Cost-Effectiveness of Inclisiran Versus Ezetimibe Monotherapy in Low-Risk Adults With Primary Hypercholesterolemia: A Markov Model

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Background

Low-risk adults with primary hypercholesterolemia face a long-term risk of cardiovascular events, but their short-term event risk is low.[1,2]

Inclisiran offers greater LDL-C reduction than ezetimibe, but this clinical advantage comes with substantially higher drug cost.[1]

For low-risk primary prevention, the key question is whether greater LDL-C lowering produces enough health benefit to justify the added cost. This study evaluates the cost-effectiveness of inclisiran versus ezetimibe monotherapy in this population.

Objectives

To evaluate the cost-effectiveness of inclisiran vs. ezetimibe monotherapy in low-risk adults with primary hypercholesterolemia from a US payer perspective and quantify decision uncertainty.

Methods

A cohort Markov model (Figure 1) compared inclisiran versus ezetimibe monotherapy from a US payer perspective over 10 years, with 1-year cycles.

- The model included six states. The cohort entered at age 46 years with no prior ASCVD, no lipid-lowering therapy at baseline, and median 10-year ASCVD risk ≈2.2%.[1]
- LDL-C effects from VICTORION-MONO were adherence-adjusted in the base case: −46.5% for inclisiran and −11.2% for ezetimibe.[1]
- LDL-C reduction was mapped to MI/stroke risk using CTT relative risks per 1 mmol/L LDL-C reduction.[2]
- Drug costs were from CMS Medicare pricing files; event costs, utilities, and follow-up costs were from published literature; mortality was based on US life tables.[3,4]
- All costs were reported in 2025 US dollars. Costs and QALYs were discounted 3% annually, with half-cycle correction.
- One-way, probabilistic, and scenario analyses tested parameter uncertainty, full biologic efficacy, and a 40-year horizon.

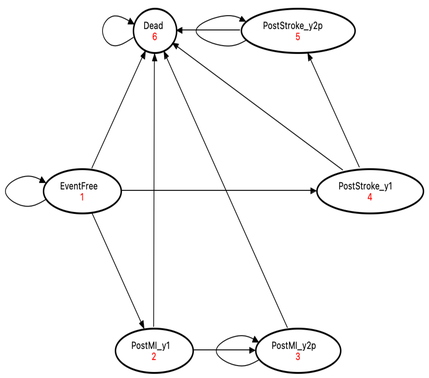
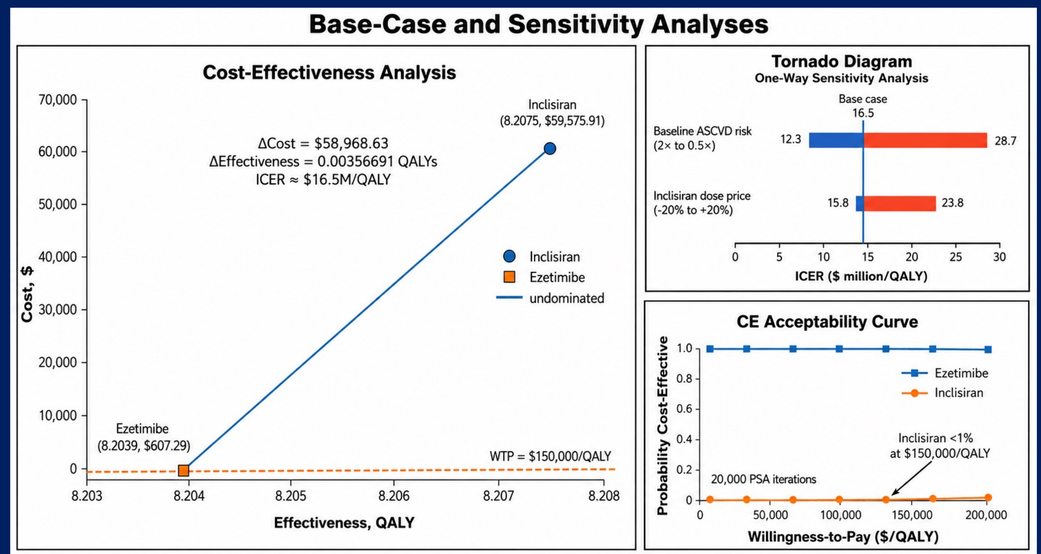


Figure 1. Markov Model

In low-risk primary-prevention adults, inclisiran produced minimal additional benefit vs. ezetimibe (ΔQALY = 0.0036) at substantially higher cost, yielding an ICER of $16.5M/QALY and <1% probability of being cost-effective at $150,000/QALY.



Abbreviations: ASCVD, atherosclerotic cardiovascular disease; CE, cost-effectiveness; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life-year; WTP, willingness-to-pay.

Figure 2. Base-Case and Sensitivity Analyses

Results

Base Case. Costs and QALYs for both inclisiran and ezetimibe are presented in Table 1.

Deterministic and Probabilistic Sensitivity Analysis. Results from one-way SA supported the base-case findings, with results driven mainly by high inclisiran cost and low baseline ASCVD risk.

Threshold analysis suggested that inclisiran would require a price reduction of approximately 98% to approach cost-effectiveness compared with ezetimibe at a willingness-to-pay threshold of $150,000/QALY.

Probabilistic sensitivity analysis indicated <1% probability of inclisiran being cost-effective at $150,000/QALY (Figure 2).

Table 1. Base-Case and Scenario Results: Inclisiran vs. Ezetimibe

Analysis	Key assumption	ΔCost	ΔQALY	ICER
Base case	10 years; adherence-adjusted	**$58,969**	**0.0036**	**$16.5M/QALY**
Biologic efficacy	10 years; adherence = 1	≈$58,969	≈0.0042	$14.1M/QALY
Lifetime horizon	40 years; age 46–86	≈$113,000	≈0.019	$6.0M/QALY

Footnote: Δ values are inclisiran − ezetimibe. Costs are 2025 US dollars and discounted at 3% annually.

Limitations

MI/stroke outcomes were modeled from LDL-C changes rather than directly observed outcomes. Adherence, costs, and utilities were derived from external sources. Generic utilities may not capture patient preferences, injection burden, or real-world payer variation.

Conclusion

In primary prevention among low-risk adults, inclisiran monotherapy is highly unlikely to be cost-effective vs. ezetimibe at current US prices; results are robust to biologic-efficacy and lifetime-horizon assumptions and are driven primarily by high drug cost and low baseline risk.

Key References

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