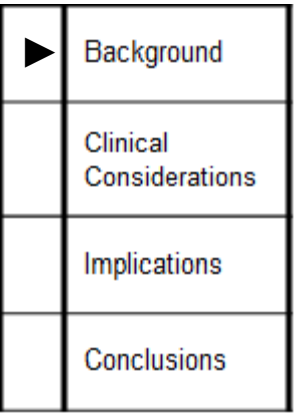
Hepatitis C Virus
Clinical Criteria Update
September 18, 2014

For:
New York State Medicaid

Purpose



- Characterize the place in therapy for the agents utilized for management of chronic hepatitis C (CHC) infection
- Provide update on recommended clinical criteria for NYS Medicaid Fee-For-Service (FFS) and Managed Care (MC) beneficiaries
- Evaluate the impact of recommended clinical criteria

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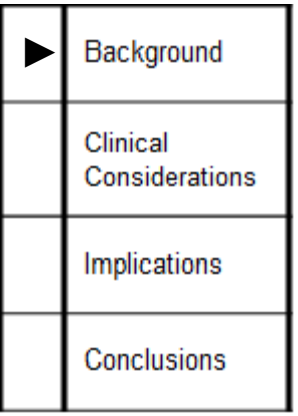
Chronic Hepatitis C

▶	Background
	Clinical Considerations
	Implications
	Conclusions

- Infectious disease defined as persistent detectable HCV RNA at 6 months post-infection
  - 6 major genotypes; genotype 1 most common in U.S.
- Disease progression is generally slow but variable
- Disease progression is accelerated by:
  - HIV, HBV co-infection
  - Alcoholic or non-alcoholic liver disease
- Major long term complications include:
  - Fibrosis
  - Cirrhosis, compensated and decompensated
  - Hepatocellular carcinoma (HCC)
- Extrahepatic manifestations may include:
  - Rheumatologic
  - Cutaneous
  - Renal

Prevalence



- The National Health and Nutrition Examination Survey (NHANES), conducted between 1999 and 2002, estimates that 3.2 million Americans are living with CHC infection, which corresponds to approximately 1.3% of United States population
  - The survey did not contain prevalence rates associated with certain populations, such as the incarcerated, homeless, nursing home residents, persons on active military duty and immigrants
- NYS DOH estimates 200,000 New Yorkers are living with HCV infection and up to 150,000 are unaware of their HCV status
- New York State Hepatitis C Testing Law was signed by Governor Andrew M. Cuomo on October 23, 2013
  - Section 2171 of the Public Health Law requires HCV screening test be offered to every individual born between 1945 and 1965
  - If the screening test is reactive, the health care provider must either offer the individual follow-up health care or a referral to a health care provider who can provide care, including hepatitis C diagnostic test

Disease Progression

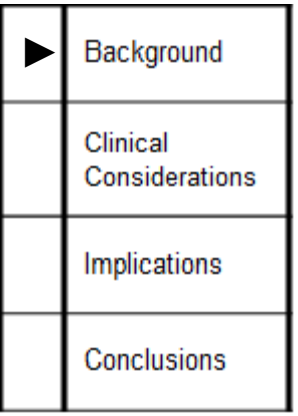
- Background
- Clinical Considerations
- Implications
- Conclusions

- Acute Phase: 0 - 6 months
  - 15 - 25% of people will spontaneously clear the virus during the acute phase
  - None of the currently available HCV agents are indicated for treatment of acute HCV
- Chronic phase: disease progresses over the next 20 to 30 years
  - 75 – 85% of patients will develop chronic infection and of that:
    - 60 – 70% of patients will develop chronic liver disease
    - 5 – 20% of patients will develop cirrhosis
    - 1 – 5% of patients will die from cirrhosis or liver cancer
- CHC liver disease severity is typically assessed by liver biopsy and defined by stage of fibrosis (i.e., METAVIR fibrosis score):

  0 = no fibrosis
  1 = portal fibrosis without septa
  2 = few septa
  3 = numerous septa without cirrhosis
  4 = cirrhosis

Centers for Disease Control and Prevention – Hepatitis C Information for Health Professionals. http://www.cdc.gov/hepatitis/HCV/HCVfaq.htm

CHC Treatment Goal



- Reduce all-cause mortality and liver-related adverse health consequences by achieving virologic cure
- Evidenced by sustained virologic response (SVR)
  - Undetectable HCV RNA at least 12 weeks after completion of treatment

AASLD/IDSA/IAS–USA. Recommendations for testing, managing, and treating hepatitis C. http://www.hcvguidelines.org.

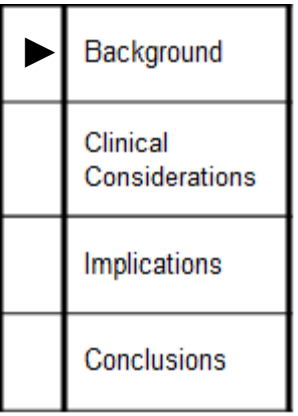
FDA-Approved Products

Table 1: Agents Approved for Treatment of Chronic Hepatitis C (CHC)

Drug (Trade Name)	FDA Approval Date	Class	FDA Indication(s)‡	Dosage Form	Adult Dose
Sofosbuvir (Sovaldi)	2013	NS5B RNA polymerase inhibitor	CHC genotype 1, 2, 3, or 4 infection including CHC/HIV coinfection and patients with hepatocellular carcinoma awaiting transplant	400 mg oral tablet	400 mg once daily
Simeprevir (Olysio)	2013	NS3/4A protease inhibitor	CHC genotype 1 infection with compensated liver disease, including cirrhosis	150 mg oral tablet	150 mg once daily
Telaprevir (Incivek)	2011	NS3/4A protease inhibitor	CHC genotype 1 infection with compensated liver disease, including cirrhosis	375 mg oral tablet	1125 mg twice daily
Boceprevir (Victrelis)	2011	NS3/4A protease inhibitor	CHC genotype 1 infection with compensated liver disease, including cirrhosis	200 mg oral capsule	800 mg 3 times daily
Pegylated interferon alpha 2a (Pegasys)	2002	Recombinant human interferon	CHC with compensated liver disease, including cirrhosis, CHC/HIV coinfection*	135 mcg pens for SC injection, 180 mcg vials and pens for SC injection	180 mcg once weekly
Pegylated interferon alpha 2b (Pegintron)	2001	Recombinant human interferon	CHC with compensated liver disease	50 mcg, 80 mcg, 120 mcg, 150 mcg vials and pens for SC injection	1.5 mcg/kg/week
Ribavirin (Copegus, Rebetol, Ribasphere)	1998	Nucleoside analog	CHC with compensated liver disease	200 mg, 400 mg, 600 mg oral tablets** 200 mg oral capsule** 40 mg/mL oral solution	<75 kg: 1000 mg daily ≥75 kg: 1200 mg daily in 2 divided doses

‡All agents must be used as a component of combination therapy for treatment of CHC; NS = nonstructural protein; SC = subcutaneous; *Pegylated interferon alpha 2a is also indicated as monotherapy for chronic hepatitis B; **200 mg ribavirin tablets and capsules are also available as generics

Compendia-Supported Use



- There are no additional uses for:
  - Boceprevir (Victrelis®)
  - Simeprevir (Olysio®)
  - Sofosbuvir (Sovaldi®)
  - Telaprevir (Incivek®)
    - Telaprevir will be discontinued by the manufacturer on October 16, 2014

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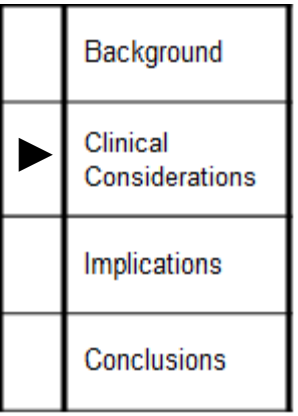
Micromedex 2.0. Truven Health Analytics.
http://www.micromedexsolutions.com/micromedex2/librarian/

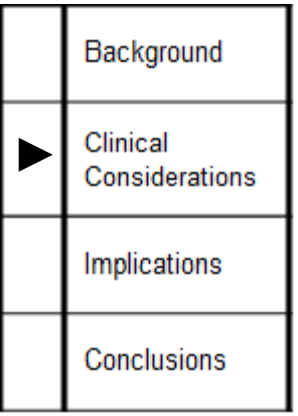
Place in Therapy



- 2011 AASLD guidelines for genotype 1 CHC:*
  - Standard of care: boceprevir or telaprevir + PR
- In January 2014, AASLD and IDSA, collaborated with IAS-USA to launch www.hcvguidelines.org
  - Disseminate expert opinion as new HCV DAA are approved and evidence emerges
  - Highlight simpler regimens with simeprevir and sofosbuvir but data are limited in specific populations
- On August 11, 2014, new section added:
  - *When and in Whom to Initiate HCV Treatment*
    - Prioritization for patients with advanced fibrosis, cirrhosis, liver transplant, or severe extra-hepatic manifestations, followed by patients that are at high risk for developing liver-related or extra-hepatic complications

*Ghany et al. Hepatology; 2011. AASLD = American Association for the Study of Liver Diseases
PR = pegylated interferon + ribavirin; IDSA = Infectious Diseases Society of America
IAS-USA = International Antiviral Society – USA; DAA = direct acting antivirals

Place in Therapy



- In April 2014, EASL guidelines were published*
  - Treatment recommendations based on HCV genotype
  - Includes all combinations recommended by AASLD/IDSA
  - Includes agents not yet available in the U.S
- Disease severity assessed prior to initiation of treatment
- All treatment-naïve and treatment-experienced patients with compensated liver disease due to CHC should be considered for treatment with the following considerations:
  - Treatment prioritized for patients with advanced fibrosis (F3-4) or with clinically significant extra-hepatic manifestations
  - Treatment justified for patients with moderate fibrosis (F2)
  - Treatment may be deferred and individualized for patients with no or mild disease (F0-1)

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* European Association for the Study of the Liver. Clinical practice guidelines: management of hepatitis C virus infection. *Journal of hepatology.* 2014;60(2):392-420.

Recommended Regimens

- Background
- ▶ Clinical Considerations
- Implications
- Conclusions

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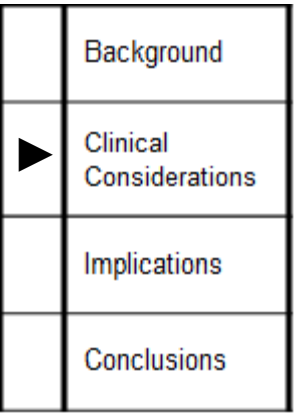
AASLD/IDSA Currently Recommended Regimens for Treatment of CHC

HCV Genotype	Treatment History	Interferon Eligible	Regimen	Duration (weeks)
1	Naïve	Yes	SOF + PEG + RBV	12
		No	SOF + SMV	12
	Prior non-response to PEG + RBV	Yes or No	SOF + SMV ± RBV	12
	Prior non-response to PEG + RBV + BOC or TPV	Yes	SOF + PEG + RBV	12 - 24
		No	SOF + RBV	24
2	Naïve	Yes or No	SOF + RBV	12
	Prior non-response to PEG + RBV	Yes or No	SOF + RBV	12*
3	Naïve	Yes or No	SOF + RBV	24
	Prior non-response to PEG + RBV	Yes or No	SOF + RBV	24
4	Naïve	Yes	SOF + PEG + RBV	12
		No	SOF + RBV	24
	Prior non-response to PEG + RBV	Yes	SOF + PEG + RBV	12
		No	SOF + RBV	24
5 or 6	Naïve	Yes	SOF + PEG + RBV	12
		No	none	none
	Prior non-response to PEG + RBV	Yes	SOF + PEG + RBV	12
		No	none	none

SOF = sofosbuvir; PEG = pegylated interferon; RBV = ribavirin; SMV = simeprevir; BOC = boceprevir; TPV = telaprevir;
*May benefit from extension to 16 weeks

AASLD/IDSA/IAS–USA. Recommendations for testing, managing, and treating hepatitis C. http://www.hcvguidelines.org.

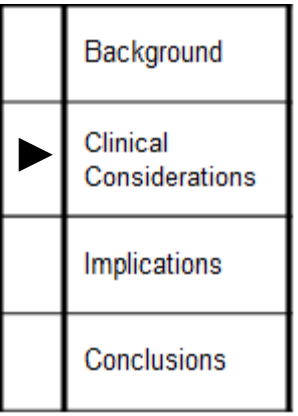
When and in Whom to Initiate HCV Treatment



AASLD/IDSA Prioritization for Initiating CHC Treatment
Highest Priority
• Persons with advanced liver disease (METAVIR score F3 or F4)
• Persons who have undergone liver transplant
• Type 2 or 3 essential mixed cryoglobulinemia with end-organ manifestations (vasculitis)
• Proteinuria, nephrotic syndrome, or membranoproliferative glomerulonephritis
High Priority
• Fibrosis (METAVIR score F2)
• HIV-1 coinfection
• HBV coinfection
• Other coexistent liver disease (e.g., nonalcoholic steatohepatitis)
• Debilitating fatigue
• Type 2 diabetes mellitus (insulin resistant)
• Porphyria cutanea tarda

AASLD/IDSA/IAS–USA. When and in whom to initiate HCV therapy. Recommendations for testing, managing, and treating hepatitis C. http://www.hcvguidelines.org/full-report/when-and-whom-initiate-hcv-therapy.

Comparator State Medicaid

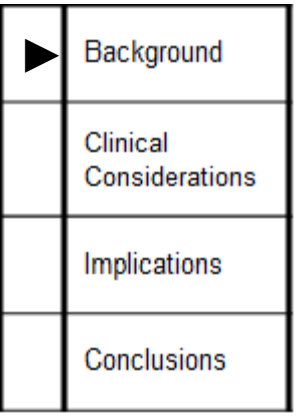


State	Sofosbuvir Requirements
California	PA required
Florida	PA required
Illinois	PA required
Massachusetts	PA required
Michigan	Sofosbuvir is not covered
Pennsylvania	PA required
Texas	Drug is not listed on the PDL

- Five comparator states require a PA for sofosbuvir. The clinical criteria were similar between the states.
- One state does not cover sofosbuvir
- One state does not list sofosbuvir on their Preferred Drug List (PDL)

NYS Medicaid Prevalence

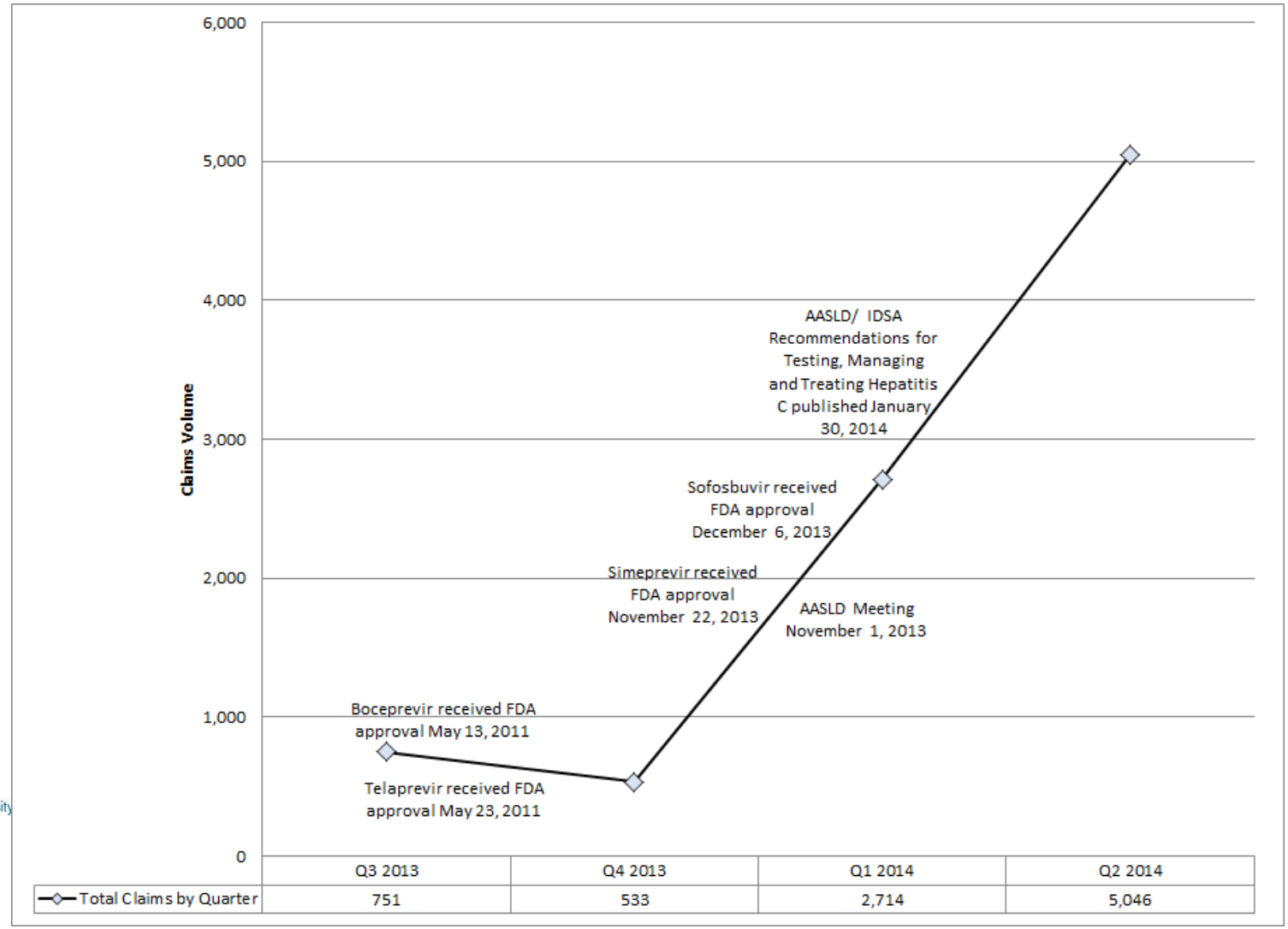
- 6,107,337 eligible beneficiaries
  - 1.5% (94,138/ 6,107,337) of beneficiaries had a diagnosis of hepatitis C (i.e. chronic, acute or unspecified)
    - 0.9% (57,897/ 6,107,337) of beneficiaries had a diagnosis of chronic hepatitis C (CHC) infection



- Highest and high priority for initiating treatment
  - 24.3% (14,070/ 57,897) of beneficiaries were co-infected with HIV and/or HBV
  - 16.3% (9,409/ 57,897) of beneficiaries had liver disease
  - 19.2% (11,531/ 57,897) of beneficiaries had extra-hepatic manifestations
- **Summary: 60.5% (35,010/ 57,897) of beneficiaries had a diagnosis of CHC and other comorbidities.**

Market Trend

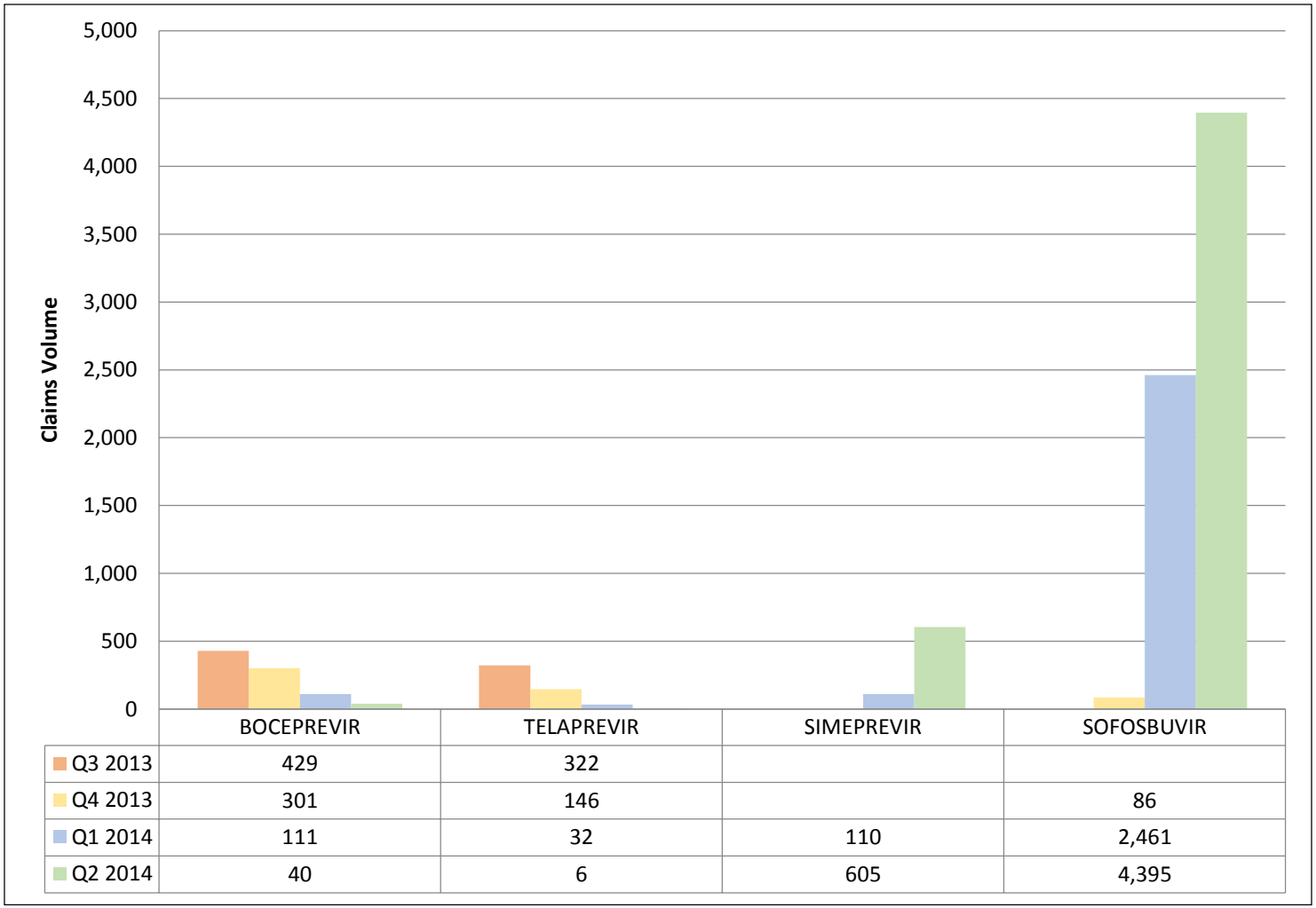
- ▶ Background
- Clinical Considerations
- Implications
- Conclusions



Time frame July 1, 2013 through June 30, 2014

Market Share Analysis

- ▶ Background
- Clinical Considerations
- Implications
- Conclusions

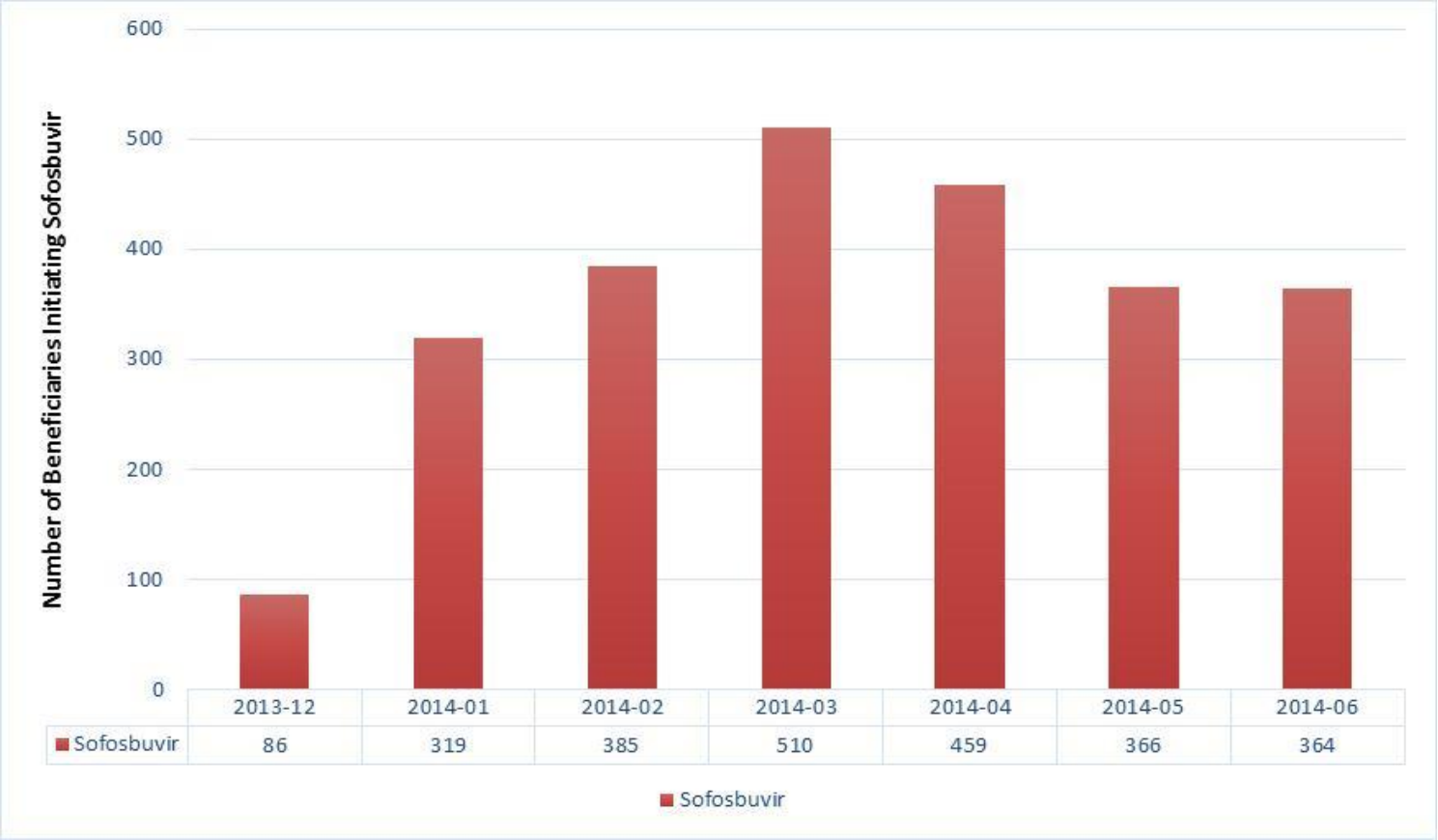


	BOCEPREVIR	TELAPREVIR	SIMEPREVIR	SOFOSBUVIR
Q3 2013	429	322		
Q4 2013	301	146		86
Q1 2014	111	32	110	2,461
Q2 2014	40	6	605	4,395

Time frame July 1, 2013 through June 30, 2014

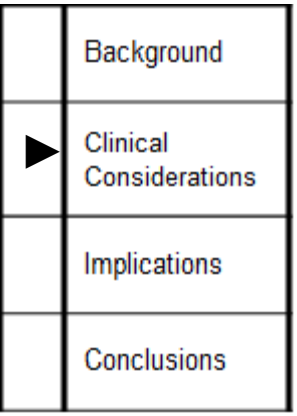
Sofosbuvir New Starts

- ▶ Background
- Clinical Considerations
- Implications
- Conclusions



- Time frame July 1, 2013 through June 30,2014
- 2,489 beneficiaries received sofosbuvir resulting in a total of 6,942 claims

Sofosbuvir Clinical Criteria
Initial Review of Criteria



1. Adult patient age ≥18 years old; AND

2. Prescribed by a hepatologist, gastroenterologist, infectious disease specialist, transplant physician, or health care practitioner experienced and trained in treatment of hepatitis C or a healthcare practitioner under direct supervision of a listed specialist; AND

Experienced and Trained in the treatment of HCV

- A current, valid, MD, DO, PA, or NP New York State license

AND

- Clinical experience is defined as the management at least 20 patients with HCV infection and treatment of 10 HCV patients in the last 12 months and at least 10 HCV-related CME credits in the last 12 months

OR

- Management and treatment of HCV infection in partnership (defined as consultation, preceptorship, or via telemedicine) with an experienced HCV provider who meets the above criteria

Sofosbuvir Clinical Criteria

Initial Review of Criteria

	Background
	Clinical Considerations
	Implications
	Conclusions

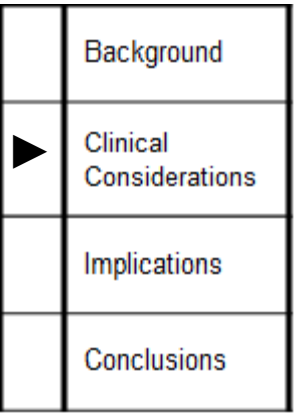
3. Patient is sofosbuvir treatment naïve (no claims history or reference in medical records to previous trial and failure of sofosbuvir); AND

4. Patient has demonstrated treatment readiness and ability to adhere to drug regimen; AND

To be evaluated by using scales or assessment tools that are readily available to healthcare practitioners at http://www.integration.samhsa.gov/clinical-practice/screening-tools or https://prepc.org/ to determine a patient's readiness (e.g. substance abuse potential) to begin hepatitis C treatment

5. Baseline HCV RNA must be submitted with a collection date within the past three months. Prescriber must submit lab documentation indicating HCV genotype and quantitative viral load; AND

Sofosbuvir Clinical Criteria
Initial Review of Criteria



6. Patient meets the diagnosis and disease severity criteria outlined in Dosing and Administration below;

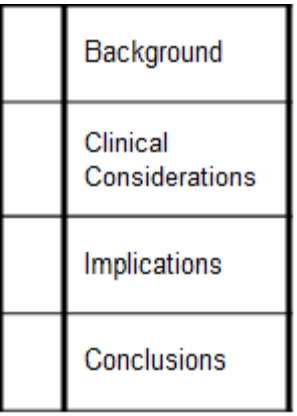
AND

– **<u>Evidence of Stage 3 or Stage 4 hepatic fibrosis including one of the following:</u>**

- Liver biopsy confirming a METAVIR score of F3 or F4; OR
- Transient elastography (Fibroscan®) score greater than or equal to 9.5 kPa; OR
- FibroSure® score of greater than or equal to 0.58; OR
- APRI score greater than 1.5; OR
- Radiological imaging consistent with cirrhosis (e.g. evidence of portal hypertension)

OR

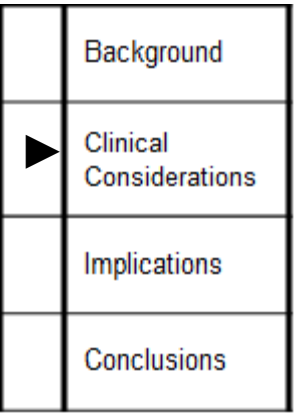
Sofosbuvir Clinical Criteria
Disease Severity Continued



6. Evidence of extra-hepatic manifestation of hepatitis C, such as type 2 or 3 essential mixed cryoglobulinemia with end- organ manifestations (e.g. vasculitis), or kidney disease (e.g. proteinuria, nephrotic syndrome or membranoproliferative glomerulonephritis**)**. Chart note documenting the presence of extra- hepatic manifestations bases on lab results or imaging results (e.g. CBC, erythrocyte sedimentation rate (ESR)/ C-reactive protein (CRP), urinalysis, BUN/ creatinine and angiography) OR

- Organ transplant; OR
- HIV-1 coinfection; OR
- HVB coinfection; OR
- Other coexistent liver disease; OR
- Type 2 diabetes mellitus (insulin resistant); OR
- Porphyria cutanea tarda; OR
- Debilitating fatigue

Sofosbuvir Clinical Criteria
Initial Review of Criteria



7. Patient agreements to complete regimen is documented in medical records submitted (e.g. dual or triple therapy as outlined in Dosing and Administration below); AND

8. Patient verbally or in writing commits to the documented planned course of treatment including anticipated blood tests and visits, during and after treatment; AND

9. Female patients of child bearing potential must have a negative pregnancy test collected within 30 days prior to the initiation of therapy OR Medical records must be submitted documenting pregnancy status.
   - *When Sovaldi is used in combination with ribavirin or peginterferon alfa/ ribavirin women of childbearing potential and their male partners must use two forms of effective contraception during treatment and for at least 6 months after treatment has concluded. Routine monthly pregnancy tests must be performed during this time. There are no data on the effectiveness of systemic hormonal contraceptives in women taking Sovaldi, therefore, two non-hormonal methods of contraception should be used during treatment with Sovaldi and concomitant ribavirin;* AND

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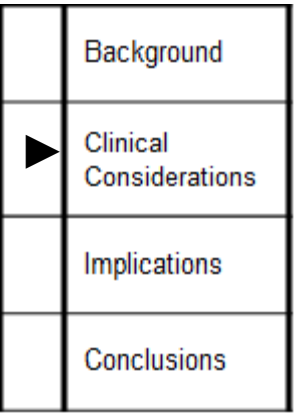
Sofosbuvir Clinical Criteria
Initial Review of Criteria

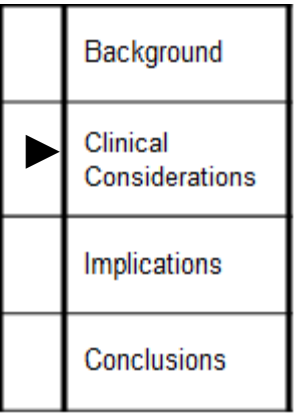


10. For HIV-1 co-infected patients, patients must have the following:
    - No detectable viral load for the past 6 months AND

11. No early refills will be allowed. Exceptions will be reviewed on a case-by -case basis in accordance with the plan's early refill exception process AND

12. The treatment started under the criteria herein defined should be continued in any setting of care governed by the Department of Health.

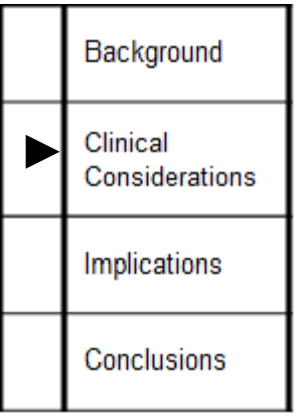
Sofosbuvir Clinical Criteria
Continuation of Therapy Criteria



1. The initial review criteria must have been met or the patient is currently on therapy and has not completed the recommended regimen.

2. Lab results (HCV RNA) collected two or more weeks after the first prescription fill date must indicate a response to therapy (≥2 log reduction in HCV RNA or HCV RNA <25 IU/mL). Copy of results must be submitted by week 6 of therapy for reauthorization of therapy.
   - *Subsequent reauthorization is contingent upon subsequent HCV viral load results* (*refer to individual regimen requirements under the "Dosing and Administration" section*)

Sofosbuvir Clinical Criteria
Continuation of Therapy Criteria



3. No sign(s) of high risk behavior (recurring alcoholism, IV drug use, etc.) or failure to complete HCV disease evaluation appointments and procedures should be evident in follow-up reviews.

4. Continuation of treatment may be authorized for members who are compliant to regimen as verified by the Prescriber and member's medication fill history (review Rx history and dispensing for compliance)

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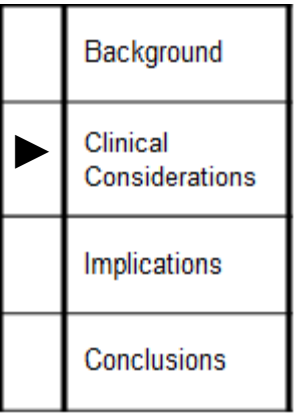
Sofosbuvir Clinical Criteria
Dosing Administration



- <u>HCV & HCV/HIV Co-Infection-Genotype 1 or 4 (Interferon Eligible)</u>

- TRIPLE THERAPY: SOVALDI + peg-interferon alfa + ribavirin

- Length of Authorization: Up to 12 weeks

  - Lab results (HCV RNA) collected two or more weeks after the first prescription fill date must indicate a response to therapy (≥2 log reduction in HCV RNA or HCV RNA <25 IU/mL).
  - Copy of results must be submitted by week 6 of therapy for reauthorization of therapy

Sofosbuvir Clinical Criteria
Dosing Administration

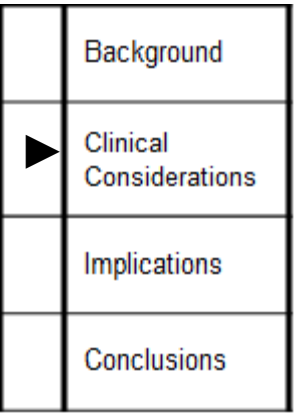
	Background
▶	Clinical Considerations
	Implications
	Conclusions

- <u>HCV & HCV/HIV Co-Infection- Genotype 1 and 4 (Interferon Ineligible)</u>

- Dual Therapy: Sovaldi + ribavirin

- Length of authorization: Up to 24 weeks
  - Beneficiary must have responded to therapy as documented by a ≥2 log reduction in HCV RNA or HCV RNA<25 IU/mL by week 4 and at week 12
  - Copy of results must be submitted by week 6 and week 14 of therapy for reauthorization of therapy

Sofosbuvir Clinical Criteria
Dosing Administration



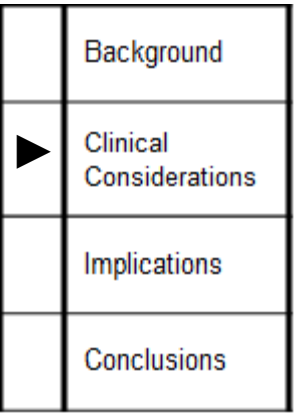
- <u>HCV & HCV/HIV Co-Infection- Genotype 2</u>

- Dual Therapy: Sovaldi + ribavirin

- Length of authorization: Up to 12 weeks
  - May be up to 16 weeks with cirrhosis

  - Beneficiary must have responded to therapy as documented by a ≥2 log reduction in HCV RNA or HCV RNA<25 IU/mL by week 4 and at week 12
  - Copy of results must be submitted by week 6 and week 14 of therapy for reauthorization of therapy

Sofosbuvir Clinical Criteria
Dosing Administration

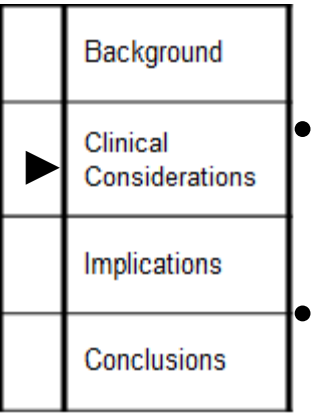


- <u>HCV & HCV/HIV Co-Infection- Genotype 3</u>
- Dual Therapy: Sovaldi + ribavirin
- Length of authorization: Up to 24 weeks

Or

- Triple Therapy: Sovaldi+ ribavirin + peg-interferon alfa
- Length of authorization: Up to 12 weeks
  - Beneficiary must have responded to therapy as documented by a ≥2 log reduction in HCV RNA or HCV RNA<25 IU/mL

Sofosbuvir Clinical Criteria
Dosing Administration



- <u>HCV Genotype 1,2, 3, or 4 Diagnosis of with Hepatocellular Carcinoma Awaiting Liver Transplant</u>
- Dual Therapy: Sovaldi +ribavirin
- Length of authorization: Up to 48 weeks

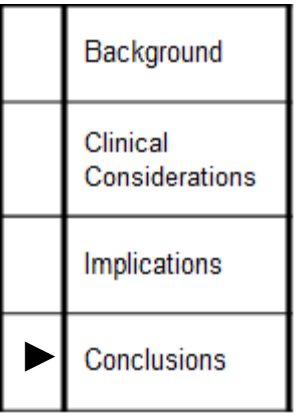
AND:

- One of the following:
  - Prescribed by or consultation, with a hepatologist, gastroenterologist or infectious disease specialist

OR

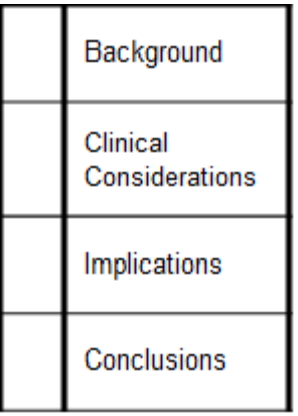
  - Patient is being managed in a liver transplant center AND
  - Documentation of hepatocellular carcinoma AND
  - Patient meet Milan criteria and awaiting liver transplantation

Conclusions



- Emerging evidence is promising
- Judicious screening and monitoring are necessary to ensure safe and effective use in appropriate patients
- Updated clinical criteria for use by NY Medicaid FFS beneficiaries will promote appropriate use and help to ensure successful outcomes

Summary



- The clinical criteria related to the following domains should be considered for all HCV agents:
  - FDA labeling information specific to therapy
  - Clinical guidelines prioritizing treatment of individuals
  - Readiness and adherence
  - Healthcare practitioners prescribing DAAs are hepatologist, gastroenterologist, infectious disease specialist, transplant physician or health care practitioner experienced and trained in the treatment of hepatitis C or a healthcare practitioner under the direct supervision of a listed specialist

- The clinical criteria should be reevaluated in 6 months post-implementation