From NASH to MASH: *How the Renamed Fatty Liver Disease Will Make a Splash on Employer Trends*

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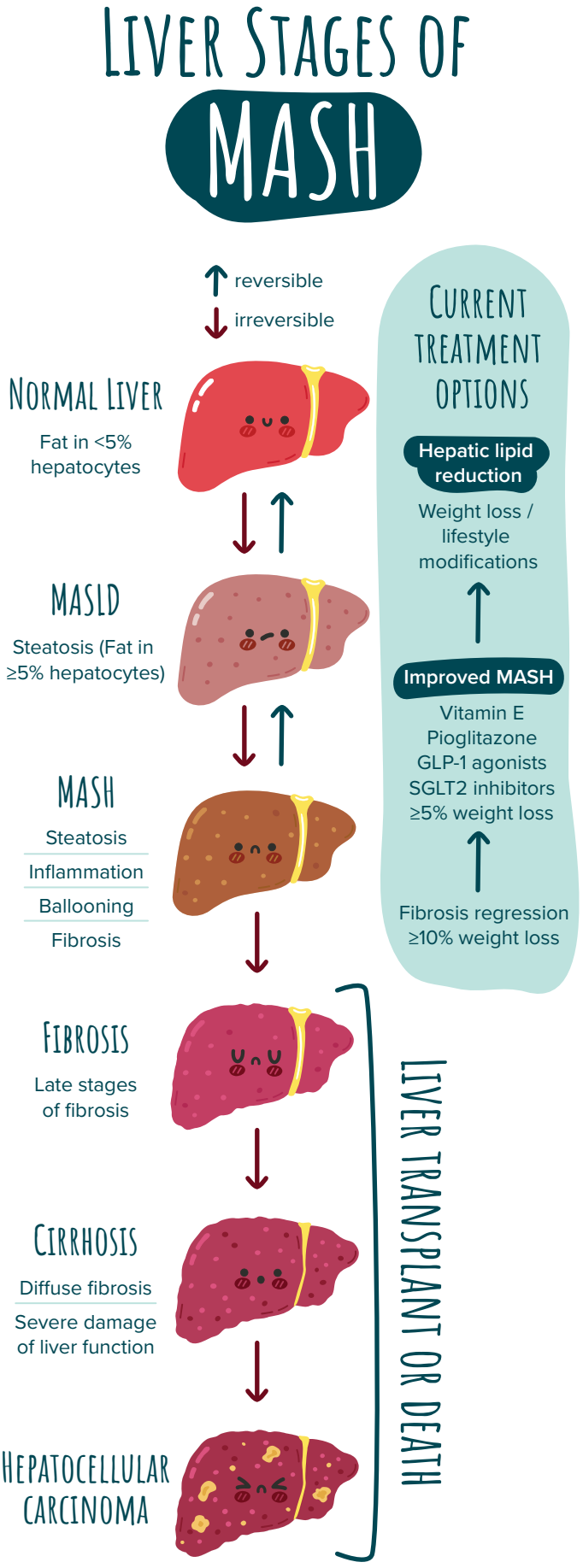
Please note: *Non-alcoholic steatohepatitis (NASH) has recently been renamed to metabolic dysfunction-associated steatohepatitis (MASH). Liver society experts, such as the American Association for the Study of Liver Diseases (AASLD), believe this new name better encompasses the condition and its causes.*

In 2018, the Employers Health clinical team published an article titled *"The Countdown to NASH: Employers Brace for the New Non-Specialty Condition,"* discussing how medications in the pipeline for the treatment of NASH, now known as MASH, were anticipated to be approved within the next few years. While not apparent at the time, it took an additional six years for the Food and Drug Administration (FDA) to approve a drug for its treatment. This article covers this condition, available treatments and the potential for management.

What is MASH?

MASH is characterized by inflammation, fat buildup and in advanced cases, fibrosis or scarring of the liver. MASH is estimated to affect between 1.5 to 6.5% of U.S. adults.

Nicknamed "the silent disease," patients typically present asymptomatic or with generalized symptoms. With a lack of symptoms, screening and diagnosis are difficult, leading experts to believe its prevalence may be larger than estimated. MASH is also linked to obesity, Type 2 diabetes and high cholesterol. Left untreated, MASH can progress into irreversible liver damage, known as cirrhosis, which can further progress into liver failure or cancer.



Over the years, the progression of this condition has become the biggest contributor to the rise in liver cancer and has replaced hepatitis C as the leading cause of liver transplantation. While certainly detrimental to patients, this disease is not without cost. Once this disease progresses into cirrhosis or liver cancer, annual costs to employer groups are estimated to be between $85,000 and $115,000. If a patient qualifies for a transplant costs increase further to an estimated $233,000 annually.
As MASH becomes more prevalent and researchers frantically search for a solution, multiple drugs are currently in the pipeline today.

How is MASH treated?

While AASLD guidelines recommend weight loss as the first strategy to reduce liver inflammation and fibrosis, there have been few options to treat MASH with medication. The quest has been on for decades to find a drug that not only resolves MASH but also helps to reduce fibrosis. Historically, vitamin E and pioglitazone have had some success in MASH resolution, but neither medication has strong evidence for reducing fibrosis.

In March 2024, the FDA approved Rezdiffra (resmetirom) as the first drug indicated for treating MASH. In clinical trials, depending on the dose, Rezdiffra was shown to improve fibrosis in 24.2 to 25.9% of participants compared to 14.2% of participants on a placebo.

Rezdiffra treatment resulted in MASH resolution in 25.9 to 29.9% of participants (depending on dose) compared to 9% of participants on a placebo. While Rezdiffra may have modest clinical effects, it is the first and only medication to succeed in reducing MASH activity and improving fibrosis.

Looking at the MASH pipeline, it may come as no surprise that GLP-1 medications could play a role in treatment, considering the relation of obesity and diabetes to MASH. Ongoing studies with semaglutide and tirzepatide are being conducted for the treatment of MASH as both combination therapy and monotherapy. Currently, the data are showing promising results in helping to reduce liver inflammation; however, like most medications used for MASH, there is little evidence to show a reduction in fibrosis.

MASH Pipeline

Product Name	Route	Drug Class	Manufacturer	Status	Estimated Approval
Wegovy (semaglutide)		GLP-1	Novo Nordisk	Phase III	2025
Lanifibranor		PPAR agonist	Inventiva	Phase III	2026
Aramchol		SCD1 inhibitor	Galmed Pharmaceuticals	Phase III	2027
Belapectin	IV	Galectin inhibitor	Galectin Therapeutics	Phase III	2025
Azemiglitazone		Thiazolidinedione	Cirius Therapeutics	Phase III	2025
Efruxifermin		Fibroblast growth factor mimetic	Akero Therapeutics	Phase III	2027

GLP-1: glucagon-like peptide 1; IV: intravenous; PPAR: peroxisome proliferator-activated receptor; SCD1: stearoyl-CoA desaturase 1

27 agents in Phase II

How might MASH be managed?

With Rezdiffra pricing at $47,400 per year combined with a robust MASH pipeline, it is imperative to begin considering how it will be managed going forward. As of April 2024, Rezdiffra remains on the new-to-market (NTM) block. Since it's the only approved product for this condition, management strategies to ensure proper use of Rezdiffra once it comes off NTM block are essential. Prior authorization criteria should require Rezdiffra to be prescribed by or in consultation with a gastroenterologist or hepatologist, with the prescriber being required to provide documentation of stage F2 to F3 fibrosis before treatment. These measures will ensure the appropriate patient populations are receiving necessary therapy and help reduce costs associated with inappropriate utilization.

Due to the high prevalence of MASH, employers should ask their medical carriers about the potential exposure to this condition. The ICD-10 code for the precursor to MASH is K76.0, known as metabolic dysfunction-associated steatotic liver disease (MASLD) and has an estimated prevalence of 32% of the U.S. population. The ICD-10 code for MASH is K75.81. Of those with MASH, about one-third of patients will be in the F2 and F3 fibrosis stages, the current target for prescription treatment.

Employers Health is here for you

As the treatment landscape for MASH matures, the Employers Health clinical team will continue to keep a close eye on clinical trials and the pipeline to ensure approved products for this indication have the appropriate utilization management strategies in place for its employer clients. When resources become available, we will be sure to keep clients updated.

TO LEARN MORE CONTACT

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