

Cost-Utility Analysis of CGRP Monoclonal Antibodies for Episodic Migraine Headaches Patients in the United States

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About me

- Fourth year Pharm.D. student at UC San Diego
- B.S. in Pharmaceutical Sciences at UC Irvine
- Hometown: Shanghai & Irvine



Migraine Headache

- Causes severe throbbing pain and/or pulsing sensation
- **21% of women and 10.7% of men** of the US population were affected by migraine as of 2018¹
- **Second largest cause of disability** worldwide following low back pain²
- Total medical expenditures of patients with a diagnosis of migraine per year were **\$2,571** higher compared to patients who did not have any signs of migraine³

Migraine Headache Classification by International Classification of Headache Disorder, 3rd edition (ICHD-3)⁴

Episodic Migraine

0 – 14 migraine days per month

Chronic Migraine

More than 14 migraine days per month

1. Burch R, Rizzoli P, Loder E. Headache. 2021;61(1):60-68. doi:10.1111/head.14024

2. Vos T, Abajobir AA, Abate KH, et al. The Lancet. 2017;390(10100):1211-1259. doi:10.1016/S0140-6736(17)32154-2

3. Hawkins K, Wang S, Rupnow M. Headache. 2008;48(4):553-563. doi:10.1111/j.1526-4610.2007.00990.x

4. Gobel H. 1. Migraine. ICHD-3. Accessed March 27, 2025. <https://ichd-3.org/1-migraine/>

Treatments for Episodic Migraine Prevention

Conventional First-line Treatments ⁵	CGRP Monoclonal Antibodies	
Divalproex, topiramate Propranolol, timolol	Erenumab (Aimovig) Eptinezumab (Vyapti) Fremanezumab (Ajovy) Galcanezumab (Emgality)	FDA Approved in 2018 FDA Approved in 2020 FDA Approved in 2018 FDA Approved in 2018

	Divalproex ER 1000 mg	Erenumab 70 mg	Eptinezumab 100 mg
Route of Administration	Oral	Subcutaneous injection	Intravenous
Clinical Efficacy over 12 weeks of treatment	-1.7 MMDs	-2.9 MMDs	-3.9 MMDs
VA FSS Price	\$12 per month	\$671 per month	\$529 per month
ICER Clinical Evidence Rating ⁶	NR	Insufficient	NR

Abbreviations: CGRP, Calcitonin Gene-Related Peptide; ER, Extended-release; FSS, Federal Supply Schedule; ICER, Institute for Clinical and Economic Review; MMD, Monthly Migraine Days; NR, Not Reported; VA, Veteran Affairs

5. Silberstein SD, Holland S, Freitag F, et al. Neurology. 2012;78(17):1337-1345. doi:10.1212/WNL.0b013e3182535d20

6. Migraine: Acute & Chronic Therapies. ICER. Accessed March 21, 2025. <https://icer.org/assessment/migraine-2018/>

Research Question

- Are CGRP receptor monoclonal antibodies cost-effective in prevention of episodic migraines compared to divalproex ER from the US healthcare payer perspective over a 10-year horizon?

Objective

- To investigate the cost-effectiveness of two CGRP receptor monoclonal antibodies, eptinezumab and erenumab, compared to divalproex ER for prevention of episodic migraine from the US healthcare payer perspective over a 10-year horizon

Study Design

A cost-utility analysis using a decisional model was constructed in R Studio using the Heemod package: <https://CRAN.R-project.org/package=heemod>

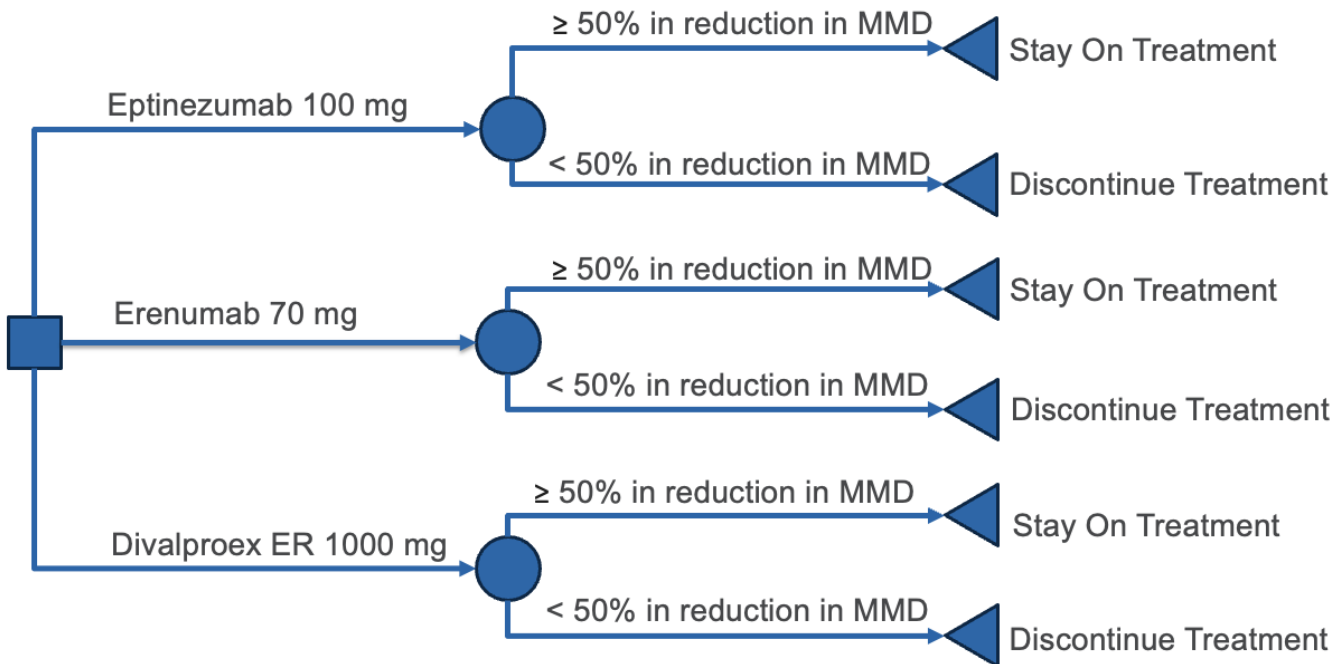
Model structure	Hybrid Decision Tree-Markov model
Simulated patient cohort^{7,8}	US adults with episodic migraine for more than 12 months
Sex	84% female
Average age	39.8 years
Time horizon	10 years
Perspective	US healthcare payer
Strategies	Divalproex ER 1000 mg daily Eptinezumab 100 mg every 12 weeks Erenumab 70 mg every 4 weeks

7. Ashina M, Saper J, Cady R, et al. Cephalalgia. 2020;40(3):241-254. doi:10.1177/0333102420905132

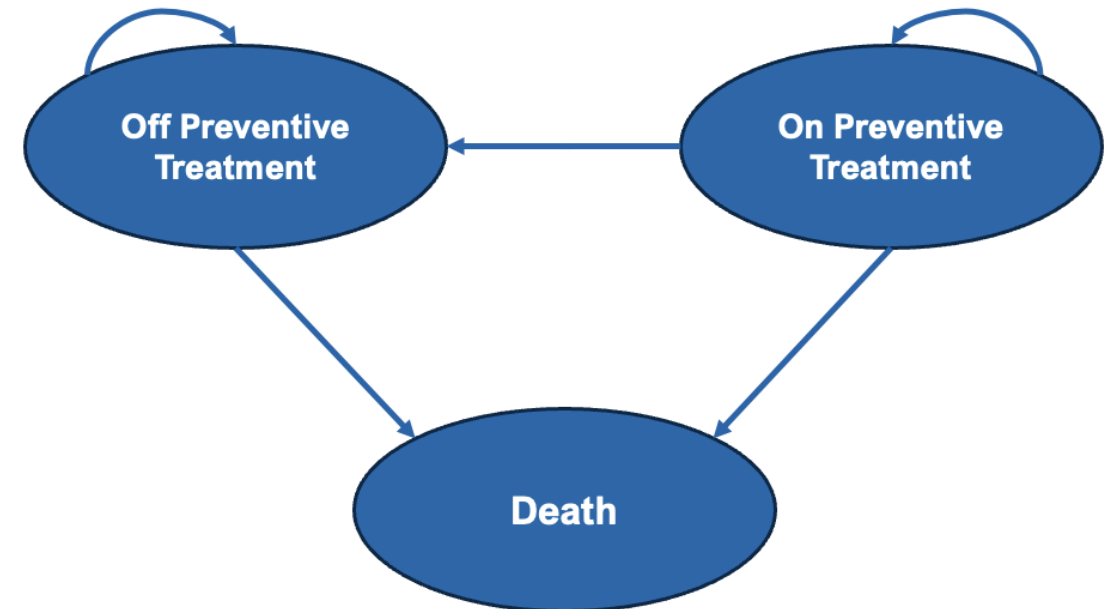
8. Burch R, Rizzoli P, Loder E. Headache. 2018;58(4):496-505. doi:10.1111/head.13281

Model Structure

- A hybrid Decision Tree-Markov model for episodic migraine over a 10-year horizon was built



Decision Tree Duration: 24 weeks



Key assumptions:

- Adequate response to treatment was determined according to the guidelines published by AHS^{5,6}
- Treatment discontinuation was only due to adverse effects in Markov model

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Abbreviation: AHS, American Headache Society

5. Silberstein SD, Holland S, Freitag F, et al. Neurology. 2012;78(17):1337-1345. doi:10.1212/WNL.0b013e3182535d20

6. Migraine: Acute & Chronic Therapies. ICER. Accessed March 21, 2025. <https://icer.org/assessment/migraine-2018/>

Methods



Probabilities

Probabilities of simulated patient cohort achieving more than 50% reduction in MMD were derived from the clinical trials

Treatment discontinuation rate was derived from clinical trials



Cost

Pharmaceutical costs were based on the US VA FSS pricing

Cost of medication administration was based on CMS physician fee schedule

Cost of migraine rescue medications and migraine-related healthcare expenditure were included



Utility

Calculated based on estimations of regression model⁹ and MMDs on and off treatments from the clinical trials

Abbreviations: MMD, Monthly Migraine Days; VA, Veteran Affairs; FSS, Federal Supply Schedule; CMS, Centers for Medicare & Medicaid Services

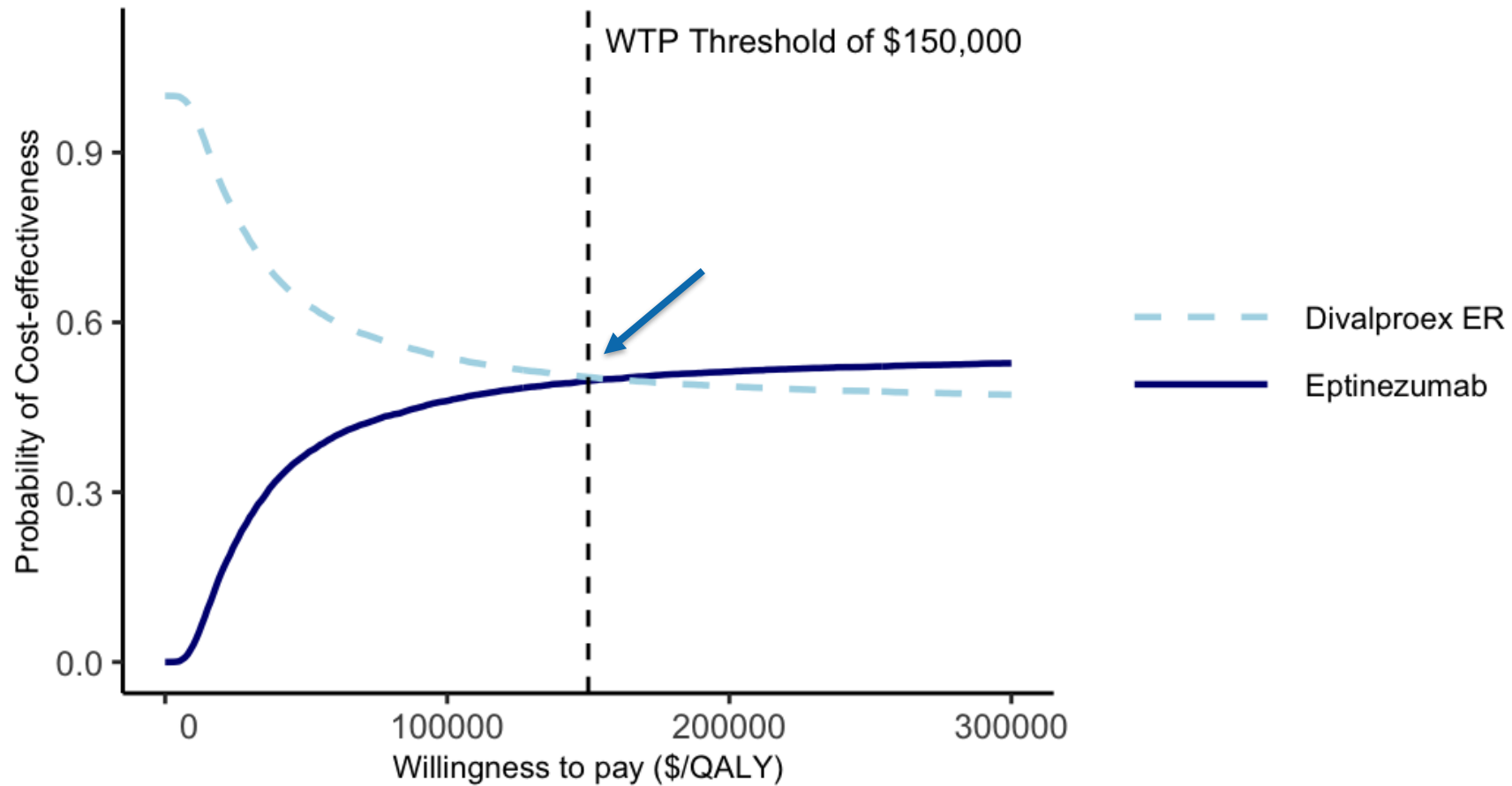
Results: Deterministic Findings

Strategy	Total costs	Drug costs	QALYs	ICER	INMB
Divalproex ER	\$41,938	\$609	5.61		
Eptinezumab	\$65,599	\$31,949	5.79	\$135,017	\$2,626
Erenumab	\$74,181	\$41,176	5.72	\$312,579	-\$16,769

Abbreviations: ICER, Incremental Cost Effectiveness Ratio; INMB, Incremental Net Monetary Benefit; QALY, Quality-adjusted Life Year

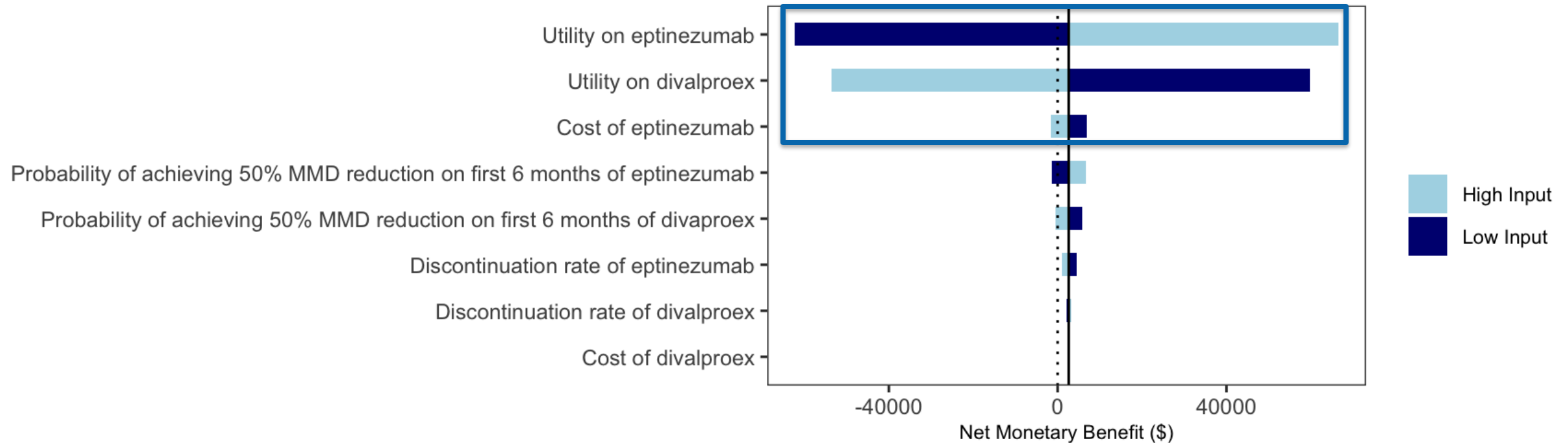
- Key takeaways:
 - Erenumab was eliminated from the list of strategies
 - Eptinezumab was cost-effective with a WTP threshold of \$150,000 per QALY gained
 - Drug costs accounted for 48.7%, 55.5%, and 1% of the total costs for eptinezumab, erenumab, and divalproex ER, respectively

Results: Sensitivity Analyses



(a) Cost-effectiveness acceptability curve

Results: Sensitivity Analyses



(b) Tornado diagram of the net monetary benefit changes between eptinezumab and divaproex

- Key takeaways:
 - Utility on both treatments had the largest impact on INMB of eptinezumab
 - INMB equals to zero when increasing the cost of eptinezumab by around 11%

Results: Scenario Analysis

- Payers may negotiate with the manufacturer if their WTP threshold is lower than \$150,000 per QALY gained
 - The manufacturer would need to reduce the total cost of eptinezumab around **20%** if the WTP threshold is \$100,000 per QALY gained

Results: Scenario Analysis

- Cost negotiation of brand name drugs:
 - **41%** reduction from VA FSS pricing based on the report by Congressional Budget Office¹⁰

Strategy	Total costs	Drug costs	QALYs	ICER	INMB
Divalproex ER	\$41,938	\$609	5.61		
Eptinezumab	\$53,904	\$18,956	5.79	\$68,283	\$14,320
Erenumab	\$59,129	\$24,552	5.72	\$166,656	-\$1,718

Abbreviations: ICER, Incremental Cost Effectiveness Ratio; INMB, Incremental Net Monetary Benefit; QALY, Quality-Adjusted Life Year

- Key takeaways:
 - A 41% cost reduction of eptinezumab lowered the ICER from \$135,017 per QALY gained to \$68,283 per QALY gained

Abbreviations: VA, Veteran Affairs; FSS, Federal Supply Schedule

Limitations

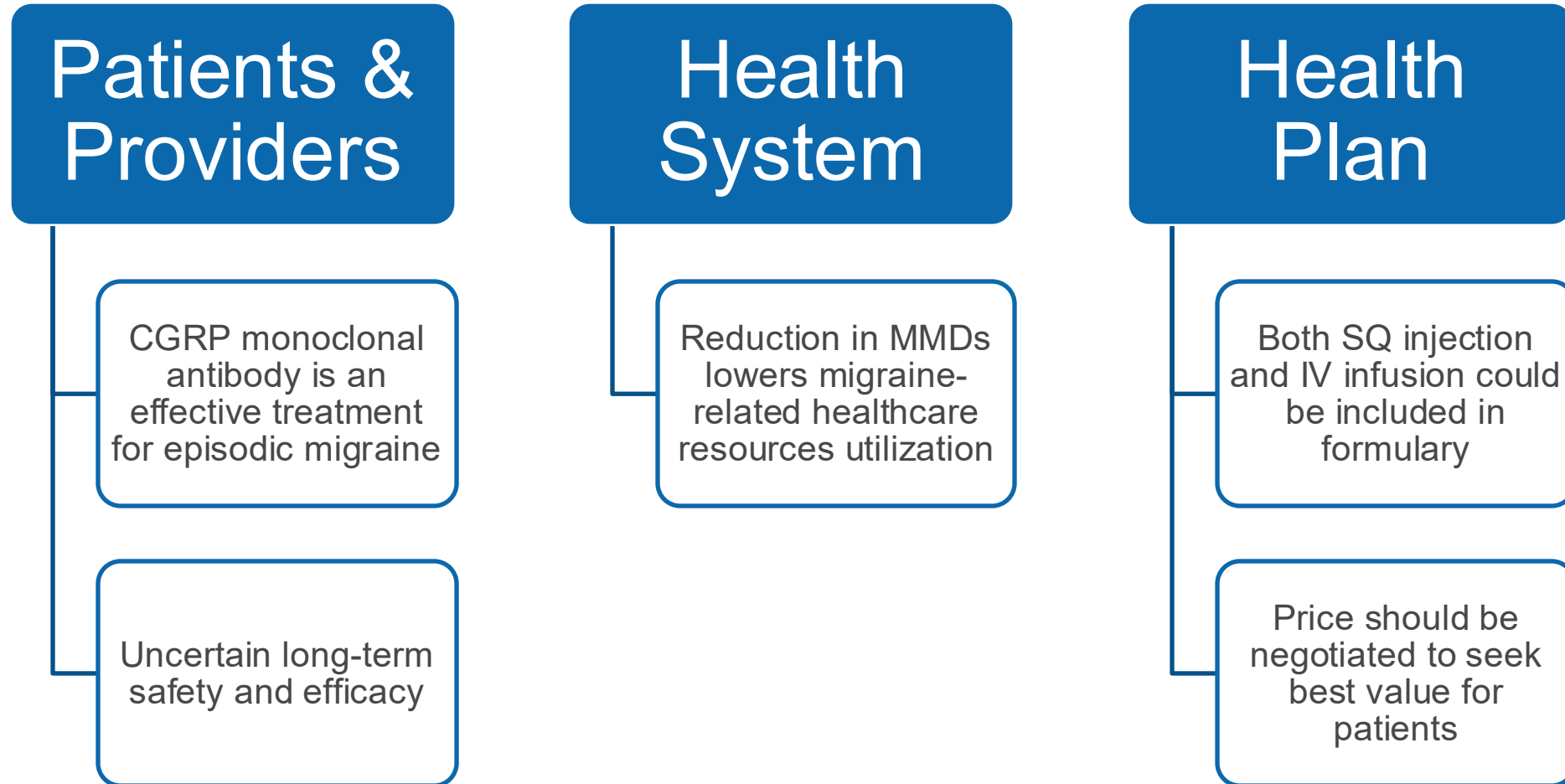
- Long-term safety and efficacy data of eptinezumab and erenumab was not available
- Societal productivity loss was not accounted for in this model
- The clinical trial of divalproex ER did not stratify the result based on episodic and chronic migraine
 - Baseline MMD was 6.3 in the clinical trial¹¹

11. Freitag FG, Collins SD, Carlson HA, et al. Neurology. 2002;58(11):1652-1659. doi:10.1212/WNL.58.11.1652

Conclusion

- CGRP monoclonal antibodies were able to
 - Reduce **frequency of migraine attacks**
 - Reduce **migraine-related healthcare utilization and expenditure**
 - Improve **quality of life**
- Payers may consider **negotiating the price of eptinezumab**
- When **biosimilars** of eptinezumab and erenumab become available in 2034 and 2035, the price reduction of both medication might favor the use of them

Implications for Integrated Health Systems



This model is open-source!

- Link to the GitHub site of this model: https://github.com/yarieldong/CGRP_CUA



Thank you!

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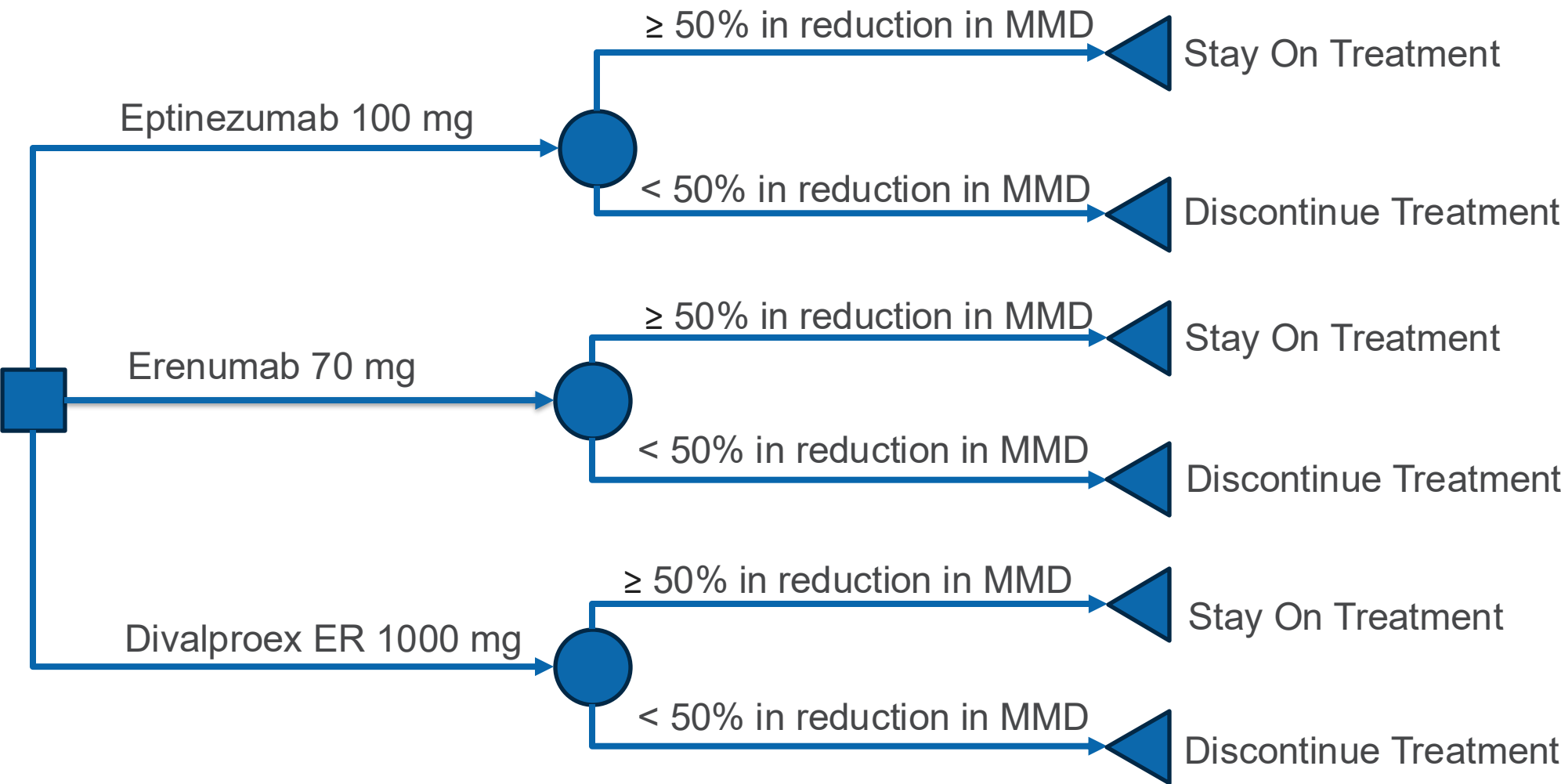
References

1. Burch R, Rizzoli P, Loder E. Headache. 2021;61(1):60-68. doi:10.1111/head.14024
2. Vos T, Abajobir AA, Abate KH, et al. The Lancet. 2017;390(10100):1211-1259. doi:10.1016/S0140-6736(17)32154-2
3. Hawkins K, Wang S, Rupnow M. Headache. 2008;48(4):553-563. doi:10.1111/j.1526-4610.2007.00990.x
4. Gobel H. 1. Migraine. ICHD-3. Accessed March 27, 2025. <https://ichd-3.org/1-migraine/>
5. Silberstein SD, Holland S, Freitag F, et al. Neurology. 2012;78(17):1337-1345. doi:10.1212/WNL.0b013e3182535d20
6. Migraine: Acute & Chronic Therapies. ICER. Accessed March 21, 2025. <https://icer.org/assessment/migraine-2018/>
7. Ashina M, Saper J, Cady R, et al. Cephalalgia. 2020;40(3):241-254. doi:10.1177/0333102420905132
8. Burch R, Rizzoli P, Loder E. Headache. 2018;58(4):496-505. doi:10.1111/head.13281
9. Jönsson L, Regnier SA, Kymes S, et al. Expert Review of Pharmacoeconomics & Outcomes Research. 2023;23(7):797-803. doi:10.1080/14737167.2023.2219898
10. A Comparison of Brand-Name Drug Prices Among Selected Federal Programs | Congressional Budget Office. February 18, 2021. Accessed March 27, 2025. <https://www.cbo.gov/publication/57007>
11. Freitag FG, Collins SD, Carlson HA, et al. Neurology. 2002;58(11):1652-1659. doi:10.1212/WNL.58.11.1652
12. Ahmed Z, Honomichl R, Thompson SF, et al. Headache: The Journal of Head and Face Pain. 2023;63(7):908-916. doi:10.1111/head.14527

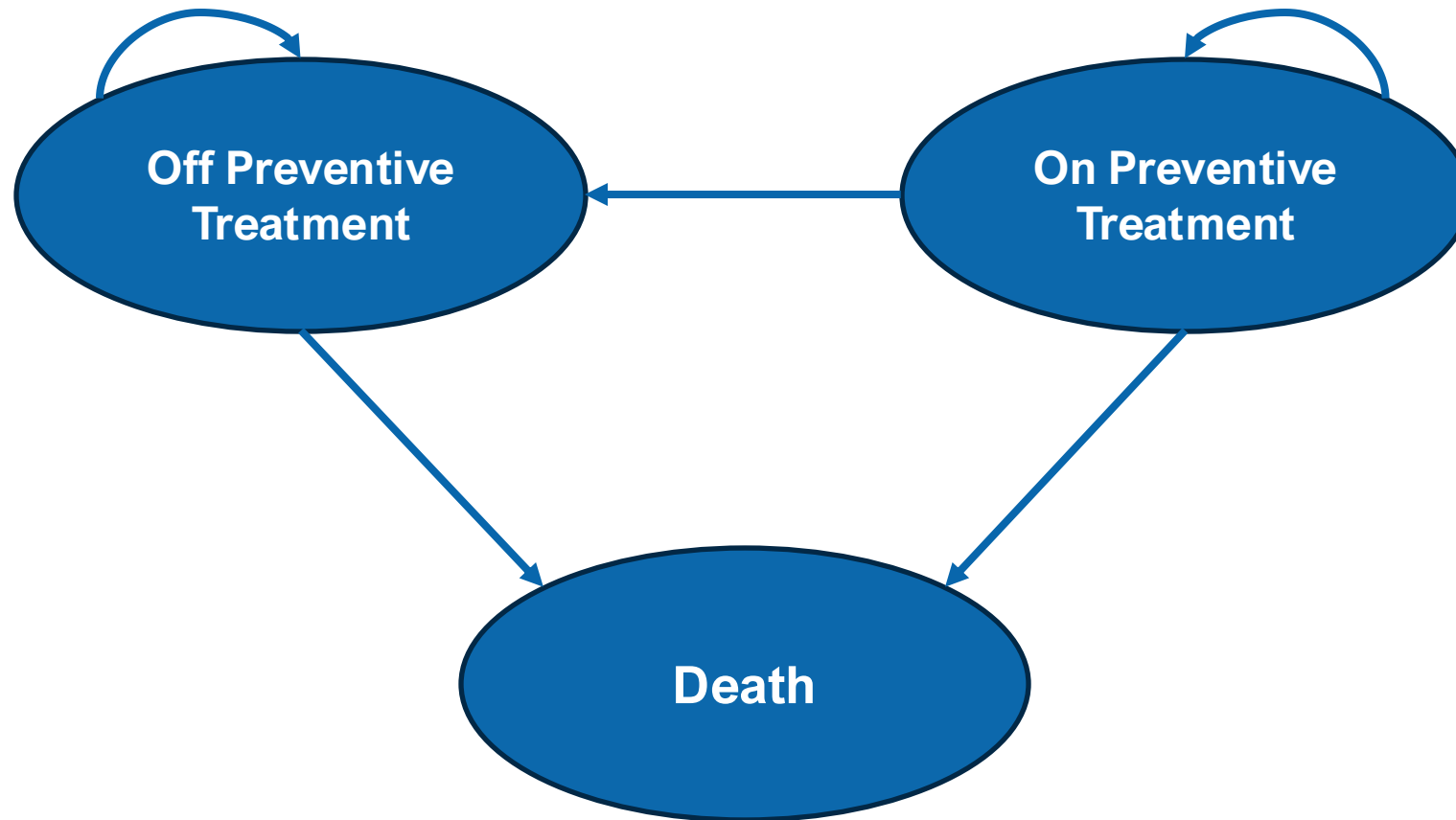
Appendix: Base-case Medical Expenditures

Strategy	Total costs	Medical resources expenditures	QALYs	Reduction of medical resources expenditures
Divalproex ER	\$41,938	\$41,329	5.61	
Eptinezumab	\$53,904	\$34,948	5.79	15.4%
Erenumab	\$59,129	\$34,577	5.72	16.3%

Appendix: Decision Tree Model



Appendix: Markov Model



Appendix: Parameters

Parameters	Value	Low Range	High Range	Distribution	Sources
Decision Tree Parameters					
Probability of achieving 50% reduction in MMD on first 6 months of divalproex	0.51	0.4335	0.5865		Freitag et al.
Probability of achieving 50% reduction in MMD on first 6 months of eptinezumab	0.75	0.6375	0.8625		PROMISE-1
Probability of achieving 50% reduction in MMD on first 6 months of erenumab	0.64	0.544	0.736		ARISE
Markov Model Parameters					
Discontinuation Rate of divalproex ER	0.0028	0.00238	0.00322	Beta	Freitag et al.
Discontinuation Rate of divalproex ER	0.0091	0.00774	0.0105	Beta	PROMISE-1
Discontinuation Rate of erenumab	0.0055	0.00468	0.00633	Beta	ARISE
Mortality	US 2021 Life Table				

Appendix: Parameters Table

Parameters	Value	Low Range	High Range	Distribution	Sources
Costs					
Divalproex ER	\$12.1	\$10.3	\$14.0	Gamma	VA FSS
Eptinezumab	\$529	\$449.28	\$607.84	Gamma	VA FSS
Erenumab	\$671	\$569.95	\$771.11	Gamma	VA FSS
Utility					
Baseline	0.05361	0.04557	0.06165	Beta	Jonsson et al. PROMISE-1
Divalproex ER	0.05622	0.04779	0.06465	Beta	Jonsson et al. Freitag et al.
Eptinezumab	0.05968	0.05073	0.06863	Beta	Jonsson et al. PROMISE-1
Erenumab	0.05811	0.04939	0.06683	Beta	Jonsson et al. ARISE

Appendix: Methods

- Statistical Analysis
 - Cost and outcomes were discounted at 3% per year
 - Expected total cost and quality-adjusted life years (QALYs) were estimated
 - **ICER and incremental net monetary benefit at WTP threshold of \$150,000 per QALY gained were calculated**
- Uncertainty Analyses
 - **One-way sensitivity analysis:** cost, utility scores on treatment, discontinuation rates, and probabilities of achieving 50% reduction in MMDs were modified
 - **Probabilistic sensitivity analysis:** 10,000 Monte Carlo simulations (cohort simulation)
 - Beta distributions for probabilities and utility values
 - Gamma distributions for cost values
 - CEAC was generated to estimate the probability of the strategies being cost-effective across various WTP thresholds

Appendix: Model Validation

- Internal model validation was performed
- Erenumab has an ICER of **\$395,000** per QALY gained compared to other first-line preventive treatments according to the study done by Institute for Clinical and Economic Review⁶
- Mortality in episodic migraine patients
 - Retrospective cohort study showed that there is no evidence for a higher all-cause mortality of EM patients compared to the natural population¹²

6. Migraine: Acute & Chronic Therapies. ICER. Accessed March 21, 2025. <https://icer.org/assessment/migraine-2018/>

12. Ahmed Z, Honomichl R, Thompson SF, et al. Headache: The Journal of Head and Face Pain. 2023;63(7):908-916. doi:10.1111/head.14527