Oscar Clinical Guideline: Rezdiffra (resmetirom) (PG198, Ver. 1)

Rezdiffra (resmetirom)

Disclaimer

Clinical guidelines are developed and adopted to establish evidence-based clinical criteria for utilization management decisions. Clinical guidelines are applicable according to policy and plan type. The Plan may delegate utilization management decisions of certain services to third parties who may develop and adopt their own clinical criteria.

Coverage of services is subject to the terms, conditions, and limitations of a member's policy, as well as applicable state and federal law. Clinical guidelines are also subject to in-force criteria such as the Centers for Medicare & Medicaid Services (CMS) national coverage determination (NCD) or local coverage determination (LCD) for Medicare Advantage plans. Please refer to the member's policy documents (e.g., Certificate/Evidence of Coverage, Schedule of Benefits, Plan Formulary) or contact the Plan to confirm coverage.

Summary

Metabolic dysfunction-associated steatotic liver disease (MASLD), formerly known as nonalcoholic fatty liver disease (NAFLD), is a condition characterized by the presence of hepatic steatosis in conjunction with at least one cardiometabolic risk factor, such as obesity, type 2 diabetes, dyslipidemia, or hypertension. The presence of inflammation and hepatocellular injury, with or without fibrosis, defines the progressive form known as metabolic dysfunction-associated steatohepatitis (MASH), previously called nonalcoholic steatohepatitis (NASH). Untreated MASH can lead to complications like cirrhosis, liver failure, and hepatocellular carcinoma.

The first-line treatment for MASLD and MASH is lifestyle modification through a hypocaloric diet, weight loss, and regular exercise. Medications may be considered for MASH, particularly in patients with advanced fibrosis. Rezdiffra (resmetirom) is a thyroid hormone receptor-beta agonist indicated for the treatment of adults with non-cirrhotic MASH with moderate to advanced liver fibrosis (stages F2 to F3) in conjunction with diet and exercise.

- Limitation of Use: Avoid use of Rezdiffra in patients with decompensated cirrhosis.

Definitions

"**Fibrosis stage**" refers to the degree of fibrosis present in the liver, graded on a 5-point scale from F0 (no fibrosis) to F4 (cirrhosis). Stages F2-F3 represent significant fibrosis.

"**MASH resolution**" is defined as the absence of hepatocellular ballooning, minimal lobular inflammation (grade 0-1), and a decrease in NAFLD activity score (NAS) by at least 2 points.

"**Metabolic dysfunction-associated steatotic liver disease (MASH)**" refers to a progressive form of nonalcoholic fatty liver disease characterized by hepatic steatosis (≥5% of hepatocytes), inflammation, and hepatocellular injury, with or without fibrosis, that was formerly termed nonalcoholic steatohepatitis (NASH).

"**MRI-PDFF**" is magnetic resonance imaging–proton density fat fraction, an imaging-based quantitative biomarker of liver fat content used to diagnose and monitor hepatic steatosis.

"**Noninvasive tests (NITs)**" refer to blood- or imaging-based tests used to diagnose and monitor MASH and fibrosis as an alternative to liver biopsy. Examples include the FIB-4 index, Enhanced Liver Fibrosis (ELF) test, vibration-controlled transient elastography (VCTE), and magnetic resonance elastography (MRE).

Medical Necessity Criteria for Initial Authorization

The Plan considers **Rezdiffra (resmetirom)** medically necessary when recent (within the last 3 months) clinical chart documentation provided indicates **ALL** of the following criteria are met:

1. The medication is prescribed by or in consultation with a gastroenterologist or hepatologist; ***AND***
2. The member is 18 years of age or older; ***AND***
3. The member has a diagnosis of noncirrhotic metabolic dysfunction-associated steatotic liver disease (MASH)[⇅] with moderate to advanced liver fibrosis (consistent with stages F2 to F3 fibrosis), confirmed by one or more of the following:
    a. Liver biopsy showing MASH and significant fibrosis (F2 or F3) without cirrhosis; ***and/or***
    b. Transient elastography (e.g. FibroScan) with liver stiffness ≥ 8.0 kPa (F2) but < 20 kPa (cirrhosis); ***and/or***
    c. Magnetic resonance elastography (MRE) with liver stiffness ≥ 3.63 kPa; ***and/or***
    d. Enhanced Liver Fibrosis (ELF) test ≥ 9.8; ***and/or***

e. Fibrosis-4 (FIB-4) index ≥ 2.67 (age > 65) or FIB-4 ≥ 1.3 (age < 65) PLUS one additional noninvasive test (transient elastography, MRE, or ELF) showing at least stage 2 fibrosis; ***AND***

⇅*formerly known as nonalcoholic fatty liver disease (NAFLD)*

4. The member has attempted at least 6 months of intensive lifestyle intervention with diet and exercise aimed at weight loss of at least 7-10%, without sufficient improvement in MASH or fibrosis; ***AND***
5. Rezdiffra (resmetirom) will be used in conjunction with diet and exercise aimed at weight loss; ***AND***
6. The member does **NOT** have cirrhosis or decompensated liver disease, as evidenced by any of the following:
    a. Liver biopsy showing cirrhosis; ***and/or***
    b. Cirrhosis of the liver with portal hypertension; ***and/or***
    c. History of liver decompensation event (e.g., ascites, variceal bleeding, hepatic encephalopathy); ***and/or***
    d. Model for End-Stage Liver Disease (MELD) score > 15; ***and/or***
    e. Transient elastography (e.g. FibroScan) with liver stiffness measurement ≥ 20 kPa; ***and/or***
    f. MRE with liver stiffness measurement ≥ 5.0 kPa; ***and/or***
    g. ELF test > 11.3; ***AND***
7. The requested dose does not exceed 100 mg per day.

If the above prior authorization criteria are met, the requested product will be authorized for 12-months.

Medical Necessity Criteria for Reauthorization

Reauthorization for 12-months will be granted if the member has recent (within the last 6 months) clinical chart documentation demonstrating **ALL** of the following criteria:

1. The member is currently receiving the medication through the Plan's benefit or has previously met Initial Authorization criteria; ***AND***
2. The member is responding positively to therapy as evidenced by one or more of the following:
    a. Improvement in steatosis, inflammation, or fibrosis based on imaging (liver ultrasound or MRI) or non-invasive tests/scores, if available; ***and/or***

b. Improvement in fibrosis stage based on available methods such as transient elastography, MRE, ELF, or clinical prediction scores (FIB-4, NAFLD fibrosis score); ***and/or***
c. Lack of disease progression or stable disease state; ***and/or***
d. Reduction in liver fat content on MRI-PDFF, if available; ***AND***

3. The member has demonstrated ongoing engagement and efforts toward weight management through adherence to the recommended diet and exercise regimen; ***AND***
4. The member has not developed cirrhosis or decompensated liver disease while on Rezdiffra (resmetirom), as evidenced by the absence of clinical signs or symptoms of decompensation (e.g., ascites, variceal bleeding, hepatic encephalopathy); ***AND***
5. The requested dose does not exceed 100 mg per day.

Experimental or Investigational / Not Medically Necessary

Rezdiffra (resmetirom) for any other indication or use is considered not medically necessary by the Plan, as it is deemed to be experimental, investigational, or unproven. Non-covered indications include, but are not limited to, the following:

- Treatment of NAFLD/MASH without significant fibrosis (stage F2-F3).
- Treatment of NASH/MASH in patients with:
    - No fibrosis (stage F0) or mild fibrosis (stage F1).
    - Cirrhosis (stage F4) or decompensated liver disease.
    - Other chronic liver diseases (e.g., hepatitis B, hepatitis C, autoimmune hepatitis, alcoholic liver disease, hemochromatosis, Wilson's disease).
- Treatment of pediatric NAFLD/MASH (age < 18 years).
- Prevention of NAFLD/MASH in patients with fatty liver or metabolic risk factors.
- Use in combination with other off-label or investigational NASH/MASH therapies (e.g., vitamin E, pioglitazone, GLP-1 RAs, FXR agonists, ASK-1 inhibitors, caspase inhibitors, etc.), outside of the context of a clinical trial.
- Use in patients who have not first attempted at least 6 months of intensive lifestyle modification focusing on weight loss of ≥ 7-10% through diet and exercise.
- Use in pre-transplant or post-transplant settings for the treatment or prevention of recurrent or de novo NASH/MASH in liver transplant recipients.

Applicable Billing Codes

ICD-10 codes considered medically necessary if criteria are met:	
Code	*Description*
K75.81	Nonalcoholic Steatohepatitis (Nash)

References

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Clinical Guideline Revision / History Information

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