Drug Monograph

Drug/Drug Class:	**Epclusa® (velpatasvir and sofosbuvir) tablet / Hepatitis C Agents**
Prepared for:	MO HealthNet
Prepared by:	Xerox Heritage, LLC

☒ **New Criteria** ☐ **Revision of Existing Criteria**

Executive Summary

Purpose:	The purpose of this monograph is to provide a review of new therapy to determine whether the reviewed drug should be made available on an open access basis to prescribers, require a clinical edit or require prior authorization for use.
Dosage Forms & Manufacturer:	Epclusa® is available in a tablet that contains 400 mg sofosbuvir and 100 mg velpatasvir respectively. Manufacturer: Gilead Sciences, Inc., Foster City, CA 94404
Summary of Findings:	The ABSTRAL phase 3 trial series demonstrated SVR12 rates ranging from 95% to 100% with Epclusa®, with or without ribavirin, typically given for 12 weeks. Epclusa® has been shown to have efficacy in HIV-HCV coinfected patients comparable to that seen in HCV-monoinfected patients. The ABSTRAL-4 trial confirmed its safety and efficacy in combination with ribavirin in patients with decompensated liver disease (Child Pugh B or C Cirrhosis).
Status Recommendation:	☐ Prior Authorization (PA) Required ☐ Open Access ☐ Clinical Edit ☒ PDL
Type of PA Criteria:	☐ Increased Risk of ADE ☐ Preferred Agent ☐ Appropriate Indications ☒ Under Solicitation

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Purpose

The purpose of this monograph is to provide a review of new therapy to determine whether the reviewed drug should be considered a prior authorization drug, a clinical edit drug or an open access drug. While prescription expenditures are increasing at double-digit rates, payers are evaluating ways to control these costs by influencing prescriber behavior and guide appropriate medication usage. This review will assist in the achievement of qualitative and economic goals related to health care resource utilization. Restricting the use of certain medications can reduce costs by requiring documentation of appropriate indications for use, and where appropriate, encourage the use of less expensive agents within a drug class.

Introduction

Hepatitis C is a liver infection caused by the Hepatitis C (HCV) virus. It is a blood-borne virus. Today, most people become infected with the virus by sharing needles or other equipment to inject drugs. For some people, hepatitis C is a short term illness but for 70-85% of people it becomes a long term, chronic infection. Chronic hepatitis C is a serious disease that can result in long term health problems, even death.

Dosage Form(s) [1]

Epclusa® is available in a tablet that contains 400 mg sofosbuvir and 100 mg velpatasvir respectively.

Manufacturer [1]

Gilead Sciences, Inc., Foster City, CA 94404

Indication(s) [1]

Epclusa® is indicated for the treatment of adult patients with chronic hepatitis C virus genotype 1, 2, 3, 4, 5, or 6 infection without cirrhosis or with compensated cirrhosis, or with decompensated cirrhosis for use in combination with ribavirin.

Clinical Efficacy [1,2] (mechanism of action/pharmacology, comparative efficacy)

Epclusa® is a fixed-dose combination of sofosbuvir and velpatasvir which are direct-acting antiviral agents against the hepatitis C virus. Velpatasvir inhibits the HCV NS5A protein necessary for viral replication. Sofosbuvir is a prodrug converted to its pharmacologically active form GS-461203 which inhibits NS5B RNA-dependent RNA polymerase, also essential for viral replication, and acts as a chain terminator.

Pharmacokinetics:

	Sofosbuvir	**Velpatasvir**
Protein binding	61-65%	>99.5%
Metabolism	Hepatic	Hepatic; substrate of P-gp, OATPs and CYP 2B6, CYP 2C8, and CYP 3A4
Excretion	Urine, 80% Feces, 14%	Urine, 0.4% Feces, 94%
Half-life	25 hours	15 hours

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ABSTRAL-1 TRIAL

STUDY DESIGN	Randomized, double-blind, placebo-controlled trial.
INCLUSION CRITERIA	Patients with genotype 1, 2, 4, 5, or 6 HCV infection without cirrhosis or with compensated cirrhosis.
EXCLUSION CRITERIA	Not specified.
TREATMENT REGIMEN	Patients were randomized to receive Epclusa once daily for 12 weeks (n=624) or placebo (n=624).
RESULTS	618/624 (99%) of the patients in the Epclusa group achieved SVR12. 206/210 of those patients with genotype 1a, 117/118 of those with genotype 1b, 104/104 of those with genotype 2, 116/116 of those with genotype 4, 34/35 of those with genotype 5, and 41/41 of those with genotype 6. None of the patients in the placebo group achieved SVR 12.
SAFETY	Not specified

ABSTRAL-4 TRIAL

STUDY DESIGN	Randomized, open label, phase 3 trial. Randomization was stratified by HCV genotype.
INCLUSION CRITERIA	Patients with genotype 1, 2, 3, 4, 5, or 6 HCV infection and Child-Pugh B cirrhosis at screening
EXCLUSION CRITERIA	Not specified.
TREATMENT REGIMEN	Patients were randomized in a 1:1:1 ratio to treatment with Epclusa for 12 weeks (n=90), Epclusa with ribavirin for 12 weeks (n=87), or Epclusa for 24 weeks.
RESULTS	Treatment with Epclusa with ribavirin for 12 weeks resulted in numerically higher SVR12 rates than treatment with Epclusa for 12 weeks or 24 weeks. Because Epclusa with ribavirin for 12 weeks is the recommended dosage regimen, the results of the 12 and 24 weeks Epclusa treatment groups were not presented. Of the patients on Epclusa and ribavirin for 12 weeks, 94% (82/87) of the patients achieved SVR12.
SAFETY	Not specified

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Contraindications [1]

- If Epclusa® is administered with ribavirin, the contraindications to ribavirin also apply

Warnings and Precautions [1]

- Serious symptomatic bradycardia when sofosbuvir is coadministered with amiodarone and another HCV direct acting antiviral
- Risk of reduced therapeutic effect due to concomitant use with inducers of P-gp and/or moderate to potent inducers of CYP
- If given with Ribavirin, the warnings and precautions for ribavirin apply

Adverse Effects [1]

Most common ≥ 5 %	Epclusa (n=624)
Headache	22%
Fatigue	15%
Nausea	9%
Asthenia	5%
Insomnia	5%

Drug Interactions [1]

- Antacids
- H2 Receptor antagonists
- Proton-pump inhibitors
- Amiodarone
- Digoxin
- Topotecan
- Anticonvulsants: carbamazepine, phenytoin, phenobarbital, and oxcarbazepine
- Antimycobacterials: rifabutin, rifampin, rifapentine
- HIV Antiretrovirals: efavirenz, regiments containing tenofovir DF, tipranavir/ritonavir
- St. John's wort
- HMG-CoA Reductase Inhibitors: rosuvastatin, atorvastatin

Dosage and Administration [1]

The recommended dose for Epclusa® is one tablet taken once daily with or without food. The treatment duration for patients without cirrhosis and patients with compensated cirrhosis is 12 weeks. For patients with decompensated cirrhosis, the treatment regimen is Epclusa® and ribavirin for 12 weeks.

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Cost

GENERIC NAME	BRAND NAME	MANUFACTURER	STRENGTH	Dose	COST/ MONTH*
Velpatasvir/ sofosbuvir	Epclusa	Gilead	100 mg/400 mg	1 tablet daily	$25,169
Ledipasvir/ sofobuvir	Harvoni	Gilead	90 mg/400 mg	1 tablet daily	$31,815
Dasabuvir/ Ombitasvir Paritaprevir Ritonavir	Viekira Pak	AbbVie	250 mg/12.5 mg/75 mg/50 mg	4 tablets daily	$28,080
Dasabuvir/ Ombitasvir/ Paritaprevir/ Ritonavir	Viekira XR	AbbVie	200 mg/ 8.33 mg/ 50 mg/ 33.33 mg	2 tablets daily	$28,080

* Maximum Allowable Cost

Conclusion

Epclusa® is the first available pangenotypic NS5A-NS5B inhibitor single-pill combination regimen, and is highly efficacious across HCV genotypes 1 to 6. It is also approved, in combination with ribavirin, for patients who have been diagnosed with cirrhosis. Having a pangenotypic option significantly streamlines the treatment plan for many doctors' offices and clinics.

Recommendation

This drug is being considered for inclusion in the state specific Preferred Drug List (PDL).

References

1. Epclusa. Retrieved 9/2/16 from https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=7f30631a-ee3b-4cfe-866b-964df3f0a44f
2. Sofosbuvir-Velpatasvir. Retrieved 9/2/16 from http://www.hepatitisc.uw.edu/page/treatment/drugs/epclusa

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