Effective Date **1/1/2024**
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Coverage Policy Number **IP0187**

Glecaprevir/Pibrentasvir

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Related Coverage Resources

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Overview

This policy supports medical necessity review for glecaprevir/pibrentasvir tablets and oral pellets (**Mavyret®**).

Coverage for glecaprevir/pibrentasvir (Mavyret) varies across plans and requires the use of preferred products in addition to the criteria listed below. Refer to the customer's benefit plan document for coverage details.

Receipt of sample product does not satisfy any criteria requirements for coverage.

Initial Approval Criteria

Glecaprevir/pibrentasvir (Mavyret) is considered medically necessary for the treatment of chronic hepatitis C virus (HCV) for all genotypes or unknown genotype status when ALL of the following criteria are met:

1. Age 3 years or older

2. Does NOT have cirrhosis or has compensated cirrhosis (Child-Pugh A)
3. Has NOT previously received treatment for their chronic HCV infection
4. Medication is prescribed by or in consultation with a gastroenterologist, hepatologist, infectious diseases physician, or a liver transplant physician
5. Preferred products are required:
   Employer Group Plans
   Documentation of failure, contraindication, or intolerance to **ONE** of the following:
   a. Epclusa® (sofosbuvir/velpatasvir) [may require prior authorization]
   b. Harvoni® (ledipasvir/sofosbuvir) [may require prior authorization]
   c. Vosevi™ (sofosbuvir/velpatasvir/voxilaprevir) [may require prior authorization]

   Individual and Family Plans:
   Documentation of failure, contraindication, or intolerance to **ONE** of the following:
   a. Epclusa® (sofosbuvir/velpatasvir) [may require prior authorization]
   b. sofosbuvir/velpatasvir [may require prior authorization]
   c. Harvoni® (ledipasvir/sofosbuvir) [may require prior authorization]
   d. ledipasvir/sofosbuvir [may require prior authorization]

Glecaprevir/pibrentasvir (Mavyret) is considered medically necessary for the treatment of chronic hepatitis C virus (HCV) genotype 1 in a treatment-experienced individual when ALL of the following criteria are met:

1. Age 3 years or older
2. Meets **ONE** of the following conditions:
   a. NS5A-Experienced, NS3/4-Naïve and **ALL** of the following:
      i. Does NOT have cirrhosis or has compensated cirrhosis (Child-Pugh A)
      ii. Had a prior null response, prior partial response, or had relapse after prior treatment with **ONE** of the following NS5A-inhibitor containing products: daclatasvir (Daklinza), ledipasvir/sofosbuvir (Harvoni), or sofosbuvir/velpatasvir (Epclusa)
      iii. Has NOT previously been treated with **ONE** of the following NS3/4A inhibitor or NS3/4A inhibitor-containing products: boceprevir (Victrelis), simeprevir (Olysio), or telaprevir (Incivek), or ombitasvir/paritaprevir/ritonavir (Technivie), ombitasvir/paritaprevir/ritonavir, dasabuvir, co-packaged (Viekira Pak/Viekira XR), sofosbuvir/velpatasvir/voxilaprevir (Vosevi), or elbasvir/grazoprevir (Zepatier)
   b. NS3/4-Experienced, NS5A-Naïve and **ALL** of the following:
      i. Does NOT have cirrhosis or has compensated cirrhosis (Child-Pugh A)
      ii. Has NOT previously been treated with **ONE** of the following NS5A-inhibitor-containing products: daclatasvir (Daklinza), ledipasvir/sofosbuvir (Harvoni), or sofosbuvir/velpatasvir (Epclusa), ombitasvir/paritaprevir/ritonavir (Technivie), ombitasvir/paritaprevir/ritonavir, dasabuvir, co-packaged (Viekira Pak/Viekira XR), sofosbuvir/velpatasvir/voxilaprevir (Vosevi), or elbasvir/grazoprevir (Zepatier)
      iii. Had a prior null response, prior partial response, or had relapse after prior treatment with **ONE** of the following NS3/4A inhibitor or NS3/4A inhibitor-containing products: boceprevir (Victrelis), simeprevir (Olysio), or telaprevir (Incivek)
   c. Pegylated Interferon/Interferon, Ribavirin, Sofosbuvir-Experienced and **ALL** of the following:
      i. Does NOT have cirrhosis or has compensated cirrhosis (Child-Pugh A)
      ii. Had a prior null response, prior partial response, or had relapse after prior treatment with **ONE** of the following regimens: interferon ± ribavirin, pegylated interferon ± ribavirin, sofosbuvir (Sovaldi) + ribavirin, sofosbuvir (Sovaldi) + pegylated interferon + ribavirin
3. Medication is prescribed by or in consultation with a gastroenterologist, hepatologist, infectious diseases physician, or a liver transplant physician
4. Preferred products are required:
   Employer Group Plans

Documentation of failure, contraindication, or intolerance to **ONE** of the following:
   a. Epclusa® (sofosbuvir/velpatasvir) [may require prior authorization]
   b. Harvoni® (ledipasvir/sofosbuvir) [may require prior authorization]
   c. Vosevi™ (sofosbuvir/velpatasvir/voxilaprevir) [may require prior authorization]

Individual and Family Plans:
Documentation of failure, contraindication, or intolerance to **ONE** of the following:
   a. Epclusa® (sofosbuvir/velpatasvir) [may require prior authorization]
   b. sofosbuvir/velpatasvir [may require prior authorization]
   c. Harvoni® (ledipasvir/sofosbuvir) [may require prior authorization]
   d. ledipasvir/sofosbuvir [may require prior authorization]

Glecaprevir/pibrentasvir (Mavyret) is considered medically necessary for the treatment of chronic hepatitis C virus (HCV) genotype 2, 4, 5, or 6 in a treatment-experienced individual when ALL of the following criteria are met:

1. Age 3 years or older
2. Does NOT have cirrhosis or has compensated cirrhosis (Child-Pugh A)
3. Had a prior null response, prior partial response, or had relapse after prior treatment with **ONE** of the following regimens: interferon ± ribavirin, pegylated interferon ± ribavirin, sofosbuvir (Sovaldi)+ ribavirin, sofosbuvir (Sovaldi) + pegylated interferon + ribavirin
4. Medication is prescribed by or in consultation with a gastroenterologist, hepatologist, infectious diseases physician, or a liver transplant physician
5. Preferred products are required:
   Employer Group Plans
   Documentation of failure, contraindication, or intolerance to **ONE** of the following:
      a. Epclusa® (sofosbuvir/velpatasvir) [may require prior authorization]
      b. Harvoni® (ledipasvir/sofosbuvir) [may require prior authorization]
      c. Vosevi™ (sofosbuvir/velpatasvir/voxilaprevir) [may require prior authorization]

   Individual and Family Plans:
   Documentation of failure, contraindication, or intolerance to **ONE** of the following:
      a. Epclusa® (sofosbuvir/velpatasvir) [may require prior authorization]
      b. sofosbuvir/velpatasvir [may require prior authorization]
      c. Harvoni® (ledipasvir/sofosbuvir) [may require prior authorization]
      d. ledipasvir/sofosbuvir [may require prior authorization]

Glecaprevir/pibrentasvir (Mavyret) is considered medically necessary for the treatment of chronic hepatitis C virus (HCV) genotype 3 in a treatment-experienced individual when ALL of the following criteria are met:

1. Age 3 years or older
2. Does NOT have cirrhosis or has compensated cirrhosis (Child-Pugh A)
3. Had a prior null response, prior partial response, or had relapse after prior treatment with **ONE** of the following regimens: interferon ± ribavirin, pegylated interferon ± ribavirin, sofosbuvir (Sovaldi) + ribavirin, sofosbuvir + pegylated interferon + ribavirin
4. Medication is prescribed by or in consultation with a gastroenterologist, hepatologist, infectious diseases physician, or a liver transplant physician
5. Preferred products are required:
   Employer Group Plans
   Documentation of failure, contraindication, or intolerance to **ONE** of the following:
      a. Epclusa® (sofosbuvir/velpatasvir) [may require prior authorization]

b. Harvoni® (ledipasvir/sofosbuvir) [may require prior authorization]
c. Vosevi™ (sofosbuvir/velpatasvir/voxilaprevir) [may require prior authorization]

Individual and Family Plans:
Documentation of failure, contraindication, or intolerance to **ONE** of the following:
a. Epclusa® (sofosbuvir/velpatasvir) [may require prior authorization]
b. sofosbuvir/velpatasvir [may require prior authorization]
c. Harvoni® (ledipasvir/sofosbuvir) [may require prior authorization]
d. ledipasvir/sofosbuvir [may require prior authorization]

Glecaprevir/pibrentasvir (Mavyret) is considered medically necessary for the treatment of chronic hepatitis C virus (HCV) in kidney or liver transplant recipients with genotype 1, 2, 3, 4, 5, or 6, when the individual meets ALL of the following criteria:

1. Age 3 years or older
2. Meets **ONE** of the following:
    a. Genotype 1 and **BOTH** of the following:
        i. NS5A-Experienced - had a prior null response, prior partial response, or had relapse after prior treatment with **ONE** of the following NS5A-inhibitor containing products: daclatasvir (Daklinza), ledipasvir/sofosbuvir (Harvoni), or sofosbuvir/velpatasvir (Epclusa)
        ii. NS3/4-Naïve - has NOT previously been treated with **ONE** of the following NS3/4A inhibitor or NS3/4A inhibitor-containing products: boceprevir (Victrelis), simeprevir (Olysio), or telaprevir (Incivek), OR ombitasvir/paritaprevir/ritonavir (Technivie), ombitasvir/paritaprevir/ritonavir, dasabuvir, co-packaged (Viekira Pak/Viekira XR), sofosbuvir/velpatasvir/voxilaprevir (Vosevi), or elbasvir/grazoprevir (Zepatier)
    b. Genotype 3 and has had a prior null response, prior partial response, or had relapse after prior treatment with **ONE** of the following regimens: interferon ± ribavirin, pegylated interferon ± ribavirin, sofosbuvir (Sovaldi) + ribavirin, sofosbuvir (Sovaldi) + pegylated interferon + ribavirin
    c. All other kidney/liver transplant recipients with genotypes 1, 2, 3, 4, 5, or 6 HCV
3. Medication is prescribed by or in consultation with a gastroenterologist, hepatologist, infectious diseases physician, or a liver transplant physician
4. Preferred products are required:
    Employer Group Plans
    Documentation of failure, contraindication, or intolerance to **ONE** of the following:
    a. Epclusa® (sofosbuvir/velpatasvir) [may require prior authorization]
    b. Harvoni® (ledipasvir/sofosbuvir) [may require prior authorization]
    c. Vosevi™ (sofosbuvir/velpatasvir/voxilaprevir) [may require prior authorization]

    Individual and Family Plans:
    Documentation of failure, contraindication, or intolerance to **ONE** of the following:
    a. Epclusa® (sofosbuvir/velpatasvir) [may require prior authorization]
    b. sofosbuvir/velpatasvir [may require prior authorization]
    c. Harvoni® (ledipasvir/sofosbuvir) [may require prior authorization]
    d. ledipasvir/sofosbuvir [may require prior authorization]

Glecaprevir/pibrentasvir (Mavyret) is considered medically necessary for the treatment of chronic hepatitis C virus (HCV) when the individual has already been started on the medication and will be completing a course of therapy.

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Continuation of Therapy

Not applicable for continuation beyond initial approval duration.

Authorization Duration

Initial approval duration:

1. **Chronic HCV Genotype 1, 2, 3, 4, 5, or 6, Treatment-Naïve without Cirrhosis or with Compensated Cirrhosis (Child-Pugh A) or Chronic Hepatitis C Virus (HCV), Genotype Unknown/Undetermined:** 8 weeks

2. **Chronic Hepatitis C Virus (HCV), Genotype 1, Treatment-Experienced**
   NS5A-Experienced, NS3/4-Naïve without Cirrhosis or with Compensated Cirrhosis (Child-Pugh A): 16 weeks
   NS3/4-Experienced, NS5A-Naïve without Cirrhosis or with Compensated Cirrhosis (Child-Pugh A): 12 weeks
   Pegylated Interferon/Interferon, Ribavirin, Sovaldi-Experienced without Cirrhosis: 8 weeks
   Pegylated Interferon/Interferon, Ribavirin, Sovaldi-Experienced with Compensated Cirrhosis (Child-Pugh A): 12 weeks

3. **Chronic HCV Genotype 2, 4, 5 or 6, Treatment-Experienced**
   Without Cirrhosis and prior treatment experience with interferon, pegylated interferon, ribavirin, and/or sofosbuvir: 8 weeks
   With Compensated Cirrhosis (Child-Pugh A) and prior treatment experience with interferon, pegylated interferon, ribavirin, and/or sofosbuvir: 12 weeks

4. **Chronic HCV Genotype 3, Treatment-Experienced**
   Without Cirrhosis or with Compensated Cirrhosis (Child-Pugh A) and prior treatment experience with interferon, pegylated interferon, ribavirin, and/or sofosbuvir: 16 weeks

5. **Hepatitis C Virus (HCV) Kidney or Liver Transplant Recipients, Genotype 1, 2, 3, 4, 5, OR 6**
   Genotype 1 NS5A-Experienced, NS3/4-Naïve: 16 weeks
   Genotype 3 Pegylated Interferon/Interferon, Ribavirin, Sovaldi-Experienced: 16 weeks
   All Other Kidney/Liver Transplant Recipients with Genotypes 1, 2, 3, 4, 5, or 6 HCV: 12 weeks

Reauthorization approval duration: not applicable

Conditions Not Covered

Any other use is considered experimental, investigational or unproven, including the following (this list may not be all inclusive):

1. **Hepatitis C Virus (HCV) Child-Pugh Class B or C Liver Disease (Moderate or Severe Hepatic Impairment).** Mavyret is contraindicated in patients with moderate or severe hepatic impairment (Child-Pugh Class B or C).

2. **Hepatitis C Virus (HCV) [any genotype], Combination with Any Other Direct-Acting Antivirals**. Mavyret provides a complete antiviral regimen.

3. **Life Expectancy Less Than 12 Months Due to Non-Liver Related Comorbidities.** Patients with a limited life expectancy that cannot be remediated by HCV treatment, liver transplantation, or another directed therapy do not require antiviral treatment.[2] Patients with a short life expectancy owing to liver disease should be managed in consultation with an expert. Little evidence exists to support initiation of HCV treatment in patients with a limited life expectancy (less than 12 months) owing to non-liver-related comorbid conditions. For these patients, the benefits of HCV treatment are unlikely to be realized and palliative care strategies should take precedence.

4. **Pediatric Patient (Less than 3 Years of Age).** The safety and efficacy of Mavyret have not been established in pediatric patients less than 3 years of age.[1]

Background

OVERVIEW

Mavyret, a direct-acting antiviral, contains glecaprevir, a pangenotypic NS3/4A protease inhibitor and pibrentasvir, a pangenotypic NS5A inhibitor.[1] It is indicated for the treatment of **chronic hepatitis C virus** (HCV) in the following scenarios:

- Patients ≥ 3 years of age with genotype 1, 2, 3, 4, 5, or 6 infection without cirrhosis or with compensated cirrhosis (Child-Pugh A).
- Patients ≥ 3 years of age with genotype 1 infection who have previously been treated with a regimen containing an HCV NS5A inhibitor or an NS3/4A protease inhibitor, but not both.

Dosing

The duration of therapy is based on prior treatment experience, genotype, and the presence or absence of cirrhosis (see Tables 1 and 2). In addition, Mavyret is recommended for 12 weeks in patients ≥ 3 years of age who are liver or kidney transplant recipients. Similar to non-transplant recipients, a 16-week treatment duration is recommended in genotype 1-infected patients who are NS5A inhibitor-experienced without prior treatment with an NS3/4A protease inhibitor or in genotype 3-infected patients who are treatment-experienced with regimens containing interferon, pegylated interferon, ribavirin, and/or Sovaldi® (sofosbuvir tablets/oral pellets).

Table 1. Recommended Duration for Treatment-Naïve Patients.[1]

HCV Genotype	Treatment Duration	
	No Cirrhosis	Compensated Cirrhosis (Child-Pugh A)
1, 2, 3, 4, 5, or 6	8 weeks	8 weeks

HCV – Hepatitis C virus.

Table 2. Recommended Duration for Treatment-Experienced Patients.[1]

HCV Genotype	Prior Treatment Experience	Duration	
		Without Cirrhosis	With Compensated Cirrhosis (Child-Pugh A)
1, 2, 4, 5, 6	PRS	8 weeks	12 weeks
3	PRS	16 weeks	16 weeks
1	NS3/4 PI[1] (NS5A-naïve)	12 weeks	12 weeks
	NS5A inhibitor[2] (NS3/4 PI-naïve)†	16 weeks	16 weeks

HCV – Hepatitis C virus; PRS – Prior treatment experience with regimens containing interferon, pegylated interferon, ribavirin, and/or Sovaldi® (sofosbuvir tablets), but no prior treatment experience with an HCV NS3/4A protease inhibitor (PI) or NS5A inhibitor; PI – Protease inhibitor; [1] Regimens containing Olysio® (simeprevir capsules) and Sovaldi, or Olysio, Victrelis® (boceprevir capsules), or Incivek® (telaprevir tablets) with interferon or pegylated interferon and ribavirin were studied; [2] Regimens containing ledipasvir/sofosbuvir or Daklinza® (daclatasvir tablets) + pegylated interferon + ribavirin [unapproved regimen] were studied.

Guidelines
The American Association for the Study of Liver Diseases/Infectious Diseases Society of America (AASLD/IDSA) provide recommendations for testing, monitoring, and treating HCV (October 24, 2022).[2] Instances in which the guidelines provide recommendations for Mavyret outside of the FDA-approved indications are outlined below.

With the availability of pangenotypic HCV treatment regimens, HCV genotyping is no longer required prior to treatment initiation for all individuals. Pretreatment genotyping is still recommended in patients with cirrhosis and/or past unsuccessful HCV treatment, because treatment regimens may differ by genotype. However, for treatment-naïve patients without cirrhosis, although genotyping may impact the preferred treatment approach, it is not required if a pangenotypic regimen is used. Treatment-naïve adults without cirrhosis are eligible for simplified treatment if they do not have hepatitis B virus (not hepatitis B serum antigen [HBsAg] positive), are not pregnant, do not have hepatocellular carcinoma, and have not had a liver transplantation. In treatment-naïve adults without cirrhosis, the recommended regimens are Mavyret for 8 weeks or sofosbuvir/velpatasvir for 12 weeks. Additional genotype-specific and/or special circumstance-specific recommendations are also provided for patients falling outside of these parameters.

Mavyret is recognized as a recommended regimen (12 weeks) for the treatment of patients with recurrent HCV post-liver transplantation (without cirrhosis or with compensated cirrhosis).

References

1. Mavyret® tablets and oral pellets [prescribing information]. North Chicago, IL: AbbVie; September 2021.
2. American Association for the Study of Liver Diseases and the Infectious Diseases Society of America. Testing, managing, and treating hepatitis C. Available at: http://www.hcvguidelines.org. Updated October 24, 2022. Accessed on March 24, 2023.