions Continued

• Consider sofosbuvir plus daclatasvir +/- ribavirin if ART cannot be modified
• Places to assess drug-drug interactions:
  – hcvguidelines.org
  – aidsinfo.nih.gov/guidelines
  – hiv-druginteractions.org
  – hep-druginteractions.org

Outline

• HIV-HCV Coinfection
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• Decompensated Liver Disease and Post-Liver Transplant
• HCV Resistance
• Future Treatment Options
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• Insurance Issues
• Case study
Renal Insufficiency Definitions

- Mild to moderate impairment:
  - CrCl 30-80 ml/min
  - No dose adjustment necessary to currently approved Direct Acting Antivirals (DAA)

- Severe impairment:
  - CrCl <30 ml/min
  - Considerations for sofosbuvir-containing regimens and ribavirin

Sofosbuvir in Renal Impairment

- Primarily renal excretion
- Insufficient data to recommend in patient with severe renal impairment or ESRD
- SOF AUC increase
  - 61% in mild impairment (GFR 50-80 ml/min)
  - 107% in moderate impairment (GFR ≥30 ml/min)
  - 171% in severe impairment (GFR <30 ml/min)
- Primary SOF-metabolite AUC increased up to 451% in severe impairment
AASLD/IDSA Guideline Recommendations in Severe Renal Impairment

• Genotype 1a, 1b, or 4
  – Elbasvir/grazoprevir for 12 weeks
• Genotype 1b for whom urgency to treat is high
  – Paritaprevir/ritonavir/ombitasvir plus twice daily dasabuvir for 12 weeks
• Genotypes 2, 3, 5, or 6 for whom urgency to treat is high
  – PEG-IFN and dose-adjusted ribavirin (200mg daily)

Treatment Options in Severe Renal Impairment

• Elbasvir/Grazoprevir
  – C-SURFER
    • Genotype 1, CKD stage 4-5, treatment naïve or IFN-experienced
    • Elbasvir/grazoprevir or placebo for 12 weeks
    • SVR12 in 99% in those that completed treatment (n=115)
Treatment Options in Severe Renal Impairment

- Paritaprevir/ritonavir/ombitasvir plus dasabuvir
  - RUBY-1
    - Randomized, open-label, Paritaprevir/ritonavir/ombitasvir plus dasabuvir +/- ribavirin
    - Genotype 1, CKD stage 4-5, no cirrhosis or coinfection
    - SVR12 rates
      - GT1a: 85% (n=13)
      - GT1b: 100% (n=7)

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Recommendations for Patients with HCV Infection Who Have Decompensated Cirrhosis

- Patients with moderate or severe hepatic impairment
- Patients with Child Pugh class B or C
- “Should be referred to a medical practitioner with expertise in that condition”


Recommended Regimens for Patients with Decompensated Liver Disease

<table>
<thead>
<tr>
<th>Therapy</th>
<th>GT 1</th>
<th>GT 2</th>
<th>GT 3</th>
<th>GT 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ledipasvir/sofosbuvir + RBV x 12 weeks</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Sofosbuvir/velpatasvir + RBV x 12 weeks</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Daclatasvir plus sofosbuvir + RBV x 12 weeks</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>

If Ribavirin Ineligible:

<table>
<thead>
<tr>
<th>Therapy</th>
<th>GT 1</th>
<th>GT 2</th>
<th>GT 3</th>
<th>GT 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ledipasvir/sofosbuvir x 24 weeks</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Sofosbuvir/velpatasvir x 24 weeks</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Daclatasvir plus sofosbuvir x 24 weeks</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>

Bold indicates Class I, Level A recommendation

SOLAR-1: LDV/SOF + RBV for HCV Patients with HCV GT 1 or 4 and Decompensated Cirrhosis

Results:

SVR12 rates were similar with 12 or 24 weeks of LDV/SOF + RBV


*Patients with CTP scores 13-15 were excluded

ASTRAL-4: SOF/VEL ± RBV in HCV Patients with HCV GT 1, 2, 3, 4, 6 and Decompensated Liver Disease

Week 0 12 24 36
n=90 SOF/VEL
n=87 SOF/VEL + RBV
n=90 SOF/VEL

Patients

<table>
<thead>
<tr>
<th></th>
<th>Median MELD (range)</th>
<th>MELD &lt; 15, n (%)</th>
<th>CTP B, n (%)</th>
<th>Ascites, n (%)</th>
<th>Encephalopathy, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SOF/VEL 12 weeks n=90</td>
<td>10 (6–24)</td>
<td>86 (96)</td>
<td>86 (96)</td>
<td>74 (82)</td>
<td>52 (58)</td>
</tr>
<tr>
<td>SOF/VEL+RBV 12 weeks n=87</td>
<td>10 (6–18)</td>
<td>83 (95)</td>
<td>77 (89)</td>
<td>65 (75)</td>
<td>54 (62)</td>
</tr>
<tr>
<td>SOF/VEL 24 weeks n=90</td>
<td>11 (6–19)</td>
<td>85 (84)</td>
<td>77 (86)</td>
<td>75 (83)</td>
<td>59 (66)</td>
</tr>
</tbody>
</table>


ASTRAL-4: Decompensated Liver Disease
SVR Results

For GT1-6, the highest SVR was seen with SOF/VEL + RBV

*Patient with nondetectable drug levels at time of virologic failure.
Charlton M, et al., AASLD, 2015, #LB-13
What Shouldn’t Be Used and Why?

• Simeprevir-based regimens
• Paritaprevir-based regimens
• Elbasvir/grazoprevir-based regimens

• Limited data and concerns for worsening liver disease in patients with Child Pugh B or C
• Reports of decompensation leading to liver failure and death
  – Paritaprevir-based regimens are contraindicated in patients with Child Pugh B or C cirrhosis
  – Elbasvir/grazoprevir contraindicated in patients with Child Pugh B or C cirrhosis

What is the Effect of Decompensated Liver Disease on Successful HCV Therapy?

• Patients with decompensated liver disease can be successfully treated
  – Recommended therapies include ledipasvir/sofosbuvir for GT 1 and 4; sofosbuvir/velpatasvir or daclatasvir plus sofosbuvir for GT 1, 2, 3, or 4
• Decompensated liver disease is more difficult to treat
  – Lower overall SVR compared to non-cirrhotic patients
    • Patients with GT 3 have lower SVR compared to other genotypes
    • Often requires concomitant ribavirin use
  – Challenge of underlying liver disease
    • Recommendation for treatment by experienced clinician
  – Avoid simeprevir
  – Elbasvir/grazoprevir and paritaprevir-based therapies are contraindicated

Recommended Regimens for Patients with HCV Post-Liver Transplant

- Ledipasvir/sofosbuvir with ribavirin x 12 weeks
  - For genotype 1 or 4 including compensated cirrhosis and decompensated cirrhosis
- Daclatasvir plus sofosbuvir with ribavirin x 12 weeks
  - For genotype 1, 2, 3 or 4 including compensated cirrhosis


SOLAR-1: LDV/SOF + RBV in Post-Transplant SVR12 Results

Error bars represent 2-sided 90% exact confidence intervals.
Reddy, AASLD, 2014, Oral #8
ALLY-1: Daclatasvir + Sofosbuvir + RBV for HCV in Post-Liver Transplant Patients

• Evaluated daclatasvir + sofosbuvir + ribavirin for 12 weeks in 53 patients status post liver transplant
• SVR rates high: Overall SVR 94% (50/53)
  – Genotype 1a 97% (30/31)
  – Genotype 1b 90% (9/10)
  – Genotype 3 91% (10/11)
  – Genotype 6 100% (1/1)


Drug Interactions with DAAs and Calcineurin Inhibitors

<table>
<thead>
<tr>
<th>HCV DAA</th>
<th>Cyclosporine</th>
<th>Tacrolimus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sofosbuvir</td>
<td>No a priori dose adjustment needed but monitor CSA levels and adjust as needed</td>
<td>No a priori dose adjustment but monitor TAC levels and adjust as needed</td>
</tr>
<tr>
<td>Ledipasvir</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Daclatasvir</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Velpatasvir</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PrOD</td>
<td>Suggested to use 1/5 of CSA dose; monitor CSA levels and adjust as needed</td>
<td>57x increase in TAC AUC. Suggested to use 0.5 mg TAC every 7 days, monitor, and adjust as needed.</td>
</tr>
<tr>
<td>PrO</td>
<td>Suggested to use 1/5 of CSA dose; monitor CSA levels and adjust as needed</td>
<td>86x increase in TAC AUC. Suggested to use 0.5 mg TAC every 7 days, monitor, and adjust as needed.</td>
</tr>
<tr>
<td>Simeprevir</td>
<td>5.8x increase in SMV; Not recommended</td>
<td>85% increase in SMV AUC. Monitor TAC levels and adjust as needed.</td>
</tr>
<tr>
<td>Elbasvir/ Grazoprevir</td>
<td>15x increase in GZR AUC and 2x increase in EBR AUC; Not recommended</td>
<td>43% increase in TAC, no a priori dose adjustment but monitor and adjust TAC levels as needed</td>
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</table>
Summary for Treatment in Post-Transplant Setting

- Limited data in post transplant setting but available data with sofosbuvir + daclatasvir and ledipasvir/sofosbuvir show high SVR
  - Other agents have limited data or concerns for drug-drug interactions

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**Recommendations for Pre-Treatment Resistance Testing in HCV**

<table>
<thead>
<tr>
<th>Year</th>
<th>Therapy</th>
<th>Resistance Recommendation</th>
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<tr>
<td>&lt;2013</td>
<td>PegIFN + RBV +/− BOC or TPV</td>
<td>No resistance testing</td>
</tr>
<tr>
<td>2013</td>
<td>PegIFN + RBV + SMV</td>
<td>Baseline for NS3 Q80k for SMV in genotype 1a</td>
</tr>
<tr>
<td>2014</td>
<td>PegIFN + RBV + SOF</td>
<td>No resistance testing</td>
</tr>
<tr>
<td></td>
<td>SOF + SMV +/− RBV</td>
<td>Baseline NS3 Q80k for SMV in genotype 1a</td>
</tr>
<tr>
<td>2014</td>
<td>LDV/SOF +/− RBV</td>
<td>No resistance testing</td>
</tr>
<tr>
<td>2014</td>
<td>PrOD +/− RBV</td>
<td>No resistance testing</td>
</tr>
<tr>
<td>2016</td>
<td>EBR/GZR +/− RBV</td>
<td>Baseline NS5A resistance testing for genotype 1a</td>
</tr>
<tr>
<td>2016</td>
<td>SOF + DCV +/− RBV</td>
<td>Baseline NS5A resistance testing for genotype 1a cirrhosis</td>
</tr>
<tr>
<td>2016</td>
<td>SOF/VEL +/− RBV</td>
<td>Baseline NS5A resistance for patients with genotype 3 and cirrhosis or prior treatment experience</td>
</tr>
</tbody>
</table>

**HCV Resistance**

- HCV replicates at a rate of up to $10^{12}$ particles produced per day
  - HCV polymerase lacks proofreading capacity making it highly error prone
  - Resistance associated polymorphisms occur naturally as minor populations
    - Carry amino acid substitutions which may alter drug target
  - Increasing interest because new therapies act directly on the hepatitis C virus, thus may be susceptible to viral mutations

HCV Molecular Targets and Associated Therapies: Proteins Encoded by HCV Genome

Slide courtesy Monique Dodd, PharmD, MLS(ASCP)

NS3 Resistance

- Q80k most common substitution affecting susceptibility of simeprevir
  - Known to reduce SVR in GT1a patients treated with simeprevir
  - Reduces susceptibility of paritaprevir
  - Substitutions at Q80 had no impact on antiviral activity of grazoprevir
- Y56, R155, A156, D168 and others
  - May affect grazoprevir and paritaprevir susceptibility
  - Combination of substitutions can have greater impact on antiviral activity than single mutations

NS5A Inhibitors and Drug Resistance

• Resistance uncommon in treatment naïve patients, except:
  – L31M - observed in approximately 6% of patients
    • Associated with >500-fold reduced susceptibility
  – Y93H - observed in approximately 14% of patients
    • Associated with >1000-fold reduced susceptibility
  – Others include: M28, Q30, A30, L28

Significance of Baseline NS5A Resistance on Treatment Outcomes in Treatment Naïve Patients

• Ledipasvir/Sofosbuvir
  – No difference in SVR 98% (1198/1219) if no baseline NS5A mutations vs 96% (356/370) if baseline NS5A mutations

• Elbasvir/Grazoprevir
  – No difference in SVR in GT1b
  – For GT1a, 58% SVR (11/19) if baseline NS5A mutations) vs 99% SVR (133/135) if no baseline NS5A mutations
    • Recommendation to add ribavirin and extend treatment duration to 16 weeks if baseline NS5A mutations identified
Significance of Resistance in Patients Who Failed NS5A Based Therapy

• Compared to treatment naïve patients, patients who failed NS5A-based therapy have
  – Higher rates of baseline NS5A mutations
  – Lower SVR
• Concerns for treatment emergent resistance and persistence of resistance post HCV therapy
  – In clinical studies, >85% of patients has NS5A RAVs after 1-2 years of treatment failure

NS5B Resistance

• Dasabuvir: non-nucleoside inhibitor
  – Low barrier to resistance
    • 1 substitution can reduce susceptibility
• Sofosbuvir: nucleotide inhibitor
  – High barrier to resistance
    • Specific mutations which decrease susceptibility are not known to occur naturally
    • To date, no clinical treatment failures due to sofosbuvir resistance

• NS5B resistance testing is not recommended
What About Resistance Testing for Genotype 3?

- Per HCV Guidelines for treatment experienced or cirrhotic patients with GT3:
  - “RAV testing for Y93H is recommended and ribavirin should be included in regimen if present”

- Of 250 patients treated with sofosbuvir/velpatasvir
  - SVR 97% if no baseline resistance
  - SVR 88% if any NS5A resistance identified
    - SVR 84% if Y93 mutation

Who Needs Resistance Testing and Which Tests?

- NS5A HCV resistance testing important for patients:
  - HCV GT1a considering elbasvir/grazoprevir
  - HCV GT3 patients who have cirrhosis or prior treatment-experience

- NS3 and NS5A resistance testing for any patients who fail all oral DAA-therapy for GT 1 or 3
  - Helps to optimize re-treatment strategy

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Sofosbuvir/Velpatasvir + Voxilaprevir for GT1, DAA experienced, ± Cirrhosis

Lawitz E. EASL 2016.
**Sofosbuvir/Velpatasvir + Voxilaprevir for GT 1-6, Treatment Experienced ± Cirrhosis**

<table>
<thead>
<tr>
<th>Population</th>
<th>SVR12</th>
<th>Duration (weeks)</th>
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<tbody>
<tr>
<td>Non-cirrhotic</td>
<td>100%</td>
<td>8</td>
</tr>
<tr>
<td>Cirrhotic</td>
<td>97%</td>
<td>12</td>
</tr>
<tr>
<td>Non-cirrhotic</td>
<td>98%</td>
<td>8 (+/-RBV)</td>
</tr>
<tr>
<td>Non-cirrhotic</td>
<td>97%</td>
<td>8</td>
</tr>
<tr>
<td>Cirrhotic</td>
<td>100%</td>
<td>12</td>
</tr>
<tr>
<td>GFR &lt;30 (Stage 4 or 5 CKD), with or without cirrhosis</td>
<td>98%</td>
<td>12</td>
</tr>
</tbody>
</table>

**Glecaprevir/Pibrentasvir**

<table>
<thead>
<tr>
<th>GT</th>
<th>Treatment History</th>
<th>Population</th>
<th>Duration (weeks)</th>
<th>SVR12</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Naïve or IFN experienced</td>
<td>Non-cirrhotic</td>
<td>8</td>
<td>97% (33/34)</td>
</tr>
<tr>
<td>1</td>
<td>Naïve or IFN experienced</td>
<td>Cirrhotic</td>
<td>12</td>
<td>96% (26/27)</td>
</tr>
<tr>
<td>1</td>
<td>Prior DAA</td>
<td>Non-cirrhotic</td>
<td>12 (+/-RBV)</td>
<td>89% (39/44)</td>
</tr>
<tr>
<td>2</td>
<td>Naïve or IFN experienced</td>
<td>Non-cirrhotic</td>
<td>8</td>
<td>98% (53/54)</td>
</tr>
<tr>
<td>3</td>
<td>Naïve</td>
<td>Non-cirrhotic</td>
<td>8</td>
<td>97% (28/29)</td>
</tr>
<tr>
<td>3</td>
<td>Naïve</td>
<td>Cirrhotic</td>
<td>12</td>
<td>100% (24/24)</td>
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<tr>
<td>4-6</td>
<td>Naïve or IFN experienced</td>
<td>Non-cirrhotic</td>
<td>12</td>
<td>100% (34/34)</td>
</tr>
<tr>
<td>1-6</td>
<td>Naïve or IFN experienced</td>
<td>GFR &lt;30 (Stage 4 or 5 CKD), with or without cirrhosis</td>
<td>12</td>
<td>98% (102/104)</td>
</tr>
</tbody>
</table>

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Specialty Pharmacy Role

Patient Evaluation
- Adherence readiness assessment
- Comorbidities impacting treatment
- Social factors
- Current pill burden
- Reinfection risk
- Appropriate clinical evaluation
- Medication reconciliation

Regimen Selection
- Drug-Drug interactions
- Dosing considerations
- Adverse effect considerations
- Resistance

Specialty Pharmacy Role

Patient Access
- Prior Authorization
- Appeal
- Patient Assistance Programs
- Financial Assistance

Medication education
- Side effect monitoring
- Adherence Action Plan and instructions for missed doses
- Follow-up plan
- Contact information

Monitoring
- Safety
- Efficacy
- Adherence
- Care Coordination
Outline

- HIV-HCV Coinfection
- Renal Insufficiency
- Decompensated Liver Disease and Post-Liver Transplant
- HCV Resistance
- Future Treatment Options
- Specialty Pharmacy Role in Treatment of Special Populations
- Healthcare Team Collaborations
- Insurance Issues
- Case study
### Specialty Pharmacy Multidisciplinary Team

<table>
<thead>
<tr>
<th>Role</th>
<th>Responsibilities</th>
</tr>
</thead>
</table>
| Physician/PA/NP     | • Patient and disease state evaluation  
                        • Clinical assessment and monitoring                                           |
| Pharmacist          | • Medication evaluation  
                        • Education  
                        • Medication and adherence monitoring                                           |
| Nurse               | • Coordination of Care  
                        • Medication administration  
                        • Lab coordination                                                            |
| Pharmacy Technician | • Refill Monitoring  
                        • PA/Appeal paperwork  
                        • Copay cards/other assistance                                                 |

**Other possible players:**
- Social worker
- Financial counselors
- Mental health professionals

### Principles of Team-Based Health Care

- Shared goals
- Clear roles
- Mutual trust
- Effective communication
- Measurable processes and outcomes

*Mitchell P. Institute of Medicine, 2012.*
Barriers to Multidisciplinary Team

- HC Team Buy-In
- Time Constraints
- PBM Restrictions
- Lack of Reimbursement
- Restricted Access

Specialty Provider Workload with Collaborative Practice

Workload Prior to Implementing Collaborative Practice
- Patient and disease state assessment
- Readiness assessment
- Medication reconciliation
- Medication education/counseling
- Laboratory and imaging evaluation
- Prescribing therapy
- Decentralized PA/appeal/financial assistance process
- On-treatment monitoring
- Post-treatment evaluation/counseling

Provider Workload With Collaborative Practice
- Patient and disease state assessment
- Readiness assessment
- Laboratory and imaging evaluation
- Prescribing therapy
- On-treatment monitoring (shared)
- Post-treatment evaluation/counseling

Pharmacist Workload With Collaborative Practice
- Medication reconciliation
- Medication education/counseling
- Centralized PA/appeal/financial assistance process
- On-treatment monitoring (shared)

Slide adapted from Cody Chastain, MD.
Pharmacists with Prescriptive Authority

- Indian Health Services
  - Clinical Pharmacy Specialists
  - Recognition of pharmacists as primary care providers with prescriptive authority
  - Scope of practice and medication prescribing authority granted by facility
- Pharmacist Clinicians
  - Licensing first recognized by New Mexico Board of Pharmacy in 1993
  - Allows prescriptive authority: guidelines or protocol submitted to Board with practitioner granting prescriptive authority within scope of practice

Outline

- HIV-HCV Coinfection
- Renal Insufficiency
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- HCV Resistance
- Future Treatment Options
- Specialty Pharmacy Role in Treatment of Special Populations
- Healthcare Team Collaborations
- Insurance Issues
- Case study
Cost of HCV Treatment

*Cost for 48 weeks

Cost related to chronic HCV Infection

<table>
<thead>
<tr>
<th>Condition</th>
<th>Cost per Patient per Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-cirrhotic liver disease</td>
<td>$17,277</td>
</tr>
<tr>
<td>Compensated cirrhosis</td>
<td>$22,752</td>
</tr>
<tr>
<td>End stage liver disease</td>
<td>$59,995</td>
</tr>
<tr>
<td>Hepatocellular carcinoma</td>
<td>$112,537</td>
</tr>
<tr>
<td>Liver transplant</td>
<td>$145,000</td>
</tr>
</tbody>
</table>
Patients with Insurance

• Identifying patient’s insurance
• Identifying preferred pharmacies
• Obtaining prior authorization form

Prior Authorization and Appeals
• PA completion
• Steps following a denial

Benefits Investigation

On-Treatment Considerations
• Avoiding lapse in treatment
• Insurance changes

Copay/Financial Assistance

Prior Authorization

• What to include:
  1. PA application provided
  2. Genotype and viral load
  3. Staging: FIB-4 score, ultrasound, CT, etc.
  4. Clinical notes
  5. Ancillary items requested by certain PBMs
     • Resistance testing (certain medications/populations)
     • Urine drug screen
     • Rehab documentation
     • Adherence readiness assessment

• Follow-up if no response in 2-3 days
APPROVED!- Now what?

• Pharmacy should run a test claim
  – Ensure approval
  – Determine copay
• Determine if patient qualifies copay assistance
  – Medicaid: does not qualify for assistance → copay
  – Medicare: obtain foundation assistance → contact patient
    • Pharmacy should do this
  – Commercial: obtain copay card if patient copay is >$10
    • Pharmacy should do this

Copay Cards: Gilead SupportPath

<table>
<thead>
<tr>
<th>Drug</th>
<th>Patient Cost</th>
<th>Copay Card Information</th>
<th>Card Details</th>
<th>Eligibility</th>
</tr>
</thead>
<tbody>
<tr>
<td>Harvoni®</td>
<td>$5</td>
<td><a href="https://www.harvoni.com/support-and-savings/copay-coupon-registration">https://www.harvoni.com/support-and-savings/copay-coupon-registration</a></td>
<td>-Max of 25% of the catalog price of a 12-week regimen</td>
<td>-Resident of US, PR, or US territories</td>
</tr>
<tr>
<td>Sovaldi®</td>
<td>$5</td>
<td><a href="https://www.sovaldi.com/coupons/">https://www.sovaldi.com/coupons/</a></td>
<td>-Valid for 6 months from 1st redemption</td>
<td>-No state or federally funded programs</td>
</tr>
<tr>
<td>Epclusa®</td>
<td>$5</td>
<td><a href="http://www.epclusainfo.com/support-and-savings/copay-coupon-registration">http://www.epclusainfo.com/support-and-savings/copay-coupon-registration</a></td>
<td></td>
<td>≥18 years old</td>
</tr>
</tbody>
</table>

Contact: 1-855-769-7284
### Copay Cards: Abbvie ProCeed

<table>
<thead>
<tr>
<th>Drug</th>
<th>Patient Cost</th>
<th>Copay Card Information</th>
<th>Card Details</th>
<th>Eligibility</th>
</tr>
</thead>
<tbody>
<tr>
<td>Viekira XR®</td>
<td>$5</td>
<td><a href="https://www.viekira.com/patient-support/financial-resources">https://www.viekira.com/patient-support/financial-resources</a></td>
<td>-Max of 25% of the catalog price</td>
<td>-Resident of US</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>-Valid for 12 uses</td>
<td>-No state or federally funded programs</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>-Expires 12 months from 1st redemption</td>
<td>-Not valid in Massachusetts</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Viekira Pak*</td>
<td>$5</td>
<td><a href="https://www.viekira.com/content/pdf/viekira-treatment.pdf">https://www.viekira.com/content/pdf/viekira-treatment.pdf</a></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Technivie®</td>
<td>$5</td>
<td><a href="https://www.viekira.com/content/pdf/viekira-treatment.pdf">https://www.viekira.com/content/pdf/viekira-treatment.pdf</a></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Contact:</strong> 1-844-277-6233</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Copay Cards: Bristol-Myers Squibb Patient Support CONNECT

<table>
<thead>
<tr>
<th>Drug</th>
<th>Patient Cost</th>
<th>Copay Card Information</th>
<th>Card Details</th>
<th>Eligibility</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daklinza®</td>
<td>$0</td>
<td><a href="https://bmsdm.sourceforge.com/patient-supportconnect/patient">https://bmsdm.sourceforge.com/patient-supportconnect/patient</a></td>
<td>-Max of $5,000 per 28-day supply of 30mg or 60mg tablets OR up to max of $10,000 per 28-day supply of 90mg</td>
<td>-Resident of US or Puerto Rico</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>-Must activate before 12/31/16</td>
<td>-No state or federally funded programs</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>-Program expires 12/31/17 (except in Mass. 6/30/17)</td>
<td>-≥18 years old</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
## Copay Cards: Merck

<table>
<thead>
<tr>
<th>Drug</th>
<th>Patient Cost</th>
<th>Copay Card Information</th>
<th>Card Details</th>
<th>Eligibility</th>
</tr>
</thead>
</table>
| Zepatier® | $5          | https://www.merckaccessprogram-zepatier.com/hcp/copay-assistance/ | -Max of 25% of the catalog price per prescription  
-Program expires 6/30/17                                                  | -Resident of US or Puerto Rico  
-No state or federally funded programs  
-≥18 years old                                                             |
|        |              | Contact: 1-866-251-6013                                      |                                                             |                                                                            |

## Copay Cards: Janssen CarePath

<table>
<thead>
<tr>
<th>Drug</th>
<th>Patient Cost</th>
<th>Copay Card Information</th>
<th>Card Details</th>
<th>Eligibility</th>
</tr>
</thead>
</table>
| Olysio® | $5          | https://olysio.janssen carepathsavings.com/Coupon/Olysio      | -Max of $50,000 per calendar year  
-Program expires 12/31/17                                                  | -Resident of US or Puerto Rico  
-No state or federally funded programs                                        |
|        |              | Contact: 1-855-565-9746                                      |                                                             |                                                                            |
Grant Funding

• Complete grant funding application
  • Yearly household income
  • Household size
  • Retired
  • File taxes
  • Submit application online

<table>
<thead>
<tr>
<th>Grant</th>
<th>Patient Cost</th>
<th>Information</th>
<th>Eligibility</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient Access Network Foundation (PANF)</td>
<td>$0</td>
<td><a href="https://pharmacyportal.panfoundation.org/Home.aspx">https://pharmacyportal.panfoundation.org/Home.aspx</a></td>
<td>-Max of $30,000/year</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Contact: 1-866-316-7263</td>
<td>-Reside in US</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>-Income below 400% or 500% FPL</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>-Any insurance</td>
</tr>
<tr>
<td>Patient Advocate Foundation (PAF)</td>
<td>$0</td>
<td><a href="https://www.copays.org/diseases/hepatitis-c">https://www.copays.org/diseases/hepatitis-c</a></td>
<td>-Max of $25,000/year</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Contact: 1-866-512-3861</td>
<td>-Reside in US</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>-Income below 400% FPL</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>-Any insurance</td>
</tr>
<tr>
<td>Good Days</td>
<td>Based on poverty percentage-up to $50</td>
<td><a href="http://www.mygooddays.org/for-patients/patient-assistance/">http://www.mygooddays.org/for-patients/patient-assistance/</a></td>
<td>-Max of $30,000/year</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Contact: 1-972-608-7141</td>
<td>-Reside in US</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>-Any insurance, must pay at least 50% of copay</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>-Income below 500% FPL</td>
</tr>
<tr>
<td>Healthwell Foundation</td>
<td>$5/fill</td>
<td><a href="https://www.healthwellfoundation.org/fund/hepatitis-c/">https://www.healthwellfoundation.org/fund/hepatitis-c/</a></td>
<td>-Max of $30,000/year</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Contact: 1-800-675-8416</td>
<td>-Reside in US</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>-Any insurance</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>-Income below 500% FPL</td>
</tr>
</tbody>
</table>
Denied- Now What?

- Call the PBM and ask about rejection.
  - Why was it rejected?
  - Is there a preferred agent?
  - What are the next steps (appeal, peer-to-peer review, external review, etc.)
  - Write appeal letter
  - Fax back appeal, original PA paperwork, and any supporting documentation (AASLD/IDSA Guidelines, clinical trial data, drug interaction analysis, etc.)

Appeal Elements

- Reason for request
- Reason for denial
- Rationale to address each reason for denial, including relevant clinical rationale where applicable
- Relevant overall patient medical history and current condition
- Summary of your professional opinion of likely outcomes with the treatment
- Restatement of request for approval

*Adapted from Abbvie Letter of Medical Necessity Template
Gilead sample Letter of Medical Necessity
Appeal Supporting Documents

• Any required appeal form from the insurer (if applicable)
• Copy of the denial letter from the insurance company
• Copy of the prescription
• Patient’s signature on consent form for treatment
• Patient’s complete medication profile including patient’s current, previous and discontinued medications
• Patient’s medical profile
• Relevant lab results, diagnostics, pathology reports, including illicit drug screening results
• Relevant treatment guidelines
• Relevant peer-reviewed journal articles
• Relevant clinical trial information
• Relevant cost information (if known)

*From Abbvie Letter of Medical Necessity Template

On-Treatment Considerations

• PA continuation requirements
  – 4 week viral load
• PA extension
  – Starting later than expected
  – On treatment viral load detectable
• Insurance changes
• Refills
  – Encourage the patient to call 7-10 days before running out
• Emergency shipments
  – Insurance
  – Manufacturer
The Un-Insured and Under-Insured

Patient Assistance Programs (PAP)
- Criteria for approval
- Process of Application

Medication Delivery
- Setting up the first fill
- Patient Support on therapy

Other Access Resources

- Hepatitis C New Drug Research

- American Liver Foundation
  – http://hepc.liverfoundation.org/resources/what-if-i-need-financial-assistance-to-pay-for-treatment/

- Life Beyond Hepatitis C
Summary

- Direct-acting antivirals can be safely and effectively used to treat patients with comorbidities, including patients with HIV-HCV coinfection, renal disease including hemodialysis, decompensated liver disease, and post-liver transplant.
- Baseline HCV resistance can affect treatment efficacy thus some patients may require baseline resistance testing.
- Potential for resistance to develop during therapy underscores importance in avoiding treatment interruptions and need for adherence.
- Cost of HCV therapies can affect access to treatment-assistance critical in appeal process and consider various patient assistance programs.

Case Study

- 45 yo male with chronic HCV and renal insufficiency evaluated for treatment of HCV. He has GT1a with a viral load of 425,000 IU/mL. Labs show a serum creatinine of 2.5 mg/dL, albumin 3.5 g/dL, AST 80 IU/mL, ALT 65 IU/ml, platelets 190,000. Transient elastography is 8 kPa.

- What are his treatment options?