Prior Authorization Review Panel

CHC-MCO Policy Submission

A separate copy of this form must accompany each policy submitted for review.
Policies submitted without this form will not be considered for review.

Plan: PA Health & Wellness	**Submission Date: 11/01/2025**
Policy Number: PA.CP.PHAR.647	**Effective Date: 11/2024** **Revision Date: 10/2025**
Policy Name: Resmetirom (Rezdiffra)	

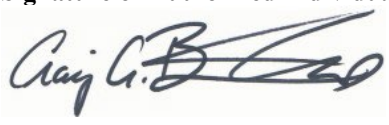
Type of Submission – Check all that apply:

- ☐ **New Policy**
- ✓ **Revised Policy***
- ☐ **Annual Review - No Revisions**
- ☐ **Statewide PDL -** *Select this box when submitting policies for Statewide PDL implementation and when submitting policies for drug classes included on the Statewide PDL.*

***All revisions to the policy must be highlighted using track changes throughout the document.**

Please provide any changes or clarifying information for the policy below:

4Q 2025 annual review: revised biopsy lookback period from 6 months to 3 years per AASLD guidance; for imaging-based biomarker examples, replaced FibroScan with VCTE as FibroScan is an example of VCTE; moved MAST, FAST, and MEFIB examples of non-invasive diagnostic scores to Appendix E; for diet and exercise criterion, removed the BMI $\geq$ 25 kg/m^2, revised "lifestyle modification" to "physician-directed weight loss program that involves a reduced calorie diet, increased physical activity, and behavioral modification," and clarified that member continues these strategies with Rezdiffra use per the PI; revised initial approval duration to 12 months; for continued therapy, added requirements for prescriber attestation of continued standard of care management and documentation of adherence to physician-directed weight loss program; references reviewed and updated. Per SDC: added redirection to Wegovy and exclusion for concurrent Wegovy use.

Name of Authorized Individual (Please type or print): **Craig A. Butler, MD MBA**	**Signature of Authorized Individual:** 

Clinical Policy: Resmetirom (Rezdiffra)

Reference Number: PA.CP.PHAR.647
Effective Date: 11/2024
Last Review Date: 10/2025

Description
Resmetirom (Rezdiffra™) is a thyroid receptor beta agonist.

FDA Approved Indication(s)
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(s) of use: Avoid use in patients with decompensated cirrhosis.

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of PA Health & Wellness® that Rezdiffra is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Metabolic Dysfunction-Associated Steatohepatitis (must meet all)**:**

1. Diagnosis of metabolic dysfunction-associated steatohepatitis (MASH; formerly known as NASH);
2. Prescribed by or in consultation with a hepatologist or gastroenterologist;
3. Age ≥ 18 years;
4. MASH with stage F2 or F3 fibrosis is confirmed by one of the following within the last 6 months (a-e):
   a. Liver biopsy within the last 3 years;
      i. b. Both of the following assessments within the last 6 months (i and ii; see Appendix E for examples)Serum-based assessment (e.g., fibrosis-4 [FIB-4], NAFLD fibrosis score [NFS], enhanced liver fibrosis test [ELF]);
      ii. Imaging-based assessment (e.g., FibroScan, magnetic resonance-based elastography [MRE], magnetic resonance imaging–proton density fat fraction [MRI-PDFF])
5. Documentation supports member's participation in a physician-directed weight loss program that involves a reduced calorie diet, increased physical activity, and behavioral modification that meets both of the following (a and b):
   a. Been actively enrolled in a physician-directed weight loss program for at least the last 6 months;

b. Will continue to be enrolled in a physician-directed diet and exercise program while concomitantly prescribed Rezdiffra;

6. Prescriber attestation that member is currently receiving standard of care management for concomitant related conditions, including type 2 diabetes, dyslipidemia, and hypertension (*see Appendix D*);
7. For member without advanced fibrosis (F3): Failure of a ≥ 6-month trial of Wegovy®, unless contraindicated or clinically significant adverse effects are experienced;*^
   **Prior authorization may be required for Wegovy*
8. Dose does not exceed the appropriate weight-based dose (a or b) and 1 tablet per day:
   a. Actual body weight < 100 kg: 80 mg per day;
   b. Actual body weight ≥ 100 kg: 100 mg per day.

Approval duration: 12 months

B. Other diagnoses/indications

1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

II. Continued Therapy

A. Metabolic Dysfunction-Associated Steatohepatitis (must meet all)**:**

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies;
2. Member is responding positively to therapy as evidenced by, including but not limited to, improvement in any of the following parameters:
   a. Improvement in fibrosis ≥ 1-stage from baseline with no worsening of MASH (i.e., no worsening of hepatocellular ballooning, lobular inflammation, or steatosis);
   b. Resolution of MASH with no worsening of fibrosis;
   c. No increase in fibrosis stage and no worsening of MASH from baseline;
3. Documentation that member is actively enrolled in a physician-directed program that involves a reduced calorie diet, increased physical activity, and behavioral modification adjunct to therapy;
4. Prescriber attestation that member is currently receiving standard of care management for concomitant related condition(s), including T2DM, dyslipidemia, and hypertension;
5. Rezdiffra is not prescribed concurrently with Wegovy;

6. If request is for a dose increase, new dose does not exceed the appropriate weight-based dose (a or b) and 1 tablet per day:
   a. Actual body weight < 100 kg: 80 mg per day;
   b. Actual body weight ≥ 100 kg: 100 mg per day.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies.
   Approval duration: Duration of request or 12 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – PA.CP.PMN.53

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

AASLD: American Association for the Study of Liver Diseases
ACE: angiotensin-converting enzyme
ARB: angiotensin receptor blocker
BMI: body mass index
DPP-4: dipeptidyl peptidase 4
ELF: enhanced liver fibrosis
FDA: Food and Drug Administration
FIB-4: fibrosis-4
GLP-1: glucagon-like peptide 1
MASH: metabolic dysfunction-associated steatohepatitis
MASLD: metabolic dysfunction–associated steatotic liver disease
NAFLD: nonalcoholic fatty liver disease
MRE: magnetic resonance elastography
NASH: non-alcoholic steatohepatitis
NFS: NAFLD fibrosis score
PCSK9: proprotein convertase subtilisin/kexin type 9
SGLT2: sodium-glucose co-transporter 2
T2DM: type 2 diabetes mellitus
VCTE: vibration-controlled transient elastography

Appendix B: Therapeutic Alternatives

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Wegovy® (semaglutide)	Initiate at 0.5 mg SC once weekly and titrate to achieve maintenance dose of 2.4 mg once weekly. If patients do not tolerate the maintenance dosage of 2.4 mg once weekly, the dosage can be decreased to 1.7 mg once weekly.	2.4 mg/week

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

None reported

Appendix D: General Information

- In June 2023, the nomenclature describing NASH and nonalcoholic fatty liver disease (NAFLD) was changed by an international liver disease societies consensus to MASH and metabolic dysfunction-associated steatotic liver disease (MASLD), respectively.

- MASH is defined by the presence of ≥ 5% hepatic steatosis with inflammation and hepatocyte injury (hepatocyte ballooning), with or without evidence of liver fibrosis.
- Standard of care management for concomitant related conditions:
  - Type 2 diabetes management may include metformin, glucagon-like peptide 1 (GLP-1) receptor agonist, sodium-glucose co-transporter 2 (SGLT2) inhibitor, sulfonylurea, dipeptidyl peptidase 4 (DPP-4) inhibitors, pioglitazone, or insulin.
  - Dyslipidemia management may include a statin, ezetimibe, fibrate, omega-3 fatty acids, or proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors.
  - Hypertension management may include an angiotensin-converting enzyme (ACE) inhibitor, angiotensin receptor blocker (ARB), calcium channel blocker, or a thiazide diuretic.

Appendix E: Serum- and Imaging-Based Liver Assessment

- Examples of liver assessment scores combining serum-based and imaging-based tests to help identify MASH:
  - FAST score, as measured by FibroScan and serum aspartate aminotransferase (AST)
  - MAST score, as measured by MRI-PDFF, MRE, and serum AST
  - MEFIB score, as measured by FIB-4 and MRE

Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
MASH	Recommended dose is based on actual body weight: • < 100 kg: 80 mg PO daily • ≥ 100 kg: 100 mg PO daily	See dosing regimen

V. Product Availability

Oral tablets: 60 mg, 80 mg, 100 mg

VI. References

1. Rezdiffra Prescribing Information. West Conshohocken, PA: Madrigal Pharmaceuticals; March 2024. Available at: https://www.madrigalpharma.com/wp-content/uploads/2024/03/Prescribing-Information.pdf. Accessed July 14, 2025.
2. Harrison SA, Bedossa P, Guy CD, et al. A Phase 3, randomized, controlled trial of resmetirom in NASH with liver fibrosis. N Engl J Med. 2024;390(6):497-509.
3. American Diabetes Association Professional Practice Committee. Standards of Care in Diabetes-2025. Diabetes Care. 2025;48(Suppl 1):S1-S352.
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.
5. Cusi K, Isaacs S, Barb D, et al. American Association of Clinical Endocrinology (AACE) clinical practice guideline for the diagnosis and management of nonalcoholic fatty liver disease in primary care and endocrinology clinical settings: co-sponsored by the American Association for the Study of Liver Diseases (AASLD). Endocr Pract. 2022;28(5):528-562.
6. Kanwal F, Shubrook JH, Adams LA, et al. Clinical care pathway for the risk stratification and management of patients with nonalcoholic fatty liver disease. Gastroenterology. 2021;161(5):1657-1669.

7. Rinella ME, Lazarus JV, Ratziu V, et al. A multisociety Delphi consensus statement on new fatty liver disease nomenclature. Ann Hepatol. 2024;29(1):101133.
8. Sterling RK, Duarte-Rojo A, Patel K, et al. AASLD Practice Guideline on imaging-based noninvasive liver disease assessment of hepatic fibrosis and steatosis. Hepatology. Published online March 15, 2024.
9. Noureddin M, Charlton MR, Harrison SA, et al. Expert panel recommendations: practical clinical applications for initiating and monitoring resmetirom in patients with MASH/NASH and moderate to noncirrhotic advanced fibrosis. Clin Gastroenterol Hepatol. 2024;22(12):2367-2377.
10. 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.
11. Younossi ZM, Zelber-Sagi S, Lazarus JV, et al. Global Consensus Recommendations for Metabolic Dysfunction-Associated Steatotic Liver Disease and Steatohepatitis. Gastroenterology. Published online April 11, 2025.
12. Cusi K, Abdelmalek MF, Apovian CM, et al. Metabolic dysfunction-associated steatotic liver disease (MASLD) in people with diabetes: The need for screening and early intervention. A consensus report of the American Diabetes Association. Diabetes Care 2025;48:1057-1082.

Reviews, Revisions, and Approvals	Date
Policy created	10/2024
4Q 2025 annual review: revised biopsy lookback period from 6 months to 3 years per AASLD guidance; for imaging-based biomarker examples, replaced FibroScan with VCTE as FibroScan is an example of VCTE; moved MAST, FAST, and MEFIB examples of non-invasive diagnostic scores to Appendix E; for diet and exercise criterion, removed the BMI ≥ 25 kg/m^2, revised "lifestyle modification" to "physician-directed weight loss program that involves a reduced calorie diet, increased physical activity, and behavioral modification," and clarified that member continues these strategies with Rezdiffra use per the PI; revised initial approval duration to 12 months; for continued therapy, added requirements for prescriber attestation of continued standard of care management and documentation of adherence to physician-directed weight loss program; references reviewed and updated. Per SDC: added redirection to Wegovy and exclusion for concurrent Wegovy use.	10/2025