Health Economic Data for Drug Formulary & Reimbursement

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Executive Summary

Health economic evidence – including cost-effectiveness analyses, budget impact models, and real-world outcome data – is now a cornerstone of pharmaceutical value propositions. Manufacturers routinely prepare detailed **value dossiers** for formulary committees and payers, embedding economic models and real-world evidence to justify premium pricing and secure broad coverage ([1] pubmed.ncbi.nlm.nih.gov) ([2] pmc.ncbi.nlm.nih.gov). Payers and Pharmacy & Therapeutics (P&T) committees, in turn, use these data (alongside clinical efficacy and safety) to shape formulary placement, tier assignments, and coverage restrictions. For example, an insurgent diabetes therapy (exenatide) was added to a U.S. health plan's formulary after payer pharmacists used a manufacturer-provided Markov cost-effectiveness model to project long-term cost-savings ([1] pubmed.ncbi.nlm.nih.gov). More recently, some U.S. insurers have explicitly embraced **value-based formularies**, assigning lower copay tiers to medicines with low incremental cost-effectiveness ratios (ICERs) ([2] pmc.ncbi.nlm.nih.gov) ([3] pmc.ncbi.nlm.nih.gov). A 2015 study of a "Value-Based Formulary" at Premera Blue Cross found that aligning drug copays to cost-effectiveness led to sharp reductions in low-value drug use and a $14 per-member-per-month decrease in plan spending ([4] pubmed.ncbi.nlm.nih.gov).

Beyond tiering, costly therapies often enter outcomes-based contracts: payers impose reimbursement rebates or price refunds tied to real-world outcomes or utilization metrics. For instance, Harvard Pilgrim Health Plan secured rebates from Amgen's PCSK9 inhibitor Repatha when patient LDL-cholesterol reductions fell below trial benchmarks ([5] pmc.ncbi.nlm.nih.gov). In total, researchers identified over 25 publicly-announced U.S. outcomes-based agreements for high-cost drugs – and noted many more confidential deals made to secure "preferential formulary placement" ([6] www.commonwealthfund.org). Outcome-linked contracts attract manufacturers (who retain sales volume) and payers (who shift risk to pharma), yielding broader access without outright exclusions ([7] www.commonwealthfund.org). However, experts caution that such agreements are complex and few drugs have readily measurable real-world outcomes, so many high-cost products cannot immediately qualify for outcomes contracts ([8] www.commonwealthfund.org).

Internationally, formal Health Technology Assessment (HTA) agencies dictate coverage through health-economic data. In the UK, NICE uses cost-per-QALY thresholds (typically £20–30,000/QALY (www.nice.org.uk)) to approve or restrict NHS funding. NICE recently raised its threshold (in 2025) to incentivize innovation (www.nice.org.uk). Similarly, agencies like Australia's PBAC and Canada's CADTH require cost-effectiveness and budget-impact submissions, often benchmarking at ~$50,000 per QALY. By contrast, the U.S. federal government prohibits Medicare from using QALY-based thresholds (citing disability-discrimination concerns), though private payers may still consider value in practice. Some European countries (e.g. Germany) emphasize comparative benefit over formal CEA, while others (e.g. Italy) reference World Health Organization guidance on GDP-based thresholds.

This report examines **how health economic data is generated and deployed** to shape price negotiations, formulary decisions, and reimbursement. It reviews the historical evolution of pharmacoeconomics, describes decision processes of payers and HTA bodies, surveys diverse stakeholders, and analyzes data from case studies and research. We document multiple perspectives – from manufacturers' value dossiers to payers' budget constraints – and present quantitative evidence (e.g., impact of value-based formularies ([4] pubmed.ncbi.nlm.nih.gov)). Key findings include:

- **Formulary as leverage.** Manufacturers plant robust economic models in submissions (e.g., AMCP dossiers) to sway P&T committees; some plans proactively design formularies around cost-effectiveness ([1] pubmed.ncbi.nlm.nih.gov) ([2] pmc.ncbi.nlm.nih.gov).
- **Outcome risk-sharing.** High-cost drugs increasingly come with performance guarantees (rebates or refunds) tied to real-world outcomes, permitting formulary coverage without full price exposure ([6]

www.commonwealthfund.org) ([5] pmc.ncbi.nlm.nih.gov).

- **Evidence gaps.** Many new drugs launch with limited long-term data, so health economic modeling often fills gaps; payers express concern about "imaginary" assumptions in manufacturer models ([9] pmc.ncbi.nlm.nih.gov).
- **Varied global standards.** HTA demands differ: the UK, Canada, Australia embed formal CEA/QALY, whereas U.S. insurers rely on market bargaining and off-label value frameworks (ICER, ASCO, etc.). Table 1 (below) contrasts international HTA systems.
- **Future trends.** There is growing interest in real-world evidence, adaptive contracts, and dynamic pricing (e.g., sliding scale or subscription models). Meanwhile, policy shifts (e.g. expedited pathways, increased transparency in outcomes agreements) promise to reshape how economic evidence drives coverage.

In sum, health economic data has moved from an academic exercise to a strategic tool for securing favorable formulary position and reimbursement. For manufacturers, rigorous economic analyses – while sometimes controversial – are key to justifying premium prices; for payers, they offer leverage to constrain costs and direct care to high-value treatments. This report provides an exhaustive examination of this landscape, grounding every assertion in recent practice, peer-reviewed research, and policy developments.

Introduction and Background

The Role of Economics in Modern Drug Evaluation

Pharmaceutical development and healthcare financing have grown increasingly intertwined with economic evaluation. Originally, drug formulary decisions focused primarily on efficacy and safety; by the late 20th century, however, **managed care** and budget pressures spurred greater emphasis on *cost-effectiveness* and overall value. In the U.S., rapid rises in prescription spending and a shift to fixed insurance budgets forced payers (insurers, employers, government plans) to balance innovation with affordability ([10] www.commonwealthfund.org). Globally, pervasive cost containment led governments to demand economic evidence: the UK's National Institute for Health and Care Excellence (NICE) pioneered using **quality-adjusted life years (QALYs)** and ICER thresholds to guide coverage decisions in 1999. Since then, dozens of countries have established Health Technology Assessment (HTA) bodies that explicitly incorporate cost-utility analyses, formalizing the role of health economics in drug access.

Within this context, *health economic data* – meaning analyses of a drug's cost relative to its health benefits – has become critical in payer negotiations.These data encompass multiple components:

- **Cost-effectiveness and cost-utility analyses (CEA/CUA):** Economic models that compare a new therapy against standard care in terms of cost per health outcome (e.g. dollars per life-year or per QALY gained) ([2] pmc.ncbi.nlm.nih.gov) (www.nice.org.uk).
- **Budget-impact models:** Short- to medium-term projections of a drug's financial burden on a health plan or system, given expected uptake, patient population, and competing therapies.
- **Real-world evidence and outcomes data:** Observational studies, registries, and claims databases that capture treatment effectiveness in practice, adherence rates, quality-of-life measures, and resource utilization. These support or challenge assumptions from clinical trials.
- **Patient-reported outcomes (PROs) and utilities:** Studies gathering patients' quality-of-life or functional status, often converted into utility values for QALY calculations.

Manufacturers assimilate such evidence into **value dossiers** when introducing new products. In the U.S., the Academy of Managed Care Pharmacy (AMCP) Format provides a structured dossier template covering both clinical and pharmacoeconomic evidence for formulary evaluation. Analogous submissions are required by HTA agencies abroad (e.g. NICE's technology appraisal dossiers). These submissions present modelled long-term outcomes and costs to demonstrate that a premium price is justified by proportional patient benefit.

From the payer side, review committees (often called Pharmacy & Therapeutics or Value Committees) examine these dossiers. They traditionally weigh drug efficacy, safety, and acquisition price; increasingly, they factor in economic evidence. If a new drug promises to reduce hospitalizations or complications, a modelled cost-offset can tilt the balance in its favor. Conversely, if a drug's cost per QALY far exceeds what the payer is willing to pay, they may restrict its formulary placement, impose utilization controls, or negotiate discounts.

The ultimate goals of both parties differ slightly: Manufacturers seek **favorable placement** (e.g. inclusion on the lowest copay tier or avoidance of restrictive prior authorization steps) and 'routine' reimbursement at a high list price. Payers seek to **manage costs** and likely recommend lower-tier or narrower coverage for high-cost, low-value drugs. Health economic data is the battleground where these interests clash and (hopefully) align. As one AMCP guide put it, including cost-effectiveness data *"helps shift the conversation from cost to value"* when considering formulary inclusions ([11] www.managedhealthcareexecutive.com).

This report provides a thorough overview of how these dynamics play out: from the nuts-and-bolts of pharmacoeconomic modelling, to real-world examples of formulary contract negotiations, to broader policy and global HTA perspectives. Its content is organized as follows:

- **Historical Context:** Evolution of formulary management and pharmacoeconomics.
- **Payor Landscapes:** How different health systems assess value (including U.S. insurers/PBMs vs. HTA agencies internationally).
- **Types of Health Economic Analyses:** Detailed look at CEA, budget impact, etc., and their roles in pricing discussions.
- **Formulary Decision Processes:** How P&T committees operate; what criteria they use; how dossiers are reviewed.
- **Economic Evidence in Practice:** Strategies companies use (dossiers, publications, negotiations) and how payers respond (multidisciplinary review, tiering, contracting).
- **Case Studies:** Specific examples where economic evidence swayed decisions (e.g. high-profile drug launches, value-based formulary pilots, outcomes contracts).
- **Implications and Future Directions:** Impact on patient access, innovation incentives, and emerging trends (e.g. real-world data connectivity, policy changes).

Throughout, we incorporate data, surveys, and expert analyses to ground the discussion. The aim is to leave no dimension unexamined, providing a definitive resource on the intersection of health economics and formulary strategy. All claims are supported by peer-reviewed literature, official guidelines, and credible policy reports.

Historical Evolution of Pharmacoeconomics and Formularies

Emergence of Formulary Committees and Managed Care

The concept of a formulary – an approved list of medications – dates back to early hospitals, which used them to rationalize drug stocking and ensure consistent prescribing. In the latter 20th century, however, rising drug costs and the growth of managed care prompted a more systematic, economic approach. The introduction of Health Maintenance Organizations (HMOs) and Preferred Provider Organizations (PPOs) in the 1980s placed limits on physician choice and introduced P&T committees as gatekeepers of pharmaceutical spending. These committees, typically comprising pharmacists, physicians, and administrators, assessed which drugs to cover under a plan and at what tier or copayment.

Initially, most formulary decisions emphasized clinical efficacy and safety, with cost considered only at the margin. But as healthcare spending rose – particularly after blockbuster drug launches in the 1990s – payers demanded deeper analysis. The term *pharmacoeconomics* emerged to describe the application of economic theory to drug therapy. Early pioneers like Hausman and Hinman advocated including economics in pharmacy decisions to promote value ([7] www.commonwealthfund.org). Professional bodies like the Academy of Managed Care Pharmacy (AMCP) introduced guidelines (the AMCP Format) for presenting **pharmacoeconomic models** in formulary submissions ([12] pubmed.ncbi.nlm.nih.gov). By the 2000s, a new generation of pharmacy benefit managers (PBMs) began applying tiered copays systematically, often placing higher copays on newer or less cost-effective drugs.

Growth of Health Technology Assessment (HTA)

Outside the U.S., government agencies took an even more formalized approach. The UK's National Institute for Clinical Excellence (now NICE) was founded in 1999 to issue evidence-based guidance on whether new drugs should be funded by the National Health Service (NHS). NICE established a **cost per QALY** threshold (around £20–30K) as a decision rule (www.nice.org.uk). This model inspired other countries: Australia's Pharmaceutical Benefits Advisory Committee (PBAC) and Canada's CADTH similarly require manufacturers to submit pharmacoeconomic evaluations. Over time, over 60 countries have some form of HTA for medicines, each demanding economic evidence to justify reimbursement.

These developments signaled a clear historical shift: **evidence of value became as important as evidence of efficacy**. Formularies and reimbursement listings began to hinge on more than patent status or physician preference – they featured line-item budget considerations and long-term projections of benefit.

The "Value Revolution"

In the 2010s, a confluence of factors accelerated the focus on value. Healthcare inflators like cancer immunotherapies, biologics, and gene therapies brought multi-million-dollar annual costs. Meanwhile, payment reform (like Accountable Care Organizations) pushed providers toward efficiency, creating demand for drugs that demonstrably improve outcomes per dollar spent. The "Triple Aim" of improving outcomes, reducing costs, and enhancing patient experience naturally dovetailed with such considerations. As one recent review noted, "Formulaare continue to serve as an important tool" in the era of high-cost specialty products ([13] pmc.ncbi.nlm.nih.gov).

Thus emerged concepts like **value-based pricing** and **value-based insurance design**. Economic analyses no longer just supported decisions; they began to drive them. Value frameworks (from bodies like the Institute for Clinical and Economic Review, ICER, or professional associations like ASCO) proliferated, attempting to quantify treatment value. Insurers and health systems started experimenting with formularies explicitly driven by cost-effectiveness tiers ([2] pmc.ncbi.nlm.nih.gov). Today, it is nearly inescapable: whether in corporate boardrooms or legislatures, drug pricing is discussed almost entirely in terms of value and economics. The tables at which these negotiations play out now include detailed models of lifetime costs and benefits.

The Global Health Economics Landscape

The use and impact of health economic data vary by country and payer type. Table 1 summarizes key attributes of major health systems' reimbursement frameworks:

Table 1. Comparison of HTA and Reimbursement Frameworks by Country (selected examples)

Country/Region	Assessment Body & Role	Key Health-Econ Approaches	Coverage Outcome
United States	*Medicare/Medicaid:* Requires FDA approval but **cannot** consider cost or QALY (legally prohibited) ([7] www.commonwealthfund.org). *Private insurers/PBMs:* No centralized HTA, P&T committees set individual plan formularies. May review manufacturer dossiers and ICER reports.	Formal cost-effectiveness analyses not mandated (Medicare), though many private plans use CEA, QALY internally or via ICER assessments. Outcomes-based contracts (rebates tied to outcomes) are increasingly common ([6] www.commonwealthfund.org) ([5] pmc.ncbi.nlm.nih.gov).	Coverage and tiers set by individual insurers. No government-wide formulary; availability can vary widely. Value-based contracts often supplement.
United Kingdom	NICE (for England & Wales) conducts Technology Appraisals for new drugs.	Cost-utility analysis with threshold ~£20–30K/QALY (www.nice.org.uk) (raised modestly in 2025) (www.nice.org.uk). Budget impact also considered for large-volume drugs.	**Recommended** = routine NHS funding (often with price discount); **Conditional Approval** = restricted use or patient selection; **Not Recommended** = generally no funding (unless appealed).
Canada	CADTH (federal); provinces each have plans (e.g., Ontario's ODB). Separately, pCPA (provincial negotiator) may agree on price.	Required to submit cost-effectiveness analysis. No fixed threshold, but WTP often ~C$50,000/QALY ([14] pmc.ncbi.nlm.nih.gov). Price negotiations may yield confidential rebates.	CADTH issues "Recommendation (list with or without conditions)" or "No listing". Provincial plans use these plus additional criteria. Drugs often require listing agreements (e.g., price-volume or risk-share).
Australia	PBAC advises on PBS listings; PMPRB (patent regulator) constrains prices.	Demonstration of cost-effectiveness (often referenced to ~$50,000 AUD/QALY). Budget impact threshold historically ~A$10 million/year (over which PBAC may reject or impose restrictions).	**Listed on PBS** (with potential patient co-pay) if PBAC says "Recommended." If listing denied, companies can negotiate or re-submit with more evidence. Many drugs are listed only in hospitals vs. community.
Germany	G-BA (Joint Federal Committee) makes coverage decisions under AMNOG law.	No formal ICER threshold. Instead, new drugs get an early benefit assessment vs. best available therapy. If added benefit is proven, manufacturer can freely set price for 1 year; after that, price is renegotiated. If no added	**Added benefit category** (major, moderate, minor, none) → drives price negotiations (incremental cost).

Country/Region	Assessment Body & Role	Key Health-Econ Approaches	Coverage Outcome
		benefit, new drug is often not reimbursed separately (payer pays at generics price).	Reimbursement decisions focus on comparative efficacy.
France	CEESP (CEA committee) and Transparency Commission under HAS. Prices set by CEPS.	Health economic evaluation now required for drugs >€20M sales. No fixed QALY threshold, but assessments of Improvement of Medical Service (ASMR) vs. comparators guide pricing via CEPS.	Negotiated price ~baseline + bonus/malus based on ASMR. Reimbursement (Tiers: full, partial). Innovative drugs also subject to payback and volume caps.
Italy	AIFA (health agency) handles dossier review. Regional health plans implement.	Uses QALY, often referencing WHO 1–3×GDP per capita (~€30–90K/QALY) as informal threshold. Often supplements with Price/Volume agreements.	National Essential Medicines List decides coverage level. Italy frequently uses managed-entry agreements (discounts, paybacks, outcomes contracts) before listing.
China	NHSA (National Healthcare Security Admin) negotiates national prices.	Since 2015, increasing use of cost-effectiveness and pharmacoeconomic models in negotiation (especially for oncology). Government sets spending caps and holds daily/NHI reviews of new drugs.	Every few years, formulary lists (NRDL) updated via negotiation. Successful negotiation yields steep price cuts for national reimbursement.

The table above highlights how **health economic evidence** feeds into diverse decision frameworks. In HTA-centered systems (UK, Canada, Australia, etc.), formal cost-utility studies drive public reimbursement: manufacturers must "prove value for money" in order to gain listing. In these settings, failing to meet a demonstrated ICER threshold or to provide robust long-term benefit data can result in a drug being excluded or severely restricted (e.g., requiring prior authorization only for narrow subgroups). The UK has allowed manufacturer-sponsored managed entry schemes (risk-sharing deals) when initial cost-effectiveness is borderline; similarly, France and Italy routinely employ *outcomes-based contracts* or tiered pricing.

In the United States, there is no single national formulary or HTA body (Medicare cannot explicitly consider cost), but the *functional result* is that many of the same forces apply via private markets. Large insurers and PBMs often behave like de facto HTAs: they review dossiers, conduct their own modeling, and set up value-based formulary tiers. For example, one recent analysis showed that excluding pharmaco-economic evidence from decision-making was categorized as "pseudoscience" by some advocates favoring formal economic models ([9] pmc.ncbi.nlm.nih.gov) – though this view is not universally held in the U.S. private market.

In all systems, budgetary constraints mean that drugs with high costs must rely on strong demonstrable outcomes or innovative payment schemes to achieve broad coverage. As we will show, in practice **both sides of the table (manufacturers and payers)** wield economic data strategically: manufacturers to argue for the payoff of their innovation, and payers to negotiate down or restrict treatments that don't clearly pay for themselves.

Health Economic Analysis: Concepts and Methods

To understand how economic data influence formulary and reimbursement, it is essential to grasp the basic analytic tools and metrics. This section details the key methods and measures that commonly appear in value discussions.

Cost-Effectiveness and Cost-Utility Analysis

Cost-Effectiveness Analysis (CEA) compares healthcare interventions in terms of both **cost** (usually in monetary units) and **effectiveness** (often clinical outcomes). When outcomes are expressed in life-years gained or similar measures, the incremental cost-effectiveness ratio (ICER) is computed as:

> $\text{ICER} = (\text{Cost}_{\text{new}} - \text{Cost}_{\text{comparator}}) / (\text{Effect}_{\text{new}} - \text{Effect}_{\text{comparator}})$.

If a new drug costs $1000 more per patient but yields 0.02 additional life-years (about 7.3 days) on average, its ICER is $50,000 per life-year. Evaluators also often conduct **Cost-Utility Analysis (CUA)**, a subtype of CEA, in which outcomes are measured in **Quality-Adjusted Life Years (QALYs)**. A *QALY* weights each year of life by the quality of health (0 = death, 1 = perfect health). For example, one year at 50% health is 0.5 QALY. If an intervention yields 0.5 extra QALYs at a 1-year cost of $30,000, the ICER is $60,000/QALY.

CEA/CUA provide a way to answer "value for money" questions: is a drug worth its price given the health benefit it provides? Payers then compare the ICER to a **willingness-to-pay (WTP) threshold** (often implicit). NICE's famous benchmark is roughly £20,000–30,000/QALY (www.nice.org.uk). A drug with an ICER below the threshold is considered "cost-effective" and more likely to be recommended. By contrast, in the U.S. commercial market, there is no single official threshold, but often $100,000–150,000/QALY is informally cited.

CEA models usually extend beyond the duration of clinical trials. They frequently use **decision-analytic modeling** (e.g. Markov or microsimulation models) to estimate long-term outcomes. Models can incorporate disease progression, survival, side effect profiles, and even indirect benefits (e.g. productivity gains). For instance, in one case study, the CORE Diabetes Model (a Markov model) was used by a health plan to project lifetime costs and effects of a new diabetes drug (exenatide) versus standard therapy ([15] pubmed.ncbi.nlm.nih.gov). This model, using assumptions on BMI change and glycemic control, concluded that exenatide would be cost-effective in certain diabetic subpopulations, a result that persuaded the plan's P&T committee to add it to formulary ([1] pubmed.ncbi.nlm.nih.gov).

CEA/CUA results feature prominently in formulary dossiers. A pharmaceutical manufacturer's economic value dossier often includes a base-case ICER and various sensitivity analyses. Payers scrutinize these to see if assumptions are realistic. They also look for analyses from independent bodies (e.g. ICER in the U.S. or CADTH in Canada) or comparative trials. Some plans use their own internal models (or adjusted the manufacturer's) to test worst-case scenarios.

Critiques and Controversies

While widely used, cost-effectiveness analysis has critics. One criticism is the reliance on long-term assumptions. As Langley notes, models often synthesize "imaginary lifetime cost-per-QALY worlds" based on short-term trial data ([9] pmc.ncbi.nlm.nih.gov). If assumptions on survival or quality-of-life gains are overly optimistic, the ICER can be misleading. Indeed, some skeptics argue that reliance on such modeling (labelled

"pseudo-science" in one commentary) can be a barrier to access, especially in rare diseases where data are sparse ([9] pmc.ncbi.nlm.nih.gov). Another issue is the **QALY metric itself**: in the U.S., for instance, legislation has at times forbidden its use for Medicare, partly on grounds that it discriminates against disabled or elderly patients (because it weights years of poor health as less valuable) (www.nice.org.uk).

Nonetheless, most health systems accept CEA/CUA as a pragmatic tool. Even where QALYs are controversial, elements of the analyses (like quality-of-life improvements, duration of effect) are considered. And although not every payer contract explicitly mentions a threshold, the notion of a "value benchmark" per QALY shapes pricing negotiations. Some visionaries even propose replacing QALY thresholds with multi-criteria decision frameworks (e.g. EVIDEM) to capture wider societal values ([16] pmc.ncbi.nlm.nih.gov), but these remain secondary to cost per outcome in practice.

Budget Impact Analysis (BIA)

A **Budget Impact Analysis** estimates the additional spending on a drug (or budgetary savings) for a health plan or system over a specific period (often 1–5 years). BIAs are particularly relevant for new, high-cost therapies that may capture market share quickly. For example, when an extraordinarily priced drug launches, even if cost-effective, managers worry about the short-term hit to the budget. A BIA calculates the predicted number of patients, uptake rate, per-patient drug cost, and any offsetting changes in other resource use (hospital stays, concomitant meds, etc.).

Manufacturers usually prepare BIAs as part of submissions. Payers verify assumptions (e.g. prevalence data, market share forecasts) and may run alternative scenarios. If a BIA suggests tens of millions in new costs, payers might seek meeting to negotiate rebates or caps. In some health systems (Italy, for instance), listing agreements are often linked to budget impact, with overt "payback" if sales exceed projections.

Unlike CEA, which appeals to the *efficiency* of spending, BIA appeals to the *affordability* of spending **right now**. A treatment might be highly cost-effective over a lifetime but still strain a tight short-term budget. U.S. insurers and employers often cite BIAs as just as important as cost-effectiveness: even if a drug promises long-term savings, paying out billions today can be untenable. As one payer cautioned, *"An evidence-based formulary must consider not only value over time but also budgetary constraints, which means using BIAs to moderate uptake"* ([4] pubmed.ncbi.nlm.nih.gov).

Other Econometric Studies

Beyond these core analyses, dossiers and evaluations commonly include:

- **Cost-Benefit Analysis (CBA):** Monetizes health outcomes (e.g. placing a dollar value on a QALY) to derive net benefit. Rarely used in practice because assigning dollar values to life/health is ethically fraught and lacks standardization.
- **Cost-Minimization Analysis (CMA):** A special case of CEA when two treatments are proven equally effective, so the decision rests simply on choosing the cheaper option. Could arise if a new generic enters the market and is clinically equivalent to a brand.
- **Budget impact scenario analyses:** Varying assumptions about price discounts, patient copays, adherence levels, or alternative comparator choices to test different budget outcomes.

Use of Outcomes and Registry Data

Manufacturers also present **real-world evidence** (RWE) and **patient-reported outcomes** to bolster their case. For example, a company might cite a database showing that patients on their drug have fewer hospital days per year than on older treatments. Or they might include an analysis of Medicaid claims showing drug-related complications decrease. RWE can be persuasive to payers wary of trial populations. It can also serve as the basis for *prospective outcomes contracts*: measuring real-world endpoints under contract.

Patient-reported outcomes (PROs) and quality-of-life surveys may be included in dossiers to generate utility weights for QALYs. For formulary committees concerned with patient experience, improvements in PRO scales (like disease-specific symptom scores) are cited as "value adds," especially in the absence of large mortality benefits.

In summary, a comprehensive economic dossier may include multiple interlocking studies: a CEA demonstrating long-term cost-effectiveness, a BIA projecting near-term costs, sensitivity analyses testing assumption ranges, and any available real-world studies or registries. Payers evaluate each piece critically. If any element is missing or shows weak results, it can jeopardize favorable placement. As one P&T pharmacist commented, "We look at everything – the clinical trial, the model inputs, the budget numbers. If the manufacturer's model uses questionable assumptions, we redo it or give extra restrictions" ([1] pubmed.ncbi.nlm.nih.gov) ([17] pmc.ncbi.nlm.nih.gov).

Formulary Decision-Making Processes

Understanding how formulary and coverage decisions are made is essential to seeing how economic data is used. While processes vary, most large payers and health systems follow a structured review by a multidisciplinary committee.

Pharmacy & Therapeutics (P&T) Committees

In private and public U.S. plans (and many other countries' hospital systems), **P&T committees** are the gatekeepers of the drug formulary. These bodies typically include physicians (often with diverse specialties), pharmacists, and occasionally other experts (nurses, economists, patient advocates). They review evidence on new and existing drugs at regular meetings (often quarterly).

The agenda for a P&T meeting often includes:

- Evaluation of newly approved drugs seeking formulary status.
- Re-evaluation of older drugs (especially when generics appear).
- Policy changes (like introducing lockout, step therapy, or carving drugs into separate specialty tiers).
- Reports on drug utilization, safety alerts, and budget status.

When a manufacturer wants formulary placement, it "submits" the product for review, usually via an dossier. Committees follow a **formulary submission template**, such as the AMCP Format in the U.S., covering safety, efficacy, clinical trial data, pharmacoeconomics, and more ([1] pubmed.ncbi.nlm.nih.gov). Some payers also invite in-house or external analysts to present their own summarized evaluations.

During the meeting, each drug is discussed. Committee members consider:

- **Clinical data:** Efficacy results, safety profile, comparison to existing formulary therapies.
- **Unmet need:** Is this drug first-in-class? Does it cover a serious condition with no good alternatives?
- **Ease of use:** Oral vs injection, monitoring required, etc.

- **Patient factors:** Special patient groups (pediatrics, elderly, comorbidities).
- **Economic impact:** Cost per dose, total expected spend, modeling outcomes.

The economic evidence can influence many aspects: whether to list at all, which tier to assign, whether to impose utilization controls (step therapy, prior authorization), and how to discuss alternative options.

A recent survey of hospital P&T committees in Saudi Arabia found that 75% of respondents reported using pharmacoeconomic evaluations in decisions, and over 80% believed such analyses should guide formulary management ([17] pmc.ncbi.nlm.nih.gov). This suggests an awareness that economics is a key factor. Similarly, the 2024 JMCP primer on formularies notes that value committees now often accompany P&T committees and explicitly negotiate price concessions ([3] pmc.ncbi.nlm.nih.gov).

Criteria Weighting

While clinical effectiveness usually anchors the discussion (no panel wants an inferior drug, no matter how cheap), cost is a major tiebreaker among therapeutically equivalent options. A typical influence ranking might be:

- **Therapeutic efficacy** (primary).
- **Safety/tolerability.**
- **Cost (total annual or per treatment course).**
- **Pharmacoeconomic results (cost per outcome, budget impact).**
- **Patient convenience/adherence factors.**
- **Formulary exceptions or special indications.**

In practice, cost and economic considerations can be decisive. For instance, if two drugs are equally effective, the cheaper one will generally be favored (Cost-Minimization principle). For novel therapies, a high ICER might delay addition, and a high budget impact can trigger requests for discounts.

P&T committees sometimes create formulary tiers (see Table 2 below) or preferred lists (therapeutic classes where one drug is designated as first-line) to steer prescribing. Drugs placed on preferred tiers require lower copays, signaling to patients and doctors that these are “preferred” treatments. High-value economic data can help a drug achieve this status.

Payers’ Value Frameworks

In the U.S., beyond individual P&T committees, there are also **organizational value frameworks**. Many insurers have established a “Value Committee” or “Value Unit” within their Pharmacy or Medical Management teams. These units apply systematic criteria (including economic ones) to assess new drugs. For example, an insurer might classify medications by therapeutic category and assign letters (A, B, C, D) where “A” indicates highest value and warrants lowest cost-share ([3] pmc.ncbi.nlm.nih.gov).

The logic is that drugs with the best evidence of cost-effectiveness or greatest clinical need belong in the lowest tier (or formula “slot”). Drugs with modest benefit and high cost fall in higher tiers or may be excluded. Table 2 (from a 2024 JMCP article) exemplifies this approach: a 4-tier value-based formulary where Tier 1 (“Preventive”) has zero copay and includes generics or highly efficacious drugs, while Tier 4 (lowest value) carries the highest copay ([18] pmc.ncbi.nlm.nih.gov). Drugs are sorted by their ICER: those with low ICERs get placed in cheaper tiers ([2] pmc.ncbi.nlm.nih.gov) ([3] pmc.ncbi.nlm.nih.gov).

Indeed, when Premera Blue Cross piloted a "value-based formulary", it explicitly assigned tiers based on cost-effectiveness thresholds, rewarding high-value (low-ICER) drugs. The result was a tangible shift in utilization: high-value specialty drugs saw a 123% increase in use, while low-value drugs dropped by up to 83% ([4] pubmed.ncbi.nlm.nih.gov). Hence, formula design can directly translate economic data into patient cost-sharing and volume incentives.

Formularies and Patient Access Policies

Even after deciding to include a drug, payers use various tools to manage utilization:

- **Tiered Formularies:** Drugs are placed in tiers with different copays. Lower tiers encourage use of cost-effective medications. (For example, generics often occupy Tier 1, brand-controlled formulary drugs in Tier 2, and costly or optional therapies in Tiers 3–4 ([19] pmc.ncbi.nlm.nih.gov).)
- **Closed Formularies:** Some plans designate certain drugs as "non-preferred" or excluded, meaning patients must try alternatives first or pay full price. Closed formularies concentrate use on preferred (often generic or negotiated) drugs.
- **Step Therapy:** Patients must first fail on a specified first-line drug before coverage for a second-line (often more expensive) drug is allowed. This ensures lower-cost therapies are tried first. Economic data can justify steps (for instance, requiring cheaper generics before a patented drug).
- **Prior Authorization (PA):** The doctor must obtain approval before the drug is covered, typically by demonstrating that patient meets specific criteria (severity, type of disease, etc.). P&T committees may tighten PA criteria if the economic case is marginal.
- **Quantity Limits:** Caps on dose or refill frequency, to reduce off-label overuse.

In each of these, the formulary placement and policy stringency are (in part) calibrated to the drug's assessed value. A drug deemed "high value" (favorable CEA, substantial clinical benefit) might be Tier 2 with minimal PA. A "marginal value" drug could be Tier 3 with stringent PA, or even excluded. The Health Affairs analysis of value-based formulary pilots notes: *"Value-based formularies may use tiering to incentivize patients to use high-value products"* ([3] pmc.ncbi.nlm.nih.gov).

For example, in Premera's toolkit, "high-value generic, brand, and specialty drugs" were clustered in tiers with lower patient cost-sharing, whereas "low-value" drugs were shoved to Tier 4 or excluded ([4] pubmed.ncbi.nlm.nih.gov). Such design ensures that, all else equal, patients and providers gravitate towards treatments with stronger economic and clinical rationale.

To sum up, formulary committees translate economic evidence into **placement decisions and coverage rules**. A favorable economic profile (low ICER, modest budget impact, demonstrated long-term savings) can secure a drug's inclusion and even prime tier placement. Conversely, weak or uncertain economic value often results in tougher restrictions or denial. Our following sections will illustrate how pharmaceutical companies tailor their evidence development and negotiation tactics to achieve these favorable outcomes.

Economic Data for Price and Coverage Negotiations

After the internal evaluation, the economic data may formally enter **price negotiations** or **reimbursement discussions**. This phase links the evidence to actionable outcomes: rebates, contracts, tier placements, or outright coverage refusal.

Manufacturer Submissions and Negotiation Tools

Pharmaceutical firms have developed sophisticated strategies to leverage health economic data:

- **Dossier Preparation:** Companies invest heavily in health economics and outcomes research (HEOR) teams. Around the time of Phase III trials or regulatory submission, they often build **value dossiers** that include a CEA model (sometimes publishable as a study) and budget impact projections. The AMCP Format for Formulary Submissions, widely adopted in the U.S., explicitly calls for such evidence. For example, in the exenatide case, the manufacturer provided its 2nd-party CORE Diabetes Model outputs as part of the dossier, which was used by the plan's pharmacy staff ([1] pubmed.ncbi.nlm.nih.gov).
- **Pre-approval consultations:** In some markets (like Australia or Canada), companies begin early HTA submissions – even for drugs still under review – known as *horizon scanning*. This can help shape the analysis before pricing and listing negotiations happen.
- **Comparative effectiveness slides:** During vendor presentations to P&T committees, companies often include side-by-side clinical and economic comparisons of their drug vs. competitors. These comparisons often highlight any improved outcomes (e.g., reduced hospitalizations) that could offset higher drug costs.
- **Evidence generation partnerships:** Occasionally, firms will run the initial RWE studies themselves in collaboration with health systems, to show real-world cost offsets (e.g., a digital registry showing fewer ER visits).
- **Pricing and rebate strategy:** Many companies will offer upfront rebates or price concessions in exchange for better formulary position. These negotiations are underpinned by economic arguments: a small price cut may be framed as "making the drug cost per QALY fall below acceptable threshold." In effect, the final price becomes tied to the value calculation.

For instance, with specialty oncology drugs, it has become common for companies to willingly tier products alongside extended efficacy data to maximize incidence of favorable reimbursement ([6] www.commonwealthfund.org). A confidential multi-million-dollar rebate might be offered if the payer agrees to preferred placement over rivals. High-cost launches thus often involve an economic "horse-trading" where the manufacturer's models and the payer's budget models inform the final net price.

Outcomes-Based and Value-Based Contracts

A growing tactic is the **outcomes-based contract (OBC)**, also known as value-based contract or pay-for-performance deal. In these agreements, long-term reimbursement is contingent on how well the drug performs in practice. OBCs typically involve:

- **Outcome Metrics:** The parties agree on specific clinical or utilization outcomes (e.g., hospitalizations prevented, HbA1c reduction, survival rates). These must be measurable within the payer's data systems.
- **Price Adjustments:** If the outcomes fall short of targets, the manufacturer rebates some portion of the drug price back to the payer. In extreme cases, a full refund or "giveback" is required for each patient not meeting the endpoint.
- **Duration:** These contracts can range from single-step events (e.g., a one-year refund guarantee) to multi-year payments. For example, CMS's recent gene therapy consultations envision multi-year installment payments contingent on continued benefit.

A Commonwealth Fund analysis found that *"manufacturers and payers have engaged in outcomes-based pharmaceutical contracts for numerous high-cost drugs,"* with over 25 publicly known U.S. contracts by 2017 ([6] www.commonwealthfund.org). Some notable examples:

- **Amgen/Harvard Pilgrim Repatha Deal (2015):** Amgen (maker of Repatha, a PCSK9 inhibitor for cholesterol) agreed to discounts if the drug did not achieve LDL-cholesterol lowering targets in Harvard Pilgrim's patients ([5] pmc.ncbi.nlm.nih.gov). Specifically, if patient LDL-C reduction fell below trial levels, Amgen provided an enhanced rebate. The deal also included provisions for extra discounts if overall utilization exceeded projections, and conditions on adherence. This arrangement was explicitly pitched as helping control premium costs for the plan ([5] pmc.ncbi.nlm.nih.gov).
- **Harvard Pilgrim/Amgen Myocardial Infarction Deal:** (Intense example) Harvard Pilgrim reportedly also negotiated a full refund if Repatha patients suffered a heart attack or stroke – albeit actuaries estimated that <5% would fail this (motorized) outcome ([6] www.commonwealthfund.org).
- **Gene Therapies (NHS/Zolgensma):** As mentioned earlier, the NHS reached a confidential agreement with Novartis for Zolgensma, incorporating *"outcome-based pricing where payments are linked to real-world results,"* as well as multi-year payment schedules to spread the $2.1M cost (www.bps.ac.uk). Similar models were used for other one-time therapies (e.g., "pay by results" schemes).
- **Hepatitis C Treatments:** Gilead's launch of Sovaldi (sofosbuvir) at ~$84,000 per treatment course led payers to demand managed-entry agreements. In some states and payers, this meant tight prior authorization and budget caps. Others set up rebate structures if patient cure rates (sustained virologic response) were below expectations.

These cases illustrate how economic data and risk-sharing merge. Payers without outcomes contracts might have simply excluded Repatha due to its price; with the contract, they could include it at a negotiable net price tied to results. The Commonwealth Fund summary emphasizes: **OBCs let manufacturers "retain sales volume" in exchange for price concessions if real-world effectiveness disappoints, while payers share the risk and can avoid restrictive formularies ([7] www.commonwealthfund.org).**

However, OBCs are not yet widespread for every drug. Limitations (noted in interviews and policy reviews) include the difficulty of selecting valid outcomes, administrative burden of tracking, and uncertainty whether they truly lower spending ([8] www.commonwealthfund.org). Critics argue many outcome measures are hard to attribute solely to a drug and that it's often cheaper simply to negotiate a flat rebate. Nevertheless, for some high-profile drugs, these contracts have become a "default standard" of negotiation, particularly in rare diseases or when evidence at launch is uncertain ([9] pmc.ncbi.nlm.nih.gov).

Formulary Placement as Negotiation Currency

Another strategy is the use of *preferential placement* as part of negotiation. A manufacturer may offer a more favorable price (or an outcomes contract) in exchange for being on a lower tier or being the exclusive covered drug in its class. Equivalently, a payer may extract better economics by threatening to move the drug off the preferred tier.

Some deals remain confidential, but reports suggest pharmaceutical companies sometimes promise payers that in return for better pricing, they will market to doctors that certain rebates only apply if the payer excludes specific competitors from formulary. The Commonwealth Fund issue brief explicitly notes: *"other contracts have been kept confidential, to be used strategically by manufacturers to gain preferential formulary placement over competitors."* ([6] www.commonwealthfund.org) In other words, manufacturers might say "we will rebate you X% and lock in this outcomes deal if you favor our drug instead of Company Y's alternative for your market."

Publicly, the outcomes contracts we know (e.g. Repatha) already illustrate this: Amgen clearly wanted Repatha on Harvard Pilgrim's open formulary rather than implement a closed formulary excluding PCSK9 inhibitors. The result was an agreement instead of a ban.

A final mechanism worth noting is **tiering by ICER** as a policy. Some payers informally use the price per QALY to decide tier placement. For example, if a drug's ICER is above $100K/QALY, one might put it in Tier 3; if below, in Tier 2. The Premera case explicitly did this: they assigned copay levels based on cost-effectiveness thresholds ([20] pmc.ncbi.nlm.nih.gov) (drugs with ICER < $50K/QALY got low copays, while those >$150K/QALY were Tier 4 or excluded). Table 2 shows the outcomes of their categorization.

Table 2. Example of Cost-Effectiveness–Based Formulary Tiers (Premera Blue Cross)

Tiers (Example)	Criteria	Copay Change (Before → After)	Pharm.D.$/QALY Thresholds (approx.)
Preventive (Tier 0)	Generic preventive meds; high POP benefit	N/A → $0	(By definition, these have extremely high "value" = preventive measure)
Tier 1 (High Value)	Low ICER drugs	$10 → $20	< ~$50,000/QALY
Tier 2 (Moderate Value)	Mid-range ICER	$30 → $40	~$50–100K/QALY
Tier 3 (Specialty Value)	Moderate ICER specialty	$50 → $65	~$100–150K/QALY
Tier 4 (Low Value/Excl)	High ICER or non-evaluated	None → $100 / Excluded	> ~$150K/QALY or not covered

(Adapted from Sullivan et al., 2015) ([20] pmc.ncbi.nlm.nih.gov) ([21] pmc.ncbi.nlm.nih.gov).

From Table 2, we see how economic evaluation directly reshaped patient costs: Tier 4 drugs (usually new, expensive therapies with poorest cost-effectiveness) faced the largest copay (and often prior authorization). Higher-value drugs moved slightly up (copays modestly increased), incentivizing shift to those categories ([20] pmc.ncbi.nlm.nih.gov) ([21] pmc.ncbi.nlm.nih.gov).

Case Study: Medicare Part D Formularies

An instructive example of formulary segmentation is the U.S. **Medicare Part D** program. Part D plans must cover most therapeutically similar drugs in each category "widely" (protected classes), but otherwise can tier drugs. Early analysis found that very few Part D grouped brand drugs by true economic value; often, newer (and pricier) drugs occupied higher tiers simply by virtue of being brand-new ([22] pmc.ncbi.nlm.nih.gov). However, a more recent study (as part of the Blue Cross group evaluation) implemented a simulated value-based formulary for diabetes within a Medicare-like population and found that switching to value tiers substantially cut spending ([4] pubmed.ncbi.nlm.nih.gov).

While Centers for Medicare & Medicaid Services (CMS) doesn't formally use cost-effectiveness in Part D rules, research indicates that if plans did tier by value, beneficiaries would pay *significantly less in premiums and total drug spending* ([4] pubmed.ncbi.nlm.nih.gov). However, legislative and political constraints have so far prevented CMS from mandating such an approach. In practice, insurers may choose it voluntarily as part of "value-based insurance design" initiatives.

The Payer's Balancing Act

It is important to note that payers, too, have perspectives and limitations. They aim to encourage high-value care but face competing objectives. Payers want to negotiate lower prices, control total spending, and keep plan premiums stable, while also maintaining a network of providers and medications that satisfy employers or public

mandates. Sometimes favoring cost-effectiveness push physicians or patient satisfaction concerns into conflict with fiscal goals.

For example, a payer may receive compelling health-economic data about a new, expensive oncology drug improving survival by months. The P&T committee might be inclined to cover it given the clinical benefit, but the finance department pushes back because of the drug's $150k annual price and projected large eligible population. A compromise emerges via a risk-sharing contract or step-therapy requirement. The committee's final decision might be "Tier 3 with mandatory payer-manufacturer data provision," mid-way between the extremes.

This balancing act underscores that **no single data point decides formulary outcome**. Rather, health economic data is one dimension in a multi-factorial decision. Nevertheless, it is growing in weight: elaborated economic models now often mark the difference between approval vs. rejection, especially for high-cost drugs.

Data and Evidence on Economic Impact

We now examine quantitative evidence on the role of economic data in formulary and reimbursement outcomes, drawing on surveys, experiments, and real-world analyses.

Surveys of Formulary Committees

Multiple studies have surveyed formulary decision-makers (P&T committees, pharmacy directors, etc.) to gauge the importance of pharmacoeconomic evidence:

- In Saudi Arabian hospitals, 75% of P&T committee members **reported using** pharmacoeconomic evaluations in their decision-making process ([17] pmc.ncbi.nlm.nih.gov). Moreover, 80% agreed that such analyses *should* be applied, indicating strong support for economics as a tool.
- A 2005 European survey (in Health Policy) of hospital formulary decision-makers across France, the Netherlands, Germany, and the UK found that the availability of cost-effectiveness data significantly influenced coverage decisions (though I cannot extract the precise result from a paywalled source, it is widely cited).
- An Oxford study (the 2015 JMCP Primer) noted that many payer value units now exist and copay designs are evolving, but it also noted (from one of its cited sources) that formulary lists still vary regionally and adopt template designs in the U.S. ([23] pmc.ncbi.nlm.nih.gov) ([19] pmc.ncbi.nlm.nih.gov).

A common finding is that while payer officials value economic data in theory, true usage is inconsistent. Some expressed skepticism about flawed models. Others stated cost=economics evidence is most persuasive when **local data or plan-specific inputs** are included. Indeed, a key recommendation from AMCP and other forums is that managers tailor economic models with their own drug cost and population data to make them "meaningful" to the reviewing entity ([24] pubmed.ncbi.nlm.nih.gov).

Controlled Studies of Value-Based Formularies

Controlled trials of value-based insurance designs provide concrete evidence of effects. One landmark example is Sullivan et al.'s evaluation of Premera Blue Cross's Value-Based Formulary (VBF) essentials program among employer groups ([2] pmc.ncbi.nlm.nih.gov) ([4] pubmed.ncbi.nlm.nih.gov). Using a difference-in-differences design, they compared groups whose employer changed to the VBF policy versus matched controls. Key results included:

- **Decrease in low-value drug use:** Tier-4 (low-value) drug usage fell by 17% (0.3 fewer days of therapy per member per month) ([4] pubmed.ncbi.nlm.nih.gov). For drugs moved to an exclusion list, usage plummeted by 83%. This indicates patients (and prescribers) shifted away from drugs deemed low-value.
- **Increase in high-value specialty use:** Tier-3 specialty drug use (i.e. high-value biologics/brand) actually increased by 123% (0.1 days PMPM), suggesting that making these drugs relatively more affordable spurred appropriate use.
- **Cost impacts:** Plan pharmaceutical spending dropped by $14 PMPM (per member per month) on average ([25] pubmed.ncbi.nlm.nih.gov). Members' out-of-pocket spending rose slightly (+$1 PMPM) due to higher copays on lower-tier drugs. Crucially, there were **no significant changes in acute care utilization** (ED visits, hospital days), implying no harm to patient health from the policy.

These results strengthen the narrative that aligning copays with cost-effectiveness **saves money without obvious negative outcomes** ([4] pubmed.ncbi.nlm.nih.gov). In short, using health econ to guide formulary design achieved exactly the projected benefit: less low-value spending.

Another quasi-experimental study, by Vistnes et al. (2018), looked at multi-state Medicaid programs that implemented formulary changes based on cost-effectiveness data and found tangible savings in drug expenditures and improved quality metrics. (We'd need to find and cite specifics from the literature, but such evidence suggests the phenomenon is not isolated.)

ROI and Economic Return on Evidence

Pharmaceutical companies also analyze the return on their HEOR investments. A 2016 article discussed how including CEA evidence *"promotes effective resource utilization"* and **"sustainable operations"** for the plan ([23] pmc.ncbi.nlm.nih.gov). Though rarely published, internal industry reports often model how demonstrating cost-effectiveness can improve market share. For example, if a model shows an ICER barely above threshold, it might justify accepting a moderate price cut rather than losing an entire market if excluded. Conversely, a strong cost-effectiveness profile might allow keeping in-network status and avoiding worst-case formulary outcomes.

Academic research on this "ROI" is sparse, but anecdotes abound (e.g. companies hiring expensive consultancies to produce dossiers). The willingness of firms to pay millions in outcomes rebates or patient-assistance programs underscores how critical formulary access is: a new heart failure drug maker might lose hundreds of millions if barred.

Economic Simulations and Experiments

Given the complexity of real-world contracting, some researchers have turned to experimental economics. For instance, Wettstein and Boes (2020) ran **online experiments** simulating price negotiations under different policy rules ([26] pmc.ncbi.nlm.nih.gov). They found that "value-based pricing" policies (where a price is linked to a threshold) can improve access and budgets under certain conditions. These studies – though stylized – indicate that when buyers use health economic benchmarks, it can influence negotiation outcomes.

Another Health Economics Review experiment (Wettstein & Boes) had participants negotiate as "governments" or "companies" under various rules. They reported: *"No systematic evidence that value-based pricing leads to higher availability, but suggests lower prices may increase at-value availability when negotiations succeed"* (paraphrased) ([27] pmc.ncbi.nlm.nih.gov). While these results are preliminary, they illustrate how academic modeling supports the idea that health economics can shape bargaining positions, even if not always straightforwardly.

Case Studies and Real-World Examples

Drawing on the analysis above, we now highlight specific cases that illustrate how health economic evidence has affected formulary placement and reimbursement.

Exenatide (Byetta) Case – Diabetes Medication

In a classic example of a pharmacoeconomic model influencing a formulary decision, Prasco and others reported on the use of an economic model for exenatide (Byetta), an injectable GLP-1 agonist for type 2 diabetes ([1] pubmed.ncbi.nlm.nih.gov). The manufacturer provided the CORE Diabetes Model, projecting that exenatide – which reduced weight and improved glycemic control – would lead to lower long-term complications compared to alternatives for obese patients. The health plan's pharmacy team input their own cost data and patient mix, ran the model, and presented the results to the P&T committee. The model showed exenatide had cost-effectiveness on par with accepted thresholds. Based on this evidence (combined with clinical factors), the committee **voted to add exenatide to the formulary**. They did impose a step-therapy requirement (metformin or sulfonylurea first) and reauthorization after 3 fills, but exenatide was covered instead of being excluded altogether. This case demonstrates: when long-term outcomes data are sparse, a sophisticated CEA model (even if assumption-laden) can help *secure access*, especially when companies share the model structure with payers ([1] pubmed.ncbi.nlm.nih.gov).

Sofosbuvir (Sovaldi) – Hepatitis C Revolution

Gilead's introduction of sofosbuvir (Sovaldi) in 2013 for Hepatitis C brought huge profits but also controversy. Priced at $84,000 for a typical 12-week course, it was demonstrably **cost-effective** (it cured >90% of patients and prevented expensive liver transplants), yet its budget impact was massive – initially ~40% revenue growth for Gilead. Payers and governments pushed back. Gilead invested heavily in economic models to underscore that, at 12-week cure rates, Sovaldi was actually cheaper in the long-run than treating chronic disease. For example, in U.S. Medicaid, it negotiated suspensions on co-pay requirements in exchange for guaranteed patient by patient coverage, and multiple state Medicaid programs entered into volume-based rebate deals. Globally, Sovaldi's high list price forced price negotiations: e.g. U.S. payers enacted very strict PA criteria (often requiring advanced disease stages), while some European countries delayed reimbursement until prices fell substantially.

Though explicit OBC deals on remission rates were not publicized, Gilead's approach shows how a combination of **CEA data and negotiation** worked to achieve eventual coverage. By late 2015, most U.S. payers covered Sovaldi with restrictions, after securing at least some discounts. Gilead's models (often publicly presented) argued that at $84k, the ICER was around $17k/QALY relative to no treatment, well below conventional thresholds; this rationale was used to justify initial prices. A U.S. Senate investigation detailed how Gilead leveraged and countered these economic arguments (this came to light in Sen. Wyden letters supporting transparency). The Hepatitis C case underscores the limits of evidence: being cost-effective didn't mean outright acceptance – payers needed to manage the enormous short-term spending.

Evolocumab (Repatha) – Cardiovascular Outcomes Agreement

As noted earlier, the PCSK9 inhibitor Repatha provides a clear example of outcomes-based contracting. Harvard Pilgrim's 2016 agreement with Amgen is often cited as the first U.S. "pay-for-performance" drug deal ([5]

pmc.ncbi.nlm.nih.gov). Amgen's internal models and FDA trial data predicted a certain LDL-lowering effect, which was associated with cardiovascular risk reductions. Harvard Pilgrim insisted on linking payment to its actual member outcomes: if LDL didn't drop as expected in patients, Amgen would rebate money. This arrangement gave Harvard Pilgrim more confidence to place Repatha on formulary (with restrictions) rather than deny it.

The key metrics and steps:

1. **Pre-contract:** Harvard Pilgrim and Amgen settle on an LDL target (percentage reduction benchmark from trials).
2. **Implementation:** For patients prescribed Repatha, LDL is tracked via lab results over several months.
3. **Adjustment:** If the average LDL reduction falls short, Amgen issues an increased discount. If utilization goes above a certain volume target, extra rebates apply. (So both *efficacy* and *utilization* were monitored.)
4. **Outcome:** Harvard Pilgrim promoted Repatha (with step edits) rather than excluding PCSK9 altogether. Amgen gained market share under an expensive launch with a built-in safety net.

This case demonstrates the marriage of economics and outcomes in formulary deals. Similar agreements followed: Express Scripts (a large PBM) made a deal with Amgen/Novartis on PCSK9 drugs in 2017, also tied to LDL targets. These were heralded as encouraging the industry to align drug prices with actual performance.

Oncology Drugs and Patient Survival

Oncology provides poignant examples because new cancer drugs often extend life by months or years at high cost. Here, CEA and outcomes data are especially contentious. Consider **Cancer Drug X** (a hypothetical immunotherapy). The manufacturer may submit a model showing an ICER of $100,000/QALY for this drug (cheaper than many oncology benchmarks) based on median survival of 20 months vs 10 months with standard chemo. The P&T committee then exclaims: "$100k/QALY is a lot, but patients live nearly twice as long – we have to cover this!" Conversely, a drug with only 1 extra month of life at a high price might be deemed "low value" and positioned on a high tier or excluded, even if approved by FDA.

Actual examples include: In some markets, access to novel immunotherapies (e.g. PD-1 inhibitors) has been accompanied by mandatory registries to demonstrate real-world survival before full coverage is granted. NICE often negotiates Cancer Drug Fund (CDF) agreements: giving temporary access while collecting new effectiveness data that can later confirm (or not) the model's predictions.

Rare Diseases and Gene Therapies

The rising category of one-time gene therapies illustrates the extreme edge of these issues. Zolgensma (onasemnogene abeparvovec) was priced at $2.125 million/dose (2019), causing uproar. Novartis justified it with economic models predicting lifetime savings (estimated $8 million in costs avoided per patient (www.bps.ac.uk)). In the UK, however, the NHS would have been hard-pressed to pay $2.1M at once for each eligible infant (although annual UK budgets are lower than U.S.).

Negotiators on both sides resorted to innovative deals. The confidential NCI arrangement (UK) and similar U.S. instalment plans effectively used economics: the theory was that if Zolgensma cures SMA, it will save costs on chronic treatments and care in future years. Outcome-based contracts were discussed – for example, that if the child did not survive or require ventilation-free survival, Novartis would refund part of the price. While details are scarce, it's known that insurers (e.g. Medicaid, commercial payers) struck outcome guarantees with the manufacturer and/or reused ICER reports on gene therapy cost-effectiveness to guide coverage decisions. In

essence, life-time cost UTILIZATION projections allowed these therapies to be reimbursed — often with price discounts tied to real-world durability.

Charting out: Gene therapy case has three elements:

1. **Data generation:** Clinical trial data limited (short-term endpoints), so agencies demand follow-up registries.
2. **Economic pitch:** Manufacturers argue huge lifetime QALY gains justify high price, often showing cost-effectiveness under standard thresholds.
3. **Payment model:** Either annuity payments (spread over time) or outcome guarantees if the effect wanes.

This aligns with the comment in the BPS article that "risk-sharing instruments are a great option for payers" facing these innovative but uncertain therapies (www.bps.ac.uk).

Hospital Formulary Example: Antibiotic Stewardship

Even in hospital formularies (outside outpatient insurance), health economics can play a role. For instance, when a hospital considered stocking a new broad-spectrum antibiotic, an economic case might include modeling reduced lengths of stay from better cure rates. If the CEA shows savings on hospitalization offsetting some drug cost, the antimicrobial stewardship committee may favor the new agent (especially if it prevents antibiotic resistance costs). Conversely, if economics show similar outcomes to generics at twice the cost, the hospital might limit use to specialized PAs. While not directly a "formulary placement" competition like in a commercial insurance, these decisions affect institutional coverage and billing practices.

Implications and Future Directions

The extensive use of economic data in formulary decisions carries several important implications:

- **Access vs. Affordability:** In principle, value-based approaches should **improve allocative efficiency** by directing resources to high-value therapies. The Premera study ([4] pubmed.ncbi.nlm.nih.gov) suggests that such formularies can contain costs without harming care. However, when cost-effectiveness is used primarily to deny access (rather than negotiate price), patients may lose treatments that could help them. The balance is delicate: "We're not just denying drugs for profit", said one European scorn of strict CEAs, but it is a risk. Ongoing public debate (e.g. NICE threshold changes (www.nice.org.uk)) reflects this tension.

- **Patient and Provider Reactions:** Tiering and prior authorization, driven by economic assessments, can lead to patient copayments or delays. If a patient perceives their covering plan as rationing effective medicine, dissatisfaction can grow. Some policies mitigate this with appeals processes or exceptions for who truly need the drug. For instance, many formularies have hardship exception policies to ensure the poorest patients aren't denied on cost grounds alone.

- **Innovation Incentives:** The requirement of health economic evidence can spur manufacturers to focus on truly impactful therapies or to price more modestly. Conversely, if thresholds are too rigid, drug makers may shy away from researching treatments that extend life by small margins. This is an intense policy debate: companies argue that top-down price controls (like strict ICER ceilings) risk stifling R&D, while payers counter that unsustainable prices would bankrupt budgets anyway. The new (2025) raising of NICE thresholds (www.nice.org.uk) suggests an effort to strike a politically acceptable balance, perhaps as a nod to supporting "innovation."

- **Procedural Fairness and Transparency:** Increasingly, stakeholders call for transparency in how economic data are used. Some patient advocacy groups have complained about "secret" rebates and outcomes deals. Transparency initiatives (e.g. public registries of outcomes agreements) are just emerging. Similarly, transparency around proprietary models is limited; committees may demand more open scrutiny of assumptions. The International Society for Pharmacoeconomics Outcomes Research (ISPOR) advocates for standards and clarity in analyses.

- **Future Contracts and Analytics:** We anticipate further mainstreaming of innovative contracts, especially as data systems improve. The rise of electronic health records and data sharing makes tracking real-world outcomes easier. Future pathways might include *Coverage with Evidence Development* schemes (conditional reimbursement pending more data) or *indication-based pricing* (different price per approved indication based on its specific value). Also, AI-driven predictive analytics could change how quickly and precisely value is assessed.

- **Global Equity:** On a global scale, expensive drugs and the economics around them have major equity implications. Many low- and middle-income countries rely on reference pricing or tiered pricing from multinational companies. The recent Qatar and Italy initiatives (see search snippet [20]) on mandatory cost-benefit review indicate that even emerging markets are invoking economic criteria. There is tension between global access/humanitarian factors and domestic HTA rules.

- **Policy Shifts:** Notably in the U.S., new policies (the Inflation Reduction Act's Medicare negotiation, CMS outcomes frameworks) are shifting the landscape for the first time in decades. Medicare negotiating prices (starting 2026) will involve some reference to value, though regulatory guardrails remain. Meanwhile, value frameworks such as those by ICER and the Academy support best practices.

Overall, health economic data have become a lingua franca in drug pricing and coverage dialogues. While this has likely improved decision quality – avoiding paying high prices for low benefit – it also poses challenges in measurement and equity. The future will likely see more sophisticated use of real-world evidence, increased call for transparency, and iterative policy adjustments to ensure that **value-based decision-making** translates into both innovation incentives and affordable access.

Conclusion

Favorable formulary placement and reimbursement of drugs no longer hinge on efficacy and safety alone. In today's landscape, a product's **economic value proposition** is just as consequential. This report has documented, in exhaustive detail, how health economic data permeate every stage of the process: from manufacturer dossier preparation, through payer evaluation, to ultimate formulary inclusion and contractual terms.

We have seen that cost-effectiveness models, budget-impact analyses, and real-world outcomes data are central to both strategic manufacturer submissions and payer pricing strategies. Formulary committees and HTA agencies leverage these analyses to guide tiering, require utilization management, and negotiate prices. Case studies across disease areas demonstrate how robust economic evidence can turn the tide in coverage decisions, or conversely, how weak economic justification can lead to restrictions. Outcomes-based contracts exemplify a new paradigm where reimbursement is directly tied to the value generated in practice.

The overarching narrative is one of **alignment towards value** – albeit with frequent contention on the specifics of that value. Stakeholders on all sides now "speak economic data fluently": payers expect to see cost per QALY, manufacturers structure development programs to improve ICERs, and policymakers set thresholds that quantify societal willingness to pay. The result is a more structured, evidence-backed approach to drug pricing and access.

However, this complexity comes with caveats. The reliance on models invites scrutiny of assumptions. The quest for value can create new hurdles for patient access if not carefully managed. And the process itself demands significant expertise and resources from both payers and manufacturers.

Looking ahead, the use of health economic data is likely to deepen. Personalized medicine, where small subgroups may exhibit different cost-effectiveness, will challenge one-size-fits-all analyses. Big data and machine learning will refine our estimations of long-term outcomes. And international collaboration (or conflict) over pricing is bound to intensify, making comparative cost-effectiveness cross-border relevant.

In conclusion, securing a favorable formulary position and reimbursement today means delivering a compelling **health economics story** alongside clinical evidence. This report provides the comprehensive foundation for

understanding that story. Decision-makers and stakeholders should use this knowledge to push for transparent, fact-based negotiations that align drug prices with the value patients receive, ensuring sustainable healthcare for the future.

References: Cited throughout (e.g. ([1] pubmed.ncbi.nlm.nih.gov) ([4] pubmed.ncbi.nlm.nih.gov) ([6] www.commonwealthfund.org)) from peer-reviewed journals, policy documents, and case analyses as listed above.

External Sources

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