BULEVIRTIDE FOR CHRONIC HEPATITIS DELTA IN ROMANIA: A REAL-WORLD-DATA-DRIVEN COST-UTILITY AND BUDGET IMPACT ANALYSIS

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Introduction

- Chronic hepatitis Delta (CHD) is the most aggressive form of viral hepatitis, with a significant contribution to cirrhosis, HCC, and liver-related mortality in the absence of efficient antiviral therapy.
- In Romania, HBV/HDV-related cirrhosis and HCC remain leading causes of LT contrasting with Western European trends dominated by ALD and MASLD.
- This unique epidemiological context heightens the potential system-level impact of therapies that prevent progression to decompensation and LT.
- Bulevirtide (BLV) has been recently approved for the treatment of compensated CHD in Romania.

Aim

To assess the cost-utility and 5-year budget impact of bulevirtide (BLV) compared with Best Supportive Care (BSC) for the treatment of chronic hepatitis Delta (HDV) in Romania, from the perspective of the Romanian public payer (National Health Insurance House), using real-world local clinical data.

Method

- A Markov cohort state-transition model was adapted to the Romanian healthcare setting, simulating liver disease progression through health states based on the METAVIR scoring system (F0-F4, decompensated cirrhosis, hepatocellular carcinoma, liver transplantation, post-transplant, and liver-related death). Cycle length was set at one year, with a lifetime horizon for the cost-utility analysis and a 5-year horizon for the budget impact analysis. Costs (2024/2025 RON) and outcomes were discounted at 3% annually. Baseline distribution, demographics, and virologic/biochemical response rates were derived from a retrospective cohort of 175 Romanian HDV patients treated with BLV. Deterministic and probabilistic sensitivity analyses were performed.

Results

BLV produced an incremental gain of 3.36 discounted life-years (LYs) and 3.08 quality-adjusted life-years per patient versus BSC (10.52 vs 7.16 LYs; 8.13 vs 5.05 QALYs). Treatment averted over 1,180 decompensated cirrhosis cases, more than 800 hepatocellular carcinomas, and 87 liver transplants.

ICERs were 843,091 RON/LY and 918,829 RON/QALY. It should be noted that the drug cost considered in the model reflects the public price and does not account for the confidential agreement or mandatory clawback local tax.

The BIA demonstrated a negligible PMPM impact, rising from 0.002 to 0.024 RON over 5 years.

KEY RESULTS

+3.36 Life-years gained — Discounted: 10.52 vs. 7.16 BSC	**+3.08** QALYs gained — Discounted: 8.13 vs. 5.05 BSC	**−239** Liver-related deaths — 657 vs. 896 BSC · NNT 4.18
−119 Decompensation events — 265 vs. 383 BSC · NNT 8.42	**−82** Hepatocellular carcinoma — 319 vs. 401 BSC · NNT 12.17	**−9** Liver transplants — 22 vs. 31 BSC · NNT 114.41

Hepcludex vs. best supportive care (BSC). Life-years and QALYs are discounted; event counts are lifetime model totals.
NNT = number needed to treat. ICER 918,829 RON per QALY gained; budget impact 0.024 RON PMPM at year 5.

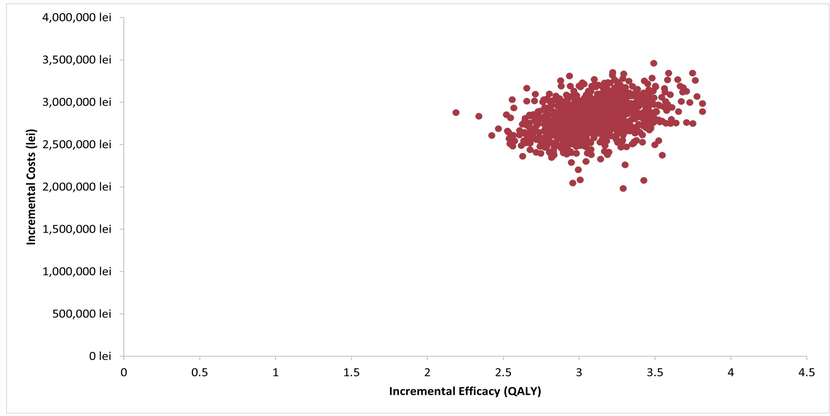

Figure 1. *Probabilistic sensitivity analysis.*

Even in the "worst-case" simulations (the far-left points of the cloud), the patient still gains over 2.2 QALYs. This confirms that the clinical advantage of BLV (disease modification) is not an artifact of specific base-case assumptions. Regardless of how we vary the inputs (within reasonable bounds), the therapy consistently delivers substantial life-year and quality-of-life gains over BSC.

From a decision-making perspective (National Health Insurance House, National Drug Agency), the results unequivocally categorize BLV as a "Type 1" intervention (More Effective / More Costly).

The top 3 drivers of the economic model, accounting for the widest variation in ICER, are:

- *Drug Acquisition Cost (BLV – Wholesale Acquisition Cost): Varying the price yields a difference of 182,434 RON in the ICER.*
- *Utility Values (Quality of Life - Responders F2): ability to keep patients in a "better" health state (F2 or Compensated Cirrhosis) with a higher quality of life, rather than just extending life in a severe state.*
- *Adherence: This supports the need for a patient support program or strict monitoring (continuation criteria) every 6 months to ensure only adherent, responding patients remain on therapy, thereby protecting the payer's budget.*

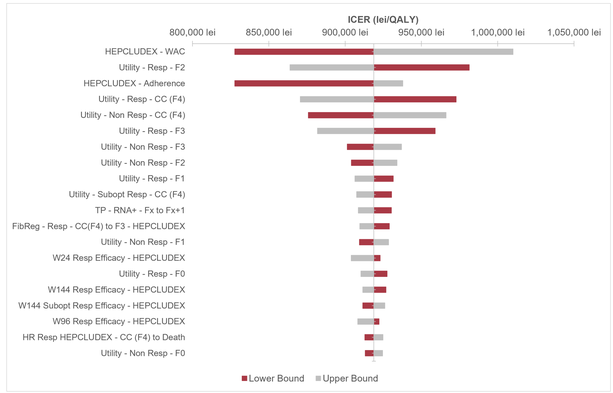

Figure 2. *Deterministic sensitivity analysis.*

Conclusions

- BLV acts as a disease-modifying therapy, substantially extending survival and preserving quality of life in Romanian HDV patients.
- Although upfront public costs might be considered significant, the impact on the National Health Insurance Fund remains minimal due to disease rarity and severity, supporting reimbursement to address a critical unmet medical need.

References

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2. Therapeutic Protocol J05AX28 bulevirtide – National Health Insurance Agency; Ministry of Health Order 1857/441/2023

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