

Resmetirom (REZDIFFRA)

Goal(s):

- To ensure appropriate use of resmetirom in patients with nonalcoholic steatohepatitis (NASH)/metabolic dysfunction-associated steatohepatitis (MASH).

Length of Authorization:

- Up to 12 months

Requires PA:

- All pharmacy point-of-sale claims

Covered Alternatives:

- Current PMPDP preferred drug list per OAR 410-121-0030 at www.orpdl.org
- Searchable site for Oregon FFS Drug Class listed at www.orpdl.org/drugs/

Approval Criteria		
1. What diagnosis is being treated?	Record ICD10 code.	
2. Is this an FDA approved indication and age? Note: resmetirom is currently approved for people 18 years and older	Yes: Go to #3	No: Pass to RPh. Deny; medical appropriateness
3. Is the request for continuation of therapy previously approved by the fee-for-service program?	Yes: Go to Renewal Criteria	No: Go to #4
4. Does the patient have a diagnosis of NASH (or MASH) as confirmed by liver biopsy (lifetime)?	Yes: Go to #8	No: Go to #5
5. Is there documentation that the patient does NOT have: <ul style="list-style-type: none"> Ongoing or recent (within 2 years) significant alcohol use Chronic or active viral hepatitis Note: significant alcohol use can be patient-specific but is typically defined as greater than 21 drinks/week (or >30 g/day) in men and greater than 14 drinks/week (or >20 g/day) in women.	Yes: Go to #6	No: Pass to RPh. Deny; medical appropriateness

Approval Criteria

<p>6. Is there provider attestation or documentation that other causes of hepatic steatosis are not suspected based on patient history/presentation or have been ruled out?</p> <p>Examples of other secondary causes of hepatic steatosis: Wilson's disease, lipodystrophy, abetalipoproteinemia, medications (e.g., amiodarone, methotrexate, tamoxifen, corticosteroids).</p>	<p>Yes: Go to #7</p>	<p>No: Pass to RPh. Deny; medical appropriateness</p>
<p>7. Is there documentation that the patient has, or is receiving drug treatment for, at least 3 of the 5 metabolic risk factors associated with MASH?</p> <p>Risk Factors:</p> <ul style="list-style-type: none"> • Overweight or obesity or increased waist circumference (BMI \geq 25 kg/m² or ethnicity adjusted equivalent) • Hypertension • Type 2 diabetes mellitus • Hypertriglyceridemia • Decreased level of high density lipoprotein (HDL) 	<p>Yes: Go to #8</p>	<p>No: Pass to RPh. Deny; medical appropriateness</p>
<p>8. Does the patient have fibrosis stage 2 or 3 as shown by appropriate diagnostic test within past 24 months?</p> <p>Note: appropriate tests may include biopsy, vibration controlled transient elastography (VCTE), magnetic resonance elastography (MRE), enhanced liver fibrosis test (ELF).</p>	<p>Yes: Go to #9</p>	<p>No: Pass to RPh. Deny; medical appropriateness</p>
<p>9. Is the medication being ordered by, or in consultation with, a hepatologist or gastroenterologist?</p>	<p>Yes: Go to #10</p>	<p>No: Pass to RPh. Deny; medical appropriateness</p>
<p>10. Will the patient be engaged in a weight management lifestyle modification program in addition to pharmacotherapy?</p> <p>Note: Resmetirom is currently approved in conjunction with diet and exercise</p>	<p>Yes: Go to #11</p>	<p>No: Pass to RPh. Deny; medical appropriateness</p>

Approval Criteria

<p>11. Does the patient have comorbidities of:</p> <ul style="list-style-type: none"> • Hypertension OR • Dyslipidemia OR • Overweight with body mass index (BMI) $\geq 25 \text{ kg/m}^2$ or Obesity BMI $\geq 30 \text{ kg/m}^2$ 	<p>Yes: Go to #12</p>	<p>No: Go to #13</p>
<p>12. Is there documentation that the patient is prescribed or has a contraindication to guideline directed medication or lifestyle therapy for <u>each</u> diagnosed comorbidity?</p> <p>Example:</p> <ul style="list-style-type: none"> • Hypertension-blood pressure at goal range or receiving treatment with antihypertensives • Dyslipidemia-lipid panel at goal or receiving statin therapy • Overweight or obesity-lifestyle management and treatment with glucagon-like peptide-1 receptor agonists (GLP-1 RA) 	<p>Yes: Go to #13</p>	<p>No: Pass to RPh. Deny; medical appropriateness.</p> <p>Recommend optimize risk factor treatment. Avoid <i>simultaneous</i> initiation of treatments with overlapping side effect profile (diarrhea, nausea) as resmetirom (e.g., GLP-1 RA)</p>
<p>13. Does the patient have comorbid type 2 diabetes mellitus?</p>	<p>Yes: Go to #16</p>	<p>No: Go to #14</p>
<p>14. Is there documentation that the patient has been screened for type 2 diabetes mellitus within past 12 months?</p>	<p>Yes: Go to #15</p>	<p>No: Pass to RPh. Deny; medical appropriateness.</p>
<p>15. Was the screening for type 2 diabetes mellitus negative?</p> <p>Note: screening options include hemoglobin A1c (HbA1c, goal $<6.5\%$), fasting blood glucose (goal $<126 \text{ mg/dL}$), or oral glucose tolerance test (goal $<200 \text{ mg/dL}$)</p>	<p>Yes: Approve for 12 months</p>	<p>No: Go to #16</p>

Approval Criteria

16. Is there documentation that the patient:
- Has a HbA1C <7% within past 6 months OR
 - Is prescribed or has a contraindication to metformin and a glucagon-like peptide 1 (GLP-1) receptor agonist, and a sodium-glucose cotransporter-2 (SGLT2) inhibitor.

Yes: Approve for 12 months

No: Pass to RPh. Deny; medical appropriateness.

Recommend optimize risk factor treatment. Avoid *simultaneous* initiation of treatments with overlapping side effect profile (diarrhea, nausea) as resmetirom (e.g., metformin or GLP-1 RA)

Renewal Criteria

1. Does the provider attest that the patient remains on, and is adherent to, pharmacotherapeutic or lifestyle therapy for any current metabolic comorbidities?

Yes: Go to #2

No: Pass to RPh. Deny; medical appropriateness

2. Does the provider attest that the patient has been adherent to therapy with resmetirom OR is adherence apparent from medication claims history?

Yes: Go to #3

No: Pass to RPh. Approve once, for 3 months.

Request documentation of adherence.

3. Has the patient had a complete metabolic panel, liver enzymes, or other appropriate biochemical or noninvasive imaging test within the past 12 months to assess for potential disease progression?

Yes: Go to #4

No: Pass to RPh. Approve once, for 3 months.

Recommend biochemical monitoring.

Additional example tests: fibrosis-4 index (FIB-4), enhanced liver fibrosis test (ELF), vibration controlled transient elastography (VCTE), magnetic resonance elastography (MRE)

Renewal Criteria

<p>4. If resmetirom initiation was more than 3 years ago, has the patient had noninvasive imaging (e.g., VCTE or MRE) or repeat liver biopsy to assess for progression of fibrosis in the past 3 years?</p> <p>If not applicable because resmetirom started less than 3 years ago skip to question #6</p>	<p>Yes: Go to #5</p>	<p>No: Pass to RPh. Approve once, for 3 months.</p> <p>Recommend noninvasive imaging or repeat biopsy.</p>
<p>5. Does the patient have evidence of stage F4 fibrosis (cirrhosis) OR has fibrosis stage worsened (e.g., stage F2 to F3) since starting resmetirom.</p>	<p>Yes: Pass to RPh. Deny; medical appropriateness</p>	<p>No: Go to #6</p>
<p>6. Is there documentation of a risk/benefit assessment for ongoing treatment with resmetirom with possible resolution of metabolic comorbidities?</p>	<p>Yes: Approve for 12 months</p>	<p>No: Pass to RPh. Approve once, for 3 months.</p> <p>Recommend provide additional documentation.</p>

P&T/DUR Review: 8/24 (SF)
Implementation: 9/1/24