Resmetirom (REZDIFFRA)
in Metabolic Dysfunction-associated Steatohepatitis (MASH)
Criteria for Use
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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 ≥ 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 15 kPa / vibration-controlled transient elastography (VCTE) consistent with cirrhosis, or liver biopsy indicating cirrhosis (METAVIR stage F4)
- ☐ Uncontrolled liver disease associated with conditions other than metabolic dysfunction[1] or untreated hepatocellular carcinoma
- ☐ Significant ingestion of alcohol for greater than 3 consecutive months within the previous 1 year with significant alcohol ingestion defined as greater than or equal to 2 alcoholic drinks per day for men and ≥ 1.5 alcoholic drinks per day for women[2]
- ☐ 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.)
- ☐ Rosuvastatin and simvastatin daily dosages greater than 20 mg or pravastatin and atorvastatin daily dosages greater than 40 mg

Inclusion Criteria

ALL the following criteria must be selected to meet criteria.

- ☐ Prescribed by a VA / VA Community Care gastroenterologist / hepatologist or locally designated expert
- ☐ Active participation for ≥ 6 months in a comprehensive lifestyle intervention (CLI) before initiation of resmetirom therapy and documented discussion about continuing participation in CLI during resmetirom therapy[3,4]
- ☐ 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
- ☐ Medications that can cause or exacerbate steatohepatitis have been changed to alternative agents as applicable and clinically appropriate[5]

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

Other Justification

- ☐ _____

Footnotes

1 E.g., biliary obstruction, viral hepatitis, autoimmune hepatitis, hereditary liver disease, drug-induced liver disease, etc.

2 One alcoholic drink = 355 mL of 5% alcohol by volume [ABV] beer; 148 mL of 12% ABV wine; 44 mL of 40% ABV distilled spirits.

3 For description of CLI, see https://dvagov.sharepoint.com/sites/vhancp/move/SitePages/Comprehensive-Lifestyle-Intervention-Materials.aspx

4 If BMI is ≥ 27 kg/m^2, adjunctive GLP-1RAs should be added after a trial of ≥1 other weight management medication if weight loss is less than 7% to 10% with CLI alone pursuant to GLP-1RA in weight management CFU.

5 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.

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