Annual Hepatitis C Update
Target Audience: Pharmacists
ACPE#: 0202-0000-18-064-L01-P
Activity Type: Knowledge-based
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Disclosures

Linda Spooner: Nothing to disclose
Paulina Deming: Nothing to disclose

Target Audience:

ACPE#:

Activity Type:

The American Pharmacists Association is accredited by the Accreditation Council for Pharmacy Education as a provider of continuing pharmacy education.
Learning Objectives

At the completion of this knowledge-based activity, participants will be able to:
1. Identify important changes in recently updated guidelines that have the potential to influence the management of hepatitis C virus (HCV) infection.
2. Describe clinically important drug updates, adverse effects, and drug-drug interactions associated with new drug classes used in the treatment of HCV infection.
3. Outline strategies for improving patient adherence to drug therapy for HCV infection and reducing comorbidities.
Assessment Question #1

Use of which of the following antiepileptic drugs results in a clinically significant drug-drug interaction with sofosbuvir?

A. Phenytoin
B. Levetiracetam
C. Lacosamide
D. Topiramate
Assessment Question #2

Four weeks after initiating therapy with velpatasvir/sofosbuvir for his genotype 3 HCV infection, Mr. Jones reports that he misses at least one dose of medication each week. Which of the following is the most appropriate action for the specialty pharmacist to take?
A. Inform him that his adherence is at 85% and that this is appropriate to achieve virologic suppression
B. Notify the prescriber that Mr. Jones’ treatment should be discontinued due to nonadherence
C. Ask Mr. Jones about his daily routine to identify why doses are being missed
D. Change Mr. Jones’ treatment to one of shorter duration
Assessment Question #3

Which of the following is an approved but not recommended regimen as per the AASLD guidelines for the treatment of HCV genotype 1a?

A. Elbasvir/grazoprevir plus ribavirin x 12 weeks
B. Glecaprevir/pibrentasvir x 8 weeks
C. Ledipasvir/sofosbuvir x 8 weeks
D. Sofosbuvir/velpatasvir x 12 weeks
Assessment Question #4

A 37 yo female without cirrhosis is on hemodialysis has HCV GT 2. What therapy is appropriate for treatment of her HCV?

A. Elbasvir/grazoprevir x 12 weeks
B. Glecaprevir/pibrentasvir x 8 weeks
C. Glecaprevir/pibrentasvir x 12 weeks
D. Sofosbuvir/velpatasvir/voxilaprevir x 12 weeks
Session Outline

- General overview of hepatitis C virus (HCV) infection
  - HCV background
  - Pharmacotherapy update
- Case application to illustrate advanced topics
  - Criteria for treatment selection
  - Recommended regimens
  - Unique populations
- Resources
  - For treatment and adherence
HCV Epidemiology

- Approximately 4 million persons in the United States infected
  - More common in blacks and in men
  - More than 16,000 new cases yearly
- 85% of new cases become chronic
- Leading cause of
  - Chronic liver disease
  - Cirrhosis
  - Liver cancer
  - Liver transplantation
- Risk factors for transmission
- Genotype (GT) 1 most common in United States
- Treatment goal: sustained virologic response (SVR) = cure
Hepatitis C: Progression of Disease

Normal Liver → Chronic Hepatitis → Cirrhosis → HCC / ESLD / Death

HCV Infection → 20-25 years → 25-30 years

Extrahepatic Manifestations Associated with HCV Infection

- Hematologic
  - Aplastic anemia
  - Thrombocytopenia

- Dermatologic
  - Porphyria cutanea tarda
  - Cutaneous necrotizing vasculitis

- Renal
  - Glomerulonephritis
  - Nephrotic syndrome

- Endocrine
  - DM
  - Hypothyroidism

- Ocular
  - Corneal ulcer
  - Uveitis

- Neuromuscular
  - Weakness, myalgia, arthritis
  - Peripheral neuropathy

- Psychiatric
  - Depression
HCV Screening: Who?

- One-time screening for
  - All individuals born between 1945 and 1965
  - People with behaviors, exposures, or conditions associated with increased risk of infection
    - HIV-positive individuals
    - Illicit drug use (intravenous or intranasal)
    - Long-term hemodialysis
    - Children born to HCV-positive mother
    - Recipients of blood transfusions/organ transplantation prior to HCV screening
    - Received tattoo in unregulated setting
    - Unexplained chronic liver disease

AASLD/IDSA/IAS–USA. RECOMMENDATIONS FOR TESTING, MANAGING, AND TREATING HEPATITIS C. HTTP://WWW.HCVGUIDELINES.ORG. ACCESSED NOVEMBER 7, 2023
HCV Assessment

- HCV antibody
  - Screening test
- HCV RNA
  - Quantitative viral load
- HCV GT
  - Guide treatment selection
- Noninvasive assessments of disease progression (discussed later)
- Additional information
  - Hepatitis A/B serologies
  - HIV testing
  - Basic metabolic panel/complete blood count

AASLD/IDSA/IAS–USA. HTTP://WWW.HCVGUIDELINES.ORG. ACCESSED 11/7/17
Chronic HCV Infection
Primary Treatment Goal

- Sustained virologic response (SVR)
  - Clinical cure
- Undetectable HCV RNA (viral load) following treatment
  - Currently 12 weeks following end of treatment (SVR 12)
- Requires strict adherence to treatment regimens
  - Need to emphasize to patients!
  - Will discuss later with case example
Differences in HCV Therapy: Then and Now

<table>
<thead>
<tr>
<th>Interferon Based</th>
<th>Direct-Acting Antivirals (DAA) Based</th>
</tr>
</thead>
<tbody>
<tr>
<td>▪ Injectable</td>
<td>▪ Oral</td>
</tr>
<tr>
<td>▪ Long duration of treatment</td>
<td>▪ Short durations</td>
</tr>
<tr>
<td>▪ High side effect profile</td>
<td>▪ Minimal side effects</td>
</tr>
<tr>
<td>▪ Multiple laboratory abnormalities</td>
<td>▪ Minimal laboratory abnormalities</td>
</tr>
<tr>
<td>▪ Low cure rates</td>
<td>▪ High cure rates</td>
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</tbody>
</table>
The Evolution of Highly Effective Treatment
# HCV Direct Acting Antivirals (DAAs)

<table>
<thead>
<tr>
<th>Target</th>
<th>NS3/4A: Protease Inhibitors (-previr)</th>
<th>NS5A: Replication Complex Inhibitors (-asvir)</th>
<th>NS5B: Polymerase Inhibitors (-buvir)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Boceprevir*</td>
<td>Ledipasvir</td>
<td>Nucleotide: Sofosbuvir</td>
</tr>
<tr>
<td></td>
<td>Telaprevir*</td>
<td>Ombitasvir</td>
<td>Non-nucleoside: Dasabuvir</td>
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<td></td>
<td>Simeprevir</td>
<td>Daclatasvir</td>
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<tr>
<td></td>
<td>Paritaprevir</td>
<td>Elbasvir</td>
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<td></td>
<td>Grazoprevir</td>
<td>Velpatavir</td>
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<td></td>
<td>Glecaprevir</td>
<td>Pibrentasvir</td>
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<tr>
<td></td>
<td>Voxilaprevir</td>
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*Removed from the market*
Ledipasvir/Sofosbuvir

- Approved Oct. 2014
- Combination of
  - NS5B polymerase inhibitor (Sofosbuvir);
  - NS5A inhibitor (ledipasvir)
- Administration
  - One tablet once daily with or without food
  - Requires acidic environment for absorption
- Indicated for GT 1 and 4

ION Phase 3 Program (ION-1, ION-2, ION-3)

Efficacy Summary

- **97% (1886/1952) overall SVR rate**

Error bars represent 95% confidence intervals.

Elbasvir/ Grazoprevir (EBR/GZR)

- Approved Feb. 2016
- Fixed-dose combination tablet
  - 50 mg elbasvir (NS5A replication complex inhibitor)
  - 100 mg grazoprevir (NS3/4A protease inhibitor)
- Dosing: 1 tablet per day with or without food
  - Indicated for HCV genotypes 1 and 4
    - Patients with GT 1a require pre-treatment resistance testing
    - If present, must add ribavirin and extend treatment duration to 16 weeks
Elbasvir-Grazoprevir in Treatment-Naïve HCV GT 1, 4 or 6
C-EDGE TN: Results

Primary efficacy analysis included all patients who received \( \geq 1 \) dose of drug.

Sofosbuvir/Velpatasvir

- Approved June 2016

- Fixed-dose combination of sofosbuvir (NS5B inhibitor) and velpatasvir (NS5A inhibitor)

- Indicated for chronic HCV genotypes 1, 2, 3, 4, 5, or 6

- Administration
  - One tablet once daily with or without food
  - Requires acidic environment for absorption
ASTRAL-1: SOF/VEL for 12 weeks in GT 1, 2, 4, 5 or 6

![SVR12 (%) Bars](image)

- Total: 618/624
- Non-Cirrhotic: 496/501
- Cirrhotic: 120/121
- Treatment-Naïve: 418/423
- Treatment-Experienced: 200/201

99% 99% 99% 99% 99%

Error bars represent 95% confidence intervals.
Sofosbuvir/Velpatasvir/Voxilaprevir

- Approved July 18, 2017
- Combination of
  - NS5B polymerase inhibitor (Sofosbuvir);
  - NS5A inhibitor (Velpatasvir);
  - NS3/4A protease inhibitor (Voxilaprevir)
- Duration of therapy 12 weeks
- Administration
  - One tablet once daily with food
Sofosbuvir/Velpatasvir/Voxilaprevir Indications: DAA Treatment Experienced Patients

- Patients with genotype 1, 2, 3, 4, 5, or 6 who were previously treated with an NS5A inhibitor

- Patients with genotype 1a or 3 infection previously treated without an NS5A inhibitor
  - No advantage of using sofosbuvir/velpatasvir/voxilaprevir over sofosbuvir/velpatasvir for retreatment of patients with GT 1b, 2, 4, 5, or 6
SVR12 Results Overall and by Cirrhosis Status

**Overall***:
- 96 SVR12 %
- 6 relapses
- 1 on-treatment failure
- 2 withdrew consent
- 1 LTFU
- 253/263

**No Cirrhosis**: 99 SVR12 %
- 140/142
- 1 withdrawing consent
- 1 LTFU

**Cirrhosis**: 93 SVR12 %
- 113/121
- 6 relapses
- 1 on-treatment failure
- 1 withdrew consent

* p < 0.001 for superiority compared with prespecified 85% performance goal for SOF/VEL/VOX

** Exposure was consistent with non-adherence
Glecaprevir/Pibrentasvir

- Approved Aug. 3, 2017
- Combination of
  - Glecaprevir - an NS3/4A protease inhibitor
  - Pibrentasvir - an NS5A inhibitor
- Indicated for HCV GT 1-6
  - Duration of therapy:
    - 8 weeks for treatment naïve
    - 12-16 weeks for treatment experienced
- Dosage and administration: 3 tablets once daily with food
Glecaprevir-Pibrentasvir for 8 or 12 weeks in Non-Cirrhotic GT 1

**Baseline Characteristics**


**ITT-PS ITT-PS-PP**

- **Patients (%) with SVR 12**
  - **GLE-PIB x 8 Weeks**
    - ITT-PS: 99.1\% (332/335)
    - ITT-PS-PP: 99.7\% (331/332)
  - **GLE-PIB x 12 Weeks**
    - ITT-PS: 100\% (331/331)
    - ITT-PS-PP: 100\% (332/332)

**ITT-PS population:** ITT excluding patients with HIV coinfection or treatment experience with sofosbuvir.

**ITT-PS-per protocol (PP) population:** ITT-PS excluding patients with premature discontinuation of study drug, virologic failure before Week 8, and missing SVR12 data.

Zeuzem S et al. AASLD 2016. Slide courtesy of Hepatitis C Online.
Glecaprevir-Pibrentasvir in Genotype 1-6 with Renal Disease
EXPEDITION-4: Results

- Source: Gane E, et. al, AASLD 2016. Abstract 935.

- ITT, intent-to-treat analysis; mITT, modified intent-to-treat analysis

Gane E et al. AASLD 2016 Slide courtesy Hepatitis C Online
Side Effect Profile of the DAAs

- Overall very well tolerated

- Most commonly reported side effects:
  - Headache
  - Fatigue
  - Nausea
  - Diarrhea (reported with voxilaprevir)
Laboratory Abnormalities

- Overall not common
- Most common laboratory abnormalities:
  - ALT elevations
    - Elbasvir/grazoprevir
    - Concomitant use of ethinyl-estradiol with glecaprevir/pibrentasvir
      - Should avoid use
  - Bilirubin elevations
    - Many DAAs inhibit bilirubin transporters
  - Anemia with concomitant use of ribavirin
    - Ribavirin causes hemolytic anemia
## Special Populations: Use of HCV DAAs in Renal Insufficiency and Cirrhosis

<table>
<thead>
<tr>
<th></th>
<th>Ledipasvir/sofosbuvir</th>
<th>Elbasvir/grazoprevir</th>
<th>Sofosbuvir/velpatasvir</th>
<th>Sofosbuvir/velpatasvir/voxilaprevir</th>
<th>Glecaprevir/pibrentasvir</th>
</tr>
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<tbody>
<tr>
<td><strong>Use in renal impairment or end-stage renal disease?</strong></td>
<td>≥ 30 mL/min</td>
<td>Safe to use in all levels of renal impairment including dialysis</td>
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</tr>
<tr>
<td><strong>Use in cirrhosis?</strong></td>
<td>Childs Class A, B or C</td>
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<td>Childs Class A, B or C</td>
<td>Childs Class A</td>
<td>Childs Class A</td>
</tr>
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*APhA2018 Annual Meeting & Exposition*
Main Drug Interaction Concerns for DAAs

- New DAAs overall have low potential for causing drug-drug interactions
  - Amiodarone with sofosbuvir and other DAA: Serious symptomatic bradycardia
- Potential for other drugs to lower DAA concentrations:
  - Strong CYP3A inducers: carbamazepine, oxcarbazepine, phenobarbital, phenytoin
  - Strong intestinal P-glycoprotein inducers: rifabutin, rifampin, rifapentine
  - St. John’s wort
- Statins:
  - Interactions vary by DAA and statin
- Acid suppressive therapy:
  - Ledipasvir and velpatasvir solubility decreases with increases in pH
    - Requires acidity for absorption
  - Ethinyl Estradiol contraindicated with glecaprevir/pibrentasvir
HEP Drug Interaction Checker

Access our comprehensive, user-friendly, free drug interaction charts. Providing clinically useful, reliable, up-to-date, evidence-based information.

Start Now

www.hep-druginteractions.org
Also available as an app: hepichart
AASLD Guidelines for Treatment-Naïve GT1 Patients without Cirrhosis

**Recommended Duration Rating**

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<td>12 weeks</td>
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<td>Sofosbuvir/velpatasvir</td>
<td>12 weeks</td>
<td>1A</td>
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**What’s Changed?**
Recommended regimens are:
- Ribavirin free
- 8 or 12 weeks in duration

**Alternatives**
- Ombitasvir/paritaprevir/ritonavir with dasabuvir with or without ribavirin; simeprevir plus sofosbuvir; sofosbuvir plus daclatasvir
- For GT1a- elbasvir/grazoprevir plus ribavirin if NS5A RAS identified
HBV Reactivation Risk in HCV

- FDA warning issued 2016 following 24 reported cases of HBV reactivation in patients treated with HCV DAAs
  - 2 deaths
  - 1 liver transplant
- Mechanism of reactivation unclear
  - HCV DAAs do not have immunosuppressive effects
- Current recommendations are to “evaluate patients for potential coinfection of HCV and HBV”
Project ECHO HBV Monitoring for Patients on HCV Treatment

Check HBsAg, anti-HBc and anti-HBs

- (+) anti-HBc
- (-)

HBsAg
- (-)
  
Liver Panel* every 4 weeks
- ALT ≥2x baseline OR ≥2xULN
- YES
- (-)
  
HBsAg‡
- (+) HBVDNA quant
  
Consult viral hepatitis specialist regarding the management of HBV treatment after completing HCV DAA treatment
  
Start TDF or ETV
- AND

HBVDNA quant
- (+)
  
Start TDF or ETV
- AND

HBV Vaccination if anti-HBs negative

No additional HBV monitoring required

* Liver panel every 4 weeks while on HCV treatment and at 12 weeks post-treatment.
‡ HBsAg can be drawn at the same as HBVDNA for convenience or can ask for HBsAg with reflex HBVDNA.

Used with permission from: National Viral Hepatitis Roundtable and Center for Health Law and Policy Innovation. Available at: https://stateofhepc.org/
Case Application

- Several cases and interactive questions to address:
  - Criteria for treatment
  - Recommended regimens
  - Unique populations
Assessing Extent of Liver Disease

- PJ is a 50 year old man with a past medical history of HTN, DM, and illicit drug use. His last use of illicit drugs was over a year ago, and he continues participating in a methadone clinic. Last year, he was diagnosed with HCV infection by the clinic following a screening test. He now presents for initial assessment prior to selection of HCV treatment.

- How should the status of PJ’s liver be assessed?

- How can the results of various methods of assessment be optimized?
Assessing Extent of Liver Disease

- Noninvasive methods
  - Liver-specific physical examination
  - Labwork
    - LFTs, PT, CBC with platelet count
    - Serum fibrosis marker panels
  - Liver imaging studies
  - Vibration-controlled transient elastography (VCTE)
  - CT scan
  - Ultrasound
  - Calculations
    - Serum AST-to-platelet ratio index (APRI)

- Invasive methods
  - Liver biopsy
    - Any role for this?
Case: A 26 yo female with chronic HCV GT 3 is evaluated for HCV treatment. She has a history of alcohol and injection drug use. Is she a candidate for therapy?

A. She is a candidate irrespective of ongoing alcohol or illicit drug use.

B. She is a candidate if she has abstained from alcohol and illicit drug use.

C. She is a candidate if she has abstained from alcohol and illicit drug use with documentation of participation in a recovery program.

D. She is a candidate if she has abstained from alcohol and illicit drug use with documentation of participation in a recovery program and/or urine drug screening for at least 6 months.
Sobriety Restrictions for HCV Treatment - November 2017

- No data to support pretreatment screening for alcohol use
- AASLD guidelines DO NOT recommend sobriety restrictions
  - Sobriety restrictions:
    - Create barriers to treatment
    - Add unnecessary cost and effort
    - May exclude populations likely to benefit from therapy

National Viral Hepatitis Roundtable and Center for Health Law and Policy Innovation. Available at: https://stateofhepc.org/
Treatment as Prevention: Why People Who Inject Drugs (PWIDs) Should Receive HCV Treatment

- HCV efficiently transmitted through injection drug use
- Global HCV prevalence among PWIDs: estimated 10 million
  - Among middle and high income countries, on-going injection drug use causes >80% of HCV transmission
  - In U.S., estimated 1.5 million PWIDs with HCV
    - Majority of new cases of HCV are in former or current PWIDs
- Proposed strategies to increase HCV treatment optimize harm reduction
  - Utilizing opioid substitution treatment (OST) programs
  - Combining efforts of OST and needle syringe programs

Increase in Acute HCV Among Young Adults

- 364% increase in acute HCV reported between 2006-2012 among persons ≤30 years of age in Kentucky, Tennessee, Virginia, West Virginia

- Primarily affected:
  - Non-Hispanic, white residents from urban and non-urban areas
  - Non-urban areas more than double rate for urban residents
  - Injection drug use most commonly reported risk factor

Zibbell et al. MMWR 2016;64(No.17)
Can Active Drug Users Adhere to HCV Therapy and Achieve Cure?

<table>
<thead>
<tr>
<th></th>
<th>Immediate Treatment Group</th>
<th>Deferred Treatment Group</th>
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<tbody>
<tr>
<td></td>
<td>Mean Drug Adherence (%)</td>
<td>SVR12, n/m (%)</td>
</tr>
<tr>
<td>All patients</td>
<td>99.3</td>
<td>184/201 (91.5)</td>
</tr>
<tr>
<td>Patients with positive UDS at Day 1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Opioids</td>
<td>99.1</td>
<td>37/44 (84.1)</td>
</tr>
<tr>
<td>Amphetamine</td>
<td>99.9</td>
<td>9/10 (90)</td>
</tr>
<tr>
<td>Cocaine</td>
<td>97.5</td>
<td>19/20 (95)</td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td>99.7</td>
<td>46/51 (90.2)</td>
</tr>
<tr>
<td>Cannabinoids</td>
<td>99.7</td>
<td>56/60 (93.3)</td>
</tr>
</tbody>
</table>

n= number of all randomized patients achieving SVR12; m= number of all randomized patients with positive UDS for the indicated drug at day 1

A 45 yo male with HCV GT 1a is evaluated for treatment. He is non-cirrhotic and treatment naïve. His HCV RNA is 8 million IU/mL. His insurance preferred therapy is elbasvir/grazoprevir and a pre-treatment resistance test shows a relevant mutation.

Which of the following is the best treatment according to the AASLD guidelines?

A. Elbasvir/grazoprevir x 12 weeks
B. Elbasvir/grazoprevir and ribavirin x 12 weeks
C. Elbasvir/grazoprevir and ribavirin x 16 weeks
D. Ledipasvir/sofosbuvir x 12 weeks
## AASLD Guidelines for Treatment-Naïve GT1a Patients without Cirrhosis

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<thead>
<tr>
<th>Alternative</th>
<th>Duration</th>
<th>Rating</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elbasvir/grazoprevir plus ribavirin</td>
<td>16 weeks</td>
<td>11a, B</td>
</tr>
<tr>
<td><em>If baseline NS5A RAS</em></td>
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</table>
A 55 yo male failed a prior treatment course of ledipasvir/sofosbuvir. He has compensated cirrhosis. How should he be retreated?
AASLD Guidelines Regarding Retreatment

- For NS5A inhibitor DAA experienced patients with GT1:
  - Recommended: sofosbuvir/velpatasvir/voxilaprevir x 12 weeks
  - Alternative: glecaprevir/pibrentasvir x 12 weeks
Unique Populations

- Case studies
  - Patient in unique living situation
  - Patient with seizure disorder
  - Patient co-infected with HIV
  - Challenging prior authorizations
Unique Living Situations

- JO is a 70 year old man with Alzheimer disease who lives in an assisted living facility. He presents for a teaching session to review his HCV therapy. He is accompanied by an LPN who assists him with daily administration of his medications. He will be initiating sofosbuvir/velpatasvir for 12 weeks.

- How should the approach for the teaching session be adjusted to accommodate JO’s living situation?

- What role does the LPN play in JO’s treatment?

- What special considerations need to be kept in mind here?
Unique Living Situations and Considerations

- Long-term care facilities (LTCFs)
  - Range from full time nursing home care to assisted living programs
  - May include rehabilitation facilities
- Halfway houses
- Homelessness/shelters
- Sudden changes in living situation
  - Admission to hospital
  - Incarceration
  - Eviction
LT CFs

- Challenges
  - Numerous providers
  - Communication difficulties
  - Inconsistent use of documentation on medication administration records (MAR)
  - Refills
  - Medication deliveries/pickups/storage

- Optimal management
  - Communication (written/electronic)
  - Assessment of MAR at each visit/medication reconciliation
  - Determination of responsibilities of medication refills/pickups at each visit
  - Safe storage
  - Patient involvement
Halfway Houses/Shelters/Homelessness

- Challenges
  - Safe medication storage
  - Inconsistent daily routines

- Optimal management
  - Discussion with patient to determine exactly how the living conditions may impact treatment
    - Examples
  - Provision of tools to overcome potential obstacles
    - Lock boxes
    - Storage of medications at clinic
      - Legal issues?
      - Alarm reminders/time of day to take medications
Sudden Changes in Living Situations

- Includes
  - Emergency Department visit/hospital admission
  - Incarceration
  - Eviction

- Challenges
  - Potential treatment interruption
  - Security of medications
  - Potential for addition of medications that interact

- Optimal management
  - Teaching session points
Patients with Seizure Disorder

- MK is a 59 year old man with a history of long-standing seizure disorder managed with phenytoin, levetiracetam, and as needed diazepam. He reports having 3-4 seizures per month despite therapeutic serum concentrations of his antiepileptic drugs. He was diagnosed with HCV infection 15 years ago, but elected to avoid interferon-based treatment because of concerns it could exacerbate his seizure disorder.

- He is now interested in pursuing treatment for his HCV infection.

- What is the concern with initiation of DAA treatment in MK?

- How can this result in treatment delays?
Patients with Seizure Disorder

- Challenges
  - Drug interactions
  - Communication with neurologist
  - Delays in therapy
  - Prior authorization criteria

- Optimal management
  - Assessment of potential drug interactions at first entry into care
  - Use of drug interaction assessment tools
  - Education and communication with physicians regarding drug interactions and ramifications
  - Discussion with patient
    - Rationale for need to change antiepileptic drug regimen
    - Crucial importance of calling HCV practitioner if any medications are changed
Patients with HIV Co-Infection

- GG is a 36-year-old white woman with no known allergies who presents to the HCV clinic for further information and evaluation. Her past medical history includes:
  - HCV infection, GT 1a, HCV RNA < 6 million IU/mL, non-cirrhotic, diagnosed 8 weeks ago
  - HIV infection
    - Diagnosed last year
    - Stable on efavirenz/tenofovir disoproxil fumarate/emtricitabine (Atripla)
      - VL < 20 last month, CD4 670
  - Uses an oral contraceptive pill for birth control

- Which HCV treatment regimens are options for GG?
- Do any adjustments need to be made in GG’s antiretroviral therapy (ART)?
Patients with HIV Co-Infection

- Challenges
  - Drug interactions
    - Criteria for switching ART
  - Different HIV and HCV providers
  - Social issues

- Optimal management
  - Drug interactions assessment
  - Communication between all providers
  - Understanding unique considerations for co-infected individuals
Challenging/Difficult Prior Authorizations

- ZV is a 25 year old woman presenting to clinic for HCV treatment selection. She underwent treatment 10 years ago with peg-interferon and ribavirin, but did not achieve SVR. She is not using birth control, as she is trying to get pregnant.

- ZV has genotype 1a infection (F4 per VCTE) and has compensated cirrhosis. Upon completion of prior authorization forms, you are informed that she has been approved for treatment with ledipasvir/sofosbuvir plus ribavirin x 12 weeks.

- Do you agree with the treatment regimen that was approved for ZV?
- How do you appeal rejections/approvals for suboptimal treatment options?
- What role does the pharmacist play?
Challenging/Difficult Prior Authorizations

- **Challenges**
  - Individualized treatment that falls outside of what the insurance will approve
  - Lengthy communications/lack of communication/frustrations
  - Appeals may be difficult
    - Vary by company
    - Differing approaches

- **Optimal management**
  - Familiarity with treatment guidance document and clinical data
  - Proper documentation
  - Communication with companies regarding prior authorization criteria updates
Online Resources

- AASLD/IDSA HCV Guidance: Recommendations for Testing, Managing, and Treating Hepatitis C
  - https://www.hcvguidelines.org/
- University of Liverpool HEP Interactions
  - http://www.hep-druginteractions.org/
- Hepatitis C Online
  - https://www.hepatitisc.uw.edu/
- Clinical Care Options HCV
  - https://www.clinicaloptions.com/Hepatitis/Topics/HCV.aspx
Best Practices for Counseling Patients About Their HCV Therapy

- The pharmacist serves as a
  - Cheerleader
  - Motivator
  - Supporter
  - Listener
  - Communicator

- Counseling approaches
  - Treatment initiation
  - Ongoing therapy
Initiation of Therapy: Patient Counseling

- Pathophysiology of HCV
- Goals of treatment and rationale
- Monitoring parameters (HCV RNA, other labs)
- Medication counseling
  - Rationale for therapy choice
  - Dosing (frequency, time of day, food requirements)
  - Crucial importance of adherence
  - Identification of potential barriers that would reduce adherence
  - Adverse effects
- Special reminders
  - Any new prescriptions, call prescriber/pharmacist for drug interaction assessment
  - Mail order/specialty pharmacy considerations
- Patient resources
Ongoing Therapy: Patient Counseling

• Brief, but still crucial
• Open-ended questions regarding
  • Adherence
  • Adverse effects
  • New medications
• Laboratory follow up
• Post-treatment follow up
Conclusions

- HCV treatment continues to be dynamic
- Challenging to maintain current knowledge
- Vital role of pharmacists continues to persist
  - Obtaining approval for treatment
  - Adherence
  - Avoidance of drug interactions
Assessment Question #1

Use of which of the following antiepileptic drugs results in a clinically significant drug-drug interaction with sofosbuvir?

A. Phenytoin
B. Levetiracetam
C. Lacosamide
D. Topiramate
Assessment Question #2

Four weeks after initiating therapy with velpatasvir/sofosbuvir for his genotype 3 HCV infection, Mr. Jones reports that he misses at least one dose of medication each week. Which of the following is the most appropriate action for the specialty pharmacist to take?

A. Inform him that his adherence is at 85% and that this is appropriate to achieve virologic suppression
B. Notify the prescriber that Mr. Jones’ treatment should be discontinued due to nonadherence
C. Analyze factors that prevent him from taking his medications consistently
D. Change Mr. Jones’ treatment to one of shorter duration
Assessment Question #3

Which of the following is an approved but not recommended regimen as per the AASLD guidelines for the treatment of HCV genotype 1a?

A. Elbasvir/grazoprevir plus ribavirin x 12 weeks
B. Glecaprevir/pibrentasvir x 8 weeks
C. Ledipasvir/sofosbuvir x 8 weeks
D. Sofosbuvir/velpatasvir x 12 weeks
Assessment Question #4

A 37 yo female without cirrhosis is on hemodialysis has HCV GT 2. What therapy is appropriate for treatment of her HCV?

A. Elbasvir/grazoprevir x 12 weeks
B. Glecaprevir/pibrentasvir x 8 weeks
C. Glecaprevir/pibrentasvir x 12 weeks
D. Sofosbuvir/velpatasvir/voxilaprevir x 12 weeks