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A Budget Impact Model for Two Investigational Agents for the Treatment of Nonalcoholic Steatohepatitis (NASH)

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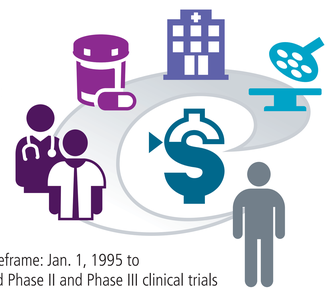
INTRODUCTION

- NASH is a type of nonalcoholic fatty liver disease (NAFLD) that affects approximately 15 million adults in the U.S.[1,2]
- Although largely asymptomatic, NASH can progress to cirrhosis, liver failure, and liver cancer, and is projected to become the most common indication for liver transplantation between 2020 and 2025.[1,2]
- There are no Food and Drug Administration (FDA)-approved therapies for NASH. The American Association for the Study of Liver Diseases (AASLD) recommends pioglitazone and vitamin E as options for select patients.[1]
- Several agents are currently in development for NASH, of which obeticholic acid and elafibranor are being tested in Phase III registration trials.[3,4]
- Given limited treatment options for NASH, the clinical interest in using novel therapies may be great once they become available.[1]
- A budget impact model may provide valuable insight to health insurers on the financial consequences of adopting novel therapies.
- A budget impact model was created to forecast the clinical and economic impact of two emerging investigational agents, elafibranor and obeticholic acid.

OBJECTIVE

To describe the pharmacy budget impact of elafibranor and obeticholic acid on a sample state Medicaid plan in the first year following their FDA-approval for the treatment of NASH.



METHODS

- A Medline search was conducted (timeframe: Jan. 1, 1995 to Oct. 30, 2017) to identify all published Phase II and Phase III clinical trials of elafibranor and obeticholic acid for NASH.
- Conference abstracts, manufacturer press-releases, and value assessments evaluating elafibranor and obeticholic acid for NASH during the same timeframe were also reviewed.
- A clinical and economic assessment was performed to determine the budget impact.
  - The relative efficacy as well as the safety and tolerability of both medications were evaluated to predict their place in therapy.
  - Key considerations for market uptake were identified to estimate unmanaged product uptake in the first year of market availability.
  - Available epidemiological data was extrapolated to estimate the proportion of members enrolled in a sample state Medicaid plan who would be treatment candidates.
  - Annual drug cost was estimated using the wholesale acquisition cost of Ocaliva® (obeticholic acid).

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RESULTS

Clinical Assessment

Table 1:
Evaluation of Elafibranor and Obeticholic Acid[1-6]

	Elafibranor	Obeticholic acid (OCA)
	Projected market entry: **2019**	
Mechanism of action	Dual PPAR-α/δ agonist	FXR ligand
Key clinical trial	Phase II GOLDEN-505 study*	Phase II FLINT study*
Study population	N=274; adults with NASH (NAS≥3) without cirrhosis	N=283; adults with NASH (NAS≥4) without cirrhosis†
Primary endpoint	Proportion of patients achieving resolution of NASH without worsening of fibrosis	Proportion of patients achieving ≥2 point reduction in NAS without worsening of fibrosis
Intervention	Elafibranor 80 mg or 120 mg orally once daily or placebo for 52 weeks	OCA 25 mg orally once daily or placebo for 72 weeks
Results	**Resolution of NASH:** 19% for elafibranor vs 12% for placebo (P=0.045)	**Improved liver histology:** 45% for OCA vs 21% for placebo (P=0.0002)
Key considerations for market uptake	• Positive effects on lipids and glucose • Mild decrease in renal function • Granted Fast Track designation	• FDA-approved for PBC • Modest weight loss • Associated with pruritus and dyslipidemia • Granted Breakthrough Therapy designation
	• May resolve NASH, but ~80% of patients may not respond to treatment • If untreated, NASH may progress until liver transplant is required • No FDA-approved treatments indicated for NASH	• May improve liver histology • Clinical trials evaluated surrogate endpoints

* Randomized, placebo-controlled † Patients must have score of ≥1 in each component of NAS score Abbreviations: FXR=farnesoid X nuclear receptor, NAS=NAFLD activity score, PBC=primary biliary cholangitis, PPAR=peroxisome proliferator-activated receptor

Economic Assessment

- Estimated annual drug cost: $74,551
- Estimated prevalence of NASH: 3.5% to 5%[1,2]
- An estimated ~5% of patients who have NASH have been diagnosed.[1,2]
- Approximately 567,000 individuals in the U.S. may have the diagnosis and be eligible for treatment.[2]
- NASH is a chronic condition and treatment is continued until progression to cirrhosis (at which time a liver transplant may be required) or until resolution.[1]

Budget Impact

Medicaid plan of 100,000 covered lives:

If low [10%] uptake
(n=18 to 25):
$1.3 to $1.9 million per year

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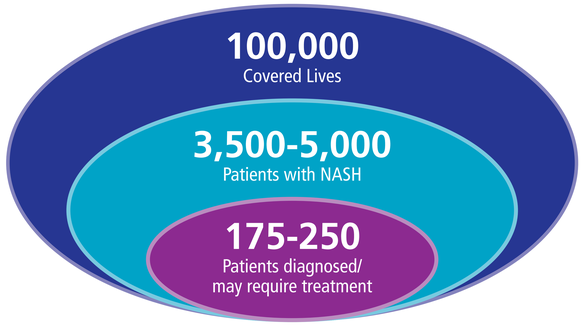
If all diagnosed patients treated
(n=175 to 250):
$13 to $18.6 million per year

Figure 1:
Projected Pharmacy Budget Impact in Year One



DISCUSSION

NASH is associated with significant morbidity and mortality and if left untreated, may progress to liver transplantation.[1]

Based on available peer-reviewed literature, elafibranor and obeticholic acid may offer clinical advantages over currently available non-FDA approved therapies.[2-5]

Despite the treatment advancements these agents may offer, only ~20% of patients responded to therapy in clinical trials.[3,4]

The FDA-approval of elafibranor and obeticholic acid for NASH may present opportunities for innovative cost-containment strategies.

- **Supplemental rebate:** Selection of a preferred NASH agent
- **Value-based contracts:** Payment contingent on agreed-upon clinical outcomes
- **Adherence monitoring:** Promotion of appropriate medication use

Plan-specific projections may be made by utilizing medical claims data to determine the exact prevalence of NASH within the plan membership.

LIMITATIONS

- Clinical impact was based on Phase II trial data which assessed surrogate endpoints; Phase III trials are ongoing.
- Several assumptions were made in estimating budget impact:
  - Prevalence of disease in the Medicaid plan
  - Number of members diagnosed
  - Number of members that would seek treatment
  - Cost of the agents
- The current analysis did not utilize medical claims data to determine the prevalence of disease in a specific population.
- Uptake of new therapies is difficult to assess due to the many variables that may influence it.

CONCLUSIONS

- New agents for the treatment of NASH are likely to have a significant impact on state Medicaid program budgets.
- The projected budget impact of elafibranor and obeticholic acid highlights the need for innovative cost-containment strategies.
- Proactive pipeline monitoring and high-level budget impact modeling may assist state Medicaid programs in preparing for high-cost specialty medications that are likely to have significant cost implications.

FUTURE STUDIES

Continuous review and adjustment to assumptions made in this budget impact model are necessary as more clinical and economic data become available.

DISCLOSURES/ACKNOWLEDGMENTS

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