# Wyoming Drug Utilization Review

## Metabolic dysfunction-associated steatohepatitis (MASH)

**Written by Christa Vanlandingham, PharmD 2026**

Metabolic dysfunction-associated steatohepatitis (MASH), formerly known as nonalcoholic steatohepatitis (NASH), is a progressive form of metabolic dysfunction-associated steatotic liver disease (MASLD) characterized by hepatic inflammation and injury that can progress to fibrosis, cirrhosis, liver failure, or hepatocellular carcinoma (1,2). MASH has become a leading cause of chronic liver disease and liver transplantation in the United States (1,2). As of 2020, MASLD affected an estimated 33.7% of U.S. adults, with 5.8% progressing to MASH, a rate projected to rise to 6.7% by 2030 (2). Many patients remain asymptomatic or experience nonspecific symptoms such as fatigue, upper abdominal pain, bloating, thirst, or sleep disturbances (3). Major risk factors include type 2 diabetes, insulin resistance, obesity, dyslipidemia, and other metabolic disorders. Fibrosis and cirrhosis represent progressive stages of liver injury, with fibrosis marked by reversible scarring from chronic inflammation while cirrhosis is the irreversible end stage characterized by widespread scarring, nodular formation, and structural distortion of the liver (3).

Lifestyle modifications are the cornerstone management for patients with MASH. In individuals who are overweight, sustained weight loss of ≥ 5% is recommended to reduce hepatic steatosis, 7-10% to decrease hepatic inflammation, and ≥10% is recommended to improve MASH related fibrosis (4). Weight loss should be achieved with a combination of dietary changes and regular physical activity. Following a balanced, Mediterranean-style diet that includes whole grains, fruits, vegetables, and healthy fats has shown to be beneficial. Exercise recommendations include at least 150 minutes of moderate intensity or 75 minutes of vigorous exercise per week. However, maintaining lifestyle changes long term can be challenging and many patients may require pharmacological interventions as well to achieve and sustain treatment goals (4).

Pharmacologic therapy for MASH is broadly categorized into non-glucose lowering medications and glucose lowering medications. One of the main non-glucose lowering agents is resmetirom (Rezdiffra), which is currently recommended for non-cirrhotic MASH with significant fibrosis in stage F2 or F3 (4). Resmetirom, an oral, liver selective thyroid receptor β1 agonist reduces intrahepatic triglycerides by enhancing hepatic lipophagy, promoting mitochondrial biogenesis, and inhibiting hepatic lipogenesis (4,5). Collectively, the mechanism of resmetirom is only FDA approved for non-cirrhotic MASH and is offering advancements in treating this disease state. This recommendation is based on results from the MAESTRO-NASH trial conducted in 2019 that demonstrated improvement in liver histology, resolution of steatohepatitis, and decreased fibrosis when compared to the placebo (4). This agent is to be utilized in adjunct with lifestyle modification and other agents. However, there is limited research and literature discussing the long-term safety and efficacy profile of resmetirom, and its high cost may limit accessibility and widespread use (4).



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Glucose lowering agents are commonly used in addition to lifestyle modifications for patients with MASH, particularly when other comorbidities such as type two diabetes and obesity (4). Current MASLD clinical practice guidelines recommend the use of these agents primarily to treat comorbidities but not as MASH-targeted therapy. Among glucose lowering agents, glucagon-like peptide 1 receptor agonists (GLP-1 RA) such as semaglutide and liraglutide demonstrate significant weight loss, increased insulin sensitivity, and cardiovascular benefits. These agents also have peripheral effects including increased lipolysis, lipid oxidation, and energy expenditure which help to reduce hepatic fat. More recently semaglutide (Wegovy) received FDA approval for the treatment of MASH following the ESSENCE trial which demonstrated steatohepatitis resolution without worsening fibrosis when compared to placebo (6). Ongoing research continues to explore potential benefits of other GLP-1 RA, including liraglutide, tirzepatide, as well as triple incretin agent retatrutide (4).

Pioglitazone has also been shown to improve steatosis, inflammation, and hepatocellular ballooning in patients with MASH, particularly patients with type 2 diabetes. However, its side effect profile such as weight gain, fluid retention, increased risk of bone fractures, and a possible association with bladder cancer has limited its use and continued research for use in MASH. Current guidelines suggest that pioglitazone may be considered in select patients with non-cirrhotic MASH after discussing the risks and benefits. However, it is not strongly recommended due to lack of robust evidence in randomized controlled phase three trials. While other glucose lowering agents such as SGLT-2 inhibitors and metformin support weight loss and improve insulin sensitivity, evidence is limited and does not show consistent improvement of fibrosis and histological endpoints of MASH. Currently, these agents are only used as adjunctive therapy rather than MASH-targeted.

There are several other agents that have been investigated for the treatment of MASH, including vitamin E, ursodeoxycholic acid, obeticholic acid, and omega-3 polyunsaturated fatty acids (4). However, current evidence regarding their use remains inconclusive, and clinicians should carefully consider potential benefits against risk. Vitamin E has shown some improvement in steatohepatitis among non-diabetic patients but carries concerns related to long-term safety, such as cardiovascular mortality and prostate cancer risk that are still unclear. Ursodeoxycholic acid and omega-3 fatty acids may improve biochemical markers of liver injury or lipid parameters, but they have not demonstrated consistent histologic improvement in fibrosis or steatosis. Obeticholic acid showed improved hepatocellular ballooning and lobular inflammation but is limited by adverse effects such as pruritus and elevated LDL cholesterol. Additionally, it showed no improvement or resolution of steatohepatitis. Overall, while these agents have been explored, their limited efficacy and safety considerations restrict their routine use in MASH management, and more randomized controlled trials need to be conducted to support the use of these agents (4).

Metabolic dysfunction-associated steatohepatitis (MASH) is a growing disease state within the United States, driven by increasing rates of type two diabetes and obesity. While lifestyle modification through sustained weight loss remains the cornerstone of therapy, pharmacologic treatment options continue to be developed and researched. Resmetirom and semaglutide are currently the only agents FDA approved, marking important improvements in targeted therapy for non-cirrhotic MASH with significant fibrosis. However, many other agents including vitamin E, pioglitazone, and other glucose-lowering therapies demonstrate variable efficacy, they are limited by safety concerns or insufficient evidence. Continued research, including large-scale randomized controlled trials, is needed to better define long-term outcomes, safety, and cost-effectiveness of emerging therapies for the treatment of MASH.

**References**


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**The P&T Committee met for its quarterly business meeting on February 12, 2026.**

Highlights of this meeting include:

Go-live for the new PBA system is currently scheduled for April 15, 2026.

The Department of Health has been actively working on the Rural Health Transformation program. Additional information can be found at https://health.wyo.gov/admin/rural-health-transformation-program/.

The once per lifetime limit on Hepatitis C treatment will be removed going forward.

Lynkuet, Redemplo, Voyxact, Omlonti, Pivya, Myqorzo, Exdensur, Yartemlea and Yeztugo were limited to indication and referred to the Department of Health for cost analysis and PDL placement.

Cardamyst and Itvisma were limited to indication.

All prior authorization criteria are open for public comment. Comments should be sent by email to alewis13@uwyo.eduby April 15, 2026.

The next P&T Committee meeting will be held May 14, 2026 in Cheyenne. An agenda will be posted approximately two weeks prior to the meeting.

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March 2026

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