MEDICAL POLICY STATEMENT		
Original Effective Date	**Next Annual Review Date**	**Last Review / Revision Date**
05/21/2014	**03/24/2017**	**05/03/2016**
Policy Name		**Policy Number**
Hepatitis C - Oral		**SRx-0003**
Policy Type		
☒ **Medical**	☐ **Administrative**	☐ **Payment**

Medical Policy Statements prepared by CSMG Co. and its affiliates (including CareSource) apply to Medical health benefit plans administered by CSMG and its affiliates and are derived from literature based on and supported by applicable federal or state coverage mandates, clinical guidelines, nationally recognized utilization and technology assessment guidelines, other medical management industry standards, and published MCO clinical policy guidelines. Medically necessary services include, but are not limited to, those health care services or supplies that are proper and necessary for the diagnosis or treatment of disease, illness, or injury and without which the patient can be expected to suffer prolonged, increased or new morbidity, impairment of function, dysfunction of a body organ or part, or significant pain and discomfort. These services meet the standards of good medical practice in the local area, are the lowest cost alternative, and are not provided mainly for the convenience of the member or provider. Medically necessary services also include those services defined in any federal or state coverage mandate, Evidence of Coverage documents, Medical Policy Statements, Provider Manuals, Member Handbooks, and/or other policies and procedures.

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A. SUBJECT

Hepatitis C - Oral

Ohio Medicaid Preferred Drug List

Kentucky Medicaid Preferred Drug List

Just4Me Preferred Drug List

- Simeprevir **(Olysio)**
- Sofosbuvir **(Sovaldi)**
- Ledipasvir and sofosbuvir **(Harvoni)**
- Ombitasvir/paritaprevir/ritonavir with dasabuvir **(Viekira)**
- Ombitasvir/paritaprevir/ritonavir **(Technivie)**
- Daclatasvir **(Daklinza)**
- Elbasvir and Grazoprevir **(Zepatier)**

B. BACKGROUND

The CareSource Medication Policies are therapy class policies that are used as a guide when determining health care coverage for our members with benefit plans covering prescription drugs. Medication Policies are written on selected prescription drugs requiring prior authorization or

Step-Therapy. The Medication Policy is used as a tool to be interpreted in conjunction with the members specific benefit plan.

The intent of the oral Hepatitis C Medication (PA) Program is to encourage appropriate selection of therapy for patients according to product labeling and/or clinical guidelines and/or clinical studies, and also to encourage use of preferred agents.

I. **Chronic Hepatitis C**
   A. **Simeprevir (Olysio)** are hepatitis C virus (HCV) protease inhibitor indicated, in combination with Sofosbuvir and or peginterferon alfa and ribavirin, for the treatment of genotype 1 chronic hepatitis C (CHC) in adult patients with compensated liver disease, including cirrhosis, who are treatment-naïve or who have been previously treated with interferon-based treatment, including prior null responders, partial responders and relapsers
   B. **Sofosbuvir (Sovaldi)** is a hepatitis C virus (HCV) nucleotide analog NS5B polymerase inhibitor indicated for the treatment of genotype 1, 2, 3, or 4 chronic hepatitis C (CHC) infection as a component of a combination antiviral treatment regimen
   C. **Ledipasvir and sofosbuvir (Harvoni)** is a fixed dose combination of ledipasvir, a hepatitis C virus (HCV), NS5A inhibitor, and sofosbuvir, an HCV nucleotide analog NS5B polymerase inhibitor, and is indicated for the treatment of chronic hepatitis genotype 1, 4, 5 or 6 in adults
   D. **Ombitasvir/paritaprevir/ritonavir with dasabuvir (Viekira)** is indicated for genotype 1 chronic hepatitis. Viekira Pak includes ombitasvir, an HCV NSA5A inhibitor, paritaprevir, an HCV NS3/4A protease inhibitor, ritonavir, a CYP3A inhibitor and dasabuvir, an HCV non-nucleoside NS5B inhibitor
   E. **Ombitasvir/paritaprevir/ritonavir (Technivie)** is a fixed dose combination of obitasvir, an HCV NSA5A inhibitor, paritaprevir, an HCV NS3/4A protease inhibitor, and ritonavir, a CYP3A inhibitor. It is indicated for use in combination with ribavirin for the treatment of patients with genotype 4 chronic hepatitis C virus infection without cirrhosis
   F. **Daclatasvir (Daklinza**) is a hepatitis C virus NS5A inhibitor indicated for use with sofosbuvir for the treatment of chronic HCV genotype 1 (without cirrhosis) and 3 infections
   G. **Elbasvir and Grazoprevir (Zepatier)** is a fixed-dose combination product containing elbasvir, a hepatitis C virus (HCV) NS5A inhibitor, and grazoprevir, an HCV NS3/4A protease inhibitor, and is indicated with or without ribavirin for treatment of chronic HCV genotypes 1 or 4 infection in adults.

C. DEFINITIONS

- **GFR** - Glomerular Filtration Rate is a test to estimate how much blood passes through the glomeruli each minute. Glomeruli are tiny filters in the kidneys that filter waste from the blood.
- **RNA** – Ribonucleic Acid is a polymeric molecule. It is involved in a varied kind of biological role in coding, decoding, regulation, and expression of genes.
- **APRI** – AST Platelet Ratio Index is used as an alternative to a liver biopsy procedure for treatment indication in chronic hepatitis C.
- **SVR4** – Sustained Virologic Response Rate at week 4 for predictive clearance of virus.
- **SVR12** – Sustained Virologic Response Rate at week 12 for predictive clearance of virus.
- **Elastography (Fibroscan and US Elastography)** - The Fibroscan device (Echosens) works by measuring shear wave velocity using a 50-MHz wave passed into the liver from a small transducer on the end of an ultrasound probe. The probe also has a transducer on the end that can measure the velocity of the shear wave (in meters per second) as the wave passes

through the liver. The shear wave velocity is then converted into liver stiffness, which is expressed in kilopascals. This technology measures the velocity of the sound wave passing through the liver and then converts that measurement into a liver stiffness measurement; the entire process is often referred to as liver US (ultrasonographic) elastography.

- Previous Abuser – Current abuser of illicit drugs or excessive alcohol abuse and previous abuse history of illicit drugs or excessive alcohol abuse within the last 5 years
- **Highest Priority for Treatment Owing to Highest Risk for Severe Complications:**
  - advance fibrosis (Metavir F3) or compensated cirrhosis (Metavir F4)
  - organ transplant
  - Type 2 or 3 essential mixed cryoglobulinemia with end organ manifestations
  - Proteinuria, nephrotic syndrome or membraneoproliferative glomerulonephritis

D. POLICY

I. CareSource will approve the use of simeprevir (Olysio), sofosbuvir (Sovaldi), ledipasvir and sofosbuvir (Harvoni), ombitasvir/paritaprevir/ritonavir with dasabuvir (Viekira), ombitasvir/paritaprevir/ritonavir (Technivie), daclatasvir (Daklinza), & Elbasvir and Grazoprevir (Zepatier) and consider their use as medically necessary when used in combination with and/or ribavirin when the following criteria have been met for Chronic Hepatitis C:

A. Hepatitis C Therapy is considered medically necessary for the treatment of chronic hepatitis C virus (HCV) infection when **ALL** of the following criteria **AND** the specified criteria for the requested medication are met:

1. **Documented diagnosis of Hepatitis C**
2. **Prescribed by a Board Certified hepatologist, gastroenterologist or infectious disease specialist or Nurse Practitioner working with the above specialists**
3. Adults age 18 and older
4. Not currently enrolled in hospice or life expectancy greater than one year
5. Negative pregnancy test for female of child bearing potential
6. Not currently participating in alcohol abuse or illicit substance abuse program:
   6.1 One confirmed negative urine drug and alcohol screen within the last 60 days. Laboratory documentation must be provided
   6.2 Previous abusers must meet **ALL** the following:
   a. Enrolled for at least 6 months in counseling services or receiving therapy from an addiction specialist prior to starting hepatitis treatment – Documentation must be provided
   b. Confirmed current monthly negative urine drug and alcohol screen for 3 consecutive months

B. Provided detectable HCV RNA levels are higher than 12 IU/ml (Wthin three months of planned treatment date)

C. Confirmed Genotype and subtype when applicable

D. Evidence of stage 3 or 4 liver fibrosis confirmed by liver biopsy, Elastography only **Unless any below are met (Fibrosis stage F0-4 covered)**

1. Hepatocellular carcinoma meeting Milan criteria (awaiting liver transplantation)
2. HCV/HIV-1 co-infection
3. Post liver transplantation

Listed in order of Evidence, then alphabetically
CareSource follows only Class 1, Level A or B from the AASLD guidelines and other evidence based guidelines

Recommendations are based on scientific evidence and expert opinion. Each recommended statement includes a Roman numeral (I, II, or III) that represents the level of the evidence that supports the recommendation, and a letter (A, B, or C) that represents the strength of the recommendation.

Classification	Description
I	Conditions for which there is evidence and/or general agreement that a given diagnostic evaluation, procedure, or treatment is beneficial, useful, and effective
II	Conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness and efficacy of a diagnostic evaluation, procedure, or treatment
IIa	Weight of evidence and/or opinion is in favor of usefulness and efficacy
IIb	Usefulness and efficacy are less well established by evidence and/or opinion
III	Conditions for which there is evidence and/or general agreement that a diagnostic evaluation, procedure, or treatment is not useful and effective or if it in some cases may be harmful

Level of Evidence	Description
Level A	Data derived from multiple randomized clinical trials, meta-analyses, or equivalent
Level B	Data derived from a single randomized trial, nonrandomized studies, or equivalent
Level C	Consensus opinion of experts, case studies, or standard of care

Adapted from the American College of Cardiology and the American Heart Association Practice Guidelines. (American Heart Association, 2011); (Shiffman, 2003)

Genotype	Cirrhosis	Treatment -naïve	Treatment - experience (RBV, IFN)[1]	Treatment - experience (Sovaldi + RBV +/- IFN)[2]	Treatment - experience (Incivek, Victrelis, Olysio + RBV + IFN)[3]	Treatment	Duration
1a	Without Cirrhosis	Yes	Yes	No	No	Zepatier	12 weeks
		Yes	Yes	No	Yes	Harvoni	12 weeks
		Yes	Yes	No	No	Viekra Pak + weight based RBV	12 weeks
		Yes	Yes	No	No	Sovaldi + Olysio	12 weeks
		Yes	No	No	No	Daklinza + Sovaldi	12 weeks
1a	Compensated Cirrhosis	Yes	Yes	No	No	Zepatier	12 weeks or 16 weeks with RBV[1]
		Yes	Yes	No	Yes	Harvoni	24 weeks or 12 weeks with RBV[1,3]
		Yes	Yes	No	No	Viekra Pak + weight based RBV	24 weeks
		Yes	No	No	No	Sovaldi + Olysio + weight based RBV	24 weeks
1b	Without Cirrhosis	Yes	Yes	No	No	Zepatier	12 weeks
		Yes	Yes	No	Yes	Harvoni	12 weeks

		Yes	Yes	No	No	Viekra Pak + weight based RBV	12 weeks
		Yes	Yes	No	No	Sovaldi + Olysio	12 weeks
		Yes	No	No	No	Daklinza + Sovaldi	12 weeks
Genotype	Cirrhosis	Treatment -naïve	Treatment - experience (RBV, IFN)[1]	Treatment - experience (Sovaldi + RBV +/- IFN)[2]	Treatment - experience (Incivek, Victrelis, Olysio + RBV + IFN)[3]	Treatment	Duration
1b	Compensated Cirrhosis	Yes	Yes	No	No	Zepatier	12 weeks
		Yes	Yes	No	Yes	Harvoni	24 weeks or 12 weeks with RBV[1,3]
		Yes	Yes	No	No	Viekra Pak	12 weeks
		Yes (Alternative Treatment)	No	No	No	Sovaldi + Olysio + weight based RBV	24 weeks
2	Without Cirrhosis	Yes	Yes	No	No	Sovaldi + weight based RBV	12 weeks
2	Compensated Cirrhosis	None	None	None	None	None	None
3	Without Cirrhosis	Yes	Yes	No	No	Daklinza + Sovaldi	12 weeks
		Yes	Yes	No	No	Sovaldi + weight based RBV + PEG-IFN	12 weeks
		Yes	Yes	No	No	Sovaldi + weight based RBV	24 weeks
3	Compensated Cirrhosis	Yes	Yes	No	No	Sovaldi + weight based RBV + PEG-IFN	12 weeks
		Yes	No	No	No	Sovaldi + weight based RBV	24 weeks
4	Without Cirrhosis	Yes	Yes	No	No	Technivie + weight based RBV	12 weeks
4	Compensated Cirrhosis	Yes	Yes	No	No	Technivie + weight based RBV	12 weeks
5	Without Cirrhosis	None	None	None	None	None	None
5	Compensated Cirrhosis	None	None	None	None	None	None
6	Without Cirrhosis	None	None	None	None	None	None
6	Compensated Cirrhosis	None	None	None	None	None	None

Recommended Regimens for Patients with Genotype 1 or 4 HCV Infection with Decompensated Cirrhosis (Moderate or Severe Hepatic Impairment; CTP Class B or C) Who May or May Not be Candidates for Liver Transplantation, Including Those with Hepatocellular Carcinoma

Genotype	Cirrhosis	Treatment	Duration
1	Decompensated	Harvoni	12 weeks + low dose RBV or 24 weeks if RBV ineligible
		Daklinza + Sovaldi	12 weeks + low dose RBV or 24 weeks if RBV ineligible
4	Decompensated	Harvoni	12 weeks + low dose RBV or 24 weeks if RBV ineligible
		Daklinza + Sovaldi	12 weeks + low dose RBV or 24 weeks if RBV ineligible

II. Simeprevir **(Olysio)**
Additional Prior Authorization Criteria:
A. Screening HCV genotype 1a and 1b infection for no presence of virus with the NS3 Q80K polymorphism
B. concurrently

III. Elbasvir and grazoprevir **(Zepatier)**
Additional Prior Authorization Criteria:
A. Testing prior to initiation:
1. Genotype 1a: Testing for the presence of virus with NS5A resistance-associated polymorphisms is recommended.
2. Obtain hepatic laboratory testing.

Note: Documented diagnosis must be confirmed by portions of the individual's medical record which will confirm the presence of disease and will need to be supplied with prior authorization request. These medical records may include, but not limited to test reports, chart notes from provider's office or hospital admission notes.

Refer to product package insert for dosing, administration and safety guidelines.
ALL other uses of oral Hepatitis C medications are considered experimental/investigational and therefore, will follow CareSource's Off-Label policy.

CONDITIONS OF COVERAGE
HCPCS N/A – Pharmacy Only
CPT

Step Therapy
Under some plans, including plans that use an open or closed formulary, some of the medications in this policy may be subject to step-therapy. Refer to the CareSource formulary tool or PDL for further guidance.

PLACE OF SERVICE
Office, Home
This medication can be self-administered and can be billed through the pharmacy benefit.

AUTHORIZATION PERIOD
Initial authorization:
Coverage of **Olysio** will be 12 to 24 weeks.

Renewal authorization:
Recommended coverage after treatment week 6 is based on the following criteria: If the viral load is the same at wk 4(compared to baseline) then can stop therapy. For example a patient that is being treated with 24 wks of SOF/SIM that has a minimally detectable viral load at wk 4 (i.e, 30 IU/mL) then tx is working and should stay on tx.

If the viral load is less than or equal to 25 IU/ml then coverage for an additional 6 weeks of triple therapy without cirrhosis, or 18 weeks with cirrhosis.

Initial authorization:
Coverage of **Zepatier, Sovaldi, Harvoni or Viekira** will be 12 to 24 weeks.

Renewal authorization:
- Extension of initial request of treatment duration greater than 12 weeks will require reauthorization between 12 and 14 weeks with an SVR 12 level submission
- Renewal authorization approved if **ALL** of the following are met:
  - Compliant with drug therapy regimen by paid pharmacy claims
  - HCV RNA levels < 25 iu/ml at 12 weeks

Initial authorization:
Coverage of **Daklinza and Technivie** will be 12 weeks.

Renewal authorization:
- Extension of initial request of treatment duration greater than 12 weeks will require reauthorization between 12 and 14 weeks with an SVR 12 level submission
- Renewal authorization approved if **ALL** of the following are met:
  - Compliant with drug therapy regimen by paid pharmacy claims
  - HCV RNA levels < 25 iu/ml at 12 weeks

ALL authorizations are subject to continued eligibility.

E. RELATED POLICIES/RULES

F. REVIEW/REVISION HISTORY

Date Issued:	05/21/2014
Date Reviewed:	05/21/2014, 01/13/2015, 03/24/2015, 06/02/2015, 11/11/2015
Date Revised:	01/13/2015 - Revisions of off market medications, criteria change 03/24/2015 – Add Harvoni and Viekira

06/02/2015 – Add Elastography testing information
11/11/2015 – Add Technivie and Daklinza
12/15/2015 – Revision to RNA level and removal of hepatic decompensation for Olysio
05/03/2016 – Update to add Zepatier, added grid with genotype and medications

G. REFERENCES

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19. Technivie [package insert] North Chicago, IL, AbbVie Inc.: Revised October 2015
20. Zepatier [package insert] Merck Sharpe Revised January 2016

The Medical Policy Statement detailed above has received due consideration as defined in the Medical Policy Statement Policy and is approved.

Independent medical review –
05/07/2014
05/03/2016