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ARCH 4 Horizon and Long-Term Value

Executive summary

ARCH/4 — Horizon & Long-Term Value is the market-access lens that asks a different question from immediate reimbursement: *how should a company shape evidence, pricing, access, and portfolio decisions over many years so that the product keeps creating value for patients, payers, and the manufacturer?* In practical terms, it is about managing the whole access lifecycle: pre-launch evidence design, launch sequencing, post-launch uncertainty reduction, indication expansion, competitive defense, and planning for the period before and after loss of exclusivity. This report assumes **no single target country** and therefore uses a cross-market perspective, with emphasis on **England, France, Germany, broader European regulation, and selected U.S. examples** because these systems are among the most influential for market access and HEOR practice. [1]

A lifecycle approach matters because HTA bodies and payers increasingly make decisions under uncertainty, then revisit those decisions as evidence evolves. NICE explicitly defines managed access as a route for medicines that are too uncertain for routine reimbursement but promising enough for time-limited access with additional evidence generation; EMA's conditional marketing authorisation similarly allows earlier approval on less comprehensive data when unmet need is high, provided further post-authorisation evidence is generated. In other words, market access is no longer a single "yes/no at launch" event; it is an iterative value-management process. [2]

For market access and HEOR teams, ARCH/4 has four core implications. First, **value must be modelled over a long horizon**, not just at launch, using lifetime or sufficiently long time horizons where benefits and costs persist. NICE, HAS, and IQWiG all emphasise that the analytic horizon should capture all important differences in outcomes and costs, while also testing uncertainty from extrapolation. Second, **evidence plans must extend beyond registration trials**, using registries, long-term follow-up, surrogate validation, post-registration studies, and real-world data to support reassessment and indication expansion. Third, **commercial strategy must be dynamic**, with pricing architecture, contractual flexibility, and portfolio timing aligned to long-term net present value rather than short-term list price optimisation. Fourth, **governance must be trigger-based**: companies need explicit rules for when new data, policy shifts, safety signals, or competitive events require a change in access strategy. [3]

In practice, the most successful ARCH/4 strategies usually combine five things: early horizon planning; a reference-case economic model plus scenario layers; a lifecycle evidence plan with clearly assigned data custodians; payer engagement around uncertainty-management tools; and KPI dashboards linked to escalation triggers. Real-world examples show that this can work, but also that good commercial terms alone are not enough. England's inclisiran population health agreement improved affordability and national funding, yet uptake still materially lagged the original ambition, showing that service readiness and implementation capacity are as important as the deal structure. By contrast, cystic-fibrosis modulator access in England shows how long-run registry-based evidence collection can support a bridge from interim access to broader routine use. [4]

Executive recommendations

- Build **one integrated ARCH/4 lifecycle plan** per asset, covering launch sequence, evidence generation, pricing architecture, indication timetable, and loss-of-exclusivity transition, rather than treating these as separate workstreams. [5]
- Use a **stack of models**, not a single model: base-case cost-effectiveness, budget impact over time, scenario analysis, and where relevant risk-adjusted NPV and real-options logic. [6]
- Treat post-launch evidence as a **designed asset**, not a compliance exercise: specify registries, endpoints, comparators, follow-up duration, ownership, and reassessment milestones before launch. [7]
- Negotiate **uncertainty-management mechanisms** with payers only when paired with operational delivery plans; otherwise even strong agreements may underperform in real use. [8]
- Use **trigger-based governance** so that new safety, durability, competitor, or policy signals automatically prompt model refresh, evidence-plan revision, or pricing/access negotiations. [9]

What ARCH 4 means and why it matters

A lifecycle view of HTA and market access is no longer peripheral. HTAi's lifecycle HTA discussion describes HTA as a process that determines the value of a technology at different points in its lifecycle — from pre-market through post-market and ultimately to disinvestment — and argues that a more holistic lifecycle approach is increasingly needed because evidence, context, and stakeholder needs evolve over time. A linked Value in Health paper on life-cycle HTA frames the problem even more directly: standard HTA can struggle with **health-system sustainability, evolving evidence, and uncertainty**, and lifecycle HTA aims to address exactly those issues. [5]

Within that broader logic, **ARCH/4 — Horizon & Long-Term Value** can be defined as the strategic discipline of maximizing access-adjusted value over the full product and portfolio lifecycle. It is not merely "forecasting future revenue." It connects long-term clinical value, evidence maturity, payer willingness to fund, financial timing, disease-area evolution, and competitive positioning. For HEOR teams, ARCH/4 is the point where reimbursement modelling becomes portfolio strategy; for market access teams, it is where launch planning turns into longitudinal value stewardship. [10]

This matters because many innovative medicines now reach payers before all long-term uncertainty is resolved. NICE's managed-access framework explicitly states that medicines may receive faster access when they are promising but too uncertain for routine use, with additional evidence collected under a time-limited agreement. EMA's conditional marketing authorisation takes a similar regulatory stance: immediate availability may be justified on less comprehensive data if unmet need is substantial and the sponsor can provide more evidence post-authorisation within agreed timelines. These structures formalise the idea that **initial access is provisional, and long-term value must be earned over time**. [11]

For ARCH/4, the central objectives are therefore broader than "win reimbursement." They are to: sustain credible value as evidence matures; preserve optionality for future indications and formulations; avoid destroying global price architecture through short-term tactics; align affordability with durability of benefit; and prepare for both upside events, such as label expansion, and downside events, such as competitor entry or weak real-world persistence. That is why this lens is especially important for products with long-acting benefits, one-time administration, broad cardiovascular or metabolic populations, oncology assets with serial indication expansion, and chronic therapies whose real-world persistence determines actual value. [12]

Strategic decisions and value modelling

Strategic questions and decision criteria

ARCH/4 starts with a set of recurring strategic questions. **Where should the product launch first? Which indication should be pursued first or next? When should broader populations be opened? Which evidence gaps should be solved now versus deferred to managed access or post-launch studies? How should one product's timing interact with the rest of the portfolio?** These are not abstract questions: NICE topic scheduling uses expected regulatory approval dates and submission readiness; its prioritisation framework is explicitly built to identify and route new topics and updates to existing guidance. In other words, access systems themselves operate on a horizon basis, so company strategy must do the same. [13]

A rigorous ARCH/4 decision framework usually uses six criteria. The first is **value density**: how much incremental health gain and payer relevance exists in the candidate launch or indication. The second is **uncertainty reducibility**: whether the remaining uncertainty can realistically be reduced through follow-up, registries, or real-world data. The third is **budget absorption capacity**: whether the health system can absorb the product across the eligible population over the relevant years. The fourth is **strategic spillover**: whether an early indication will help or hurt later submissions, such as by shaping a reference price, anchoring a clinical narrative, or generating usable evidence. The fifth is **delivery feasibility**: whether the system can actually identify, refer, infuse, monitor, and fund patients. The sixth is **option value**: whether a decision today preserves or destroys future strategic choices, such as later expansion into earlier lines of therapy. This set of criteria is consistent with lifecycle HTA thinking, NICE's emphasis on extrapolation and implementation issues, and WIPO's discussion of managerial flexibility in biotech and pharmaceutical valuation. [14]

A practical method is to score every launch/indication option with a **decision matrix** that includes: expected incremental QALYs; expected ICER range; payer budget impact over one, three, and five years; durability uncertainty; time-to-evidence maturity; probability of approval and reimbursement; cannibalisation or synergy with the existing portfolio; operational complexity; and impact on international reference pricing where relevant. The highest-value choice is not always the one with the highest headline price. Sometimes the best ARCH/4 path is to begin with a narrower, higher-certainty population; sometimes it is to accept lower early net revenue in exchange for faster learning, stronger registry evidence, or larger long-run addressable value. NICE, HAS, and IQWiG all support this general logic by emphasising justified time horizons, extrapolation discipline, and explicit treatment of uncertainty. [15]

Value metrics and modelling approaches

At minimum, ARCH/4 uses **cost-effectiveness analysis** and **budget impact analysis**. But long-term strategy usually needs a broader modelling stack. NICE states that the time horizon should be long enough to reflect all important differences in costs or outcomes and that a lifetime horizon is usually appropriate when survival or long-running benefits differ. NICE, HAS, and IQWiG all also require explicit treatment of uncertainty and, where extrapolation is needed, scenario analysis. ISPOR's budget impact good-practice update likewise stresses affordability and population health implications, not merely average cost-effectiveness. [16]

For portfolio and investment decisions, however, companies usually need to add **NPV**, **risk-adjusted NPV**, and sometimes **real-options** approaches. WIPO's biotech/pharma valuation guidance notes that risk-adjusted NPV is widely used because it applies stage-specific probabilities of success to future cash flows, and that real-options analysis is valuable when managerial flexibility itself has value — for

example, the option to defer, expand, partner, bundle, or discontinue depending on later information. In the health-value literature, real option value can also refer to clinical value unlocked when patients survive long enough to benefit from future innovation, which is conceptually different from financial real-options analysis but strategically related in ARCH/4 because both forms of option value reward preserving future possibilities. [17]

The methodological implication is straightforward: **do not make ARCH/4 decisions from a single ICER or a single launch NPV**. Build at least four linked model layers: a payer-facing reference-case CEA; a one- to five-year budget-impact model; a manufacturer or portfolio NPV/rNPV model; and a scenario engine that can show how results change with durability, uptake, competitor entry, indication timing, and discount/payment architecture. This is especially important for gene and cell therapies, where the relationship between one-off cost, long-term durability, and annual payer budgets can produce very different conclusions depending on payment timing and discount assumptions. [18]

Model comparison table

Model	Main question answered	Core inputs	Strengths	Limitations	Typical data sources
Cost-effectiveness analysis	Is the intervention good value for money versus relevant comparators over the appropriate horizon?	Clinical efficacy/ effectiveness, utilities, costs, survival/ extrapolation, comparators, discount rates	Core HTA currency; ties health gain to cost; supports reimbursement arguments	Sensitive to extrapolation and utility mapping; can understate affordability challenges	RCTs, indirect treatment comparisons, utilities, claims/EHR costs, literature, HTA inputs [19]
Budget impact analysis	Can the payer afford the product in the near to medium term?	Eligible population, uptake, displacement, costs, timing, payment mechanics	Critical for ARCH/4 affordability decisions; useful for launch sequencing and contracting	Often ignores longer-term downstream benefits if horizon is too short	Epidemiology, claims, treatment patterns, price/rebate assumptions, coverage rules [20]
NPV	What is the present value of future net cash flows?	Revenue, costs, taxes, discount rate, launch timing, exclusivity	Clear investment metric for lifecycle strategy	Does not inherently handle development/ reimbursement probability	Forecast sales, pricing files, COGS, SG&A, tax, exclusivity assumptions [21]

Model	Main question answered	Core inputs	Strengths	Limitations	Typical data sources
Risk-adjusted NPV	What is expected asset value after stage-specific risk adjustment?	NPV inputs plus probabilities of technical, regulatory, and access success	Better fit than plain NPV for pharmaceutical assets under uncertainty	Probability choices can be contentious; still limited on flexibility value	Pipeline probabilities, historical success rates, regulatory benchmarks, internal forecasts [22]
Scenario and sensitivity analysis	Which assumptions drive results and where are decision cliffs?	Structural assumptions, parameter ranges, price points, durability, uptake, competition	Essential for ARCH/4 governance; highlights triggers for strategic change	Can proliferate into too many scenarios without decision discipline	All of the above plus expert elicitation [23]
Real-options analysis	What is the value of preserving future choices such as expansion, deferral, or abandonment?	Volatility, decision points, milestone timing, probabilities, payoff distribution	Captures managerial flexibility and staged decision-making	More complex; harder to communicate to external payers	Internal pipeline strategy, partnership options, forecast ranges, milestone maps [24]
Annuity / installment payment modelling	How does spreading payments over time affect affordability, access, and risk-sharing?	Upfront price, installment structure, rebate triggers, durability assumptions, budget thresholds	Highly relevant for one-time therapies; can align payment timing with benefit realisation	Depends on contract enforceability, accounting rules, patient mobility, and data tracking	Contract terms, budget rules, outcomes definitions, claims/ registry follow-up [25]

Recommended minimum input set for ARCH 4 models

Input class	Why it matters over the horizon	Typical source
Epidemiology and diagnosed prevalence	Determines market size now and under future case-finding scenarios	Registries, literature, claims, public health datasets [26]
Treatment-pathway evolution	Future standard of care changes can invalidate the original model	Guidelines, payer policy, clinician interviews, competitor intelligence [27]

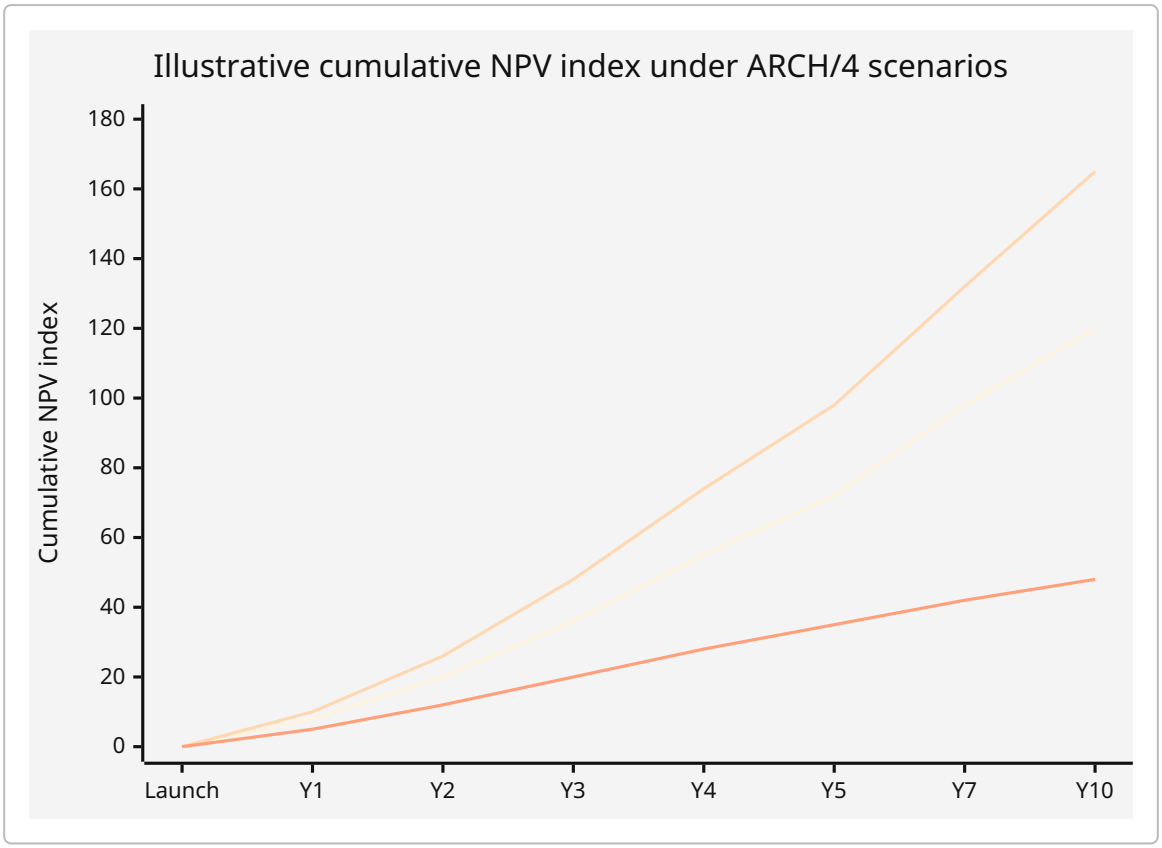
Input class	Why it matters over the horizon	Typical source
Long-term effectiveness and durability	Main driver of value for chronic and one-time therapies	Extension studies, registries, post-marketing studies, long-term follow-up [28]
Real-world adherence/ persistence	Converts trial efficacy into real-world effectiveness and budget impact	EHR, claims, pharmacy data, patient support data [29]
Access frictions and site capacity	Can delay or cap realised uptake even under good reimbursement	Referral data, infusion-center capacity, implementation audits [30]
Exclusivity and IP timing	Determines long-run price erosion and lifecycle windows	Patent estate, SPC calendars, legal review, public registers [31]
Competitive and pipeline risk	Can change ICERs, market share, and payer leverage	Trial databases, company disclosures, horizon scanning [13]

The discounting question deserves specific attention. NICE allows alternative analyses using **1.5%** discounting for both costs and health effects in specific circumstances involving very long-term sustained benefit, while its reference-case framework otherwise requires standard discounting. HAS uses the public discount rate and requires sensitivity analysis around the discount rate, including higher and zero-rate tests; for very long horizons it notes a declining rate after 30 years down to **1.5%**. IQWiG discusses sensitivity testing with discount rates between **0% and 5%**, with differential discounting also assessed in sensitivity analysis. For ARCH/4, that means discounting is not merely a technical detail: it can materially change the product's long-term value case, especially in curative and preventive settings. [32]

The same applies to **surrogate endpoints**. NICE's manual states that surrogate outcomes are most useful for QALY estimation when there is strong evidence that they predict survival or HRQoL, and that uncertainty in the surrogate-to-final-outcome relationship should be quantified and explored in probabilistic and scenario analyses. NICE's 2025 surrogate-endpoint collaboration further notes that many technologies are assessed before definitive long-term data exist and that much of their value may ultimately depend on those long-term effects. For ARCH/4, surrogates should therefore be treated as a bridge — useful, often necessary, but always temporary unless validated. [33]

Illustrative line chart

The figure below is **illustrative only**. It shows how cumulative NPV can diverge over time under different ARCH/4 scenarios as assumptions on durability, uptake, evidence maturation, and pricing flexibility change. The chart is not based on a specific product; it visualises the modelling logic described above. [34]



Actionable recommendations for modelling

A strong ARCH/4 modelling program should do five concrete things. It should keep a **single evidence-to-value backbone model** and derive country variants from it, rather than rebuilding from scratch country by country. It should predefine a **durability playbook** with pessimistic, base, and optimistic waning scenarios. It should pair every payer-facing model with a **manufacturer-side rNPV view** so that access concessions can be judged against total lifecycle value. It should include an **implementation realism layer** — site readiness, diagnosis rates, referral friction, adherence — because those variables often explain the difference between access on paper and access in practice. And it should maintain a documented set of **re-run triggers**, such as a new hazard ratio, a competitor entering an earlier line, or a change in a budget-impact threshold. [35]

Lifecycle evidence and real-world evidence

ARCH/4 depends on a principle that many organisations still under-execute: **launch with an evidence continuum, not just a dossier**. NICE's real-world evidence framework is explicit that real-world data can be used to reduce uncertainty and improve guidance, and that high-quality RWE requires prespecified questions, data of suitable provenance and quality, transparency, and methods that minimise bias. NICE also encourages companies to engage early on how real-world data will be used within evidence-generation plans. [29]

That principle is mirrored across Europe. HAS provides formal instructions for post-registration studies requested by the Transparency Committee, including timelines, required synopsis elements, data-source specification, endpoint selection, comparators, and follow-up duration. Importantly, HAS states that when major uncertainties are identified, it may request additional data at re-evaluation and specify whether existing registries or databases are sufficient or whether ad hoc data collection is needed. This

is a classic ARCH/4 mechanism: uncertainty is not merely acknowledged; it is operationalised into a study obligation with a reassessment timetable. [36]

For advanced therapies, long-term follow-up is central. FDA's guidance on long-term follow-up after gene therapy notes that gene therapies may produce permanent or long-acting changes and therefore may require extended monitoring for delayed adverse events. The guidance recommends that LTFU be designed according to product characteristics and risk, and it notes that for integrating vectors the duration may extend to **15 years**. That should fundamentally shape market-access planning: the evidence horizon is often far longer than the launch horizon. If the funding model assumes durable value but the evidence plan does not observe durability for long enough, the ARCH/4 strategy is incomplete. [37]

What evidence is usually needed over the lifecycle

For most products, the lifecycle evidence stack has four layers. The first is **registration evidence** establishing efficacy and short-term safety. The second is **bridging evidence**: external controls, indirect comparisons, or surrogate validation used in the first reimbursement submission. The third is **post-launch effectiveness evidence**, often based on registries, claims, and treatment-pattern data, to confirm persistence, heterogeneity, and resource use in practice. The fourth is **long-horizon value evidence**, which may include long-term survival, delayed adverse events, organ preservation, productivity or caregiver effects where relevant, and durability of response. ARCH/4 requires all four layers to be planned as a single program. [38]

Practical methods for lifecycle evidence generation

Registries are often the most important post-launch infrastructure, especially in rare disease and advanced therapy areas. EMA's registry-based studies guidance emphasises data collection, data quality management, and data analysis to achieve higher-quality evidence, and notes that post-authorisation registry-based studies should be registered in the EU PAS Register. In England, the cystic fibrosis data-collection agreement built on the UK CF Registry, with NICE, NHS England, the Cystic Fibrosis Trust, and Vertex as parties — an unusually clear example of registry infrastructure embedded directly into lifecycle access strategy. [39]

Long-term follow-up studies are essential when the product may create delayed harms or the value proposition depends on durable benefit. FDA's gene-therapy guidance makes this explicit for delayed adverse events and for risk reassessment as data accumulate. ARCH/4 teams should therefore prespecify not only duration but also adjudication rules, visit burden, data linkage method, and who funds the follow-up when patients move between providers or payers. [37]

Surrogate-endpoint programs should include a validation strategy from the start. NICE's manual sets out levels of evidence for surrogate relationships and prefers meta-analytic validation using randomised controlled trials that report both surrogate and final outcomes. This means that when a product relies on surrogate endpoints at launch, the ARCH/4 evidence plan should include a pathway for upgrading the evidence tier after launch — for example through extended trial follow-up, pooled analyses, or registry linkage to final outcomes. [40]

Post-marketing studies should be designed for decision use, not just publication. HAS requires clarity on study type, data sources, endpoints including patient-relevant measures, comparators, and follow-up duration. NICE's RWE framework similarly expects prespecified public protocols and analysis plans. In ARCH/4 terms, that means no "generic registry" and no "we will collect outcomes later." The evidence

plan must specify the question, the decision it supports, and the time when the decision will be revisited. [41]

Actionable recommendations for evidence generation

Companies should create an **evidence generation charter** approved before submission, defining each evidence gap, the study or data source assigned to close it, the metric that will count as success, and the committee or payer audience that will use the result. They should nominate a **data custodian** for every key dataset, pre-negotiate data-sharing permissions where possible, and align registry variables with both regulatory safety needs and HTA modelling needs. They should also distinguish clearly between **evidence to maintain access**, **evidence to expand access**, and **evidence to defend price**, because those goals often require different endpoints and different follow-up periods. [38]

Commercial and payer levers over time

Commercial tactics

ARCH/4 commercial strategy is about **pricing architecture over time**, not just a launch price. For some products, the problem is preserving a premium while uncertainty declines. For others, the problem is broadening access without collapsing the global price corridor. That is why commercial tactics such as confidential discounts, launch sequencing, indication-based pricing, bundling, combination-therapy frameworks, and lawful lifecycle IP strategy belong inside the ARCH/4 lens rather than being treated as separate commercial topics. [42]

Pricing over time should usually be treated as a path, not a point. One practical rule is to separate the *visible architecture* from the *effective net price path*. This can be done through confidential rebates, volume-linked arrangements, or time-limited access terms, especially where international reference pricing matters. The strategic question is not “how much is the price?” but “how does the price evolve as evidence, population size, and competitive intensity evolve?” That is especially relevant for products whose first reimbursed population is small and high-need, but whose later expansions reach broader, lower-value, or less certain groups. [43]

Indication-based pricing is particularly important in multi-indication oncology and rare-disease lifecycle management. OHE notes that indication-based pricing allows medicine prices to vary by indication and helps health systems capture value as drugs gain multiple or new indications. The logic is straightforward: if the same molecule has very different incremental value across indications, a single uniform price can either overpay in low-value settings or under-reward in high-value ones. In practice, implementation varies by market, but ARCH/4 teams should at least model it, even where the contract eventually uses commercial flexibility rather than formal indication-specific tariffs. [44]

Bundling and combination therapies are now a growing ARCH/4 issue, especially in oncology. EFPIA and OHE both describe the challenge: combinations create value-attribution problems, affordability issues, and legal/commercial complexity when multiple manufacturers are involved. A combination may be clinically superior but commercially blocked if value cannot be allocated in a way that keeps the whole regimen cost-effective. ARCH/4 teams therefore need combination-specific pricing frameworks, early legal review, and joint-evidence planning well before the combination submission occurs. [45]

Lifecycle IP strategy can legitimately support long-term value when it reflects real therapeutic innovation — for example a new formulation, device, pediatric program, or manufacturing improvement that changes outcomes or usability. In the EU, supplementary protection certificates can

extend protection for pharmaceutical products, up to the statutory limits, and pediatric work can add a further six months in some cases. But ARCH/4 should distinguish clearly between **value-creating lifecycle innovation** and strategies that may be seen by payers or competition stakeholders as low-value “evergreening.” The latter can create reputational, policy, and access backlash even if legally defensible in some contexts. [46]

Payer engagement and policy levers

On the payer side, ARCH/4 is where **conditionality** becomes a core tool. NICE managed access is explicitly designed for promising but uncertain medicines, with a data collection agreement plus a patient-access and/or commercial access arrangement, typically for the shortest period needed up to a maximum of five years. NHS England’s Innovative Medicines Fund applies this logic to non-cancer medicines and states that managed access should be reserved for medicines with plausible potential to be cost-effective and priced responsibly during the uncertain period. [47]

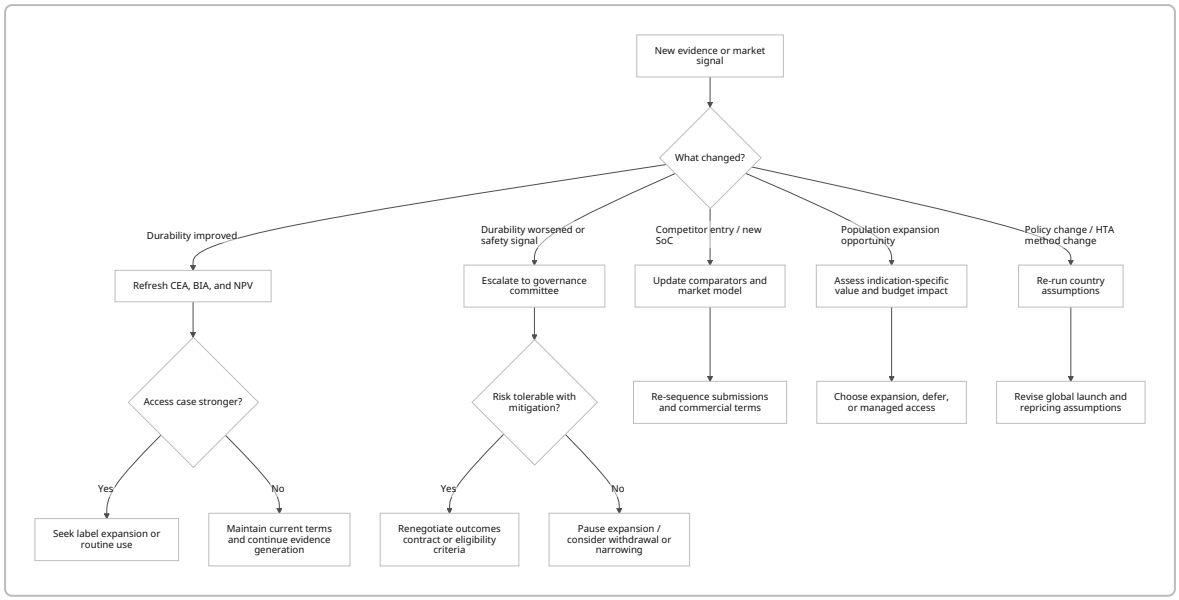
Regulatory policy can support this strategy. EMA’s conditional marketing authorisation allows earlier access on less comprehensive data when the benefit of immediate availability outweighs the risk of remaining uncertainty, provided post-authorisation obligations are fulfilled. EMA also encourages early scientific advice and early involvement of HTA bodies through parallel consultation. That combination is highly ARCH/4-compatible because it lets sponsors design a joined-up regulatory-plus-HTA horizon plan rather than discovering payer concerns after approval. [48]

Outcomes-based contracts and annuity-style structures are especially relevant for one-time therapies. The CMS Cell and Gene Therapy Access Model is a major recent example: a multi-year voluntary model in which CMS negotiates key terms, including pricing discounts and outcomes-based rebates, and supports states with implementation and data-collection infrastructure. CMS presents the model explicitly as a way to increase access, improve outcomes, and reduce financial and administrative burden for Medicaid programs. This is a clear signal that outcomes-linked payment and operational support are moving from theory into institutional policy. [49]

Performance-based annuities serve a related function. NEWDIGS describes them as a way to both spread costs over time and manage performance risk, while published analyses show that annuity payment structures can expand access under budget-impact constraints compared with full upfront payments. For ARCH/4, the lesson is that payment timing is itself a market-access variable, particularly in systems where annual budget caps or budget-impact tests drive implementation. [50]

Mermaid flowchart for decision triggers

The flow below is a recommended **ARCH/4 governance logic** for when strategy should remain stable, when it should shift, and who should intervene.



Actionable recommendations for commercial and payer strategy

Use **pricing corridors** with pre-agreed guardrails rather than ad hoc discounting. Build **indication-entry gates** so that broader populations are opened only when predefined value and affordability criteria are met. For one-time therapies, model at least one **installment or outcomes-linked option** even if the final deal is conventional, because the exercise clarifies what affordability problem is truly being solved. For combinations, establish a **combination readiness team** spanning market access, legal, finance, and HEOR at least 12 to 18 months before expected regulatory filing. And for lifecycle IP, require a simple question at governance level: **what patient or system benefit does this increment actually create?** If the answer is weak, the ARCH/4 case is weak too. 51

Risk management, KPIs, and case studies

Risk categories and triggers for strategy shifts

ARCH/4 needs a risk framework that is broad enough to capture the real causes of value erosion. The major categories are **clinical**, **regulatory**, **financial**, **competitive**, **implementation**, and **reputational/policy** risk. Clinical risk includes weaker durability, late adverse events, biomarker drift, or lower real-world persistence than expected. Regulatory risk includes post-authorisation obligations not being completed on time, conditional approval conditions not being met, or guidance updates under managed access returning a worse-than-expected conclusion. Financial risk includes budget-impact shocks, discount escalation, or lower uptake due to service bottlenecks. Competitive risk includes new mechanisms, earlier-line entrants, or superior combinations. Implementation risk includes site capacity, diagnostic rates, referral friction, and patient support underperformance. Reputational/policy risk includes criticism of pricing tactics, weak transparency, or lifecycle IP strategies perceived as extractive rather than value-creating. 52

A useful ARCH/4 KPI set should include both **value KPIs** and **control KPIs**. Value KPIs include population reached, persistence, observed event reduction, confirmed duration of response, time to reimbursement expansion, and cumulative net revenue versus plan. Control KPIs include percentage of required evidence milestones delivered on time, registry completeness, median time from diagnosis to treatment start, number of centres activated, budget impact versus threshold, and time from new evidence signal to model refresh. Where managed access applies, governance should also track

whether evidence generation remains “on track” and whether corrective action is needed — exactly the sort of oversight NICE describes for managed-access oversight groups and interim evidence reviews. [53]

KPI and trigger table

Risk area	Example KPIs	Trigger for action	Typical ARCH/4 response
Clinical durability	Response persistence, survival trend, biomarker sustainability	Durability curve falls below pre-specified scenario band	Refresh model; reconsider price path or expansion timing
Safety	Delayed adverse-event rate, discontinuation, serious safety reports	Confirmed new safety concern or rising trend	Narrow eligibility, update monitoring, renegotiate terms, pause expansion
Regulatory / HTA	Study milestones met, reassessment readiness, evidence completeness	Missed milestone or unfavorable interim evidence review	Escalate to governance, revise protocol, increase data-collection support
Financial	Net budget impact, rebate burden, cumulative NPV vs plan	Budget test exceeded or NPV falls below hurdle rate	Reprice, sequence differently, shift customer mix, use installment structure
Competitive	Share, comparator outcomes, line-of-therapy shifts	Competitor moves earlier line or alters SoC	Re-run comparators, reprioritise indications, change narrative
Implementation	Site activation, referral-to-treatment time, diagnosis yield	Uptake materially below forecast despite reimbursement	Invest in operational enablement, not just contracting
Policy / reputation	Payer sentiment, media pressure, policy consultations	Visible backlash to price or IP strategy	Simplify offer, improve transparency, retreat from low-value tactics

Case studies

Luxturna and the long arc of gene-therapy value

Luxturna is a useful ARCH/4 case because it combined early high-price access, outcomes-linked contracting in the United States, and a long need for durability evidence. EMA concluded that Luxturna’s benefits outweighed its risks and authorised it in the EU. NICE subsequently recommended it in England with a simple discount patient-access scheme. In parallel, Spark disclosed in an SEC filing that it had reached an agreement in principle with Harvard Pilgrim for an outcomes-based rebate arrangement and an innovative contracting model to reduce payer risk and financial burden. Later French reassessment cited long-term follow-up data, including registry and observational studies, and maintained substantial clinical benefit, illustrating how post-launch evidence can reinforce the long-horizon value story. The lesson is that ARCH/4 for gene therapy depends on **contract design plus durability evidence plus reassessment discipline**; any one of the three alone is insufficient. [54]

Hemgenix and managed access for one-time therapy uncertainty

NICE's 2024 guidance on Hemgenix recommended the therapy with managed access and stated that more evidence is being collected, after which NICE will decide whether it should remain available for routine use. This is a textbook ARCH/4 structure: a one-time therapy with potentially transformative long-term benefit enters the system before all durability uncertainty is resolved, and the health system explicitly buys time through managed access rather than forcing a binary full-approval or no-access choice. The lesson is that for high-cost one-time therapies, **time itself becomes a reimbursed asset**: the system funds access while evidence accrues, provided the evidence plan and the commercial terms are judged acceptable. [55]

Pembrolizumab and oncology lifecycle expansion

Pembrolizumab shows the ARCH/4 logic of serial indication expansion better than almost any product. The FDA label now spans a long list of tumour settings, and NICE has issued separate appraisals over time for different NSCLC settings, including metastatic use, neoadjuvant-plus-adjuvant use, and adjuvant treatment after resection. The commercial and HEOR lesson is that oncology value is rarely static: evidence packages, comparators, biomarker rules, treatment sequencing, and combination partners all evolve. An ARCH/4 program for oncology therefore needs repeating cycles of model refresh, indication-specific evidence, and often different pricing/access tactics by setting rather than one master access story for the molecule. [56]

Inclisiran and the gap between deal architecture and implementation

Inclisiran is one of the clearest recent examples of a horizon-oriented chronic-disease access model. NHS England and the Accelerated Access Collaborative framed the arrangement as the first NHS population health agreement; NHS funding was centralised and inclisiran was supplied in primary care at a nominal charge designed to improve affordability, with the latest NHS documentation maintaining the same price for current and new NHS patients until December 2027. Yet reported real-world implementation fell well short of the original ambition: *The BMJ* reported that roughly 30,000 patients had been prescribed inclisiran in primary care since 2021, far below the 300,000 target by 2024. The lesson is especially important for ARCH/4: **long-term value depends on delivery-system execution, not only price, reimbursement, or epidemiologic need**. [57]

Kaftrio and registry-enabled lifecycle expansion in chronic rare disease

Cystic-fibrosis modulators in England illustrate a different ARCH/4 pattern: an interim access agreement paired with structured data collection through the UK Cystic Fibrosis Registry, followed by later NICE recommendations and expansion to additional mutation groups through NHS commissioning policy. NICE's data-collection agreement explicitly names the registry manager and the key parties involved, and later NHS commissioning documents confirm expanded availability. This case shows how a disease-area registry can function as a long-term strategic asset for both patients and payers: it reduces uncertainty, supports reassessment, and enables broader access once evidence matures. The key lesson is that **registry infrastructure is itself a lifecycle market-access capability**, not just a research tool. [58]

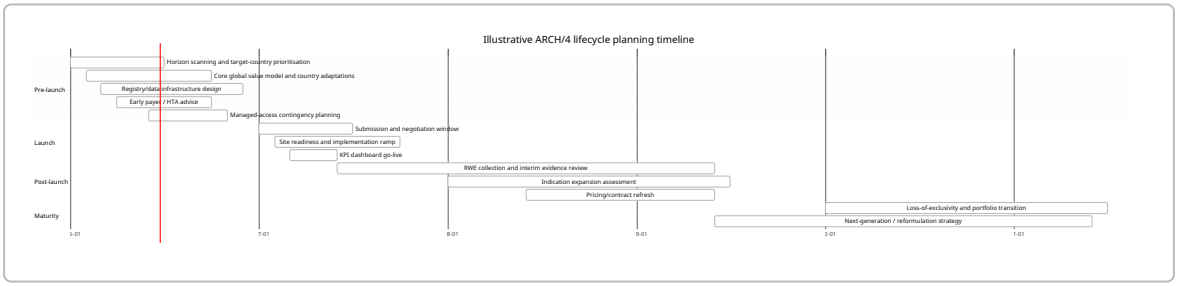
Implementation roadmap and playbook

ARCH/4 succeeds only when it is operationalised. The minimum cross-functional group should include **market access, HEOR, medical affairs, RWE/epidemiology, regulatory, pricing/commercial, legal/IP, finance, and supply/operations**. The governance model should separate three levels of decision-

making: an **asset team** that runs models and studies; an **ARCH/4 steering committee** that approves major pivots such as repricing, indication sequencing, and managed-access negotiations; and an **executive portfolio forum** that arbitrates between assets when capital or launch capacity is constrained. This structure is consistent with lifecycle HTA's emphasis on stakeholder engagement and on aligning premarket and postmarket activities rather than treating them as isolated exercises. [59]

Implementation timeline

The timing below is a recommended lifecycle plan. It is illustrative, but closely reflects the way NICE, HAS, and managed-access systems expect evidence and reassessment to unfold. [60]



One-page summary table of recommended actions by phase

Phase	Primary objective	Recommended ARCH/4 actions	Lead functions	Key deliverables
Pre-launch	Build the long-horizon value case and preserve options	Prioritise markets and indications; create global CEA/BIA backbone plus rNPV; design registry/LTFU plan; pre-negotiate data access; test managed-access and installment scenarios; map IP/exclusivity milestones	Market access, HEOR, medical, RWE, regulatory, finance, legal/IP	Target-product access profile; global value dossier; evidence generation charter; scenario library
Launch	Secure initial access without compromising long-term value	Sequence filings; negotiate confidential rebates or conditional access if needed; activate sites and referral pathways; launch dashboard for uptake, budget impact, and evidence milestones	Market access, pricing, operations, medical, field teams	Country access agreements; launch KPI dashboard; implementation readiness pack

Phase	Primary objective	Recommended ARCH/4 actions	Lead functions	Key deliverables
Post-launch	Reduce uncertainty and convert provisional access into sustained value	Run registries/post-marketing studies; validate surrogates where needed; refresh models with real-world data; assess new indications, combinations, and earlier lines; review payer contracts	RWE, HEOR, medical, access, regulatory	Interim evidence reports; updated CEA/BIA; expansion business cases
Maturity	Protect value while preparing for erosion	Reassess price architecture; use justified lifecycle innovation only where patient value is clear; prepare generic/ biosimilar defense and service differentiation; shift focus to adherence, patient segmentation, and portfolio migration	Commercial, access, medical, legal/ IP, finance	Maturity strategy, LOE plan, next-generation asset transition plan

Practical playbook

A robust ARCH/4 playbook can be run as a repeating quarterly process.

Step one: refresh the horizon map. Update expected approvals, label changes, standard-of-care shifts, budget-policy changes, and competitor launches. NICE's topic planning and prioritisation manuals show why this matters: external decision systems are themselves highly timing-sensitive. [61]

Step two: refresh the evidence map. For each unresolved uncertainty, confirm what evidence has arrived, what remains missing, and whether the original study design still answers the right question in the current treatment pathway. Lifecycle HTA literature is clear that postmarket learning must inform subsequent decisions, not sit unused in a repository. [62]

Step three: refresh the value stack. Re-run CEA, BIA, and rNPV, plus a limited set of decision-relevant scenarios. NICE, HAS, and IQWiG all support this discipline through lifetime horizon logic and explicit scenario/sensitivity analysis requirements. [63]

Step four: check operational truth. Compare modelled uptake to actual treated patients, referral timelines, site throughput, persistence, and adverse-event monitoring. The inclisiran case demonstrates why this is indispensable. [64]

Step five: decide whether to stay the course or shift strategy. The decision should be based on explicit triggers, not intuition. That is the essence of ARCH/4 governance: to make long-term value management systematic rather than reactive. [65]

Final analytical takeaway

ARCH/4 is the part of market access that turns a product from a reimbursement event into a managed long-term asset. The best ARCH/4 strategies are not those that simply maximise launch price; they are those that **preserve future optionality, design evidence around reassessment, align payment timing with value realisation, and know when to change course**. HTA and payer institutions are increasingly organised around that same logic — through lifecycle HTA, managed access, post-registration evidence, and outcomes-linked payment models — which means companies that still operate with a "launch-only" mindset are now strategically misaligned with the systems they are trying to influence. [66]

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