Rezdiffra™
resmetirom tablets
60 mg · 80 mg · 100 mg

Coverage and Access Support Guide

This guide provides information about the major types of prescription drug coverage, affordability programs, and access support resources for patients who have been prescribed Rezdiffra™

Contact your **Madrigal representative** for local coverage information for Rezdiffra™

Please see INDICATION AND IMPORTANT SAFETY INFORMATION on pages 8-9.

Madrigal is committed to Rezdiffra™ coverage for patients

Timing for coverage decisions varies by plan

Plans may require a prior authorization (PA) or medical exception for coverage. Please check the insurer's website for PA guidance, including forms and contacts. PAs can be submitted through CoverMyMeds or directly to the patient's payer.

Common PA requirements for Rezdiffra™

Age, diagnosis, and dosing	Prescribed by
• Patient's age, NASH diagnosis, Rx details, and NDC	• Or in conjunction with a specialist
Chart notes	**Medical necessity**
• Date of initial diagnosis • Relevant health conditions or symptoms • Date and results of diagnostic test to assess fibrosis: FibroScan-AST, FibroSure, MRE, FIB-4, or liver biopsy • Patient is noncirrhotic • ICD-10-CM code (K75.81, consistent with F2 or F3) • Documentation of conjoint prescription with diet and exercise	• Explanation of medical necessity, including why the patient's diagnosis, severity of condition, and impact of disease warrants treatment with Rezdiffra™
	History prior to your care
	• If applicable
	Rezdiffra™
	• Prescribing information (PI)

AST, aspartate aminotransferase; FIB-4, Fibrosis-4; ICD-10-CM, International Classification of Diseases, Tenth Revision, Clinical Modification; MRE, magnetic resonance elastography; NASH, nonalcoholic steatohepatitis; NDC, National Drug Code; Rx, prescription.

INDICATION AND IMPORTANT SAFETY INFORMATION

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.

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

ADVERSE REACTIONS

The most common adverse reactions with Rezdiffra (reported in ≥ 5% of patients and higher compared to placebo) are: diarrhea, nausea, pruritus, vomiting, constipation, abdominal pain, and dizziness. Diarrhea and nausea were the most common causes of treatment discontinuation.

Please see INDICATION AND IMPORTANT SAFETY INFORMATION on pages 8-9.

Rezdiffra™
resmetirom tablets
60 mg · 80 mg · 100 mg

Understanding Rezdiffra™ coverage for Commercially insured patients

~78% of Commercial lives have coverage for Rezdiffra™[1]

Eligible Commercially insured patients may pay as little as $10 with the Rezdiffra™ Copay Savings Program*

*Must have Commercial insurance and your insurance does not cover the full cost of your prescription. Patients who are enrolled in a state or federally funded prescription insurance program are not eligible for this offer. This includes patients enrolled in Medicare Part D, Medicaid, Medigap, Veterans Affairs (VA), Department of Defense (DOD) programs, or TriCare. Not valid to cash-paying patients. Must reside in the US or a US territory. Must be 18 years of age or older.

Terms and conditions can be found at:
https://portal.trialcard.com/madrigal/rezdiffra/terms-conditions/

Rezdiffra™
resmetirom tablets
60 mg · 80 mg · 100 mg

Please see INDICATION AND IMPORTANT SAFETY INFORMATION on pages 8-9.

Understanding Rezdiffra™ coverage for Medicare patients

The Inflation Reduction Act (IRA) brings significant changes to Medicare Part D benefit design, ushering in new affordability options in 2025[2]

Changes from the IRA may help Part D beneficiaries manage costs

Out-of-pocket (OOP) cost cap[3]

Beneficiaries will have a $2000 OOP cap. The coverage gap has been eliminated in 2025.

New payment option[4]

Beneficiaries can enroll in the Medicare Prescription Payment Plan to spread out OOP costs throughout the calendar year.

Increased income limit for LIS[2]

Income limit for Medicare Part D Low Income Subsidy (LIS, or "Extra Help"), is now 150% of the Federal Poverty Level (FPL).*

Medicare Part D has 3 phases of coverage in 2025[3]

Part D benefit will have an OOP cap of $2000

Annual Deductible	**Patient pays 100% of drug costs**	← Patient deductible is $590
Initial Coverage Phase	**Patient OOP payment is 25% of the drug cost (until they reach $2000)**	← Patient pays up to $1410
Catastrophic Coverage Phase	**Patient pays $0 for the rest of the year**	← Patient reaches OOP max of $2000

*The income eligibility threshold for the LIS Program is $22,590 for individuals and $30,660 for married couples in the lower 48 US states. Patients at or below 150% of the FPL must also meet certain resource limits. For 2024, those resource limits are at or below $17,220 (individuals) or $34,360 (married couples).[5]

Rezdiffra™
resmetirom tablets
60 mg · 80 mg · 100 mg

Please see INDICATION AND IMPORTANT SAFETY INFORMATION on pages 8-9.

The Medicare Prescription Payment Plan is a new payment option for Part D beneficiaries[4]

The Medicare Prescription Payment Plan allows Medicare Part D members to pay for prescription drugs in capped monthly installments instead of up front at the pharmacy, making medications more affordable and predictable for beneficiaries.

How the Medicare Prescription Payment Plan works

Eligibility & Enrollment

Who is eligible
The Medicare Prescription Payment Plan is available to anyone who has Medicare Part D prescription drug insurance, through either a standalone plan or Medicare Advantage.

Insurers will be educating members on the Medicare Prescription Payment Plan.

Enrollment in the Medicare Prescription Payment Plan
Patients may enroll during Open Enrollment in 2024 or at any point during the plan year, in 2025. Patients can enroll through their Part D plan via the toll-free phone number, online, or using a printed form and mailing it.

Using the Medicare Prescription Payment Plan

At the pharmacy
Patients pay $0 when picking up their prescription.

The insurer notifies the pharmacy that the beneficiary is participating in the Medicare Prescription Payment Plan.

Paying the bill
Insurer bills patients for the copayment or coinsurance in even monthly amounts.

Opting out

At any time
Patients may opt out of the Medicare Prescription Payment Plan at any time and can continue to pay their balance monthly or in 1 lump sum.

New prescriptions after stopping
Prescriptions filled after leaving the plan are billed at the regular amount and must be paid at the pharmacy.

IMPORTANT TO KNOW

Patients who have high prescription costs earlier in the year through deductibles or coinsurance are likely to benefit the most. Opting in to the Medicare Prescription Payment Plan during Open Enrollment ensures benefit for the entire plan year.

For more information on the Medicare Prescription Payment Plan:
https://www.medicare.gov/prescription-payment-plan

Please see INDICATION AND IMPORTANT SAFETY INFORMATION on pages 8-9.

The Medicare Part D LIS "Extra Help" Program assists beneficiaries with limited incomes by lowering costs[5]

The LIS Program can help cover monthly premiums, annual deductibles, and prescription copayments.[5]

Changes to the "Extra Help" Program[4-6]

Starting in 2024, the LIS Partial Subsidy was eliminated and eligibility for the Full Subsidy was expanded to include people with incomes up to 150% of the FPL. This comes to **$22,590** for an individual or **$30,660** for a married couple. Patients who qualify for LIS can still enroll in the Medicare Prescription Payment Plan to help spread out their prescription drug costs.

Eligibility for Medicare Part D "Extra Help" Program[7,8]

Automatic Enrollment	• Dual-eligible beneficiaries who qualify for both Medicare and Medicaid • Beneficiaries who receive Supplemental Security Income • Beneficiaries who qualify for a Medicare Savings Program
Proof of Eligibility Through Application	• Beneficiaries who are 65 years of age and older • A beneficiary's income relative to the FPL • Beneficiaries with disabilities who have been receiving Social Security Disability Insurance benefits for >24 months (individuals on disability can be <65 years of age)

To qualify, beneficiaries must:

☑ Be receiving Medicare ☑ Have a prescription drug plan ☑ Have limited income and assets

Out-of-pocket costs with "Extra Help"[8]

Plan premium/plan deductible:	Prescription generic drugs:	Prescription brand-name drugs:
$0	**Up to $4.50**	**Up to $11.20**

For more information on "Extra Help":
https://www.ssa.gov/medicare/part-d-extra-help,
or call 1-800-772-1213

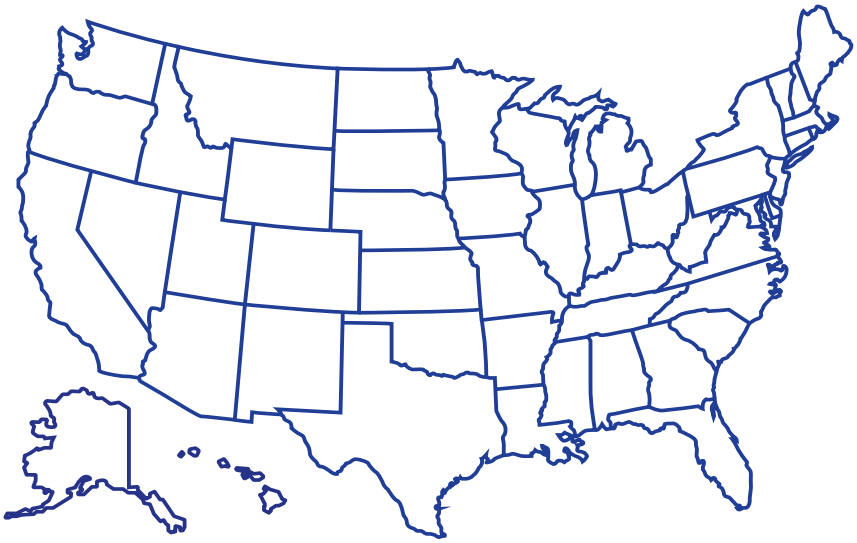
Please see INDICATION AND IMPORTANT SAFETY INFORMATION on pages 8-9.

Rezdiffra™
resmetirom tablets
60 mg · 80 mg · 100 mg

Understanding Rezdiffra™ coverage for Medicaid patients

Rezdiffra™ is covered across all 50 states[9]

Coverage criteria may vary by state[10]



Although prescription drug coverage is an optional benefit under federal Medicaid law, all states currently provide coverage for outpatient prescription drugs to eligible individuals within their state Medicaid programs.[11]

Out-of-pocket costs for Medicaid beneficiaries vary by state and income[10]

The amounts the states can charge are limited and not all beneficiaries may be asked to pay.

Out-of-pocket costs are limited to nominal amounts for people with income ≤150% of the FPL[10,12]

Preferred:	Non-preferred:
$4.00	**$8.00**

For more information about Medicaid: Medicaid.gov/about-us/beneficiary-resources/index.html#statemenu, or call 1-800-MEDICARE (1-800-633-4227)

Please see INDICATION AND IMPORTANT SAFETY INFORMATION on pages 8-9.

Rezdiffra™
resmetirom tablets
60 mg · 80 mg · 100 mg

INDICATION AND IMPORTANT SAFETY INFORMATION

INDICATION

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.

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

WARNINGS AND PRECAUTIONS

Hepatotoxicity

Hepatotoxicity has been observed in one patient. *Please see full Prescribing Information for more details on this specific case of Hepatotoxicity [see Warnings and Precautions (5.1)].*

Monitor patients during treatment for elevations in liver tests and for the development of liver-related adverse reactions. Monitor for symptoms and signs of hepatotoxicity (e.g., fatigue, nausea, vomiting, right upper quadrant pain or tenderness, jaundice, fever, rash, and/or eosinophilia [>5%]). If hepatotoxicity is suspected, discontinue Rezdiffra and continue to monitor the patient. If laboratory values return to baseline, weigh the potential risks against the benefits of restarting Rezdiffra. If laboratory values do not return to baseline, consider DI-ALH or autoimmune liver disease in the evaluation of elevations in liver tests.

Gallbladder-Related Adverse Reactions

In clinical trials, cholelithiasis, acute cholecystitis, and obstructive pancreatitis (gallstone) were observed more often in Rezdiffra-treated patients than in placebo-treated patients. If cholelithiasis is suspected, gallbladder diagnostic studies and appropriate clinical follow-up are indicated. If an acute gallbladder event is suspected, interrupt Rezdiffra treatment until the event is resolved.

Drug Interaction with Certain Statins

Dosage adjustment for certain statins is recommended. Monitor for statin-related adverse reactions including but not limited to elevation of liver tests, myopathy, and rhabdomyolysis. *Please see the upcoming Drug Interaction section of the Important Safety Information for more details.*

ADVERSE REACTIONS

The most common adverse reactions with Rezdiffra (reported in ≥ 5% of patients and higher compared to placebo) are: diarrhea, nausea, pruritus, vomiting, constipation, abdominal pain, and dizziness. Diarrhea and nausea were the most common causes of treatment discontinuation.

Hypersensitivity Reactions

Reactions such as urticaria and rash, which may reflect drug hypersensitivity, were observed in patients receiving Rezdiffra.

Laboratory Abnormalities

Increases in mean ALT and AST levels were observed in the first 4 weeks after initiating treatment with Rezdiffra. The mean elevation in ALT and AST values was less than 1.5 times baseline at 4 weeks after treatment initiation. These values returned to baseline around 8 weeks after initiating treatment.

Please see INDICATION AND IMPORTANT SAFETY INFORMATION on pages 8-9.

Rezdiffra™
resmetirom tablets
60 mg · 80 mg · 100 mg

DRUG INTERACTIONS

Clinically Significant Interactions Affecting Rezdiffra

- **Strong or Moderate CYP2C8 Inhibitors:** Resmetirom is a CYP2C8 substrate. Concomitant use with strong CYP2C8 inhibitors (e.g., gemfibrozil) is not recommended. Reduce dosage if used concomitantly with a moderate CYP2C8 inhibitor (e.g., clopidogrel).
- **Organic Anion-Transporting Polypeptides (OATP) 1B1 and OATP1B3 Inhibitors:** Resmetirom is an OATP1B1 and OATP1B3 substrate. Concomitant use with OATP1B1 or OATP1B3 inhibitors (e.g., cyclosporine) is not recommended.

Clinically Significant Interactions Affecting Other Drugs

- **Statins**
  - Limit daily rosuvastatin and simvastatin dosage to 20 mg
  - Limit daily pravastatin and atorvastatin dosage to 40 mg
- **CYP2C8 Substrates:** Resmetirom is a weak CYP2C8 inhibitor. Monitor patients more frequently for substrate-related adverse reactions if Rezdiffra is co-administered with CYP2C8 substrates where minimal concentration changes may lead to serious adverse reactions.

USE IN SPECIFIC POPULATIONS

Pregnancy

There are no available data on Rezdiffra use in pregnant women to evaluate for a drug-associated risk of major birth defects, miscarriage, or other adverse maternal or fetal outcomes. There are risks to the mother and fetus related to underlying NASH with liver fibrosis, such as increased risks of gestational diabetes, hypertensive complications, preterm birth, and postpartum hemorrhage. Report pregnancies to Madrigal's Adverse Event reporting line at 1-800-905-0324 and https://www.madrigalpharma.com/contact/.

Lactation

There is no information regarding the presence of Rezdiffra in human or animal milk, the effects on the breastfed infant, or the effects on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for Rezdiffra and any potential adverse effects on the breastfed infant from Rezdiffra or from the underlying maternal condition.

Pediatric Use

The safety and effectiveness have not been established in pediatric patients.

Geriatric Use

No overall differences in effectiveness but numerically higher incidence of adverse reactions have been observed in patients ≥65 years of age compared to younger adult patients.

Renal Impairment

The recommended dosage in patients with mild or moderate renal impairment is the same as in patients with normal kidney function. Rezdiffra has not been studied in patients with severe renal impairment.

Hepatic Impairment

Avoid use in patients with decompensated cirrhosis (consistent with moderate to severe hepatic impairment). Moderate or severe hepatic impairment (Child-Pugh Class B or C) increases resmetirom C_{max} and AUC, which may increase the risk of adverse reactions.

No dosage adjustment is recommended for patients with mild hepatic impairment (Child-Pugh Class A).

The safety and effectiveness have not been established in patients with NASH cirrhosis.

Please see the full Prescribing Information for Rezdiffra.

Rezdiffra™
resmetirom tablets
60 mg · 80 mg · 100 mg

Please see INDICATION AND IMPORTANT SAFETY INFORMATION on pages 8-9.

Madrigal Patient Support

Available at every step

Madrigal Patient Support offers dedicated support for your patients. We understand the complexities of insurance and financial assistance. Let **Madrigal Patient Support** help you navigate these challenges and ensure your patients have access to Rezdiffra™.

Call 877-219-7770 Monday through Friday, 8 AM to 8 PM ET
or visit madrigalpatientsupport.com

References: 1. Data on file. REF-00913. Madrigal Pharmaceuticals, West Conshohocken, PA. Managed Markets Insight & Technology, LLC database as of December 2024. **2.** Inflation Reduction Act and Medicare. Centers for Medicare & Medicaid Services. CMS.gov. September 10, 2024. Accessed September 19, 2024. https://www.cms.gov/inflation-reduction-act-and-medicare **3.** Final CY 2025 Part D redesign program instructions fact sheet. Centers for Medicare & Medicaid Services. CMS.gov. April 1, 2024. Accessed September 19, 2024. https://www.cms.gov/newsroom/fact-sheets/final-cy-2025-part-d-redesign-program-instructions-fact-sheet **4.** Fact sheet: Medicare Prescription Payment Plan. Centers for Medicare & Medicaid Services. CMS.gov. August 2023. Accessed September 19, 2024. https://www.cms.gov/files/document/medicare-prescription-payment-plan-factsheet.pdf **5.** Social Security Administration. Understanding the Extra Help with your Medicare Prescription Drug Plan. February 2024. Accessed September 19, 2024. https://www.ssa.gov/pubs/EN-05-10508.pdf **6.** Understanding Medicare's Part D Low Income Subsidy (LIS/Extra Help). National Council on Aging. Published March 22, 2024. Accessed September 19, 2024. https://www.ncoa.org/article/understanding-medicare-part-d-low-income-subsidy-extra-help/ **7.** US Department of Health and Human Services. Medicare & you 2025. Accessed September 19, 2024. https://www.medicare.gov/publications/10050-Medicare-and-You.pdf **8.** Help with drug costs. Centers for Medicare & Medicaid Services. Medicare.gov. Accessed September 19, 2024. https://www.medicare.gov/basics/costs/help/drug-costs **9.** US Department of Health and Human Services. Centers for Medicare & Medicaid Services. DOF. April 11, 2024. **10.** Cost sharing. Centers for Medicare & Medicaid Services. Published July 2, 2024. Accessed September 19, 2024. https://www.medicaid.gov/medicaid/cost-sharing/index.html **11.** Medicaid. Centers for Medicare & Medicaid Services. Medicaid.gov. Accessed September 23, 2024. https://www.medicaid.gov/medicaid/prescription-drugs/index.html **12.** Cost sharing out of pocket costs. Centers for Medicare & Medicaid Services. Accessed September 27, 2024. https://www.medicaid.gov/medicaid/cost-sharing/index.html

Please see INDICATION AND IMPORTANT SAFETY INFORMATION on pages 8-9.

Madrigal Pharmaceuticals

Rezdiffra™
resmetirom tablets
60 mg · 80 mg · 100 mg