2024 Rare Disease Trend Report

PERSPECTIVES FROM HEALTHCARE PAYERS AND EMPLOYERS

Alnylam®

FIFTH EDITION

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FOREWORD

The healthcare community is now well-versed in the life-changing potential of rare disease products, including cell and gene therapies. While the initial novelty has shifted from groundbreaking anticipation to a rapidly expanding portfolio of treatments, many questions — particularly around how to create and sustain access and affordability — remain unresolved. As more rare disease products have launched in the United States, stakeholders have explored various approaches and policies to manage high costs, while continuing to support innovation. Yet, the debate continues about how best to navigate access challenges as market dynamics evolve.

The 2024 Alnylam Rare Disease Trend report continues important discussions with payers and employers, expanding on previous editions to explore the emerging use of next-generation technologies, such as artificial intelligence (AI), and the impacts of the initial phases of the Inflation Reduction Act (IRA) Medicare Part D Redesign. Published to inspire open dialogue among payers, employers, providers, manufacturers, brokers and consultants, advocacy groups, and patients, this report serves to provide all stakeholders with a deeper understanding of urgent healthcare trends and challenges that must be overcome to improve patient access to rare disease products.

INTRODUCTION

This report is intended to inform stakeholders of prevailing trends in the management of high-cost rare disease products. Previous editions of this report (2020, 2021, and 2022) focused exclusively on the budget impact of rare disease products on health plans. Last year's edition (2023) introduced the employer perspective on rare disease and specialty products given their critical role in coverage decisions and relationships with payers. This year's edition (2024) builds upon the perspectives of payers and employers to identify key trends both stakeholders are implementing to navigate various market challenges and manage costs associated with rare diseases. Key questions answered within this report include:

- **How have key stakeholder priorities related to covering and managing rare diseases products shifted since this report began publication in 2020?**
- **What management and reimbursement strategies are gaining preference and why?**
- **How are self-insured vs. fully insured employers preparing for and managing benefit design and decision-making for rare disease products?**
- **How may potential legislation and policy reform in the United States shape payer and employer decision-making and engagement going forward?**
- **How are payers and employers using next-gen technology, including AI, and how does it inform coverage decision-making for new rare disease products?**

By sharing annual insights and perspectives on current and future coverage and management trends, the authors of this report aim to elevate and amplify healthcare community discussion around rare disease products. With a better understanding of how payers and employers perceive, evaluate, and prioritize the unique challenges of managing rare disease products, key industry stakeholders can stay informed about ongoing trends and adapt to market changes.

This report was sponsored and developed by Alnylam Pharmaceuticals, Inc. Alnylam is a biopharmaceutical company leading the translation of RNA interference (RNAi) into subsequent therapeutic approvals for patients who have limited or inadequate treatment options.

KEY FINDINGS

1	2	3	4
IRA COST BURDEN SHIFTS TO INFLUENCE COVERAGE AND MANAGEMENT DECISIONS IN 2025	**ECONOMIC PRESSURES ARE INCREASINGLY INFLUENCING PAYER DECISION-MAKING**	**STAKEHOLDERS WELCOME NEW COST-MITIGATION STRATEGIES**	**ETHICAL, ROI, AND IMPLEMENTATION CONCERNS SLOW AI ADOPTION AMONG PAYERS**
Payers and employers are closely monitoring the impact of the IRA Medicare Part D redesign and other macro trends. As costs are expected to shift from the government and beneficiaries to manufacturers and Part D plans, key implications may include the reevaluation of coverage decisions and more narrow formulary management across all books of business, including among rare disease products. Despite the pressure to tighten formulary approaches, payers and employers remain uncertain about potential policy changes and their tactical implications following the 2024 U.S. elections. However, both stakeholders expect to reevaluate future strategies in the 2025 plan year.	Payers and employers continue to prioritize outcomes and other clinical value drivers for management decisions, but economic factors such as treatment costs and total budget impact have increased in importance year over year. Economic pressures are driving the payer community to implement stricter approaches to control costs. These include tighter prior authorization criteria, specialty pharmacy and site-of-care mandates, and a stronger focus on practical outcomes and value-based contracts. The growing portfolio of new rare disease products is partly driving this utilization management trend. At the same time, as more therapeutic options enter the market, the rare disease space may see a shifting management paradigm and become structured more like traditional competitive disease areas. This may give payers a greater ability to control utilization and manage spend in a clinically appropriate manner.	Payers and employers alike are exploring new ways to manage rare disease products, such as cell and gene therapies, by leveraging external partners, specialized capabilities, and engaging in risk-sharing and -mitigation discussions. Employers have historically favored carve outs, but large payers are reluctant to expand their use, preferring to manage financial risks internally and stay directly connected to their member populations. Stakeholders recognize that no "perfect" solution exists for mitigating cost pressures, keeping them open to opportunities for disease- and product-specific strategies to reduce care costs.	While payers see potential in next-gen technologies like artificial intelligence (AI), they remain cautious about broadly adopting AI in managed care. This is due to concerns about ethics in coverage decisions, short-term ROI, data-sharing compliance, and the need for organizational shifts requiring time and buy-in. The novelty of AI and operational implementation barriers add to the hesitancy. In the near-term, the greatest interest lies in using novel technologies to provide tools and information to empower patients, so they can play a more active role in their healthcare.

METHODOLOGY

Alnylam Pharmaceuticals, Inc., sponsored and developed this publication in partnership with their vendor, Guidehouse. The Commercial Health Group at Guidehouse is a leading global advisory consultancy that specializes in life sciences strategy and research services.

SURVEY DEVELOPMENT

A survey was developed to capture payer and employer sentiment on management of rare disease products. The survey was designed to assess current payer and employer practices, perspectives, and priorities, and gain insights into anticipated changes in the management of rare disease products within the next plan year (2025), the next three to five plan years (2026–2030), and beyond (2030+).

The survey focused on the same themes as previous years to inform the report structure, including benefit design and utilization management, infrastructure and capabilities, payer economics, employer perspectives, and future trends. No specific products were assessed, although some may have been discussed in interviews as examples to further illustrate themes or trends. Potential respondents were screened for participation (see "Participant Selection and Demographics" below), and a total of 30 U.S.-based medical, and pharmacy directors, and employers meeting the predefined eligibility criteria were recruited to complete the survey and provided with the online link. Guidehouse partnered with a commercial vendor on Alnylam's behalf to recruit participants and transfer the survey to an online format.

RECRUITMENT AND FIELDING

Respondents were selected for relevant expertise and involvement in rare disease product evaluation. Guidehouse informed respondents that data and insights would be aggregated, and respondent identities would remain anonymous. The authors then selected participants to ensure a mix of both medical and pharmacy directors from a variety of health plan types (e.g., commercial, Medicare Advantage, and managed Medicaid), as well as a mix of stakeholders with national and regional purviews. To gain additional insights into the expected adoption of novel technological tools, a supplemental interview was held with a chief data officer (CDO) at a national health plan. In addition to payer respondents, the authors selected employers, employer benefit consultants, and employer coalition stakeholders to ensure a mix of employer perspectives.

All participants completed the survey from October 14 to October 24, 2024. While survey respondents may choose to participate in the annual updates to the research, each sample of respondents should be considered an independent sample.

PARTICIPANT SELECTION AND DEMOGRAPHICS

Research participants were required to meet specific qualifying criteria to ensure the integrity of responses across topics. Specific prequalification criteria for payers and employers included:

- **(Payers only) Current medical/pharmacy directors and/or CDO employed by a commercial, Medicare Advantage, or managed Medicaid payer, or a pharmacy benefit manager;**
- **Past experience and current active involvement in policy development within their organization, including experience in medical and utilization management of policy development for rare disease products at their organization; and**
- **Willingness and ability to discuss management approaches for rare products, such as new product evaluations, pharmacy and therapeutics (P&T) committee processes, innovative reimbursement model composition and implementation, distribution network determinations, and adoption of AI technology.**

QUALITATIVE INTERVIEWS

A set of individuals who completed the survey participated in interviews conducted over a 21-day period from September 30 to October 21, 2024. Fifteen respondents participated in 60-minute interviews to provide additional qualitative insight. Guidehouse researchers conducted all interviews over the phone in a double-blind manner, such that no respondent knew the company supporting the research and no Alnylam employee knew which specific payer stakeholders were providing input. All interviewees provided consent for using their responses in the composition of this report.

Respondents who met all eligibility criteria and completed the survey and phone interview received honoraria according to fair market value calculations.

DATA ANALYSIS, REPORTING, AND LIMITATIONS

Guidehouse collected, analyzed, and reported survey and interview responses. Data was blinded and aggregated across the entire sample of respondents. Responses reflect each participant's views and self-reported claims of their organization's internal processes and operations. All statements and opinions contained within the report reflect responses received by payer participants and do not necessarily reflect those of Alnylam or other reviewers.

PARTICIPANT SAMPLE PROFILE

Stakeholders with a strong understanding of rare and specialty product management, representing payers and employers across the United States, were selected to participate in primary research.

Payers who participated in the sample represent approximately 150 million total covered lives. Of the total covered lives represented by payers sampled, 59% represented the commercial book of business, 30% Medicare Advantage, and 11% managed Medicaid.

Of the plans sampled, the majority of commercial plan drug spend in rare is in the pharmacy benefit (58% of spend) compared to the medical benefit (42%); compared to a 46% / 54% blend for Medicare Advantage spend and 49% / 51% for managed Medicaid. The distinction between pharmacy and medical spend for Commercial, Medicare Advantage, and managed Medicaid often depends on the inclusion of specialty pharmacy networks. Plans with integrated specialty pharmacies are more likely to cover a therapy under the pharmacy benefit rather than the medical benefit when the option is available.

A supplemental interview was held with a CDO at a national health plan to gain additional insights into the expected adoption of novel technological tools, including artificial intelligence.

Employer group stakeholders consisted of benefit leadership among large self-funded employers, employer coalitions, and employee benefit consultants.

FIGURE 1A: **STAKEHOLDER SAMPLE PROFILE: RESEARCH SAMPLE MIX**

N=30 TOTAL RESPONDENTS

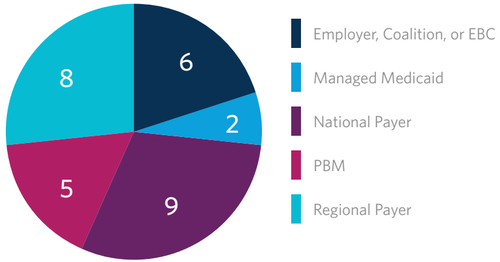


FIGURE 1B: **STAKEHOLDER SAMPLE PROFILE: COVERED LIVES MIX**

N=24 PAYERS; ~150M TOTAL COVERED LIVES

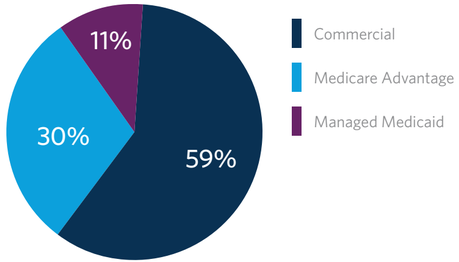
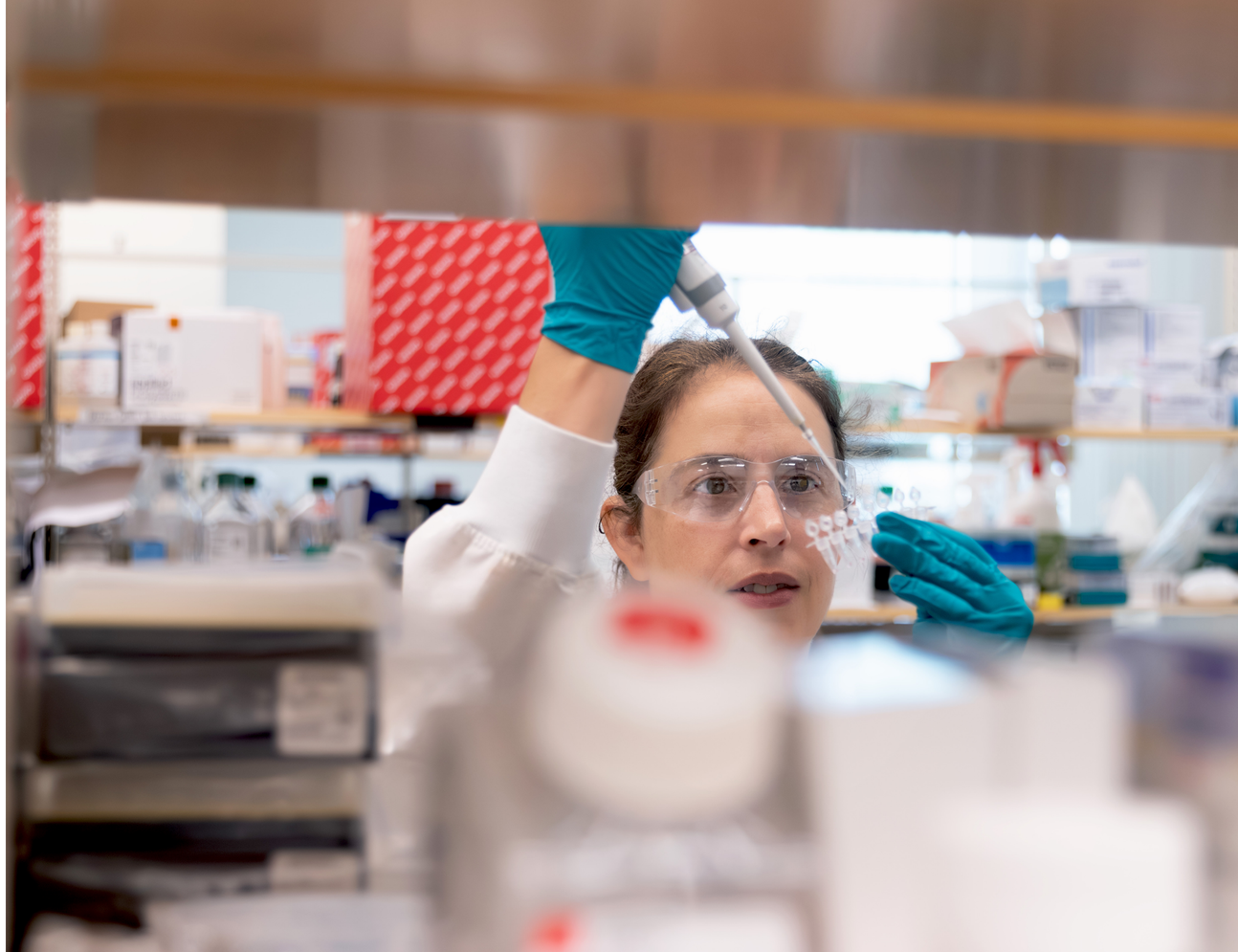


FIGURE 1C: **STAKEHOLDER SAMPLE PROFILE: Rx SPEND BY BENEFIT**

AVERAGE Rx SPEND BY BENEFIT



SECTION 1:

BENEFIT DESIGN AND UTILIZATION MANAGEMENT APPROACH

MANAGEMENT OF RARE DISEASE PRODUCTS

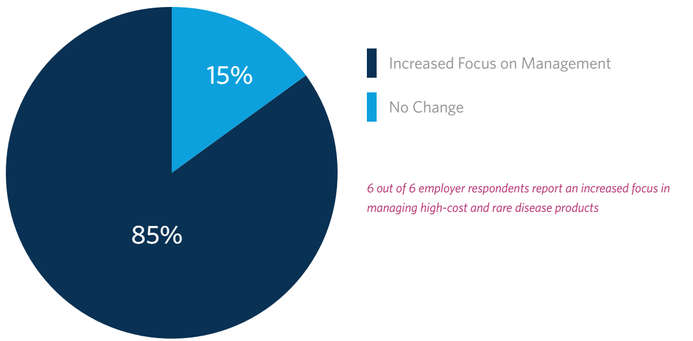
Since 2020, the U.S. Food and Drug Administration (FDA) has approved over 170 therapies for rare disease indications, driven by a commitment to support innovation for patients.[1–3] Over the years, payers and employers have remained focused on managing high-cost rare disease products. In the 2024 sample of respondents, payers representing 85% of total covered lives reported an increased focus on managing rare disease products, a priority all sampled employer group stakeholders shared (n=6).

Utilization management tactics, such as prior authorizations, are vital tools health plans deploy to ensure clinically appropriate access to medications. During primary research interviews, several payers noted they may require specific lab test documentation early in the patient journey to confirm diagnosis and ensure appropriate use. Payers may also restrict use beyond a product's FDA approved indication to manage products and control costs. Use is restricted in this manner by ensuring access to patient populations that achieved clinical benefit in a product's pivotal trial. Payer stakeholders mention this strategy is becoming more common due to a perceived increase in the number of broad FDA labels that have not been fully aligned to inclusion and exclusion criteria studied during clinical trials.

In addition to these tactics, many payers continue to implement step therapy in which patients must first try and fail what payers consider to be more cost-effective alternatives before receiving a higher-cost treatment. Payers often deploy a combination of tactics to control spending and manage utilization.

FIGURE 2: **PAYER EMPHASIS ON THE MANAGEMENT OF HIGH-COST AND RARE DISEASE PRODUCTS**

PRESENTED AS % TOTAL LIVES IN PAYER SAMPLE (N=24; ~150M LIVES)



6 out of 6 employer respondents report an increased focus in managing high-cost and rare disease products

Like previous years, payers surveyed in 2024 reported consistent utilization management approaches for rare disease products. Payers report mandating step therapy when new products enter therapeutic areas that are entrenched with established treatments, such as cardiovascular, bleeding disorders, respiratory, central nervous system (CNS), and oncology. Payers reported these therapeutic areas are the highest budget spend categories and face competition from multiple manufacturers.

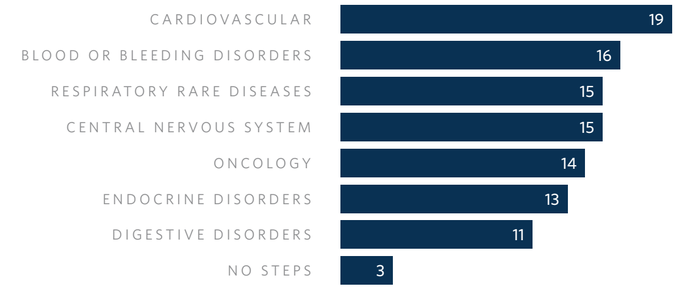
However, as noted in the 2023 report, some exceptions to standard utilization management practices exist, largely due to federal and state mandates among Medicare Advantage and managed care organizations (MCOs). These may specify or prohibit the use of inclusion and/or exclusion criteria for certain products, particularly for patients in protected classes or due to state-mandated unified formularies (e.g., managed Medicaid).

VALUE DRIVERS TO PHARMACY AND THERAPEUTICS (P&T) REVIEW PROCESS

As noted in previous editions of the report since 2020, payers continue to prioritize patient outcomes over financial considerations when making coverage and management decisions for rare disease products. However, the influence of financial factors has grown, reflecting an ongoing shift in payer priorities. While five of the top 10 value drivers for access decision-making cited in 2024 focused on clinical effectiveness, five focused on costs and contracting — up from four in 2023 and two in 2022, respectively.* This trend toward increased financial management is likely due to the aggregate increased total per member per month (PMPM) cost of rare disease products as well as the advent of multiple products within a therapeutic class, creating competition and leverage.

FIGURE 3: **IMPLEMENTED STEP THERAPY FOR MEDICAL BENEFIT HIGH-COST AND RARE DISEASE PRODUCTS BY TA**

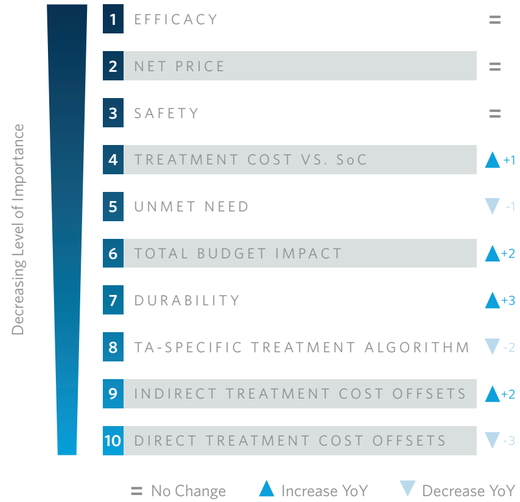
PRESENTED AS COUNT WITH MULTIPLE SELECTIONS POSSIBLE; N=24 PAYERS, COMMERCIAL BoB



**The 2022 edition of the report evaluated fewer total value drivers than 2023 and 2024. The years 2023 and 2024 had consistency in surveyed value drivers, but 2023 phrased the description as "rare disease and specialty products," while "high-cost and rare disease products" was the language used in 2024. In addition, while survey respondents may choose to participate in the annual updates to the research, each sample of respondents should be considered an independent sample.*

FIGURE 4: **2024 VALUE DRIVER IMPACT ON ACCESS DECISION-MAKING FOR HIGH-COST AND RARE DISEASE**

WEIGHTED AVERAGE RANKING BASED ON TOTAL COVERED LIVES



CONTRACTING/ECONOMIC FOCUSED

P&T committees generally approach their review of rare disease products similar to their review of specialty and traditional products. This approach generally reflects an understanding that rare diseases have smaller relative patient populations (less than 200,000 in the United States per the FDA), greater unmet need due to limited therapeutic alternatives, and expected high prices for novel treatments.

Consistent with the 2023 report, clinical efficacy (first), net price (second), and safety (third) continue to be the top three value drivers with the greatest impact on access decision-making for rare disease products. This reinforces the delicate balance of providing access to safe and effective life-changing treatment options that carry significant costs.

> *"**Efficacy and safety will always be the most important factors** when it comes to decision-making."*
>
> -NATIONAL PAYER

> *"There's no difference at our organization. **We evaluate new drugs based on clinical merit and pricing**. Our prior authorization criteria has less to do with a rare condition and more to do with a high price tag."*
>
> -NATIONAL PAYER

In addition to the increased focus on contracting and economic factors, total cost-of-care drivers have become key considerations in access decision-making. These include the standard of care (fourth), budget impact (sixth), durability (seventh), and indirect treatment cost offsets (ninth). National and large regional payers are largely driving this shift by focusing on the total budget impact across the care continuum.

FIGURE 5: **VALUE DRIVER IMPACT ON ACCESS DECISION-MAKING FOR HIGH-COST AND RARE DISEASE**

WEIGHTED AVERAGE RANKING BASED ON TOTAL COVERED LIVES

CONTRACTING/ECONOMIC FOCUSED

= No Change ▲ Increase YoY ▼ Decrease YoY

Decreasing Level of Importance

	PBMs	NATIONAL PAYERS	REGIONAL PAYERS	MANAGED MEDICAID	EMPLOYERS
1	EFFICACY =	EFFICACY =	EFFICACY =	EFFICACY =	EFFICACY NEW
2	NET PRICE ▲	NET PRICE =	NET PRICE ▲	TOTAL BUDGET IMPACT ▲	ECONOMIC BURDEN TO EMPLOYER GROUPS NEW
3	SAFETY ▼	TOTAL BUDGET IMPACT ▲	DURABILITY ▲	NET PRICE ▼	NET PRICE NEW
4	UNMET NEED ▲	TREATMENT COST VS. SoC ▼	TREATMENT COST VS. SoC ▲	TA-SPECIFIC TREATMENT ALGORITHM ▲	TOTAL BUDGET IMPACT NEW
5	TREATMENT COST VS. SoC ▲	SAFETY ▼	SAFETY ▲	SAFETY ▼	PREVALENCE NEW
6	TA-SPECIFIC TREATMENT ALGORITHM ▼	UNMET NEED ▼	CHRONIC VS. ONE-TIME ADMIN THERAPY ▲	INDIRECT TREATMENT COST OFFSETS ▲	SAFETY NEW
7	DURABILITY ▼	ECONOMIC BURDEN TO EMPLOYER GROUPS ▲	UNMET NEED ▼	UNMET NEED ▼	REAL-WORLD EVIDENCE NEW
8	TOTAL BUDGET IMPACT ▲	REIMBURSEMENT/ PAYMENT MODEL ▲	INDIRECT TREATMENT COST OFFSETS ▲	REAL-WORLD EVIDENCE ▲	PATIENT ADVOCACY NEW
9	INDIRECT TREATMENT COST OFFSETS ▲	WAC PRICE ▲	DIRECT TREATMENT COST OFFSETS =	QoL DATA ▲	TREATMENT COST VS. SoC NEW
10	COMPETITIVE PIPELINE ▲	REAL-WORLD EVIDENCE ▲	COMPETITIVE PIPELINE ▲	DIRECT TREATMENT COST OFFSETS ▼	VBC OFFERINGS NEW

National and large regional payers are increasingly focused on the total budget impact on their programs and the economic burden on employer groups, reflecting their priorities in managing internal costs and addressing the rising expenses faced by their key customers. Other than employer groups themselves, national payers were the only group to rank economic burden to employer groups as a top value driver.

In contrast, payer and employer group stakeholders continue to prioritize efficacy when making access decisions. However, compared to the 2023 report, pharmacy benefit managers (PBMs) report an increased focus on net price and direct treatment cost compared to the standard of care, underscoring ongoing efforts to establish rebate-based contracting in more competitive rare diseases. While PBMs and national payers largely drive overall trends due to their proportional representation of covered lives, several value driver differences exist across access stakeholders. Regional payers place a higher priority on durability and whether a product is administered one-time or chronically. Given fewer resources compared to national payers and less frequent member turnover, regional plans focus on the duration of a product's benefit relative to its dosing frequency and also prioritize managing cash flow.

Overall, unmet need has dropped in its perceived impact on access decision-making compared to previous editions of the trend report. This is likely due to an influx of therapies that have launched into the market in the past decade, including one-time cell and gene therapies and RNAi therapeutics. As unmet needs specific to therapeutic areas continue to be addressed, contracting and economic value drivers are receiving greater scrutiny from access decision-makers.

UTILIZATION AND INFLUENCE OF GUIDELINES AND HEALTH TECHNOLOGY ASSESSMENTS (HTA)

Payers and employers use guidelines and HTA reports, such as the Institute for the Clinical and Economic Review (ICER), as supplementary resources for research to inform coverage decisions and general awareness. However, these reports have little influence on final coverage decisions for new products.

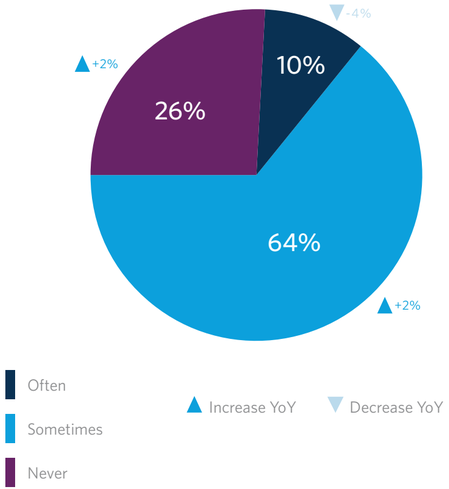
In limited cases, a professional society guideline recommendation may influence payers to consider implementing step therapy or drive off-label access given physician demand. Though these materials are generally only supplemental in shaping access policies, payers may still leverage HTA reports for more economic contracting and negotiation discussions with manufacturers.

U.S. professional society guidelines (e.g., American Heart Association, American College of Cardiology) are preferred over those from outside the United States (e.g., European Society of Cardiology). As in the 2023 report, several payers expressed concern with the applicability and relevance of guidelines from outside the United States to the U.S. health system. However, they will refer to them for reference in cases that lack clinical guidelines, such as for rare diseases, or when U.S. guidelines are unavailable or outdated. In some cases, guidelines are developed in specific countries to address the endemic impact of a rare disease in that region.

Consistent with findings from all past editions (i.e., 2020, 2021, 2022, and 2023), payers and employers indicated moderate influence of HTA reports and expect a slight increase in the influence of HTAs in coming years. Specifically, 63% of represented stakeholders reported a moderate influence — up from 60% in 2023 and 47% in 2020. In the next three to five years, 70% of access stakeholders anticipate a moderate influence and 20% anticipate a significant influence of HTA reports on coverage and management decisions for high-cost and rare diseases.

FIGURE 6: **UTILIZATION OF NON-U.S. GUIDELINES FOR DECISION-MAKING IN RARE DISEASES**

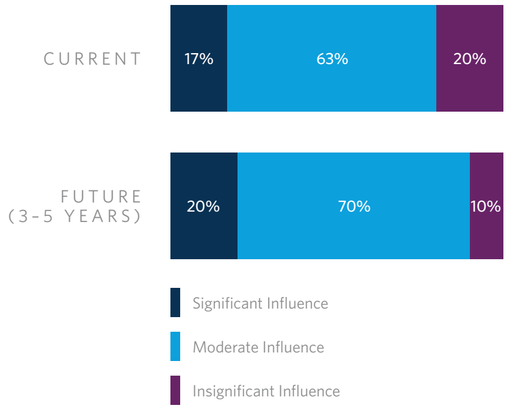
PRESENTED AS % TOTAL LIVES IN PAYER SAMPLE (N=24; ~150M LIVES)



5 out of 6 employer respondents report "sometimes" using non-U.S. guidelines; 1 out of 6 never use non-U.S. guidelines

FIGURE 7: **INFLUENCE OF HTA REPORTS SUCH AS ICER ON UTILIZATION MANAGEMENT FOR HIGH-COST AND RARE DISEASES**

PRESENTED AS % OF COUNT; N=30



*"We will **only use non-U.S. guidelines when we don't have access to U.S. perspective**, but it is not a main driver overall."*

-REGIONAL PAYER

SECTION 2:

INFRASTRUCTURE AND CAPABILITIES

VERTICAL INTEGRATION

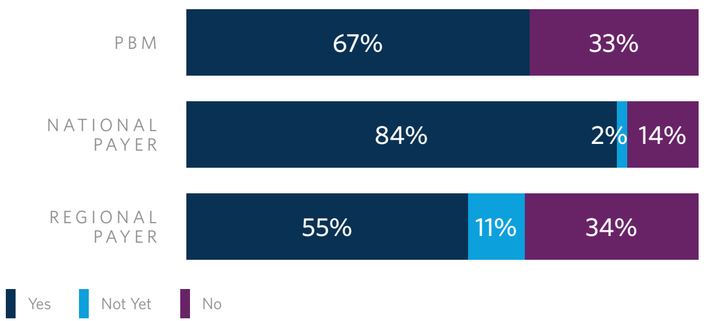
The definition of vertical integration can vary based on access stakeholder type and associated organizational strategies. For large national payers surveyed in 2024, vertical integration most often enables direct engagement with PBMs and specialty pharmacies. This integration allows for greater site-of-care control and specialty pharmacy mandate strategies, which collectively drive significant cost savings for the commercial book of business at health plans.

By aligning operations closely with PBMs and specialty pharmacies, national payers can improve overall efficiency of care coordination and delivery. This type of vertical integration reduces the overall spend associated with rare and specialty medications. However, this report does not consider managed Medicaid plans to be vertically integrated due to overarching regulatory constraints and existing partnerships with MCOs.

Alternatively, regional payers surveyed in 2024 view vertical integration as a strategy to foster collaboration with provider groups and large integrated delivery networks (IDNs). By partnering with large IDNs, regional payers reported they can create more cohesive control over clinical pathway management and value-based agreements. These agreements provide financial incentives to better equip regional payers to manage high costs and improve the quality of care provided to their members.

FIGURE 8: **PAYERS CONSIDERED TO BE VERTICALLY INTEGRATED**

PRESENTED AS % TOTAL LIVES IN PAYER SAMPLE (N=22; EXCLUDING MANAGED MEDICAID PAYERS)

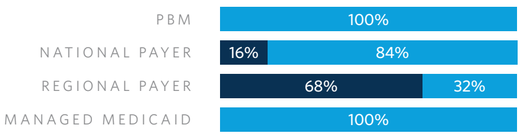


*"We are **vertically integrated because it allows us to be a lot more efficient across a range of services,** but we also offer comprehensive services that are integrated with providers."*

-REGIONAL PAYER

FIGURE 9: **UTILIZATION OF A THIRD-PARTY SPECIALTY BENEFIT MANAGER**

PRESENTED AS % TOTAL LIVES IN PAYER SAMPLE (N=24; ~150M LIVES)



4 out of 6 employer respondents report not working with a third-party Specialty Benefit Manager; 2 out of 6 use a third-party Specialty Benefit Manager

*"Our **current PBM operates as our specialty benefit manager**. We have little incentive to look beyond them or seek alternative partnerships at this point, but maybe in the future."*

-EMPLOYER

SPECIALTY BENEFIT MANAGEMENT

Payers and employers must find ways to balance the costs of specialty products while supporting the wellbeing of their members or employees. To address these challenges, a minority of stakeholders surveyed in 2024 reported they are exploring the use of third-party specialty benefit managers to provide strategic recommendations aimed at improving patient outcomes and reducing expenses in high-cost therapeutic areas.

The current level of adoption of third-party specialty pharmacy benefit managers remains relatively low, as large payers prefer to manage specialty products internally and employers prefer to work with PBMs. Regional plans report a moderate-to-high level of outsourcing specialty benefit management due to fewer available resources to manage internally. The use of these third-party specialty pharmacy benefit managers is expected to expand across organization types, particularly within the commercial book of business, driven by the increasing complexity of managing rare diseases.

CROSS-BENEFIT MANAGEMENT OF PHARMACY AND MEDICAL BENEFITS

Consistent with previous years and in the 2024 report, payers prefer to manage products under the pharmacy benefit compared to the medical benefit given the availability of more levers to control spend. This control is often demonstrated through point-of-sale adjudication and better negotiated prices under the pharmacy benefit. However, through qualitative interviews, most payers surveyed in 2024 highlighted their capabilities in managing products across both the medical and pharmacy benefits, allowing for integrated oversight. Furthermore, payers representing 86% of covered lives in the 2024 sample reported that the same group of stakeholders is responsible for reviewing products across both benefits, compared to 14% who indicated separate roles handle product reviews.

INTERACTION BETWEEN NATIONAL AND REGIONAL ACCOUNTS

Interactions among health plans vary across plan types. Based on findings in 2024, regional accounts often collaborate with national accounts to ensure coordinated coverage and maintain alignment across prior authorization criteria, promoting consistent access to care. Conversely, national accounts do not typically reach out to regional accounts for input or guidance in their decision-making processes or policy development.

SECTION 3:

EMPLOYER TRENDS

EMPLOYER INFLUENCER AND INVOLVEMENT

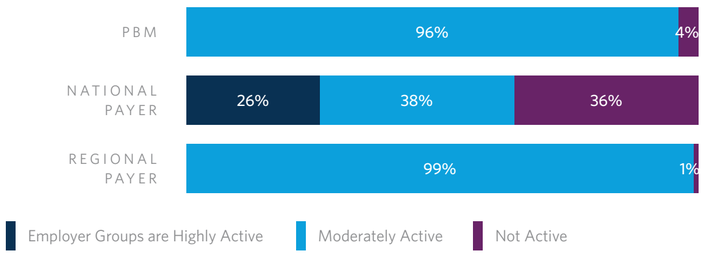
Employers are increasingly prioritizing how to manage one-off high expense claims (e.g., cell and gene therapies), also known as "catastrophic" or "lightning strike" claims. In the 2024 survey, employers considered themselves as "highly active" in benefits and coverage decisions for rare disease products. Meanwhile, payers viewed employers as only "moderately active," relying instead on employer benefit consultants (EBCs) to guide decision-making.

Both payers and employers agree the growing volume of claims for rare disease products is unsustainable, especially for self-funded employer groups that assume the entire financial risk. While much of employer group focus in 2024 has been on broader spend (e.g., management of GLP-1s), they plan to take a more proactive approach in communicating concerns to their EBCs moving forward. In some cases, they may consider carving out coverage of certain rare disease products to mitigate the catastrophic costs of "lightning strikes." Meanwhile, use of programs such as stop-loss and reinsurance varies by organization, with no expected change in adoption.

On one hand, self-funded employers have more control over the benefits they opt to cover because they pay for claims directly, rather than paying for fixed premiums. On the other hand, fully insured employers pay fixed premiums to MCOs and/or PBMs. In these cases, the payer assumes the financial risk and controls the benefits, impacting overall access to rare disease treatments due to restrictions and high costs.

FIGURE 10: **LEVEL OF ACTIVITY EMPLOYER GROUPS HAVE IN BENEFITS/COVERAGE DECISIONS IN RARE DISEASES**

PRESENTED AS % TOTAL LIVES IN PAYER SAMPLE (N=22; EXCLUDING MANAGED MEDICAID PAYERS)



3 out of 6 employer respondents report employer groups are highly active; 2 out of 6 report moderate activity; 1 out of 6 report no activity

> *"From what I have seen, **employer groups are playing a more active role** in recent years."*
>
> **-PBM**

EMPLOYER RISK MANAGEMENT AND BENEFIT DESIGN OPTIONS

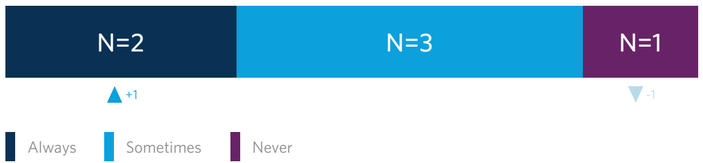
To mitigate financial risks linked to rare disease products, employers are increasingly collaborating with payers to pursue innovative strategies. By working with their actuarial counterparts, employers are exploring benefit design options to tailor coverage and make healthcare costs more predictable.

Carve outs, or benefits that are excluded ("carved out") from coverage or managed separately, have historically been used for one-time gene therapies. However, large employers are increasingly anticipating using carve outs for rare disease products better manage financial risks. This shift is largely due to concerns over financial sustainability of covering rare disease treatments, as they have noticed an increase in spend due to the emergence of multiple rare disease products. Payers, including PBMs, prefer to manage the financial risks associated with rare disease products internally, rather than use carve outs, which they say give niche vendors a market advantage. Managing these products internally allows payers to maintain control over their benefit designs and gain transparency into the access needs of their member populations.

Employers are also showing increased interest in optional riders or opt-in clauses. These risk management tools provide techniques that offer non-traditional benefits, including options for additional coverage to standard benefits, such as critical illness insurance. In the 2023 report, 73% of surveyed employers utilized riders in some capacity, whereas 83% reported doing so in 2024. (Note: individual stakeholders in 2024 sample varied from that of 2023.) The most common use of optional riders for rare disease products occurs in oncology, where additional coverage is available for employees to opt into.

FIGURE 11: **EMPLOYER USE OF OPT-IN CLAUSES IN RIDERS**

PRESENTED AS COUNT OF EMPLOYER RESPONDENTS; N=6



LEVERAGING EMPLOYER BENEFIT CONSULTANTS AND COALITIONS

Employers often turn to employer coalitions and benefit consultants for strategic guidance to navigate the complexities of health plans, particularly for supporting employees with rare diseases. These organizations help employers design benefit structures that balance cost and coverage for specialized treatments.

By joining forces as a coalition, employers leverage collective influence and bargaining power to negotiate contracts with manufacturers, payers, and policymakers. This approach can provide better access to rare disease treatments. Additionally, employer coalitions serve as a platform for employers to share experiences, insights, and best practices, allowing them to learn effective strategies for addressing challenges related to rare disease coverage.

SECTION 4:

TECHNOLOGY

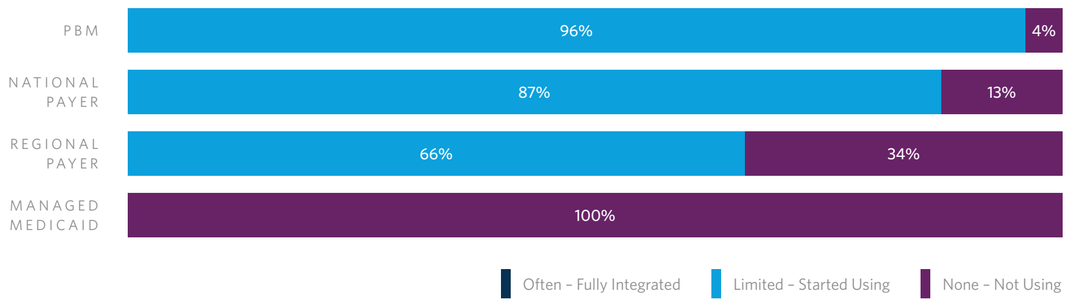
CURRENT USE OF AI TECHNOLOGY FOR ACCESS DECISIONS

More and more individuals and organizations are turning to artificial intelligence (AI) technology to improve efficiency, automate tasks, and analyze data. The 2024 trend report surveyed payers and employers to uncover insights on the impact of AI on access decision-making. Stakeholders at payer and employer organizations report the adoption of AI and other next-gen technologies has been slow, primarily due to competing budget priorities, compliance uncertainties, and technical complications.

Some pharmacy and medical directors at large plans and PBMs use internal AI chatbot software during new product reviews to access clinical trial results and disease information. However, none of the payers and employers sampled reported using AI to make coverage and management decisions for any treatment options, including those indicated for rare diseases. The payer community widely agrees that human voting members of pharmacy and therapeutics (P&T) committees, not AI, should make the final coverage and management decisions given the high level of importance and subjectivity that go into such decisions.

FIGURE 12: **LEVEL OF AI USAGE FOR COVERAGE AND MANAGEMENT DECISIONS**

PRESENTED AS % OF TOTAL LIVES IN PAYER SAMPLE (N=24. ~150M LIVES)

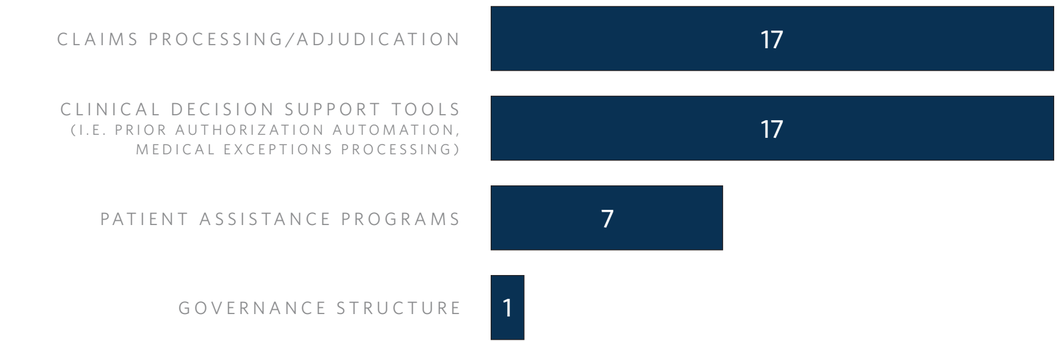


3 out of 6 employer respondents reported limit use of AI; 3 out of 6 reported no use of AI

No payer or employer stakeholder reported full implementation of AI at their organization for coverage and management decisions

FIGURE 13: **TYPE OF AI UTILIZATION AT PAYER AND EMPLOYER ORGANIZATIONS**

PRESENTED AS COUNT WITH MULTIPLE SELECTIONS POSSIBLE; N=30



Although AI is not directly used for P&T decision-making, most payers cite its adoption for automating processes related to prior authorization approvals, claim adjudications, and patient assistance programs given repetitiveness of tasks. Payers report that AI has streamlined communications with providers, enabling faster prior authorization approvals, including for rare disease products. However, they are not using AI for prior authorization denials and do not expect changes to this process, due to the subjectivity of these decisions and their importance to patients requiring coverage.

PAYER INVESTMENT IN AI TECHNOLOGY

To gain additional insights into the expected adoption of novel technological tools, a supplemental interview was held with a CDO at a national health plan for the 2024 trend report. According to the CDO, payer executives are eager to adopt AI because of its many potential capabilities, but using it for access decisions is not a top priority due to the enormous upfront investment required to fully operationalize the technology. Instead, payers are prioritizing the improvement of data connectivity and interoperability by standardizing and streamlining mainframes and electronic medical records (EMR).

*"The CEO of [large payer organization] spoke on a podcast recently on AI and he said **we have to be aware of AI and ensure that if we do use it, it has to be ethical and compliant.**"*

ETHICAL AND COMPLIANCE CONCERNS OF AI TECHNOLOGY

Ethics and compliance concerns have often driven stakeholder approach to adoption of AI technology in its early stages of commercialization. Payers and employers are taking steps to safeguard proprietary company data and member health records. These initial compliance and safety measures include corporate training on using AI and risks of sharing information. However, stakeholders sampled for the 2024 trend report are unfamiliar with related technologies, such as blockchain or decentralized digital ledgers, and do not anticipate using these capabilities in the near future to store data more securely.

ANTICIPATED FUTURE USE OF TECHNOLOGY IN RARE DISEASE MANAGEMENT

While stakeholders anticipate a gradual increase in AI uptake over the next few years, barriers such as interoperability of data systems (e.g., EMRs), low return on investment, and ethical concerns need to be navigated for widespread adoption. While technological adoption is in its early days for payers, multiple stakeholders surveyed anticipate a growing role for new technologies in patient empowerment, particularly for patients with rare diseases who may lack familiarity with information related to their condition.

Stakeholders see potential for new technologies to enhance patient assistance programs, educational materials, price transparency initiatives, and the ability to answer questions about conditions and benefits, which can be especially impactful in the rare disease space. Technology, such as digital resources, chat boxes, and out-of-pocket-costs calculators, designed to empower patients, is becoming a key focus for payers and employers. As health care moves toward precision medicine and targeted therapies, these technological innovations are becoming essential tools for supporting patients, particularly in the rare disease space.

*"Healthcare decisions have always come down to the balance of clinical outcomes vs. financial outcomes on both the payer and provider sides. If you make those two things fixed, it **comes down to patient empowerment and how a technology can empower patients.**"*

-CDO, NATIONAL HEALTH PLAN

SECTION 5:

PAYER ECONOMICS

FINANCIAL RISK MANAGEMENT TECHNIQUES

Payers and employers are continually seeking strategies to manage the financial risks of covering rare disease therapies, particularly as more novel treatments enter the market and the U.S. rare disease market size is estimated to expand from $215 billion in 2023 to over $540 billion by 2032.[4] In discussions with access stakeholders, several approaches to financial risk management were mentioned, including, but not limited to, outcomes-based contracts, conditional treatment continuation, and per member per month (PMPM) cost capitation. Among these, payers and employers consistently express a strong preference for contracts that share financial burden and risk with the manufacturer.

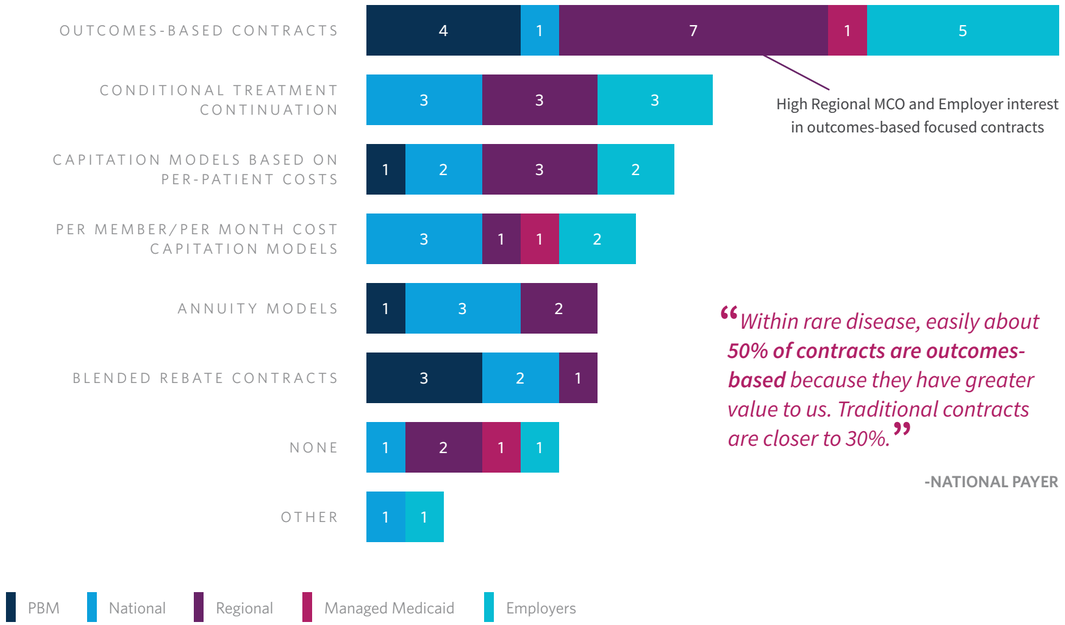
Stakeholders find innovative contracts, such as value- and outcomes-based agreements, appealing because they reduce financial uncertainty and enable access to rare disease products. Payers especially like outcomes-based contracts because they align costs with clinical outcomes, adding value that ultimately strengthens the health plan's positioning with key customers, such as large employer groups.

There was also notable interest in conditional treatment continuation contracts, which allow stakeholders to reassess terms if patients do not receive pre-specified clinical benefits. These contracts are best suited for chronic therapies with multiple payments per course of treatment (e.g., Spinraza), as they reduce financial exposure for payers and employers if the therapy fails to meet targeted outcomes.

Conversely, annuity models and blended rate contracts generated the least interest due to their complexity, which makes them less viable as effective solutions for managing high costs.

FIGURE 14: **ANTICIPATED USE OF INNOVATIVE CONTRACTS NEXT PLAN YEAR**

PRESENTED AS COUNT WITH MULTIPLE SELECTIONS POSSIBLE; N=30



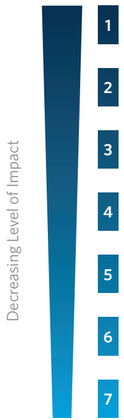
*"Within rare disease, easily about **50% of contracts are outcomes-based** because they have greater value to us. Traditional contracts are closer to 30%."*

-NATIONAL PAYER

INNOVATIVE CONTRACTS

Product cost is the primary driver of plan interest in innovative contracts, followed by whether the product is a one-time therapy or requires multiple administrations. While payers with a majority of managed Medicaid members prioritize product cost, they also focus on contracts that demonstrate improvements in downstream outcomes, reflecting their commitment to supporting vulnerable and underserved patient populations.

FIGURE 15: **PRODUCT COST HAS THE GREATEST IMPACT ON PLAN INTEREST FOR INNOVATIVE CONTRACTS FOLLOWED BY SINGLE-USE THERAPY**



OVERALL	PBMs	NATIONAL PAYERS	REGIONAL PAYERS	MANAGED MEDICAID
PRODUCT COST	ONE-TIME THERAPY	PRODUCT COST	PRODUCT COST	PRODUCT COST
ONE-TIME THERAPY	PRODUCT COST	ONE-TIME THERAPY	ABILITY TO TRACK DATA	IMPROVEMENT IN OUTCOMES
ABILITY TO TRACK DATA	ABILITY TO TRACK DATA	CHRONIC VS. MAINTENANCE THERAPY	ONE-TIME THERAPY	ONE-TIME THERAPY
IMPROVEMENT IN OUTCOMES	POPULATION SIZE	IMPROVEMENT IN OUTCOMES	IMPROVEMENT IN OUTCOMES	CHRONIC VS. MAINTENANCE THERAPY
CHRONIC VS. MAINTENANCE THERAPY	IMPROVEMENT IN OUTCOMES	ABILITY TO TRACK DATA	CHRONIC VS. MAINTENANCE THERAPY	COMPETITIVE ADVANTAGE VS. PEERS
POPULATION SIZE	COMPETITIVE ADVANTAGE VS. PEERS	POPULATION SIZE	COMPETITIVE ADVANTAGE VS. PEERS	POPULATION SIZE
COMPETITIVE ADVANTAGE VS. PEERS	CHRONIC VS. MAINTENANCE THERAPY	COMPETITIVE ADVANTAGE VS. PEERS	POPULATION SIZE	ABILITY TO TRACK DATA

Although payers are interested in outcomes-based contracting, they continue to face challenges around such contracts that need to be overcome to be beneficial and sustainable. Barriers exist with establishing and agreeing to terms with manufacturers around clearly defining outcome metrics and measuring outcomes. Payers also cite challenges with data collection due to the inconsistent electronic medical record structures and difficulties in accurately tracking utilization. Additional uncertainties include best price limitations and government legislation. Addressing such barriers would allow for more widespread adoption of outcomes-based contracts.

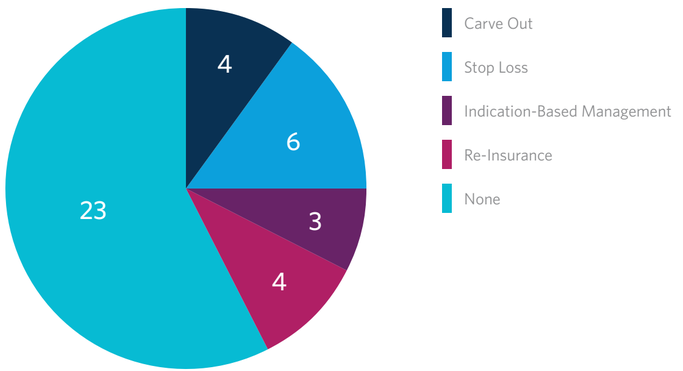
> *"Yes, value-based contracts are more common today. More manufacturers suggest it even before approval. If it's something you can pull out of claims, then it's no problem. But if it's **something you need to access and it's more nebulous, then it's challenging to track.**"*
>
> **-MANAGED MEDICAID PAYER**

RISK MANAGEMENT FOR CELL AND GENE THERAPIES

Payers and employers want to understand how cell and gene therapies will affect their organizations' coverage policies and overall costs. Both regional and national payers report taking measures to control costs for one-time gene therapies, but uncertainty remains about the management of emerging gene therapies that require repeat administrations for optimal therapeutic benefit (e.g., hemophilia). Outside of contracting strategies, most payers and employers are not yet taking steps to mitigate their financial exposure to one-time gene therapies. Among those who are taking steps, stop-loss, carve outs, and re-insurance are valued as the top financial mitigation strategies.

FIGURE 16: **TYPE OF FINANCIAL RISK MITIGATION STRATEGIES FOR HIGH-COST ONE-TIME GENE THERAPIES**

PRESENTED AS COUNT WITH MULTIPLE SELECTIONS POSSIBLE; N=30



SECTION 6:

FUTURE RARE DISEASE TRENDS

IMPACT OF THE MEDICARE PART D REDESIGN ON MANAGED CARE

When interviewed in October 2024, payers and employers reported making no significant changes to rare disease management in response to the initial phases of the IRA Medicare Part D benefit redesign. Key stakeholders highlighted minimal willingness to adopt broad tactical changes prior to knowing the outcomes and policy implications of the 2024 elections. When asked about the likely impact of the Medicare Part D redesign rollout, both payers and employers indicated they expect to reevaluate coverage decisions in 2025 due to increased financial liability under the Part D program.

The redesigned Part D benefit includes an annual $2,000 out-of-pocket (OOP) cap on beneficiary cost sharing for Part D prescription drugs that went into effect for plan year 2025. The cap on the patient contribution results in Part D plans taking on more financial responsibility, especially for higher-cost therapies. Payers indicated this greater liability, along with increasing drug prices, may lead to fewer Part D plan offerings, stricter management, and fewer products on formulary across all books of business.[5]

Employer groups and benefit consultants expect Part D plan costs to increase due to the shift in financial liability and the $2,000 Part D OOP cap. Interviewed stakeholders cited this could impact employers if payers raise premiums for their commercial plans to help offset Medicare Part D margins. However, the law includes a provision that limits premium increases to no more than 6% from the prior plan year.[6]

ADDITIONAL IRA CONSIDERATIONS

In addition to expected management changes as a result of the Part D redesign, other policy changes within the IRA are likely to influence payer tactics.

Interviewed payers expect to ask manufacturers for more competitive contracts and higher rebates under the commercial book of business due to shifting financial liability and to align with Medicare-negotiated rates for the 10 Part D drugs in the new Medicare Drug Price Negotiation Program, a separate provision of the IRA.

As policy changes from the IRA shift the financial burden from the government and patients to manufacturers and payers, rare disease products may face greater access hurdles. These potential barriers may include coverage reevaluations, stricter management, and an expectation of higher rebates across all books of business.

> *"The **Part D redesign will cause us to reevaluate our formularies**. We try to only cover what we have to and use contracting the best we can. There will be fewer drugs to choose from with our hands tied for rare diseases."*
>
> -NATIONAL PAYER

FUTURE TRENDS IN UTILIZATION MANAGEMENT OF RARE DISEASE PRODUCTS

With the U.S. election underway at the time of the survey, interviewed participants expressed uncertainty about potential policy changes, adopting a "wait and see" approach to potential implications, but expect to continue prioritizing accessibility for their beneficiaries. Payers and employers are likely to continue exploring new ways to leverage external partners, specialized capabilities, and financial risk-sharing and risk-mitigation agreements to manage rare disease products. Additional cost-control approaches for rare disease products will see broader implementation across the payer community, including stricter prior authorization criteria, specialty pharmacy requirements, and site-of-care mandates.

CONCLUSION

The research for the fifth annual Alnylam Rare Disease Trend report was conducted in September and October of 2024. As with earlier editions of the report, the 2024 Alnylam Rare Disease Trend report explores rare disease management, offering insights into best practices and novel approaches for improving access while managing the short- and long-term economics of rare diseases. This year's report expands to examine the impacts of the IRA Medicare Part D Redesign and the emerging use of artificial intelligence (AI) technology.

Similar to previous reports, payer survey findings show that clinical efficacy, net price, and safety remain the top three value drivers influencing access decisions for rare disease products. However, financial factors are playing a larger role, five of the top 10 reported value drivers now focus on contracting — up from four in 2023 and two in 2022. This trend reflects an ongoing shift in payer priorities, as they strive to provide access to safe, effective life-changing treatments, while balancing their significant costs, especially as more rare disease products enter the market. Amid increasing economic pressures, many stakeholders are expanding their use of cost-control measures, such as stricter prior authorization criteria, specialty pharmacy and site-of-care mandates, and risk-sharing agreements.

Additionally, payers and employers are closely monitoring the impact of the IRA Medicare Part D redesign. If costs shift to manufacturers and Part D plans as expected in 2025, respondents anticipate reevaluating coverage decisions and tightening formulary management. With U.S. elections in progress at the time of the research, respondents took a "wait and see" approach to potential policy changes and their implications.

Meanwhile, despite the promise of AI to create efficiencies, stakeholders largely are cautious to quickly adopt next-gen technology, citing ethical, compliance, budgetary, and logistical concerns. Regarding the use of AI for payer decisions, they generally agree that only humans should determine coverage decisions and prior authorization denials, given the critical nature and potential subjectivity of such decisions.

The Rare Disease Trend report is designed to support U.S. payers, employers, and manufacturers in understanding key trends and by benchmarking rare disease drug management practices against industry peers. In the next issue, the report will continue to examine the value drivers behind coverage and management decisions, as stakeholders navigate evolving market dynamics to connect individuals with life-changing innovations for treating rare diseases.

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