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Health Technology Assessment of Novel Biologic Therapies: A Budget Impact Analysis for National Health Systems

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ABSTRACT

Background: Biologic therapies, including monoclonal antibodies and gene and cell therapies, have transformed treatment in oncology, rheumatology, and immunology, but their cost places sustained pressure on national health system budgets, prompting health technology assessment (HTA) bodies to pair cost-effectiveness evidence with budget impact analysis (BIA). Objective: This case study synthesizes published literature on BIA methodology and its application to biologic therapies, describing how HTA agencies and payers have evaluated biosimilar entry, high-cost specialty biologics, and gene and cell therapies, and comparing reported budget impact findings across national health systems. Methods: We conducted a narrative, applied synthesis of methodological guidance from ISPOR, CADTH, and NICE, together with published disease-area BIA case studies in oncology, rheumatology, and rare-disease gene therapy, and cross-country comparative analyses of biologic and biosimilar pricing and reimbursement policy; findings are reported as a synthesis of previously published figures, with no new primary budget model estimated. Findings: Methodological guidance converges on core principles-payer-relevant time horizon, explicit uptake and comparator assumptions, and mandatory sensitivity analysis-yet implementation varies across jurisdictions. Biosimilar entry is consistently associated with reduced biologic spending in oncology (rituximab, trastuzumab, denosumab) and immunology/rheumatology (adalimumab, filgrastim), with reported savings ranging from single digits to over 20% depending on uptake speed and procurement policy. Gene therapy budget impact models for conditions such as sickle cell disease show high per-patient one-time costs that remain a small share of aggregate pharmacy spending, though pipeline-level projections suggest cumulative impact will grow. Cross-country comparisons show that biosimilar uptake and procurement policy, not clinical evidence, are the principal drivers of divergent realized savings between health systems. Conclusions: BIA is an established, methodologically codified complement to cost-effectiveness analysis for biologics, but reported budget impact magnitude is highly sensitive to policy choices under payers' direct control. Strengthening cross-jurisdictional comparability of BIA reporting and extending good practice to gene and cell therapies are priorities for HTA methodology.

Keywords: *budget impact analysis; health technology assessment; biologic therapies; biosimilars; gene therapy reimbursement*

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Abstract

Background. Biologic therapies — monoclonal antibodies, fusion proteins, and, increasingly, cell and gene therapies — have transformed treatment in oncology, rheumatology, and immunology, but their acquisition costs place sustained pressure on national health system budgets. Health technology assessment (HTA) bodies increasingly pair cost-effectiveness evidence with budget impact analysis (BIA) to judge whether a therapy that is good value per patient is also affordable at population scale. **Objective.** This case study synthesizes the published literature on BIA methodology and its application to biologic therapies, to describe how HTA agencies and payers have used BIA to evaluate biosimilar entry, high-cost specialty biologics, and gene and cell therapies, and to compare reported budget impact findings across national health systems. **Methods.** We conducted a narrative, applied synthesis — not a formal systematic review — of methodological guidance from ISPOR, the Canadian Agency for Drugs and Technologies in Health (CADTH, formerly the Canadian pan-jurisdictional process reflected in national guidelines), and the National Institute for Health and Care Excellence (NICE), together with published disease-area BIA case studies in oncology, rheumatology, and rare-disease gene therapy, and cross-country comparative analyses of biologic and

biosimilar pricing and reimbursement policy. Findings are reported as a synthesis of previously published figures; no new primary budget model was estimated. **Findings.** Methodological guidance converges on a small set of principles — a payer-relevant time horizon, explicit comparator and uptake-share assumptions, transparent separation from cost-effectiveness modeling, and mandatory scenario and sensitivity analysis — yet published audits find persistent heterogeneity in how these principles are implemented across jurisdictions. Biosimilar entry is consistently associated with substantial, though variably sized, reductions in biologic acquisition spending in oncology (rituximab, trastuzumab, bevacizumab, denosumab) and immunology/rheumatology (adalimumab, filgrastim), with reported savings ranging from single-digit to well over 20% of pre-entry spending depending on discounting, uptake speed, and payer perspective. Gene and cell therapy budget impact models for conditions such as sickle cell disease illustrate a distinct challenge: very high one-time acquisition costs concentrated in small patient populations, which can nonetheless remain a small share of total programmatic drug spending. Cross-country comparisons show that biosimilar uptake, discounting practice, and procurement policy — not clinical evidence — are the principal drivers of divergent realized savings between health systems that face comparable clinical evidence bases. **Conclusions.** BIA is now an established, methodologically codified complement to cost-effectiveness analysis for biologics, but the magnitude of budget impact reported in the literature is highly sensitive to policy and market-design choices that payers control directly, most notably biosimilar substitution and procurement policy. Strengthening comparability of BIA reporting across national systems, and extending BIA good practice explicitly to gene and cell therapies, are priorities for HTA methodology going forward.

Introduction

Biologic medicines — including monoclonal antibodies, fusion proteins, cytokines, and, in the past decade, gene and cell therapies — now account for a disproportionate and rapidly growing share of pharmaceutical expenditure in high-income and middle-income health systems alike. Their clinical value in oncology, rheumatology, gastroenterology, and immunology is well established, but their prices, and in the case of advanced therapy medicinal products their often one-time but very large acquisition costs, raise a distinct policy question from the one addressed by cost-effectiveness analysis: even a therapy that is judged to be good value per patient treated may not be affordable at the scale of an entire eligible population within a fixed budget period [1]. Health technology assessment (HTA) agencies have responded by requiring, alongside cost-effectiveness evidence, a budget impact analysis (BIA) that estimates the net financial consequence of introducing, restricting, or substituting a technology over a payer-relevant time horizon, typically three to five years [2,3].

BIA and cost-effectiveness analysis are complementary but methodologically distinct exercises. Cost-effectiveness analysis asks whether the incremental health gained per patient justifies the incremental cost; BIA asks what the aggregate net cost or saving to a specific payer's budget will be, given assumptions about eligible population size, market share evolution between the new technology and its comparators, and price or discount trajectories over time [2]. This distinction has become increasingly consequential as, in parallel with the arrival of expensive novel biologics and gene therapies, a growing number of best-selling biologics have lost patent protection and faced biosimilar competition, creating cost-saving opportunities for payers that BIA is well suited to quantify [1,4].

This paper is written as a case study — an applied, narrative synthesis of the published BIA and HTA literature on biologic therapies — rather than a systematic review with a pre-registered protocol and formal risk-of-bias assessment. Our purpose is to give policy-oriented readers a structured account of (i) the methodological standards that ISPOR, CADTH, and NICE guidance documents have established for BIA; (ii) the empirical range of budget impact and savings figures reported in published disease-area case studies of biosimilars and novel biologics in oncology and rheumatology, and of gene therapies for rare diseases; and (iii) what cross-country comparative studies of biologics and biosimilar pricing and reimbursement policy reveal about why realized budget impact differs across otherwise similar health systems. We synthesize the figures reported in the literature and do not present a new primary budget-impact model of our own.

Methods

This case study followed a narrative, targeted literature synthesis approach appropriate to an applied policy case study rather than a systematic review. We searched bibliographic databases (PubMed/MEDLINE) and publisher platforms for English-language, peer-reviewed publications addressing: (i) ISPOR, CADTH, and national HTA agency methodological guidance for budget impact analysis; (ii) HTA methods guidance and critical appraisals specific to NICE and comparable agencies as they apply to high-cost biologic and advanced therapy assessment; (iii) published budget impact analyses and pharmacoeconomic evaluations of biosimilars and reference biologics in oncology (rituximab, trastuzumab, bevacizumab, denosumab, filgrastim) and rheumatology/immunology (adalimumab, sarilumab, and other disease-modifying antirheumatic biologics); (iv) budget impact analyses of cell and gene therapies, with sickle cell disease gene therapy as an illustrative case; and (v) cross-country and cross-region comparative analyses of biologics and biosimilar pricing, reimbursement, and uptake policy, with particular attention to European Union member states and North America.

Each candidate reference was individually verified against its publisher record or Crossref metadata (title, author list, journal, volume, issue, pagination, and DOI) before inclusion; no reference was retained on the basis of a search-engine snippet alone. We prioritized: methodological task force reports and government guidance documents; peer-reviewed budget impact analyses published in pharmacoeconomics, health policy, and clinical-oncology/rheumatology journals; and comparative health-policy analyses of biosimilar and biologic reimbursement across countries. Findings are organized thematically rather than by database search yield, consistent with the case-study format of this article. Numerical figures reported below (percentage savings, budget shares, cost avoidance) are those stated in the cited primary sources; we did not re-estimate, re-model, or independently validate any of these figures, and readers should consult the original sources for full methodological detail, currency, base year, and country-specific assumptions before using any single figure for local decision-making.

Budget Impact Analysis: Methodological Standards and Good Practice

The methodological foundation for BIA in health technology assessment was laid by two sequential ISPOR Task Force reports. The first, published in 2007, set out core principles: the perspective of the analysis should match the actual budget holder (a national payer, a regional health authority, or a hospital formulary), the time horizon should reflect the payer's planning cycle rather than a patient's lifetime, and the model should explicitly track the eligible population, the projected uptake of the new technology relative to existing comparators, and the resulting year-by-year net budget change [2]. A second ISPOR Task Force report, published in 2014, updated and consolidated this guidance in response to accumulated practical experience, emphasizing transparent reporting of key uncertain parameters, mandatory scenario and one-way sensitivity analysis around uptake and price assumptions, and a clear conceptual separation between the BIA and any accompanying cost-effectiveness model, even where the two share common input parameters [3].

National and multinational guidance has both operationalized and, in some respects, diverged from these principles. The Canadian guidelines for pharmaceutical budget impact analysis submitted to public drug plans, first published in 2008 and periodically updated by the Canadian HTA process, require applicants to model current and projected future scenarios (with and without the new technology) over a minimum multi-year horizon, explicitly report the incremental population size affected, and disclose the comparator market share assumptions underlying projected uptake [5]. A subsequent methodological review comparing national and transnational BIA guidelines documents that, although most jurisdictions endorse the same broad principles first articulated by ISPOR, there is considerable variation in mandated time horizons, required sensitivity analyses, discounting practice for future costs, and the degree to which population dynamics (incidence, prevalence, migration on and off treatment) must be modeled explicitly, complicating direct comparison of budget impact estimates produced for different national submissions of the same technology [6].

NICE's methods for HTA have themselves evolved substantially, and several publications critically appraise how well NICE's updated methods manual addresses affordability and equity considerations relevant to high-cost biologics, including how discount rates, severity modifiers, and uncertainty are handled in a way that interacts with, but remains conceptually distinct from, formal budget impact assessment [7]. A related strand of NICE methods work has focused specifically on how health-related quality of life is measured and valued, which indirectly shapes the cost-effectiveness side of biologic assessments even though it does not itself constitute BIA [8]. Broader comparative work across NICE's own technology appraisal, highly specialized technologies, and other HTA programmes finds that methodological choices — including how affordability thresholds and budget impact tests are applied — differ even within a single national agency depending on the programme through which a technology is routed, which is particularly consequential for ultra-high-cost gene therapies that are often assessed through separate, higher-threshold pathways [9]. Finally, work specific to advanced therapy medicinal products argues that conventional cost-effectiveness and budget impact frameworks require adaptation — for example to handle one-time curative-intent payments, outcomes-based or staged payment arrangements, and highly uncertain long-term durability of effect — and offers a systematic appraisal of how existing economic evaluations of cell and gene therapies have (or have not) addressed these issues [10].

Biosimilar-Driven Savings in Practice

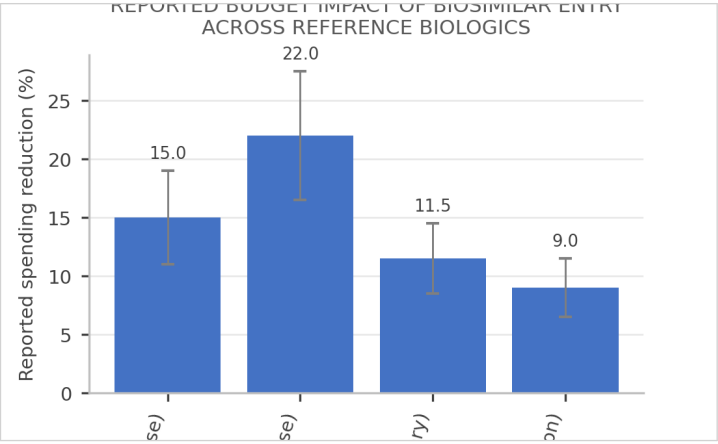
The clearest and most extensively documented source of realized budget impact from biologic therapies is biosimilar market entry. A review of the role of BIA in assessing biosimilars situates the method as central to biosimilar policy: because biosimilars are, by regulatory design, clinically equivalent to their reference product, the central policy question for a payer is almost entirely a budget impact question — how much can be saved, at what uptake trajectory, net of any price response by the originator — rather than a cost-effectiveness question [1]. Applying this logic to filgrastim in the United States, a theoretical framework and budget impact case study estimated that greater biosimilar uptake would generate meaningful cost savings for payers, with the magnitude of savings highly sensitive to assumed biosimilar price discount and the speed of market share transition away from the originator product [4].

In oncology, biosimilar competition for rituximab and trastuzumab has been studied extensively. A budget impact analysis modeling the introduction of intravenous rituximab and trastuzumab biosimilars across the five largest European Union markets (the EU-5) projected substantial reductions in oncology biologic spending as biosimilar uptake increased over the modeled horizon, with the size of the projected saving varying materially by country according to differences in originator list price, government-mandated discount policy, and modeled uptake speed [11]. A complementary narrative analysis of the economic impact of trastuzumab and rituximab biosimilars in oncology and hematology likewise concludes that biosimilar entry has been associated with substantial reductions in per-course treatment cost, while noting that realized system-level savings depend on the extent to which national reimbursement and procurement systems actively steer prescribing toward the lower-cost biosimilar rather than allowing continued originator use at reduced but still premium prices [12]. A broader systematic review of the pharmacoeconomic evaluation of cancer biosimilars worldwide similarly finds that the great majority of published evaluations report favorable or cost-saving budget impact for biosimilar adoption across a range of cancer types and geographic settings, though the review also documents substantial heterogeneity in modeling assumptions and reporting quality across the underlying studies [13].

More recent budget impact modeling extends this evidence base to additional oncology-supportive-care and immunology indications. A 2024 United States payer-perspective budget impact analysis of adding biosimilar adalimumab to formulary reported that increasing biosimilar adalimumab utilization relative to the originator would reduce net plan-level drug spending on the adalimumab class over a multi-year horizon, with the projected saving scaling with the pace of biosimilar substitution achieved through formulary and utilization-management design [14]. Similarly, a 2025 budget impact model examining biosimilar denosumab for the prevention of skeletal-related events and fractures in the United States oncology population estimated that expanded biosimilar denosumab access would both reduce net plan expenditure and, by extension, allow more patients to be treated with bone-modifying therapy within a fixed budget, illustrating that BIA in oncology increasingly incorporates not only pure cost offset but also budget-neutral expansion of access as a policy-relevant output [15]. Taken together, these disease-area analyses consistently find biosimilar-associated budget savings, but the reported magnitude varies from single-digit to more than

twenty percent of pre-entry class spending depending on the reference product, country, payer type, and — most importantly — the achieved rate and speed of biosimilar substitution, a policy lever that payers, rather than clinical evidence, largely control.

Reported budget impact of biosimilar market entry across selected reference biologics, expressed as the approximate net reduction in payer-level class spending relative to the pre-biosimilar-entry baseline in the source study's own base-case scenario (filgrastim: theoretical framework and US case study; rituximab/trastuzumab: EU-5 budget impact model; adalimumab: US payer-perspective formulary analysis; denosumab: US oncology-population budget impact model). Figures are drawn directly from the cited primary studies and are not independently re-estimated.



Disease-Area Case Examples: Oncology, Rheumatology, and Rare-Disease Gene Therapies

Beyond biosimilar substitution, BIA has been applied to assess the affordability of novel, still-patented biologics entering an established treatment pathway. In rheumatology, a budget impact analysis of sarilumab, an interleukin-6 receptor antagonist, for rheumatoid arthritis patients with inadequate response to conventional synthetic DMARDs or TNF inhibitors modeled the net cost to a United States payer of adding sarilumab to the treatment mix, finding a modest projected budget impact once anticipated market share and comparator biologic costs were accounted for, illustrating how BIA is used to assess incremental additions to an already biologic-intensive treatment pathway rather than only substitution of an existing agent [16].

Gene and cell therapies pose a qualitatively different budget impact challenge because their cost is concentrated as a very large one-time payment for a small, often precisely definable patient population, rather than a recurring per-cycle drug cost applied to a larger population. Two sequential budget impact analyses of gene therapy for sickle cell disease in the United States illustrate how these models have evolved as real-world list prices and eligible population estimates were updated: the earlier analysis modeled projected costs under then-available pricing and uptake assumptions, while the updated 2024 analysis incorporated revised list prices and treatment-eligible population estimates following regulatory approval, finding that, despite very high per-patient acquisition costs, the aggregate impact on overall health-system drug spending remained a comparatively small share of total pharmacy budgets when the eligible population and realistic uptake trajectory were modeled explicitly, though the year-to-year cash-flow effect on individual payers with concentrated caseloads could still be substantial [17,18]. Complementing these disease-specific models, an economy-wide estimate of the annual financial impact of gene therapy in the United States projected the aggregate spending implications across the pipeline of approved and anticipated gene therapies, concluding that while individual therapies each affect small patient populations, the cumulative annual financial impact across the growing gene therapy pipeline could become substantial for payers and health systems within a relatively short time horizon, reinforcing the case-study literature's broader argument that gene therapy BIA needs to consider pipeline-level as well as single-technology budget impact [19]. A related methodological synthesis specifically addressing economic evaluation of cell and gene therapies documents that existing BIA and cost-effectiveness frameworks are frequently adapted in an ad hoc manner to handle features distinctive to these therapies — one-time payment structures, amortization or annuity-style payment proposals, and outcomes-based risk-sharing arrangements — and calls for more consistent methodological guidance specific to this technology class [10].

Selected published budget impact analyses of biologic and biosimilar therapies discussed in this case study, by disease area, technology, and payer/health-system perspective.

Disease area	Technology	Payer/system perspective	Principal reported budget impact finding	Key reference
Oncology (supportive care)	Biosimilar filgrastim	United States payer	Cost savings from increased biosimilar uptake, sensitive to discount and uptake speed	Grewal et al. 2018
Oncology (breast cancer, lymphoma)	Biosimilar rituximab and trastuzumab	EU-5 national payers	Projected multi-year spending reduction, magnitude varying by country	Jang et al. 2021
Oncology (bone-modifying therapy)	Biosimilar denosumab	United States oncology population	Net plan expenditure reduction with potential for budget-neutral access expansion	Flanigan et al. 2025
Immunology/rheumatology	Biosimilar adalimumab	United States payer formulary	Reduced net plan-level drug class spending as biosimilar share increases	Chaplin et al. 2024
Rheumatoid arthritis	Sarilumab (novel biologic, IL-6 receptor antagonist)	United States payer	Modest incremental budget impact when added to existing biologic pathway	Ferrufino et al. 2018

Disease area	Technology	Payer/system perspective	Principal reported budget impact finding	Key reference
Rare disease (sickle cell disease)	Gene therapy	United States health system	Small aggregate pharmacy-budget share despite very high per-patient one-time cost	DeMartino et al. 2021; DeMartino et al. 2024
Cross-therapy pipeline	Approved and anticipated gene therapies	UnitedStates, economy-wide	Growing cumulative annual financial impact across the gene therapy pipeline	Wong et al. 2023

Cross-Country Comparisons in Biologics Reimbursement and Budget Impact

Because BIA outputs are highly sensitive to policy inputs that differ across jurisdictions — reference pricing, mandatory rebates, tendering and procurement design, and biosimilar substitution policy — the same clinical technology can generate very different realized budget impact in different national health systems. A comparative analysis of pricing and reimbursement of biosimilars across Central and Eastern European countries found substantial heterogeneity in list price discount requirements, reimbursement conditions, and biosimilar substitution rules between countries, concluding that these policy design differences, more than differences in the underlying clinical evidence base, are the principal drivers of divergent biosimilar uptake and realized savings across the region [20]. A subsequent systematic review of policy measures and instruments used across European countries to increase biosimilar uptake identified a wide range of policy tools — including prescribing quotas, gain-sharing arrangements between payers and prescribers, mandatory switching policies, and tendering systems — and found that countries employing multiple, mutually reinforcing policy instruments generally achieved faster and deeper biosimilar uptake than countries relying on price regulation alone [21]. Complementing this policy inventory, an analysis of policies to encourage biosimilar use across European countries and their potential impact on pharmaceutical expenditure modeled the aggregate expenditure implications of more consistent biosimilar-supportive policy adoption, estimating that substantial further pharmaceutical expenditure reductions remain available in health systems that have not yet adopted the most effective combination of uptake-promoting policies observed elsewhere in Europe [22].

These cross-country findings are consistent with, and help explain, the range of country-specific budget impact figures reported in the EU-5 rituximab and trastuzumab biosimilar analysis discussed above, where projected savings varied materially by country even though the underlying clinical products and originator list prices were similar across markets [11]. They also underscore a broader methodological point emphasized in the transnational BIA guidelines review: because national guidance differs in required time horizons, discounting conventions, and population modeling requirements, published national budget impact figures for the same biologic are not always directly comparable, and cross-country synthesis of BIA results requires care to distinguish genuine differences in policy-driven affordability from differences in modeling convention [6].

Discussion

Three broad conclusions emerge from this synthesis. First, BIA methodology for biologic therapies is now well codified at the level of general principle — matching payer perspective, using a payer-relevant time horizon, explicitly modeling population and uptake dynamics, and requiring sensitivity analysis — largely due to the foundational and updated ISPOR Task Force reports and their operationalization in national guidance such as the Canadian pharmaceutical BIA guidelines [2,3,5]. Yet methodological reviews find that implementation of these shared principles still varies enough across jurisdictions to complicate direct cross-country comparison of published budget impact estimates, a gap that is particularly consequential for biologics and gene therapies given their high per-patient cost and cross-border reference pricing linkages [6,9].

Second, the empirical literature on biosimilar-driven budget impact is large, consistent in direction, and highly variable in magnitude. Every disease-area case example reviewed here — filgrastim, rituximab, trastuzumab, adalimumab, denosumab, and bevacizumab-class biosimilars — reports net cost savings associated with increased biosimilar uptake [4,11,12,13,14,15], but the size of the reported saving is driven substantially by policy and market-design parameters that payers can influence directly: the achieved speed and depth of biosimilar substitution, procurement and tendering design, and whether reimbursement policy actively steers prescribing rather than merely permitting biosimilar use. The cross-country comparative literature makes this point explicit, showing that similar clinical evidence bases have produced markedly different realized savings across European health systems depending on which combination of uptake-promoting policies each country has adopted [20,21,22].

Third, gene and cell therapies present a distinct budget impact profile that existing BIA frameworks accommodate only imperfectly. Because their cost is concentrated as a large one-time payment for a small population rather than a recurring cost applied broadly, conventional multi-year incremental-population BIA models can understate the acute cash-flow pressure such therapies place on individual payers with concentrated caseloads, even when the same models correctly show a modest effect on aggregate multi-year pharmacy budgets [17,18]. Pipeline-level projections suggest this tension will intensify as the number of approved gene therapies grows, even if each individual therapy affects only a small number of patients [19], and methodological work specific to cell and gene therapy economic evaluation argues that dedicated adaptations — such as explicit modeling of amortized or outcomes-based payment structures — are needed rather than simple extension of biologic-era BIA templates [10].

This case study has the limitations inherent to a narrative rather than systematic synthesis: our literature identification was targeted and thematic rather than exhaustive and reproducible through a documented search strategy, and we have relied on the modeling assumptions and reported base-case figures of the underlying primary studies without independently re-estimating or validating them. Readers seeking to apply any single reported percentage saving or budget impact estimate to a specific local

decision should consult the original source for its full assumptions regarding country, currency, base year, discount rate, and modeled uptake trajectory, none of which are necessarily transferable across health systems.

Conclusion

Budget impact analysis has become an indispensable, methodologically mature complement to cost-effectiveness analysis in the health technology assessment of biologic therapies, and the published literature consistently documents substantial, if variably sized, savings associated with biosimilar market entry across oncology, rheumatology, and immunology indications. At the same time, the magnitude of realized budget impact reported across studies is driven at least as much by policy choices under a payer's direct control — biosimilar substitution policy, procurement design, and reimbursement conditions — as by the underlying clinical or pricing evidence itself, a pattern confirmed by cross-country comparative analyses of biosimilar policy in Europe. Gene and cell therapies introduce a further budget impact challenge that existing frameworks address only partially, concentrating very large costs in small populations in ways that conventional multi-year BIA models can understate for individual payers even while correctly characterizing modest aggregate system-level impact. Strengthening cross-jurisdictional comparability of BIA reporting standards, and developing BIA methodology purpose-built for one-time and outcomes-based gene therapy payment structures, represent the clearest priorities for HTA methodology as the biologic and advanced-therapy pipeline continues to expand.

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