Generic Name: Resmetirom

Applicable Drugs: Rezdiffra™

Preferred: N/A

Non-preferred: N/A

Date of Origin: 5/22/2024

Date Last Reviewed / Revised: 11/19/2025

PRIOR AUTHORIZATION CRITERIA

(May be considered medically necessary when criteria I through VII are met)

I. Documented diagnosis of Metabolic Dysfunction-Associated Steatohepatitis (MASH) (formerly known as NASH) AND must meet all of the following criteria:
   A. Patient is 18 years old or older.
   B. Patient has stage F2 or F3 liver fibrosis confirmed within the last 12 months by:
      i. Liver biopsy AND
      ii. Combination of FIB-4 score of 1.30 to 3.25 AND FibroScan or MRI elastography demonstrating liver stiffness of 7.5 to 14 kPa.
   C. Patient has at least three of the following five metabolic risk factors: abdominal obesity, hypertriglyceridemia, low HDL cholesterol, elevated blood pressure, impaired fasting glucose.

II. For patients with BMI < 25:
   A. Documented (healthcare provider attestation) trial and failure of 6-month trial of comprehensive lifestyle interventions including diet and exercise.

III. For patients with BMI ≥ 25:
   A. Weight loss of at least 5% since NASH diagnosis OR
   B. Documented trial of reduced-calorie diet (approximately 500 kcal/day deficit) and exercise plan (recommended increase in physical activity of a minimum 150 minutes per week) with a goal of achieving at least 5% to 10% weight loss for at least 6 months AND
   C. Documentation that the requested medication will be used as an adjunct to a reduced-calorie diet and exercise plan, as described above, with the goal of achieving at least 5% to 10% weight loss.

IV. For patients with comorbid Type 2 Diabetes Mellitus:
   A. A1c must be 9.0% or lower.
   B. Documented trial and failure, or contraindication to, both of the following treatments for at least 6 months:
      i. Pioglitazone 30-45 mg daily

ii. GLP-1 receptor agonist (such as semaglutide) at maximum tolerated dose (dose must be stable for at least 6 months) A GLP-1 receptor agonist may be approved if there is a diagnosis of type II diabetes mellitus and criteria in section I. A, B II. and C are met.

V. For patients without comorbid Type 2 Diabetes Mellitus:

A. Documented trial and failure of, or contraindication to, treatment with vitamin E 800IU daily for at least 3 months.

VI. Documentation that resmetirom will be used in conjunction with comprehensive lifestyle changes including diet and exercise. There must be a documented, detailed treatment plan of optimized care for concomitant related conditions, including dyslipidemia, T2DM, and hypertension. This could include statin and anticoagulant therapy.

VII. Resmetirom is prescribed by a hepatologist or gastroenterologist.

VIII. Refer to plan document for the list of preferred products. If requested agent is not listed as a preferred product, must have a documented failure, intolerance, or contraindication to the preferred product(s).

EXCLUSION CRITERIA

- Cirrhosis (stage F4 liver fibrosis)
- Causes of chronic liver disease other than noncirrhotic NASH (such as Hepatitis C, Wilson's disease, hepatocellular carcinoma, etc.)
- Any level of alcohol consumption
- Moderate to severe hepatic impairment (Child-Pugh Class B or C or score ≥ 7)
- Concomitant use with strong CYP2C8 inhibitors (e.g. gemfibrozil)
- Concomitant use with OATP inhibitors (e.g. cyclosporine)
- Bariatric surgery in previous 5 years
- Pregnancy

OTHER CRITERIA

- Resmetirom dosing is 80mg by mouth once daily for patients with body weight < 100 kg, or 100mg by mouth once daily for patients with body weight ≥ 100 kg.
- Compounded GLP-1 Receptor Agonists are not covered.

QUANTITY / DAYS SUPPLY RESTRICTIONS

- 30 tablets per 30 days.

APPROVAL LENGTH

- **Authorization:** 12 months.
- **Re-Authorization:** 12 months. An updated letter of medical necessity or progress notes showing the medication is effective and tolerated must be provided for re-authorization. Efficacy for this medication is defined as no worsening of fibrosis stage or improvement of fibrosis stage. Documentation of repeat biopsy OR a combination of FIB-4 score and noninvasive imaging (such as FibroScan) must be provided to assess medication efficacy. Patient must be adherent to drug therapy. Documentation of patient's current weight and BMI must be provided. Patients who have gained >5% body weight since initiation of resmetirom are not eligible for renewal.

APPENDIX

N/A

REFERENCES

1. Rezdiffra Prescribing information. Madrigal Pharmaceutical, Inc.; 2024. Accessed November 19, 2025. https://www.madrigalpharma.com/wp-content/uploads/2025/04/rezdiffra-prescribing-information-07-2024.pdf
2. Cusi, K, et. al., American Association of Clinical Endocrinology Clinical Practice Guideline for the Diagnosis and Management of Nonalcoholic Fatty Liver Disease in Primary Care and Endocrinology Clinical Settings. *Endocrine Practice*. 2022;28(5):528-562. doi:https://doi.org/10.1016/j.eprac.2022.03.010.
3. Harrison, SA, et. al., A Phase 3, Randomized, Controlled Trial of Resmetirom in NASH with Liver Fibrosis. *N Engl J Med*. 2024;390(6):497-509. doi:10.1056/NEJMoa2309000.
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6. Newsome, PN, et. al., A Placebo-Controlled Trial of Subcutaneous Semaglutide in Nonalcoholic Steatohepatitis. *N Engl J Med.* 2021;384(12):1113-1124. doi: 10.1056/NEJMoa2028395.
7. Rinella, ME, et. al., AASLD Practice Guidance on the clinical assessment and management of nonalcoholic fatty liver disease. *Hepatology*; 77(5):1797-1835, May 2023. doi:10.1097/HEP.0000000000000323
8. Vilar-Gomez E, et. al., Weight Loss Through Lifestyle Modification Significantly Reduces Features of Nonalcoholic Steatohepatitis. *Gastroenterology*. 2015;149(2):367-e15. doi:10.1053/j.gastro.2015.04.005
9. American Diabetes Association Professional Practice Committee; 4. Comprehensive Medical Evaluation and Assessment of Comorbidities: Standards of Care in Diabetes—2025. *Diabetes Care* 1 January 2025; 48 (Supplement_1): S59–S85. https://doi.org/10.2337/dc25-S004

DISCLAIMER: Medication Policies are developed to help ensure safe, effective and appropriate use of selected medications. They offer a guide to coverage and are not intended to dictate to providers how to practice medicine. Refer to Plan for individual adoption of specific Medication Policies. Providers are expected to exercise their medical judgement in providing the most appropriate care for their patients.