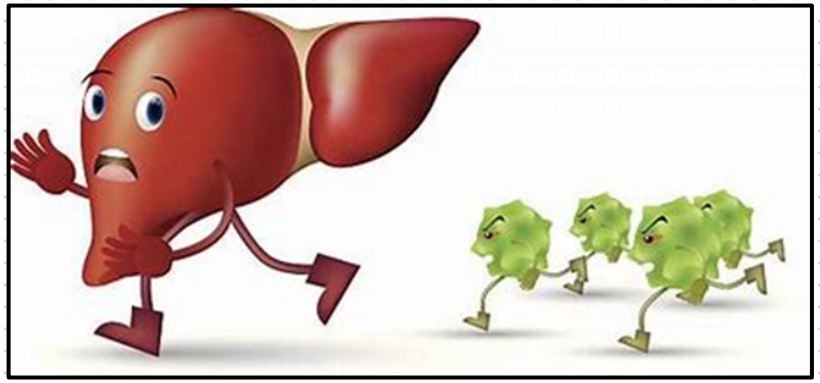

We Treat Hepatitis C: Focus on Michigan Medicaid

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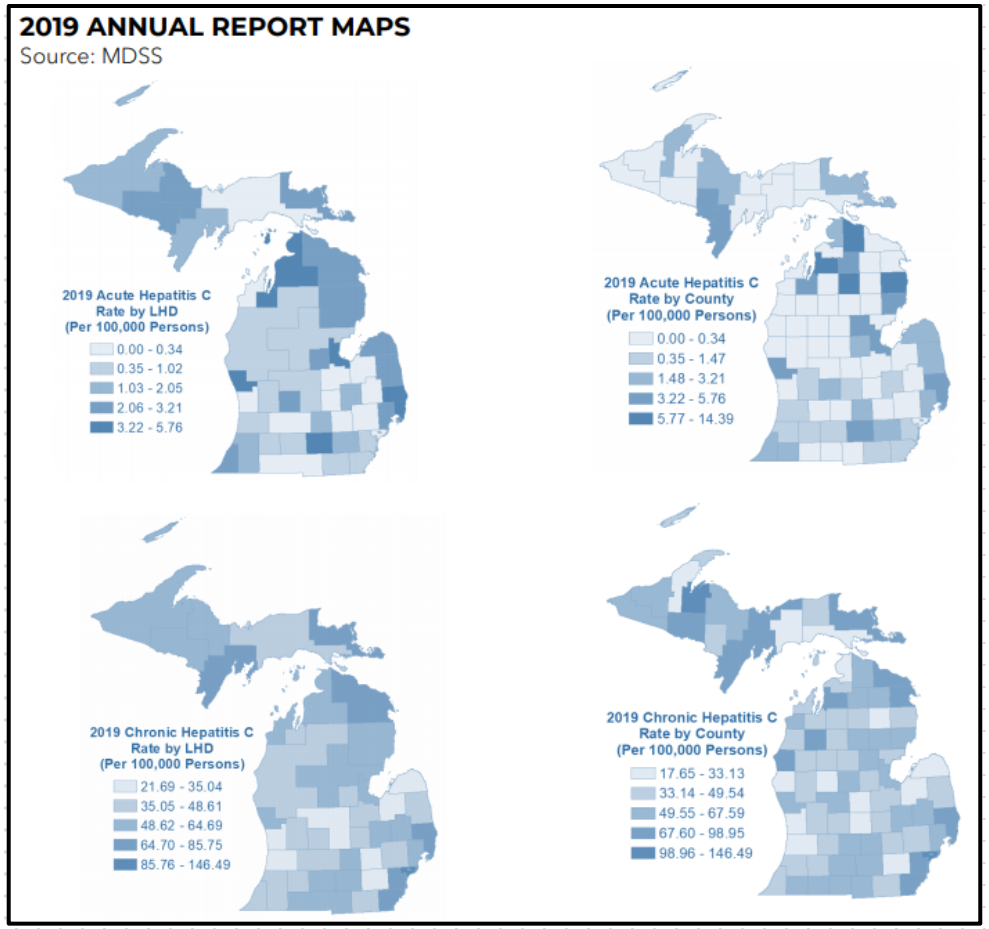
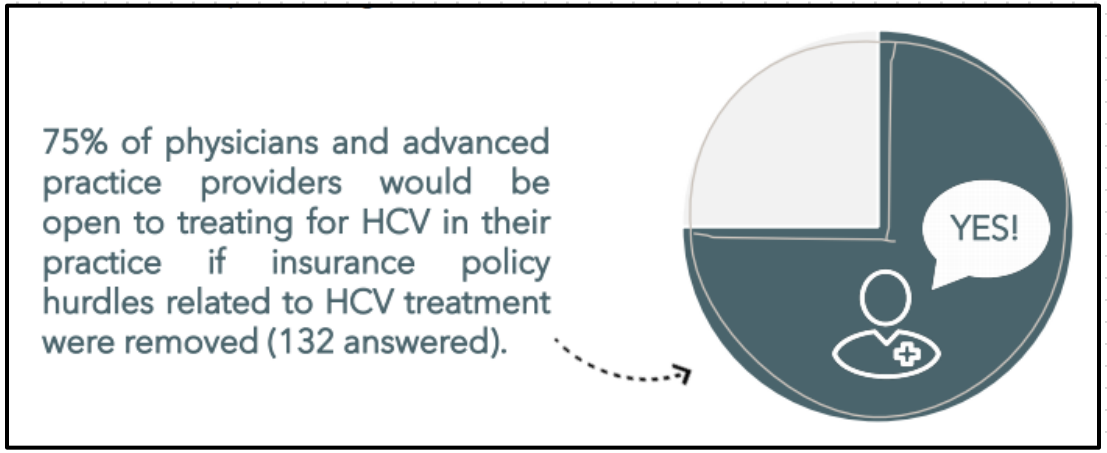
Michigan's Plan to Eliminate Hepatitis C

- Update Michiganders on Hepatitis C transmission, prevention, and curative treatment
- Expand Hepatitis C testing to all adults, all pregnant women, and anyone at risk
- Increase access to Hepatitis C treatment
- Increase access to Hepatitis C prevention through STD treatment, substance use treatment, and syringe service programs



HCV Treatment for Medicaid Enrollees

- As of April 1, 2021 Mavyret is the preferred Hepatitis C direct acting antiviral for Michigan Medicaid
- Any Medicaid enrolled prescriber can prescribe this medication with no prior approval required
- Documentation of patient sobriety no longer required

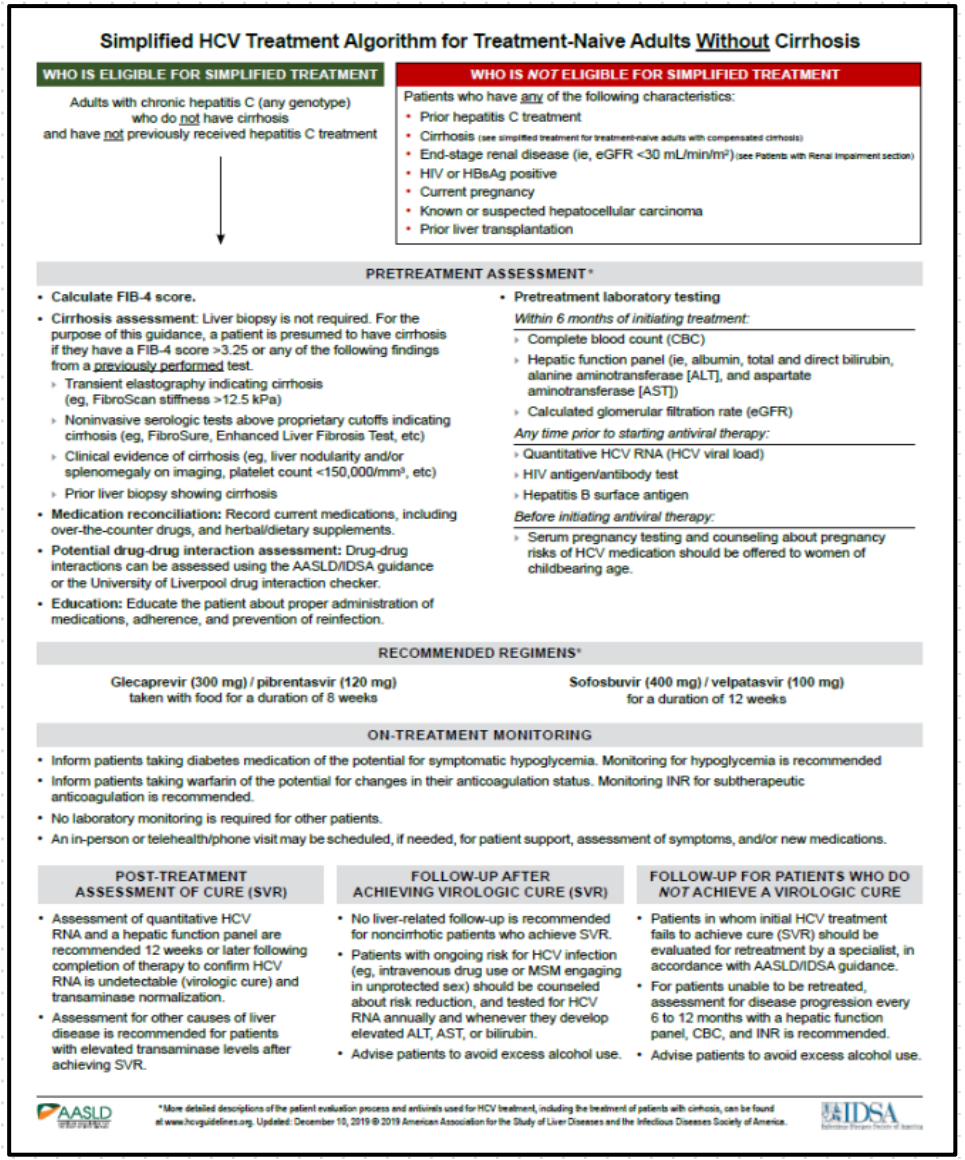


Quick Mavyret Overview

- Mavyret is a single tablet regimen containing two HCV medications:
  - glecaprevir 100 mg, an NS3/4A protease inhibitor
  - pibrentasvir 40 mg, an NS5A replication complex inhibitor
- Indicated for cure of Hepatitis C in persons at least 12 years old and ≥ 45 kg
- Dose is 3 Mavyret tablets once daily with meal for 8 weeks
- 93-100% cure rate in treatment naïve patients and all HCV genotypes
- Most common side effects are headache and fatigue
  - Discontinuation for side effects is very rare
- **Warnings:**
  - Hepatitis B reactivation can occur in HBV/HCV coinfected patients causing liver necrosis or death
  - Liver decompensation or death can occur in patients with current or prior decompensated cirrhosis
  - Certain drug interactions can cause treatment failure or increase the rate of adverse events

Adapting AASLD/IDSA Streamlined HCV Treatment to Michigan Medicaid

Without Cirrhosis



Simplified HCV Treatment Algorithm for Treatment-Naive Adults Without Cirrhosis

WHO IS ELIGIBLE FOR SIMPLIFIED TREATMENT

Adults with chronic hepatitis C (any genotype) who do not have cirrhosis and have not previously received hepatitis C treatment

WHO IS *NOT* ELIGIBLE FOR SIMPLIFIED TREATMENT

Patients who have any of the following characteristics:
- Prior hepatitis C treatment
- Cirrhosis (see simplified treatment for treatment-naive adults with compensated cirrhosis)
- End-stage renal disease (ie, eGFR <30 mL/min/m²) (see Patients with Renal Impairment section)
- HIV or HBsAg positive
- Current pregnancy
- Known or suspected hepatocellular carcinoma
- Prior liver transplantation

PRETREATMENT ASSESSMENT*

- **Calculate FIB-4 score.**
- **Cirrhosis assessment**: Liver biopsy is not required. For the purpose of this guidance, a patient is presumed to have cirrhosis if they have a FIB-4 score >3.25 or any of the following findings from a previously performed test.
  - Transient elastography indicating cirrhosis (eg, FibroScan stiffness >12.5 kPa)
  - Noninvasive serologic tests above proprietary cutoffs indicating cirrhosis (eg, FibroSure, Enhanced Liver Fibrosis Test, etc)
  - Clinical evidence of cirrhosis (eg, liver nodularity and/or splenomegaly on imaging, platelet count <150,000/mm³, etc)
  - Prior liver biopsy showing cirrhosis
- **Medication reconciliation:** Record current medications, including over-the-counter drugs, and herbal/dietary supplements.
- **Potential drug-drug interaction assessment:** Drug-drug interactions can be assessed using the AASLD/IDSA guidance or the University of Liverpool drug interaction checker.
- **Education:** Educate the patient about proper administration of medications, adherence, and prevention of reinfection.
- **Pretreatment laboratory testing**

Within 6 months of initiating treatment:
- Complete blood count (CBC)
- Hepatic function panel (ie, albumin, total and direct bilirubin, alanine aminotransferase [ALT], and aspartate aminotransferase [AST])
- Calculated glomerular filtration rate (eGFR)

Any time prior to starting antiviral therapy:
- Quantitative HCV RNA (HCV viral load)
- HIV antigen/antibody test
- Hepatitis B surface antigen

Before initiating antiviral therapy:
- Serum pregnancy testing and counseling about pregnancy risks of HCV medication should be offered to women of childbearing age.

RECOMMENDED REGIMENS*

Glecaprevir (300 mg) / pibrentasvir (120 mg) taken with food for a duration of 8 weeks

Sofosbuvir (400 mg) / velpatasvir (100 mg) for a duration of 12 weeks

ON-TREATMENT MONITORING

- Inform patients taking diabetes medication of the potential for symptomatic hypoglycemia. Monitoring for hypoglycemia is recommended
- Inform patients taking warfarin of the potential for changes in their anticoagulation status. Monitoring INR for subtherapeutic anticoagulation is recommended.
- No laboratory monitoring is required for other patients.
- An in-person or telehealth/phone visit may be scheduled, if needed, for patient support, assessment of symptoms, and/or new medications.

POST-TREATMENT ASSESSMENT OF CURE (SVR)
- Assessment of quantitative HCV RNA and a hepatic function panel are recommended 12 weeks or later following completion of therapy to confirm HCV RNA is undetectable (virologic cure) and transaminase normalization.
- Assessment for other causes of liver disease is recommended for patients with elevated transaminase levels after achieving SVR.

FOLLOW-UP AFTER ACHIEVING VIROLOGIC CURE (SVR)
- No liver-related follow-up is recommended for noncirrhotic patients who achieve SVR.
- Patients with ongoing risk for HCV infection (eg, intravenous drug use or MSM engaging in unprotected sex) should be counseled about risk reduction, and tested for HCV RNA annually and whenever they develop elevated ALT, AST, or bilirubin.
- Advise patients to avoid excess alcohol use.

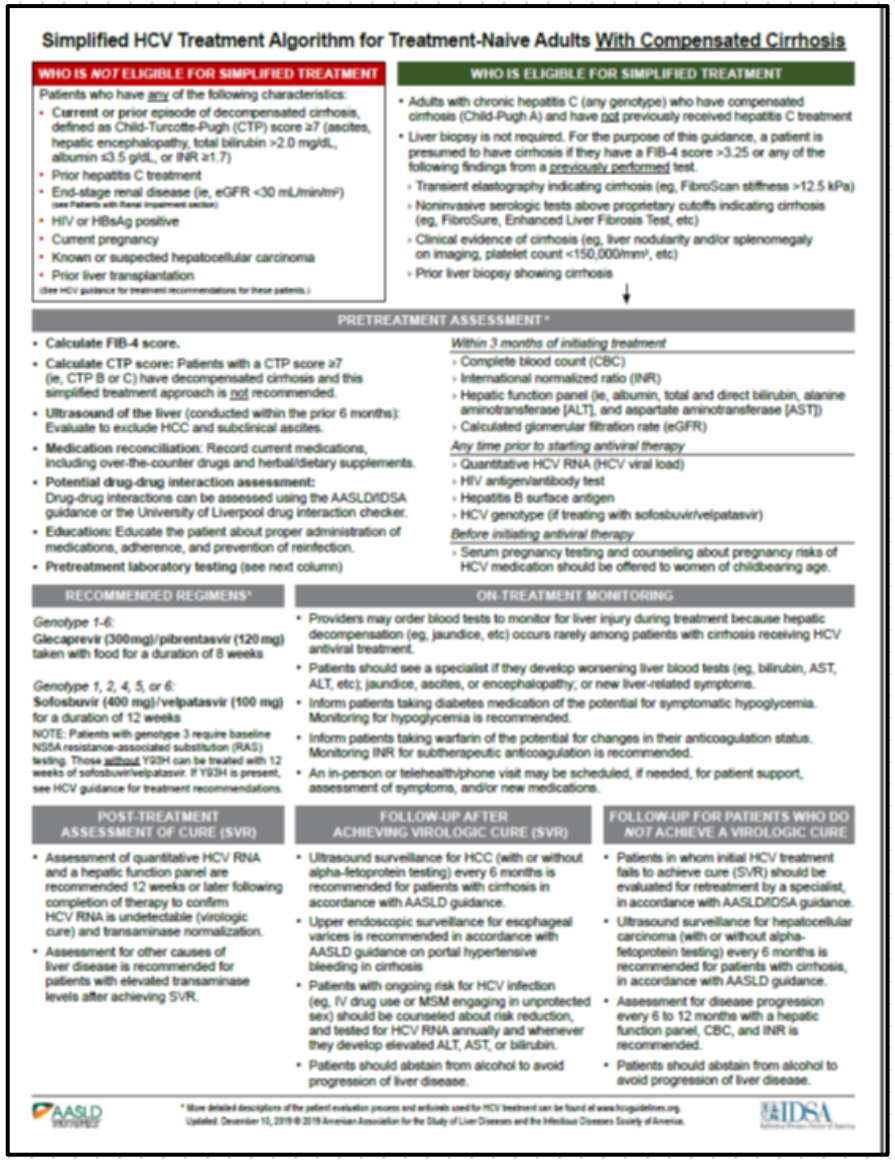
FOLLOW-UP FOR PATIENTS WHO DO *NOT* ACHIEVE A VIROLOGIC CURE
- Patients in whom initial HCV treatment fails to achieve cure (SVR) should be evaluated for retreatment by a specialist, in accordance with AASLD/IDSA guidance.
- For patients unable to be retreated, assessment for disease progression every 6 to 12 months with a hepatic function panel, CBC, and INR is recommended.
- Advise patients to avoid excess alcohol use.

*More detailed descriptions of the patient evaluation process and antivirals used for HCV treatment, including the treatment of patients with cirrhosis, can be found at www.hcvguidelines.org. Updated: December 10, 2019 © 2019 American Association for the Study of Liver Diseases and the Infectious Diseases Society of America.

AASLD IDSA

www.hcvguidelines.org
Accessed April 19, 2021

With Compensated Cirrhosis



Simplified HCV Treatment Algorithm for Treatment-Naive Adults With Compensated Cirrhosis

WHO IS *NOT* ELIGIBLE FOR SIMPLIFIED TREATMENT

Patients who have any of the following characteristics:
- Current or prior episode of decompensated cirrhosis, defined as Child-Turcotte-Pugh (CTP) score ≥7 (ascites, hepatic encephalopathy, total bilirubin >2.0 mg/dL, albumin ≤3.5 g/dL, or INR ≥1.7)
- Prior hepatitis C treatment
- End-stage renal disease (ie, eGFR <30 mL/min/m²) (see Patients with Renal Impairment section)
- HIV or HBsAg positive
- Current pregnancy
- Known or suspected hepatocellular carcinoma
- Prior liver transplantation

(See HCV guidance for treatment recommendations for these patients.)

WHO IS ELIGIBLE FOR SIMPLIFIED TREATMENT
- Adults with chronic hepatitis C (any genotype) who have compensated cirrhosis (Child-Pugh A) and have not previously received hepatitis C treatment
- Liver biopsy is not required. For the purpose of this guidance, a patient is presumed to have cirrhosis if they have a FIB-4 score >3.25 or any of the following findings from a previously performed test.
  - Transient elastography indicating cirrhosis (eg, FibroScan stiffness >12.5 kPa)
  - Noninvasive serologic tests above proprietary cutoffs indicating cirrhosis (eg, FibroSure, Enhanced Liver Fibrosis Test, etc)
  - Clinical evidence of cirrhosis (eg, liver nodularity and/or splenomegaly on imaging, platelet count <150,000/mm³, etc)
  - Prior liver biopsy showing cirrhosis

PRETREATMENT ASSESSMENT*

- **Calculate FIB-4 score.**
- **Calculate CTP score:** Patients with a CTP score ≥7 (ie, CTP B or C) have decompensated cirrhosis and this simplified treatment approach is not recommended.
- **Ultrasound of the liver** (conducted within the prior 6 months): Evaluate to exclude HCC and subclinical ascites.
- **Medication reconciliation:** Record current medications, including over-the-counter drugs and herbal/dietary supplements.
- **Potential drug-drug interaction assessment:** Drug-drug interactions can be assessed using the AASLD/IDSA guidance or the University of Liverpool drug interaction checker.
- **Education:** Educate the patient about proper administration of medications, adherence, and prevention of reinfection.
- **Pretreatment laboratory testing** (see next column)

Within 3 months of initiating treatment
- Complete blood count (CBC)
- International normalized ratio (INR)
- Hepatic function panel (ie, albumin, total and direct bilirubin, alanine aminotransferase [ALT], and aspartate aminotransferase [AST])
- Calculated glomerular filtration rate (eGFR)

Any time prior to starting antiviral therapy
- Quantitative HCV RNA (HCV viral load)
- HIV antigen/antibody test
- Hepatitis B surface antigen
- HCV genotype (if treating with sofosbuvir/velpatasvir)

Before initiating antiviral therapy
- Serum pregnancy testing and counseling about pregnancy risks of HCV medication should be offered to women of childbearing age.

RECOMMENDED REGIMENS*

Genotype 1-6:
Glecaprevir (300 mg)/pibrentasvir (120 mg) taken with food for a duration of 8 weeks

Genotype 1, 2, 4, 5, or 6:
Sofosbuvir (400 mg)/velpatasvir (100 mg) for a duration of 12 weeks

NOTE: Patients with genotype 3 require baseline NS5A resistance-associated substitution (RAS) testing. Those without Y93H can be treated with 12 weeks of sofosbuvir/velpatasvir. If Y93H is present, see HCV guidance for treatment recommendations.

ON-TREATMENT MONITORING
- Providers may order blood tests to monitor for liver injury during treatment because hepatic decompensation (eg, jaundice, etc) occurs rarely among patients with cirrhosis receiving HCV antiviral treatment.
- Patients should see a specialist if they develop worsening liver blood tests (eg, bilirubin, AST, ALT, etc); jaundice, ascites, or encephalopathy; or new liver-related symptoms.
- Inform patients taking diabetes medication of the potential for symptomatic hypoglycemia. Monitoring for hypoglycemia is recommended.
- Inform patients taking warfarin of the potential for changes in their anticoagulation status. Monitoring INR for subtherapeutic anticoagulation is recommended.
- An in-person or telehealth/phone visit may be scheduled, if needed, for patient support, assessment of symptoms, and/or new medications.

POST-TREATMENT ASSESSMENT OF CURE (SVR)
- Assessment of quantitative HCV RNA and a hepatic function panel are recommended 12 weeks or later following completion of therapy to confirm HCV RNA is undetectable (virologic cure) and transaminase normalization.
- Assessment for other causes of liver disease is recommended for patients with elevated transaminase levels after achieving SVR.

FOLLOW-UP AFTER ACHIEVING VIROLOGIC CURE (SVR)
- Ultrasound surveillance for HCC (with or without alpha-fetoprotein testing) every 6 months is recommended for patients with cirrhosis in accordance with AASLD guidance.
- Upper endoscopic surveillance for esophageal varices is recommended in accordance with AASLD guidance on portal hypertensive bleeding in cirrhosis
- Patients with ongoing risk for HCV infection (eg, IV drug use or MSM engaging in unprotected sex) should be counseled about risk reduction, and tested for HCV RNA annually and whenever they develop elevated ALT, AST, or bilirubin.
- Patients should abstain from alcohol to avoid progression of liver disease.

FOLLOW-UP FOR PATIENTS WHO DO *NOT* ACHIEVE A VIROLOGIC CURE
- Patients in whom initial HCV treatment fails to achieve cure (SVR) should be evaluated for retreatment by a specialist, in accordance with AASLD/IDSA guidance.
- Ultrasound surveillance for hepatocellular carcinoma (with or without alpha-fetoprotein testing) every 6 months is recommended for patients with cirrhosis, in accordance with AASLD guidance.
- Assessment for disease progression every 6 to 12 months with a hepatic function panel, CBC, and INR is recommended.
- Patients should abstain from alcohol to avoid progression of liver disease.

*More detailed descriptions of the patient evaluation process and antivirals used for HCV treatment can be found at www.hcvguidelines.org. Updated: December 10, 2019 © 2019 American Association for the Study of Liver Diseases and the Infectious Diseases Society of America.

AASLD IDSA

Which Medicaid enrollees are eligible for streamlined HCV treatment with Mavyret?

- **Persons 12 years and older, not pregnant, with active hepatitis C**
  - Hepatitis C RNA present in blood samples
  - Other medications available for 3-12 year olds
  - Defer treatment in pregnant and lactating women
- **Persons whose medications do not have important Mavyret drug-drug interactions**
  - Medicaid patients requiring a different hepatitis C drug will need a prior authorization; the PA does not include a specialist nor a sobriety requirement
- **For additional information about HCV and other direct acting antiviral medications, please see the HCV Elimination in Michigan slide set and video available on this website.**

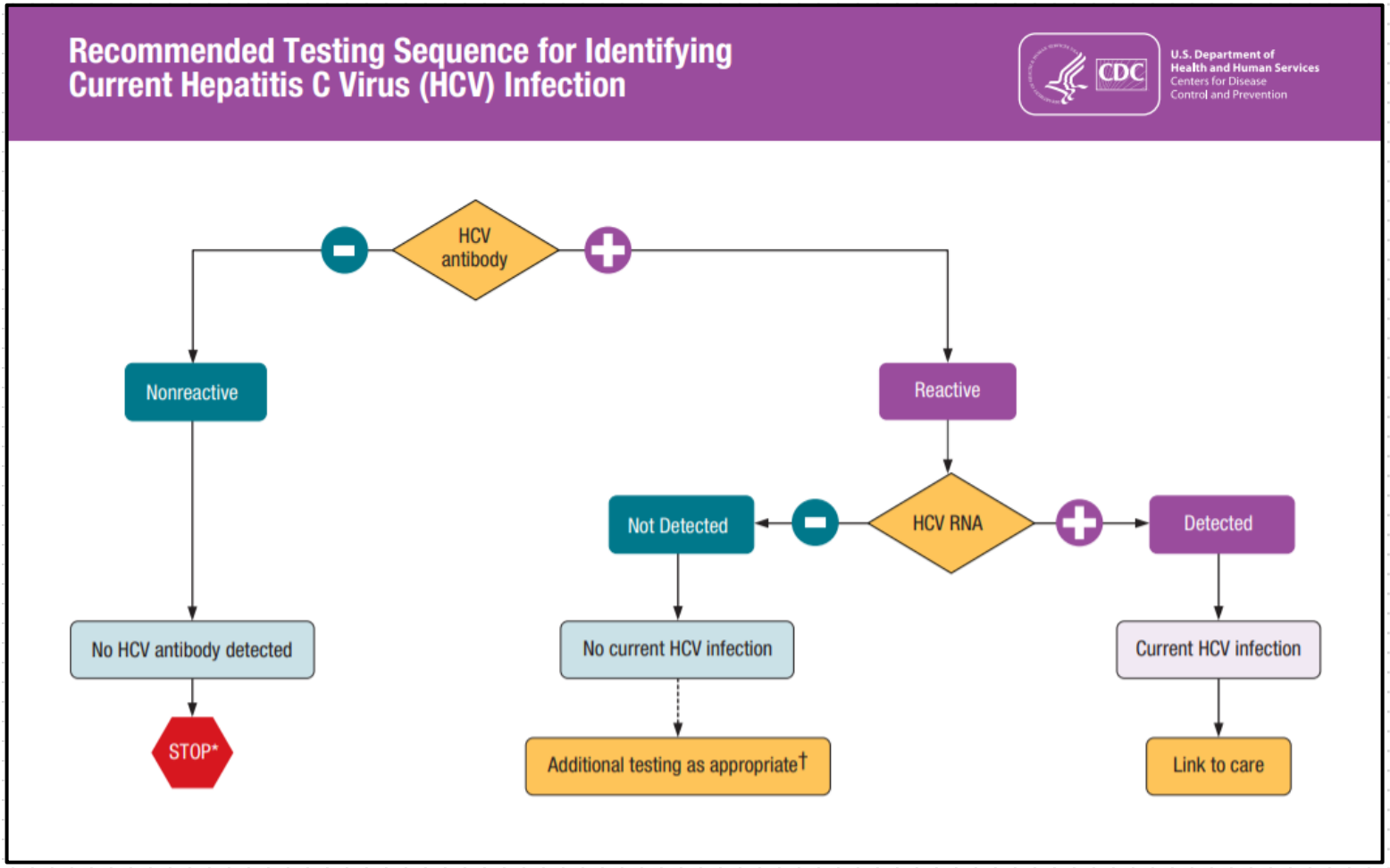
While most patients can be treated in primary care, some should be referred to a specialist

- **Patients who should be referred to a specialist or co-managed with a specialist:**
  - Patients with prior hepatitis C treatment failure
  - Patient with active hepatitis B: Hep B Surface antigen **OR** isolated Hep B Core total antibody
  - Active HIV infection
  - Persons with decompensated cirrhosis
  - Prior liver transplant or other organ transplant
  - Liver cancer

Screen and confirm active HCV infection

- Hepatitis C antibody is a screening test
  - About 20% of persons clear hepatitis C infection
  - These individuals remain antibody positive without active viral infection
- Confirm infection with Hepatitis C RNA or viral load test
- Some laboratories offer reflex testing – a sample positive for hepatitis C antibody is automatically tested for HCV RNA without obtaining another sample
  - Pricing differs among laboratories but reflex testing saves the provider and patient an extra visit and an extra blood draw.

HCV Diagnostic Testing



Some laboratories offer reflex testing: a sample positive for hepatitis C antibody is automatically tested for HCV RNA without obtaining another sample

HCV Baseline Assessment: Focused History

- Prior HCV diagnosis?
  - If so, when initially diagnosed?
- Was there prior HCV treatment?
  - Which meds?
  - Was treatment unsuccessful?
- Review symptoms of liver decompensation or portal hypertension
  - Jaundice, ascites, encephalopathy, GI bleeding
  - History of decompensated cirrhosis requires referral to a specialist for treatment
- Other health conditions that require consultation for HCV treatment
  - HBV, HIV, pregnancy
- Update the medication list including supplements
  - Is Mavyret compatible?
- What was the presumed route of HCV acquisition and are their ongoing potential exposures?
  - Opportunity for drug or alcohol treatment or HIV/STD testing and treatment
- What is patient's experience with medication adherence?
  - Planning intensity of monitoring on treatment

Assessing Drug Interactions

- Most common or important drug interactions with Mavyret
  - Contraindicated due to low Mavyret levels: ***atazanavir, rifampin***
  - Not recommended due to reduced effect: ***carbamazepine, efavirenz, St. John's wort***
  - Not recommended due to increased ALT on treatment: ***estrogens***
  - Reduce dose or discontinue during Mavyret treatment: ***statins***
- Check for interactions with all the medications and supplements
  - Liverpool University Drug Interaction Checker
    - Website: Liverpool HEP Interactions (hep-druginteractions.org)
    - Smartphone app: Hep iChart
  - AASLD website: hcvguidelines.org
  - Mavyret Prescribing Information
- Mavyret is known to be safe with buprenorphine, methadone, and naloxone
  - It is expected to be safe with naltrexone

Mavyret full prescribing information; hep-druginteractions.org

HCV Baseline Assessment: Clinical Exam

- Clinical evidence of health behaviors: drug injection or alcohol
- Clinical evidence of obesity or metabolic syndrome
- Clinical presence of liver dysfunction
  - Enlarged or shrunken nodular liver
  - Splenomegaly
  - Spider hemangioma and palmer erythema
  - Jaundice
  - Purpura or evidence of abnormal bleeding
  - Ascites
  - Encephalopathy

Baseline Assessment: Laboratory Testing

For all patients:

- CBC with differential and platelet count
- Chemistry (creatinine, AST, ALT, bilirubin, albumin)
- PT/INR
- Serum pregnancy test (if applicable)
- Hepatitis B surface antigen, B surface antibody, B core total antibody (not IgM)
- Hepatitis A total antibody (not IgM)
- HIV testing (HIV 1/2 antigen antibody combo test)

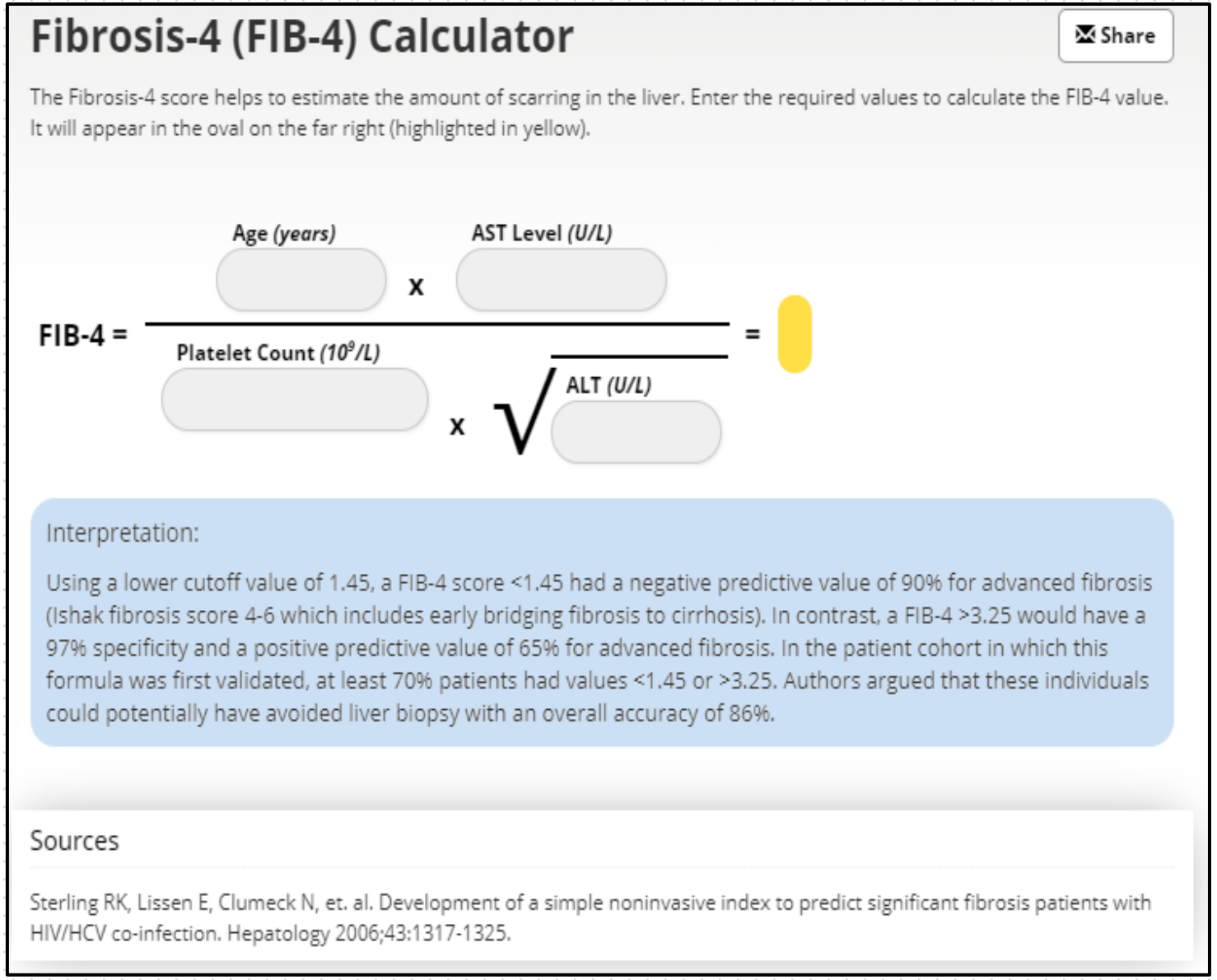
Needed only in special circumstances:

- Commercial blood tests for fibrosis: HCV FibroSure, FibroSpect, FibroMeter, etc.
- HCV genotype
- HCV resistance associated variant testing (NS5A RAVs, NS3/4A RAVs)
- Testing for other causes of liver disease

Assessing Liver Fibrosis

- Streamlined assessment for cirrhosis:
  - FIB-4: calculated from age, AST, ALT, and platelet count
    - >3.25 considered cirrhosis
  - Current or prior clinical evidence of cirrhosis:
    - Prior commercial lab test result of F4 (F4 fibrosis=cirrhosis)
    - Prior elastography result >12.5 kPa
    - Nodular liver or splenomegaly on ultrasound
    - Platelet count <150,000
    - Prior liver biopsy showing cirrhosis
- Commercial blood tests of liver fibrosis give more specific results
  - (FibroSure, FibroTest, FibroMetric, etc.)
- Elastography
- Liver ultrasound has poor sensitivity for cirrhosis but is used to screen for hepatocellular cancer

Assessing Liver Fibrosis



Fibrosis-4 (FIB-4) Calculator

Share

The Fibrosis-4 score helps to estimate the amount of scarring in the liver. Enter the required values to calculate the FIB-4 value. It will appear in the oval on the far right (highlighted in yellow).

$$\text{FIB-4} = \frac{\text{Age (years)} \times \text{AST Level (U/L)}}{\text{Platelet Count } (10^9/L) \times \sqrt{\text{ALT (U/L)}}} =$$

Interpretation:

Using a lower cutoff value of 1.45, a FIB-4 score <1.45 had a negative predictive value of 90% for advanced fibrosis (Ishak fibrosis score 4-6 which includes early bridging fibrosis to cirrhosis). In contrast, a FIB-4 >3.25 would have a 97% specificity and a positive predictive value of 65% for advanced fibrosis. In the patient cohort in which this formula was first validated, at least 70% patients had values <1.45 or >3.25. Authors argued that these individuals could potentially have avoided liver biopsy with an overall accuracy of 86%.

Sources

Sterling RK, Lissen E, Clumeck N, et. al. Development of a simple noninvasive index to predict significant fibrosis patients with HIV/HCV co-infection. Hepatology 2006;43:1317-1325.

[Fibrosis-4 (FIB-4) Calculator - Clinical Calculators - Hepatitis C Online (uw.edu)]

Assessing Cirrhosis: Child-Turcotte-Pugh (CTP) Score

	1 points	2 points	3 points
Albumin g/dl	>3.8	3.5-2.8	<2.8
Bilirubin mg/dl	< 2	2-3	>3
INR	<1.7	1.7-2.3	>2.3
Ascites	None	Moderate (diuretic responsive)	Severe
Encephalopathy	None	Mild-Moderate (grade 1-2)	Severe (grade 3-4)

A: 5-6 points, compensated, 2 yr survival 85%

B: 7-9 points, decompensated, 2 yr survival 57%

C: ≥ 10 points, decompensated, 2 yr survival 35%

Child-Turcotte-Pugh (CTP) Calculator - Clinical Calculators - Hepatitis C Online (uw.edu)

Management of Cirrhosis

- Can treat patients who never had liver decompensation with Mavyret for 8 weeks
- Refer patients who have or have had ***decompensated liver*** disease to hepatologist or liver transplant specialist

- Surveillance for hepatocellular cancer
  - Liver ultrasound
    - Prior to treatment

      and
    - Every 6 months after treatment
  - Alpha-feto-protein (AFP) in addition is optional

- Assessment for portal hypertension
- EGD for surveillance for varices
- No EGD is necessary if:
  - Elastography result <20 kPa

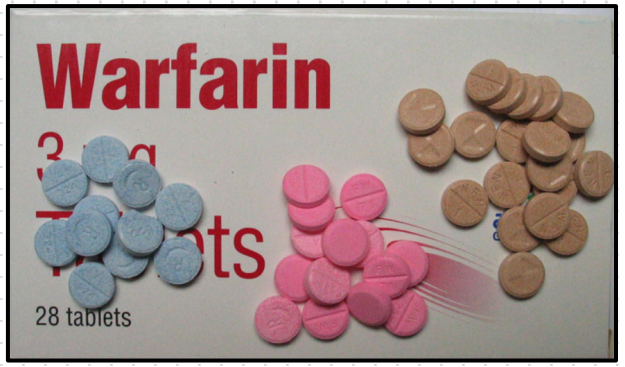
    and
  - Platelet count ≥ 150,000

Treatment with Mavyret

- Three tablets by mouth once daily with food for 8 weeks
- Carton with one month supply contains 4 weekly cartons
  - Each weekly carton contains 7 wallets with 3 tablets each
  - Patient may access medication directly from pharmacies, by mail order, or may pick up at your facility
- Most patients need monitoring for adherence only
  - No labs are necessary during treatment for the majority of patients
- Adherence management may involve:
    - One phone call during initial treatment and a second call when starting 2nd month
    - More frequent phone calls, telehealth visits or face-to-face encounters
    - Daily text, phone call, or in-person reminders

Monitoring on Treatment

- Patients on diabetic medications need monitoring for hypoglycemia as their liver function improves on treatment
- Patients on anticoagulants like warfarin need monitoring for anticoagulation effect as their liver function improves on treatment
- Additional lab monitoring during treatment is at the discretion of the provider
- Lab testing with ALT, AST and HCV RNA is required 12 weeks after completion of treatment



Follow-up After Treatment

- Cure is defined as undetectable HCV RNA on a blood sample obtained at least 12 weeks after completion of treatment
  - Sustained Virologic Response at 12 weeks (SVR12)
  - Persons who do *not* achieve SVR12 must be reassessed for the cause of treatment failure
  - Persons who achieve SVR12 but have elevated ALT or AST must be assessed for other causes of liver disease
- Persons with ongoing HCV exposure after cure should be monitored with repeat HCV RNA at least annually
- Persons with cirrhosis need:
  - Ongoing HCC surveillance with ultrasound every six months

    and
  - Periodic re-evaluation for esophageal varices

Resources for Providers

- MDHHS website: We Treat Hepatitis C
  - Mi.gov/WeTreatHepC
- MATEC 24/7 consults
  - (313) 408-3483
- Henry Ford Hepatitis C consultation line M-F, 9-5pm
  - (313) 575-0332
- Michigan Medicine viral hepatology
  - (844) 233-0433
- AASLD website:
  - hcvguidelines.org
- Liverpool drug interaction website:
  - https://www.hep-druginteractions.org/checker
  - Smartphone app: Hep iChart
- University of Washington Hepatitis C Course Modules
  - https://www.hepatitisc.uw.edu/

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- HCV Guidance: Recommendations for Testing, Managing, and Treating Hepatitis C
  - https://www.hcvguidelines.org/
- Frequently Asked Questions for Providers
  - https://www.cdc.gov/hepatitis/hcv/index.htm
- University of Washington Hepatitis C Course Modules
  - https://www.hepatitisc.uw.edu/

Questions?

WSU-AREC@gmail.com

Questions answered within 24 – 48 hours

WAYNE STATE
School of Medicine

AIDS Research and Education Center