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HPR118

The Role of Invasive Diagnostics in Prior Authorization for MASH

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Objective

- Prior authorization (PA) criteria in the US often include patient eligibility requirements
- While PA criteria may align with clinical trial inclusion and exclusion criteria, deviations may occur due to real-world applicability, cost, and clinical guidelines
- For conditions involving invasive diagnostic tests, PA requirements face challenges, balancing between clinical trial criteria to maintain clinical rigor or diverging from these to reduce barriers to access
- This study evaluates the alignment between PA criteria and clinical trial inclusion/exclusion criteria for a recently approved noncirrhotic nonalcoholic steatohepatitis (NASH) / metabolic dysfunction-associated steatohepatitis (MASH) treatment

Methods

- PA criteria for resmetirom, approved for NASH with moderate to advanced liver fibrosis, were reviewed, focusing on requirements such as liver biopsy, stages of liver fibrosis, and metabolic risk factors
- Major commercial formularies, including Cigna / Express Scripts, Aetna / CVS Caremark, Prime Therapeutics, Anthem / Elevance, and UnitedHealthcare / Optum were reviewed
- Payer policies were compared to pivotal clinical trial inclusion and exclusion criteria to assess alignment

Results

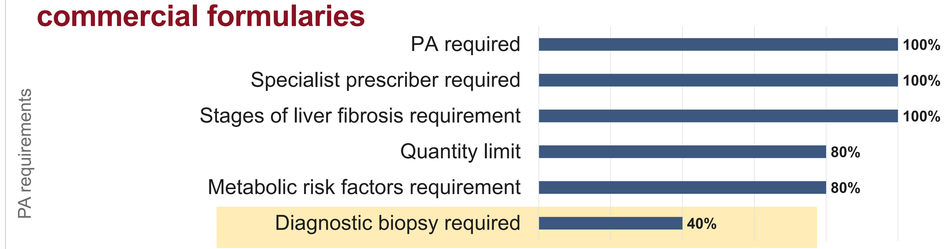
- The American Gastroenterological Association (AGA)[1] and American Association for the Study of Liver Diseases (AASLD)[2] have provided guidance on the use of noninvasive tests (NITs) for diagnosing MASH in clinical practice
  - While AGA emphasizes the use of NITs for screening, risk stratification, and monitoring, the AASLD still recognizes the role of liver biopsy in cases where NITs yield inconclusive results or when histological confirmation is necessary (**Table 1**).
- The clinical trial criteria for resmetirom[3] included metabolic risk factors, a baseline or recent liver biopsy showing NASH with stage 2 or 3 fibrosis, and a NAFLD Activity Score (NAS) of at least 4, with a second liver biopsy performed at 36 weeks (**Table 3**)
- While liver biopsy is considered the gold standard for confirming NASH, its invasiveness and risks limit feasibility, making NITs safer, more accessible alternatives for diagnosis and monitoring
  - Among the five formularies reviewed, two required a diagnosis via liver biopsy for PA, while the others accepted NITs (**Figure 1** and **Table 2**)

Table 1. Recommendations based on AGA[1] and AASLD[2] guidelines regarding biopsy vs NITs for diagnosing MASH

	Clinical scenario	Recommendation
American Gastroenterological Association (AGA) recommendations	Initial evaluation of patients with suspected MASH	Use **NITs for risk stratification**. FIB-4 Index score <1.3 suggests **low likelihood of advanced fibrosis** and may **exclude need for further testing**
	Patients with FIB-4 Index >1.3	Perform additional **NITs** (e.g., VCTE or MRE) to **further assess fibrosis stage**
	Monitoring disease progression or treatment response	Use serial **NITs over time** to guide clinical management decisions
	Patients with NITs suggesting advanced fibrosis (F3) or cirrhosis (F4)	Initiate surveillance for complications, such as HCC screening and variceal assessment
American Association for the Study of Liver Diseases (AASLD) recommendations	Indeterminate or conflicting NIT results	Consider **liver biopsy** to clarify uncertainties, particularly **when NITs provide discordant findings** or when **alternative liver diseases are suspected**
	Need for definitive histological assessment	Perform **liver biopsy** in cases where **detailed histopathological evaluation is required** for clinical decision-making

AASLD, American Association for the Study of Liver Diseases; AGA, American Gastroenterological Association; FIB-4, Fibrosis-4; HCC, hepatocellular carcinoma; MRE, magnetic resonance elastography; NIT, noninvasive test; VCTE, vibration-controlled transient elastography

Figure 1. Overview of PA criteria for resmetirom across major commercial formularies



Data presented as n=5 (%).
PA: prior authorization

Table 2. Detailed PA criteria for resmetirom across major commercial formularies

	Cigna[4] / Express Scripts[5]	Aetna [8–9]/ Caremark[6–7]	Prime Therapeutics[10]	UHC[11–12] / Optum[13–14]	Anthem / Elevance[15]
Tier placement	Specialty / non-preferred	NF / non-preferred	Specialty	Specialty / non-preferred	Specialty
PA required?	Y				
QL?	Y	N	Y	Y	Y
Specialist Rx required?	Y				
Diagnostic biopsy required?	Y	N	N	N	Y
If no biopsy, how confirmed?	n/a	ONE of the following: MRE or biopsy	At least TWO of the following: VCTE, ELF, or MRE	ONE of the following: FAST, MAST, or MEFIB	n/a
Stages of liver fibrosis criteria?	Stage F2 fibrosis OR stage F3 fibrosis at baseline (documentation required)				
Metabolic risk factors criteria?	Y	N	Y	Y	Y

FAST, FibroScan-AST; MAST, derived from MRI, MRE, and AST; MEFIB, MRE combined with FIB-4; VCTE (e.g., Fibroscan), Vibration-Controlled Transient Elastography; ELF, Enhanced Liver Fibrosis (ELF™) Test; NF, non-formulary; N, no; MRE, Magnetic resonance elastography; Rx, prescriber; PA, prior authorization, Y, yes; QL, quantity limit; UHC, United Healthcare

Table 3. Key resmetirom clinical trial inclusion and exclusion criteria[3]

	Criteria	Details
Inclusion Criteria	Age	Adults (typically ≥18 years)
	Diagnosis	Biopsy-confirmed MASH with fibrosis (F1-F3 stages)
	Metabolic risk factors	Evidence of metabolic dysfunction (e.g., obesity, type 2 diabetes, dyslipidemia)
	Liver fat	Elevated liver fat content on imaging (MRI-PDFF or CAP)
	Other conditions	Stable medical conditions, controlled diabetes (if present)
Exclusion Criteria	Cirrhosis	F4 fibrosis (compensated or decompensated cirrhosis)
	Other liver diseases	Hepatitis B/C, autoimmune hepatitis, primary biliary cholangitis, Wilson's disease, etc.
	Alcohol use	Excessive alcohol consumption
	Uncontrolled comorbidities	Unstable cardiovascular disease, active malignancy, or severe kidney disease
	Recent weight loss	Rapid weight loss or bariatric surgery within the past 6-12 months

MRI-PDFF, Magnetic Resonance Imaging-Proton Density Fat Fraction; CAP, Controlled Attenuation Parameter; MASH, Metabolic Dysfunction-Associated Steatohepatitis; HBV, Hepatitis B Virus; HCV, Hepatitis C Virus; PBC, Primary Biliary Cholangitis.

Conclusions

- Our findings indicate that 3/5 reviewed plans do not mandate liver biopsy as a PA requirement, despite its use in clinical trials
- This reflects a growing emphasis on balancing diagnostic accuracy with patient safety and accessibility
- These findings highlight a divergence from clinical trial requirements, with payer criteria aligning more closely with real-world practices to reduce procedural risks and barriers to care

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