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Section:	Prescription Drugs	Effective Date:	July 1, 2026
Subsection:	Endocrine and Metabolic Agents	Original Policy Date:	August 9, 2024
Subject:	Rezdiffra	Page:	1 of 5

Last Review Date: June 11, 2026

Rezdiffra

Description

Rezdiffra (resmetirom)

Background

Rezdiffra (resmetirom) is a partial agonist of the thyroid hormone receptor-beta (THR- β) which is the major form of THR in the liver. Stimulation of THR- β in the liver reduces intrahepatic triglycerides (1).

Regulatory Status

FDA-approved indication: Rezdiffra is a thyroid hormone receptor-beta (THR- β) agonist 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) (1).

Limitations of Use: Avoid use of Rezdiffra in patients with decompensated cirrhosis (1).

Rezdiffra may cause hepatotoxicity and gallbladder-related adverse reactions. Patients should be monitored for elevations in liver tests and for the development of liver-related adverse reactions. If hepatotoxicity is suspected, Rezdiffra should be discontinued and the patient should be monitored. Gallbladder diagnostic studies and appropriate clinical follow-up is indicated if cholelithiasis is suspected. If an acute gallbladder event is suspected, interrupt Rezdiffra treatment until the event is resolved (1).

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The safety and effectiveness of Rezdiffra in pediatric patients less than 18 years of age have not been established (1).

Related policies

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Rezdiffra may be considered **medically necessary** if the conditions indicated below are met.

Rezdiffra may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 18 years of age or older

Diagnosis

Patient must have the following:

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

AND ALL of the following:

- a. Moderate to advanced liver fibrosis (stages F2 to F3) as confirmed by **ONE** of the following:
 - i. Liver biopsy, performed within the last 6 months
 1. Nonalcoholic Fatty Liver Disease Activity score (NAS) ≥ 4 OR if NAS <4 , hepatocyte ballooning and steatosis are present
 - ii. Elastography (e.g., Fibroscan), computed tomography, or magnetic resonance imaging within the last 3 months
- b. Patient has **THREE** or more of the following conditions that are managed according to standard of care:
 - i. Central obesity
 - ii. Hypertriglyceridemia
 - iii. Reduced high-density lipoprotein cholesterol (HDL)

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- iv. Hypertension
- v. Elevated fasting plasma glucose (i.e., diabetes or pre-diabetes)
- c. Prescribed by, or in consultation with, an endocrinologist, gastroenterologist or hepatologist
- d. Used in conjunction with diet and exercise

AND NONE of the following:

- a. Stage F4 liver fibrosis (cirrhosis)
- b. Significant alcohol consumption (≥ 2 alcoholic drinks per day) for a duration of more than 3 months in the last year
- c. Diagnosis of hepatocellular carcinoma (HCC)
- d. Chronic liver diseases (e.g., primary biliary cholangitis, primary sclerosing cholangitis, Hepatitis B positive, Active Hepatitis C, etc.)

Prior – Approval *Renewal* Requirements

Age 18 years of age or older

Diagnosis

Patient must have the following:

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

AND ALL of the following:

- a. Improvement in fibrosis by at least 1 stage within 1 year of treatment **OR** patient has had no worsening of fibrosis after 2 years or more of therapy
- b. Patient has not progressed to stage F4 (cirrhosis)
- c. Metabolic risks are managed to standard of care
- d. Used in conjunction with diet and exercise

AND NONE of the following:

- a. Significant alcohol consumption (≥ 2 alcoholic drinks per day) for a duration of more than 3 months in the last year
- b. Diagnosis of hepatocellular carcinoma (HCC)
- c. Chronic liver diseases (e.g., primary biliary cholangitis, primary sclerosing cholangitis, Hepatitis B positive, Active Hepatitis C, etc.)

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Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Quantity 100 mg per day

Duration 12 months

Prior – Approval *Renewal* Limits

Same as above

Rationale

Summary

Rezdiffra is a thyroid hormone receptor-beta agonist indicated for the treatment of noncirrhotic nonalcoholic steatohepatitis with moderate to advanced liver fibrosis. Rezdiffra may cause hepatotoxicity and gallbladder-related adverse reactions. The safety and effectiveness of Rezdiffra in pediatric patients less than 18 years of age have not been established (1).

Prior authorization is required to ensure the safe, clinically appropriate, and cost-effective use of Rezdiffra while maintaining optimal therapeutic outcomes.

References

1. Rezdiffra [package insert]. West Conshohocken, PA: Madrigal Pharmaceuticals, Inc.; December 2025.

Policy History

Date	Reason
August 2024	Addition to PA
September 2024	Annual review
June 2025	Annual review
July 2025	Per FEP, changed NAS requirement to only apply in liver biopsy
September 2025	Annual review

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June 2026 Annual review and reference update. Per SME, changed NASH diagnosis to MASH

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on June 11, 2026 and is effective on July 1, 2026.