UnitedHealthcare Pharmacy
Clinical Pharmacy Programs

Program Number	2025 P 2338-4
Program	Prior Authorization/Medical Necessity
Medication	Rezdiffra™ (resmetirom)
P&T Approval Date	4/2024, 1/2025, 11/2025
Effective Date	2/1/2026

1. Background:

Rezdiffra™ (resmetirom) is a thyroid hormone receptor-beta (THR-beta) 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). 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.

2. Coverage Criteria[a]:

A. Initial Authorization

1. **Rezdiffra** will be approved based on **all** of the following criteria:

   a. Diagnosis of metabolic dysfunction-associated steatohepatitis (MASH) [formerly known as nonalcoholic steatohepatitis (NASH)]

   -AND-

   b. Submission of medical records documenting that disease is fibrosis stage F2 or F3 as confirmed by **one** of the following:

      (1) Liver stiffness measurement (LSM) by vibration-controlled transient elastography (VCTE) (e.g., FibroScan)
      (2) LSM by magnetic resonance elastography (MRE)
      (3) Liver biopsy within the past 12 months

   -AND-

   c. Patient has received comprehensive counseling regarding lifestyle modification (e.g., dietary or caloric restriction, exercise, behavioral support, community-based program)

   -AND-

   d. Provider attests that Rezdiffra will not be initiated at the same time as Wegovy (semaglutide) for treatment of the same indication

-AND-

e. Prescribed by or in consultation with **one** of the following:

(1) Gastroenterologist
(2) Hepatologist

Authorization will be issued for 12 months

B. Reauthorization

1. **Rezdiffra** will be approved based on **all** of the following criteria:

a. Documentation of positive clinical response to **Rezdiffra** therapy (e.g., improvement in or stabilization of fibrosis)

-AND-

b. Patient has not progressed to cirrhosis

-AND-

c. Prescribed by or in consultation with **one** of the following:

(1) Gastroenterologist
(2) Hepatologist

Authorization will be issued for 12 months

[a] State mandates may apply. Any federal regulatory requirements and the member specific benefit plan coverage may also impact coverage criteria. Other policies and utilization management programs may apply.

3. Additional Clinical Rules:

- Notwithstanding Coverage Criteria, UnitedHealthcare may approve initial and re-authorization based solely on previous claim/medication history, diagnosis codes (ICD-10) and/or claim logic. Use of automated approval and re-approval processes varies by program and/or therapeutic class.

4. References:

1. Rezdiffra [package insert]. West Conshohocken, PA: Madrigal Pharmaceuticals, Inc.; March 2024.
2. Harrison SA, Bedossa P, Guy CD, Schattenberg JM, Loomba R, Taub R, Labriola D, Moussa SE, Neff GW, Rinella ME, Anstee QM, Abdelmalek MF, Younossi Z, Baum SJ, Francque S, Charlton MR, Newsome PN, Lanthier N, Schiefke I, Mangia A, Pericàs JM, Patil R, Sanyal AJ, Noureddin M, Bansal MB, Alkhouri N, Castera L, Rudraraju M, Ratziu V; MAESTRO-NASH Investigators. A Phase 3, Randomized, Controlled Trial of

Resmetirom in NASH with Liver Fibrosis. N Engl J Med. 2024 Feb 8;390(6):497-509. doi: 10.1056/NEJMoa2309000. PMID: 38324483.
3. Rinella ME, Lazarus JV, Ratziu V, et al. A multisociety Delphi consensus statement on new fatty liver disease nomenclature. *Hepatology*. 2023;78(6):1966-1986. doi:10.1097/HEP.0000000000000520
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. doi:10.1097/HEP.0000000000000323
5. Wattacheril JJ, Abdelmalek MF, Lim JK, Sanyal AJ. AGA Clinical Practice Update on the Role of Noninvasive Biomarkers in the Evaluation and Management of Nonalcoholic Fatty Liver Disease: Expert Review. Gastroenterology. 2023;165(4):1080-1088. doi:10.1053/j.gastro.2023.06.013
6. European Association for the Study of the Liver (EASL). Electronic address: easloffice@easloffice.eu; European Association for the Study of Diabetes (EASD); European Association for the Study of Obesity (EASO); European Association for the Study of the Liver (EASL). EASL-EASD-EASO Clinical Practice Guidelines on the management of metabolic dysfunction-associated steatotic liver disease (MASLD). J Hepatol. 2024;81(3):492-542. doi:10.1016/j.jhep.2024.04.031
7. 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*. Published online October 18, 2024. doi:10.1097/HEP.0000000000001112
8. 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. doi:10.1016/j.cgh.2024.07.003

Program	Prior Authorization/Medical Necessity - Rezdiffra (resmetirom)
Change Control	
4/2024	New program
1/2025	Revised initial authorization criteria for confirming fibrosis stage F2 or F3. Added criterion to reauthorization criteria that patient has not progressed to cirrhosis. Updated references.
11/2025	Added combination use language. Added medical record submission requirement to initial authorization criteria for confirming fibrosis stage F2 or F3. Updated references.
2/2026	Administrative change to correct change control language, no change to coverage criteria.