

DRUG POLICY

Rezdiffra™ (resmetirom)

BENEFIT APPLICATION

Benefit determinations are based on the applicable contract language in effect at the time the services were rendered. Exclusions, limitations or exceptions may apply. Benefits may vary based on contract, and individual member benefits must be verified. Wellmark determines medical necessity only if the benefit exists and no contract exclusions are applicable. This medical policy may not apply to FEP. Benefits are determined by the Federal Employee Program.

DESCRIPTION

The indications below including FDA-approved indications and compendial uses are considered covered benefits provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Rezdiffra is indicated in conjunction with diet and exercise for the treatment of adults with noncirrhotic nonalcoholic steatohepatitis (NASH) with moderate to advanced liver fibrosis (consistent with stages F2 to F3 fibrosis).

This indication is approved under accelerated approval based on improvement of NASH and fibrosis. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

Limitations of Use

Avoid use of Rezdiffra in patients with decompensated cirrhosis.

POLICY

Required Documentation

Submission of the following information is necessary to initiate the prior authorization review:

1. Chart notes or medical records documenting clinical findings supporting the diagnosis of metabolic dysfunction-associated steatohepatitis (MASH)
2. Chart notes demonstrating the patient is engaging in healthy lifestyle changes (e.g., heart-healthy diet and exercise regimen)
3. For continuation of therapy requests: medical records (e.g., chart notes, laboratory tests) demonstrating positive clinical response from baseline

Prescriber Specialties

The requested medication must be prescribed by or in consultation with one of the following:

1. Gastroenterologist
2. Hepatologist
3. Cardiometabolic specialist

Criteria for Initial Approval

Metabolic dysfunction-associated steatohepatitis (MASH) [formerly known as noncirrhotic nonalcoholic steatohepatitis (NASH)]

Authorization of 12 months may be granted for treatment of metabolic dysfunction-associated steatohepatitis (MASH) when ALL the following criteria are met:

1. Member is 18 years of age or older.
2. Member has a diagnosis of metabolic dysfunction-associated steatohepatitis (MASH) with moderate to advanced liver fibrosis (consistent with stages F2 to F3 fibrosis) confirmed by one of the following:
 - A. Liver biopsy
 - B. FAST [(FibroScan-aspartate aminotransferase (AST)]
 - C. MAST [derived from magnetic resonance imaging–proton density fat fraction, magnetic resonance elastography (MRE), and AST]
 - D. MEFIB [MRE combined with fibrosis-4 index (FIB-4)]
3. Member has THREE or more of the following metabolic risk factors that are managed according to standard of care:
 - A. Obesity
 - B. Hypertriglyceridemia
 - C. Reduced high-density lipoprotein (HDL) cholesterol
 - D. Hypertension
 - E. Elevated fasting plasma glucose indicative of pre-diabetes or diabetes
4. Member does not have evidence of the following: Cirrhosis, hepatic decompensation, or hepatocellular carcinoma (HCC)
5. Member has an alcohol consumption of ≤ 20 g/day in females and ≤ 30 g/day in males
6. The requested drug will be used in conjunction with healthy lifestyle modifications (e.g., dietary or caloric restriction, exercise, behavioral support, community-based program).

Continuation of Therapy

Metabolic dysfunction-associated steatohepatitis (MASH) [formerly known as noncirrhotic nonalcoholic steatohepatitis (NASH)]

Authorization of 12 months may be granted for treatment of metabolic dysfunction-associated steatohepatitis (MASH) in members requesting reauthorization when ALL the following criteria are met:

1. Member has achieved or maintained a positive clinical response to the requested drug (e.g., improvement in liver function such as reduction in alanine aminotransferase [ALT], reduction of liver fat content by imaging such as magnetic resonance imaging-protein density fat fraction [MRI-PDFF] or FibroScan controlled attenuation parameter [CAP]).

Other

Rezdiffra (resmetirom) is considered **not medically necessary** for members who do not meet the criteria set forth above.

Dosing and Administration

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

Quantity Limits Apply

Medication	Standard Limit	FDA Recommended Dosing
Rezdifra (resmetirom) 60 mg tablets	30 tablets per 30 days	The recommended dosage of Rezdifra is based on actual body weight. For patients weighing: <ul style="list-style-type: none"><100 kg, the recommended dosage is 80 mg orally once daily.≥100 kg, the recommended dosage is 100 mg orally once daily. If Rezdifra is used concomitantly with a moderate CYP2C8 inhibitor (e.g., clopidogrel) reduce the dosage of Rezdifra. For patients weighing: <ul style="list-style-type: none"><100 kg, reduce the dosage to 60 mg once daily.≥100 kg, reduce the dosage to 80 mg once daily.
Rezdifra (resmetirom) 80 mg tablets		
Rezdifra (resmetirom) 100 mg tablets		

PROCEDURES AND BILLING CODES

To report provider services, use appropriate CPT* codes, Alpha Numeric (HCPCS level 2) codes, Revenue codes, and/or ICD diagnostic codes.

- N/A

REFERENCES

1. Rezdifra [package insert]. West Conshohocken, PA: Madrigal Pharmaceuticals; March 2024.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Waltham, MA: UpToDate, Inc.; 2024. <https://online.lexi.com>. Accessed March 12, 2025.
3. Chen VL, Morgan TR, Rotman Y, et al. Resmetirom therapy for metabolic dysfunction-associated steatotic liver disease: October 2024 updates to AASLD Practice Guidance. *Hepatology*. 2025;81(1):312-320.
4. Rinella ME, Neuschwander-Tetri BA, Siddiqui MS, et al. AASLD Practice Guidance on the Clinical Assessment and Management of Nonalcoholic Fatty Liver Disease. *Hepatology* 2023; 77(5): 1797-1835.

POLICY HISTORY

Policy #: 05.05.40

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