Drug Monograph

Drug/Drug Class:	**Vosevi® (sofosbuvir, velpatasvir, and voxilaprevir) film coated tablet/ Hepatitis C**
Prepared for:	MO HealthNet
Prepared by:	Conduent

☒ **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:	Vosevi® is available in a film coated tablet that contains 400 mg sofosbuvir, 100 mg velpatasvir, and 100 mg voxilaprevir respectively. Manufactured by: Gilead Sciences, Inc., Foster City, CA 94404
Summary of Findings:	The approval of Vosevi was based on 2, phase 3 clinical trials that included approximately 750 adults with mild cirrhosis or without cirrhosis. The first trial compared Vosevi with placebo in adults with HCV genotype 1 who previously failed treatment with an NS5A inhibitor. Patients with genotypes 2,3,4,5, and 6 received Vosevi. The second trial examined Vosevi versus sofosbuvir and velpatasvir in adults with HCV genotypes 1, 2, or 3 who previously failed treatment with sofosbuvir, but not a NS5A inhibitor drug. The results of both clinical trials showed that 96% to 97% of patients given Vosevi had no viral detection 12 weeks after treatment, suggesting that the infection had been cured.
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 [2]

Hepatitis C is a contagious liver disease that ranges in severity from a mild illness lasting a few weeks to a serious, lifelong illness that attacks the liver. It results from infection with the HCV virus, which is spread primarily through contact with the blood of an infected person. It is estimated that 2.7-3.9 million people in the United States have chronic hepatitis C.

Until the past few years, hepatitis C treatment required weekly injections and oral medications that many HCV-infected people couldn't take because of other health problems or unacceptable side effect. The treatment patterns are changing for the better. Today, chronic HCV is usually curable with oral medications taken every day for 2-6 months. Still, only about half of the people with HCV know that they're infected, mainly because they don't have any symptoms.

Dosage Form(s) [1]

Vosevi® is available in a film coated tablet that contains 400 mg sofosbuvir, 100 mg velpatasvir, and 100 mg voxilaprevir respectively.

Manufacturer [1]

Gilead Sciences, Inc., Foster City, CA 94404

Indication(s) [1]

Vosevi® is indicated for the treatment of adult patients with chronic Hepatitis C virus infection without cirrhosis or compensated cirrhosis (child-pugh A) who have genotype 1, 2, 3, 4, 5, or 6 infection and have previously been treated with an HCV regimen containing an NS5A inhibitor. It is also indicated for genotypes 1a or 3 infection and have previously been treated with an HCV regimen containing sofosbuvir without an NS5A inhibitor.

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

Vosevi® is a fixed-dose combination of sofosbuvir, velpatasvir, and voxilaprevir which are direct acting antiviral (DAA) agents against the Hepatitis C virus.

Pharmacokinetics:

	Sofosbuvir	Velpatasvir	Voxilaprevir
Distribution	61-65% protein bound	>99% protein bound	>99% protein bound
Half Life	29 hours	17 hours	33 hours

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Excretion	Urine: 80% Feces: 14 %	Urine: 0.4% Feces: 94% (77% as parent)	Feces: 94% (40% as parent)
Elimination	Glomerular filtration and active tubular secretion	Biliary excretion	Biliary excretion

Polaris 4

Treatment with Vosevi for 12 weeks resulted in numerically higher SVR12 rates than treatment with sofosbuvir/velpatasvir for 12 weeks in subject with HCV genotype 1a and 3 infection.

STUDY DESIGN	Randomized, open-label, 12 week trial that evaluated treatment with Vosevi compared to Epclusa (Sofosbuvir/Velpatasvir).
INCLUSION CRITERIA	Subjects with genotype 1, 2, 3, or 4 HCV infection without cirrhosis or other compensated cirrhosis who had previously failed a HCV DAA-containing regimen that did not include an NS5A inhibitor.
EXCLUSION CRITERIA	Not specified.
TREATMENT REGIMEN	Patients with genotype 1, 2, or 3 HCV infection were randomized 1:1 to each group. Randomization was stratified by HCV genotype and by the presence or absence of cirrhosis. Subjects with genotype 4 HCV infection were enrolled to the Vosevi group.
RESULTS	In patients with genotype 1a receiving Vosevi, 97% achieved SVR12 compared to 82% of patients receiving sofosbuvir/velpatasvir. Comparably, 96% of patients with genotype 3 receiving Vosevi achieved SVR12 compared to 85% of patients receiving sofosbuvir/velpatasvir. Comparable SVR12 rates were observed in patients with HCV genotype 1b and 2 infection treated with Vosevi versus sofosbuvir/velpatasvir.
SAFETY	On-treatment virologic failure was similar between the two groups in patients with genotype 1a and 3. Relapse rates were significantly higher in these genotype groups with sofosbuvir/velpatasvir versus Vosevi.

Contraindications [(1)]

- Rifampin

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Warnings and Precautions [1]

- Risk of Hepatitis B Virus reactivation in patients coinfected with HCV and HBV
- Serious symptomatic bradycardia when coadministered with amiodarone
- Risk or reduced therapeutic effect due to concomitant use of Vosevi with inducers of P-gp and/or moderate to potent inducers of CYP.

Adverse Effects [1]

Most common, ≥ 5%	Vosevi (n=263)	Placebo (n=152)
Headache	21%	14%
Fatigue	17%	15%
Diarrhea	13%	9%
Nausea	13%	7%
Asthenia	6%	4%
Insomnia	6%	3%

Drug Interactions [1]

- Inducers of P-gp may decrease plasma concentrations of Vosevi
- Moderate to potent inducers of CYP2B6, CYP2C8, and CYP3A4 may decrease plasma concentrations of Vosevi
- Substrates of BCRP, OATP1B1, OATB1B3, and OATP2B1. Vosevi are inhibitors of these transporters and may alter the exposure of such drugs
- Antacids
- H2 Receptor antagonist
- PPIs
- Antiarrhythmics; amiodarone, digoxin
- Anticoagulants; dabigatran
- Anticonvulsants; carbamazepine, phenytoin, phenobarbital, oxcarbazepine
- Antimycobacterials; rifampin, rifabutin, rifapentine
- Antiretrovirals; atazanavir, lopinavir, tipranavir/ritonavir, efavirenz, tenofovir disoproxil fumarate,
- St. John's wort
- HMG-CoA Reductase Inhibitors
- Cyclosporine

Dosage and Administration [1]

The FDA recommended dose of Vosevi is one tablet orally taken once daily with food.

Cost

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GENERIC NAME	BRAND NAME	MANUFACTURER	DOSE	COST/ Month*
Sofosbuvir, velpatasvir, voxilaprevir	Vosevi	Gilead	1 tablet daily	$25,169.20
Glecaprevir, pibrentasvir	Mavyret	Abbvie	3 tablets daily	$12,743.64

* Maximum Allowable Cost

Conclusion

Vosevi® is a fixed dose combination of sofosbuvir, velpatasvir, and voxilaprevir which are all direct acting antiviral agents against the Hepatitis C virus. Vosevi is the first pangenotypic fixed-dose tablet that includes medications from three different HCV antiviral classes. It plays an important role for patients who have experienced treatment failure with other DAA therapy. The recommended treatment regimen is one tablet daily with food for 12 weeks. The cost is approximately $75,000 per 12 week treatment.

Recommendation

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

References

1) Vosevi. Retrieved 11/21/2017 from: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=17ffc094-8ca7-45d2-80d8-fd043bc9a221&audience=consumer
2) Hepaptis C FAQs for the Public. Retrieved 11/21/2017 from: https://www.cdc.gov/hepatitis/hcv/cfaq.htm

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