Non-alcoholic steatohepatitis (NASH)

Disease Coverage Extract

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The approval of the first disease-specific therapies for the treatment of non-alcoholic steatohepatitis (NASH) from 2020 will drive the value of the NASH market to reach over $21bn in 2027, with a CAGR of 57%.

Visit Datamonitor Healthcare to view our Forecast, Treatment, Epidemiology, and Pipeline Analysis for the NASH market.

KEY QUESTIONS ANSWERED

- What are the unmet needs in NASH?
- What is the timeline of approval for NASH therapies?
- Which pipeline therapies will dominate the NASH market?
- How will payers react to premium prices and how will this impact the NASH market?
- Which NASH patient populations will experience the greatest uptake of novel therapies?
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DISEASE DEFINITION AND DIAGNOSIS

DISEASE DEFINITION

Non-alcoholic fatty liver disease (NAFLD) encompasses a spectrum of patients who have fatty liver in the absence of significant alcohol consumption. NAFLD patients are often segmented into non-alcoholic fatty liver (NAFL) and non-alcoholic steatohepatitis (NASH) patients. NAFLD diagnosis requires evidence of hepatic steatosis and lack of secondary causes of liver fat accumulation such as substantial alcohol consumption, long-term use of a steatogenic medicine, or monogenic hereditary disorders. NASH is defined as the presence of >5% hepatic steatosis and inflammation with hepatocyte injury, with or without fibrosis. Although the presence of fibrosis is not required for a diagnosis of NASH, fibrosis is present in over 80% of NASH patients. For this reason, NASH patients are often further segmented by their fibrosis stage (Chalasani et al., 2018).

DIAGNOSIS

Initial diagnosis of NASH is based on an analysis of a patient's clinical history and a physical examination. This diagnosis focuses on potential causes, triggers, and comorbid conditions. In order for an initial diagnosis to be made, five key criteria must be met (Chalasani et al., 2012):

- hepatic steatosis must be present
- hepatocellular injury has occurred as a result of the hepatic steatosis
- there are no competing etiologies for the hepatic steatosis
- there are no co-existing causes for chronic liver disease
- there is no significant alcohol consumption (alcohol consumption must be within guidelines).

After a physician makes an initial diagnosis of NASH, the diagnosis may then be confirmed. Techniques used to confirm NASH diagnoses include liver biopsy, fibroscan, blood tests, and the use of non-invasive scoring scales such as the NAFLD Activity Score (Chalasani et al., 2012).

Treatment guidelines recommend liver biopsy as the gold standard for NASH diagnosis

Current treatment guidelines recommend liver biopsy as the gold standard, however, use is only advised in the case of uncertain diagnosis or suspicion of advanced liver disease because of the invasive nature of the procedure. In the American Association for the Study of Liver Diseases (AASLD) and European Association for the Study of the Liver (EASL) guidelines, liver biopsy is advised in patients with metabolic syndrome who are at risk of hepatic inflammation, or when the fibrosis-4 (FIB-4) index or liver stiffness suggest the presence of fibrosis (Leoni et al., 2018).
PRODUCT PROFILE (LATE STAGE): TROPIFEXOR

PRODUCT PROFILE

ANALYST OUTLOOK

Tropifexor (Novartis/Pfizer) could stand out against the other farnesoid X receptor (FXR) agonists Ocaliva (obeticholic acid; Intercept Pharmaceuticals) and cilofexor (Gilead) due to its favorable safety profile and lack of reported pruritis. If efficacy is comparable to the aforementioned rivals, which are expected to reach the market earlier, then tropifexor's cleaner safety and tolerability profile could allow it to emerge as the preferred FXR agonist. In addition, Novartis's collaboration with Pfizer could overcome tropifexor's late entry to market as the companies have an abundance of developmental and commercial resources that small biotech companies such as Intercept or Genfit will find difficult to compete with.

Although there are currently no data relating to non-alcoholic steatohepatitis (NASH) resolution, or fibrosis regression with no worsening of NASH, tropifexor increased levels of fibroblast growth factor 19 (FGF19), thereby inhibiting bile acid synthesis from cholesterol and insulin-induced hepatic lipogenesis, which should ultimately lead to hepatic delipidation. Tropifexor was also observed to numerically reduce alanine aminotransferase (ALT), gamma-glutamyl transferase (GGT), and liver fat, measured by magnetic resonance imaging-proton density fat fraction (MRI-PDFF), compared to placebo, but the study was not powered for statistical significance. Despite previous studies demonstrating that there is a strong correlation between MRI-PDFF liver fat reductions and histological responses, further biopsy data are still required by regulators (Jayakumar et al., 2019). Novartis aims to complete the histology-based Part C of the Phase IIb trial, which uses higher doses (140µg and 200µg), in July 2019. Nevertheless, results thus far have demonstrated tropifexor's anti-inflammatory and anti-steatotic effects, which provide hope for positive data in Part C.

DRUG OVERVIEW

FXR is a nuclear receptor that regulates bile acid metabolism and signaling. Activation of the receptor inhibits bile acid synthesis from cholesterol via cytochrome P450 7A1 and increases bile acid conjugation, transport, and excretion. This protects the liver from the potentially harmful effects caused during bile acid accumulation. Tropifexor is a novel, highly potent, non-bile acid FXR agonist. It has demonstrated potent activity in rodent Parkinson's disease models by measuring the induction of FXR target genes in tissues (Tully et al., 2017).
PATIENT BASED FORECAST

FORECAST ASSUMPTIONS

Datamonitor Healthcare makes the following assumptions in its forecast of cenicriviroc for NASH:

REGULATORY

- Datamonitor Healthcare expects Allergan to submit US and EU regulatory filings in Q3 2020 based on 18-month interim data from the pivotal AURORA study. Cenicriviroc’s approval is expected in Q3 2021 in the US and EU, with subsequent launches in Q4 2021 and Q1 2022, respectively.

- Cenicriviroc is not expected to launch in Japan as there have not been any clinical trials reported in this territory.

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