

# Resmetirom (REZDIFFRA) in Metabolic Dysfunction-associated Steatohepatitis (MASH) Criteria for Use January 2026

VA Pharmacy Benefits Management Services and National Formulary Committee

*The following recommendations are based on medical evidence, clinician input, and expert opinion. The content of the document is dynamic and will be revised as new information becomes available. The purpose of this document is to assist practitioners in clinical decision-making, to standardize and improve the quality of patient care, and to promote cost-effective drug prescribing. THE CLINICIAN SHOULD USE THIS GUIDANCE AND INTERPRET IT IN THE CLINICAL CONTEXT OF THE INDIVIDUAL PATIENT. INDIVIDUAL CASES THAT ARE EXCEPTIONS TO THE EXCLUSION AND INCLUSION CRITERIA SHOULD BE ADJUDICATED AT THE LOCAL FACILITY ACCORDING TO THE POLICY AND PROCEDURES OF ITS P&T COMMITTEE AND PHARMACY SERVICES.*

The Product Information should be consulted for detailed prescribing information.

## Exclusion Criteria

If ANY of the following are selected, the patient will NOT meet criteria for resmetirom for MASH.

- Child-Pugh score  $\geq 7$  (Note: Bilirubin can be adjusted for patients with Gilbert syndrome, and score adjusted for patients taking anticoagulants.)
- Decompensated liver cirrhosis as manifested by complications of cirrhosis (e.g., noncardiac ascites, variceal hemorrhage, hepatic encephalopathy, spontaneous bacterial peritonitis, etc.)
- In most recent assessment, FibroScan greater than 18 kPa / vibration-controlled transient elastography (VCTE) consistent with cirrhosis, MRE  $> 5.0$  kPa, FIB-4  $> 2.67$  (unless LSM  $< 18$  kPa),<sup>^1</sup> or liver biopsy indicating cirrhosis (METAVIR stage F4)
- Hepatocellular carcinoma currently not actively managed by hepatology (or multidisciplinary team)
- Uncontrolled liver disease associated with condition other than metabolic dysfunction<sup>^2</sup>
- Heavy ingestion of alcohol for greater than 3 consecutive months within the previous 1 year with heavy alcohol ingestion defined as  $\geq 4$  alcoholic drinks per day for men and  $\geq 3$  alcoholic drinks per day for women<sup>^3</sup>
- Untreated hyperthyroidism or hypothyroidism
- Concomitant use of strong CYP2C8 inhibitors (e.g., gemfibrozil, etc.)
- Concomitant use of systemic organic anion transporter polypeptide (OATP) inhibitors (e.g., cyclosporine, etc.)

Warnings:

- Gallbladder-related adverse reactions such as cholelithiasis and cholecystitis have occurred during resmetirom therapy. Resmetirom should be withheld in acute gallbladder events/acute cholecystitis until the event is resolved.
- Resmetirom may increase the plasma concentration of certain statins. Limit rosuvastatin and simvastatin daily dosages to 20 mg and pravastatin and atorvastatin daily dosages to 40 mg.

## Inclusion Criteria

ALL the following criteria must be selected to meet criteria.

- Documented noncirrhotic metabolic dysfunction-associated steatohepatitis (MASH) with METAVIR F2–F3 fibrosis and nonalcoholic fatty liver disease (NAFLD) activity score (NAS) greater than or equal to 4 on liver biopsy in the past 36 months
- Prescribed by a VA/VA Community Care gastroenterologist/hepatologist or locally designated expert in the management of MASH.
- Documented plan on addressing and monitoring appropriate lifestyle interventions.^4^5
- Documented plan to change medications that can cause or exacerbate steatohepatitis to alternative agents as applicable and clinically appropriate.^6

## Additional Inclusion Criteria

If applicable, the following must be selected to meet criteria.

- For patients who are overweight/obese^7: Medical inadvisability, intolerance, or inadequate response^8 to a drug with GLP-1RA activity that has evidence confirming effectiveness for noncirrhotic MASH with moderate to advanced liver fibrosis.^9

Abbreviations: GLP-1RA, glucagon-like peptide 1 receptor agonist

## Additional Inclusion Criteria

If applicable, the following must be selected to meet criteria.

- For patients who can become pregnant: Counseling provided on potential risks vs benefits of treatment.
- For females who are breastfeeding/providing breastmilk to an infant: Counseling provided on potential risks vs benefits of treatment.

## Other Justification

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## Footnotes

- 1 Use FIB-4 with caution in patients aged > 65 years because of lower reliability.
- 2 E.g., biliary obstruction, viral hepatitis, autoimmune hepatitis, hereditary liver disease, drug-induced liver disease, etc.
- 3 One alcoholic drink = 355 mL (12 fl oz) of 5% alcohol by volume [ABV] beer; 148 mL (5 fl oz) of 12% ABV wine; 44 mL (1.5 fl oz) of 40% ABV distilled spirits.
- 4 Lifestyle counseling is an essential component of overall MASH management and includes recommendations on nutrition, exercise, and weight loss. Lifestyle counseling can be done, if feasible, by providers or as part of a comprehensive lifestyle intervention (CLI). <https://dvagov.sharepoint.com/sites/vhamove/Shared%20Documents/NCP-MOVE-CLI-Definition.pdf>.
- 5 Adjunctive glucagon-like peptide-1 receptor agonists (GLP-1RAs) should be added pursuant to GLP-1RA in weight management criteria for use.
- 6 Examples of drugs associated with development or exacerbation of steatohepatitis, MASLD, or MASH: amiodarone, androgenic steroids, atypical antipsychotics (e.g., clozapine, olanzapine), estrogens, glucocorticoids, irinotecan, methotrexate, nucleoside reverse transcriptase inhibitors, selective serotonin receptor inhibitor antidepressants, tamoxifen, valproic acid, etc.
- 7 Overweight is defined as body mass index (BMI) of 25–29.9 kg/m<sup>2</sup> (23–24.9 kg/m<sup>2</sup> in Asians) and obesity is defined as BMI ≥30 kg/m<sup>2</sup> (≥25 kg/m<sup>2</sup> in Asians).
- 8 Inadequate response refers to progression of liver fibrosis stage on imaging-based non-invasive tests (NIT) or on liver biopsy. Imaging-based NITs include VCTE (e.g., FibroScan) demonstrating > 20% worsening in liver stiffness (kPa). Worsening on liver biopsy would require demonstrating 1-stage worsening in METAVIR liver fibrosis stage (e.g., F2 to F3).
- 9 Consistent with fibrosis stages F2–F3. Example of GLP-1 receptor agonist for MASH: semaglutide.

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