# 2023 Rare & Specialty Trend Report

## PERSPECTIVES FROM HEALTHCARE PAYERS

Alnylam®

FOURTH EDITION

# CONTENTS



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# FOREWORD

When the first cell and gene therapies gained approval and hit the U.S. market in 2017, the healthcare community celebrated the scientific breakthrough and the potential and hope these therapies would inspire for future generations to live longer, healthier lives. Treatment, and even cures, for rare, complex, and chronic conditions that once seemed impossible became more possible. At the same time, payers and other risk-bearing stakeholders faced the very difficult question of how they could maintain their commitment to patient access in the future with financial prudence when many more high-cost therapies were coming to market.

Fast forward to today—the future is here. Now in the aftermath of the global COVID-19 pandemic, more and more high-cost therapies to treat complex, chronic, and rare diseases are coming to market in the near term. A recent report from CVS Health shares that there are 12 gene therapy treatments on track for approval in 2024.[1] At the same time, global economies are fluctuating, U.S. healthcare costs continue to rise, and a series of policy changes aimed at creating access begin to take effect. Now more than ever, the once looming question has become an urgent need: How can stakeholders manage uncertainty and set themselves up for sustainable success without sacrificing or jeopardizing patient access and outcomes?

To glean crucial insights into these evolving market realities, the 2023 Alnylam Rare and Specialty Trend Report continues this important discussion with payers — and expands it to include another vital risk-bearing entity, the employer community. This report's 4th edition also broadens its focus to encompass payer priorities in specialty as a whole. Its purpose is to reflect impact on market dynamics and provide a comprehensive overview of access barriers, trends, and potential solutions. Published to inspire open dialogue among payers, providers, manufacturers, employers, advocacy groups, and patients, this report serves to provide all stakeholders with a deeper understanding of the urgent and emerging healthcare challenges that must be overcome to sustainably improve patient access and outcomes beyond short-term fixes.

# INTRODUCTION

This report is intended to inform stakeholders on prevailing trends in the management of rare and specialty therapeutics. While previous editions of this report (2020, 2021, & 2022) focused exclusively on the budget impact of high-cost rare disease therapeutics on payers, this year's edition (2023) examines the potential impact of current market dynamics of high-cost therapeutics including rare and more common diseases. It also expands the payer perspective to include plan sponsors to reflect the management priorities of influential risk-bearing entities across the commercial space. Included among these trends is the lingering implications of COVID-19 cost pressures, the growing portfolio of high-cost therapies, policy and price reforms, and the risk mitigation strategies for both payers and employers. Key questions answered within this report include:

- **How have payer priorities 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 high-cost therapeutics?**
- **How will potential legislation and reform shape decision-making and engagement for payers and employers?**
- **How have payer perceptions and anticipated use of innovative reimbursement models shifted?**

By sharing annual insights and perspectives on the current and future management trends of rare and specialty therapeutics, the authors of this report aim to elevate and amplify the discussion around how to achieve best practices for sustainably providing access to novel treatment options and improving patient outcomes. With a better understanding of how payers and employers perceive, evaluate, and prioritize the unique challenges of rare and specialty products, the industry can be better positioned to achieve the shared ambition of enhancing and extending patient lives.

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

# KEY FINDINGS

| 1 | 2 | 3 | 4 |
|---|---|---|---|
| **TRENDS IN PAYER MANAGEMENT APPROACHES REFLECT MARKET SITUATIONS, NOT DRUG DESIGNATION, BY "RARE" VS. "SPECIALTY."** | **EMPLOYERS ARE EXPLORING STRATEGIES TO MANAGE THE POTENTIAL CATASTROPHIC FINANCIAL RISKS OF RARE & SPECIALTY THERAPEUTICS.** | **PAYERS ARE PRIORITIZING INTERNAL CAPABILITIES THAT HELP PROTECT THEIR ORGANIZATIONS AGAINST THE FINANCIAL RISKS OF EXTERNAL MARKET EVENTS.** | **RISK-BEARING ENTITIES CONTINUE TO TROUBLESHOOT HOW TO PAY FOR HIGH-COST DRUGS WITHOUT COMPROMISING PATIENT ACCESS.** |
| Payers do not consider rare and specialty as distinct categories that warrant differential management. Rather, they tend to use the same pharmacy and therapeutics (P&T) review processes for both, and consider the same coverage management strategies for both. Furthermore, coverage and policy decisions taken tend to be based on the clinical profile and competitive dynamics, not the drug designation.<br><br>Accordingly, coverage pattern trends with regard to competitive landscape, clinical value and differentiation, unmet need, and other market factors may begin to emerge as more high-cost drugs come to market. | In search of predictability with regard to the emerging pipeline of high-cost therapeutics, some employers are looking into traditional risk mitigation tools, such as stop-loss, reinsurance, and carve outs, and new strategies like shared-risk pool agreements.<br><br>However, few have yet to make significant changes to business processes. Self-funded employers, which typically are larger organizations, tend to be more involved in benefit design than fully insured employers that may not have the same risk exposure, scale, or resources to actively customize their benefit design. In either case, payers have an opportunity to help guide employers to prudent, available options, especially as the need to find sustainable solutions becomes more urgent. | Acutely aware they are operating in a fragmented system with rapidly evolving market dynamics for high-cost therapeutics, payers are increasingly doing their best to control what they can internally to create stability. Namely, they are reviewing their site of care mandates, specialty pharmacy integration, and subcommittee initiatives, among other internal policies, programs, and functions, to bolster their organizational resilience and long-term viability.<br><br>From a contracting perspective, payers — especially PBMs — are focused on net price and often look to near-term predictability (18–36 months into the future) for actuarial and budgeting purposes. | Payers and employers concerned they are lagging behind their peers may rest assured to learn no one has the answer — yet. To date, no universally accepted agreements or best practices have emerged to tackle the numerous associated uncertainties and unknowns. As a stopgap, payers and employers are fleshing out their coverage playbooks with individual strategies and tools to ensure they have multiple options from which to choose in the interim. |

# METHODOLOGY

Alnylam Pharmaceuticals, Inc., sponsored and developed this publication in partnership with their vendor, Guidehouse. Alnylam is a biopharmaceutical company focused on the discovery, development, and commercialization of RNA interference (RNAi) therapeutics. The Commercial Health Group at Guidehouse, a leading global consultancy that specializes in life sciences across both the commercial and public sectors, provided research services.

## SURVEY DEVELOPMENT

A survey was developed to capture payer and employer sentiment on the quantitative management of rare disease and specialty 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 and specialty within the next plan year (2024), the next 3–5 plan years (2025–2029), and beyond (2029+).

The survey focused on the same themes used to inform the report structure, including benefit design and utilization management, infrastructure and capabilities, payer economics, employer perspective, 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 & Demographics" below), and a total of 30 U.S.-based medical, 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 & FIELDING

Respondents were selected for relevant expertise and involvement in rare and specialty product evaluation. The agency 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 or managed Medicaid affiliate), as well as a mix of stakeholders with national and regional purviews. 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 September 18 to October 26, 2023. 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 & 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:**

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

## FOLLOW-UP INTERVIEWS

Participants were interviewed in tandem with the survey over a 26-day period from September 20 to October 16, 2023. Fifteen respondents participated in a 60-minute follow-up interview to provide additional, qualitative insight. Guidehouse researchers conducted all interviews over the phone in a double-blinded manner, such that no respondent knew the company supporting the research and no Alnylam employee knew which payers 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 follow-up phone interview received honoraria according to Fair Market Value calculations.

## DATA ANALYSIS, REPORTING & LIMITATIONS

Guidehouse collected, analyzed, and reported survey and interview responses. Data was blinded and aggregated across the entire sample of respondents.

Researchers had no way of validating survey responses for accuracy regarding payer practices or internal processes and operations. All statements and opinions contained within the report reflect responses received by included 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.

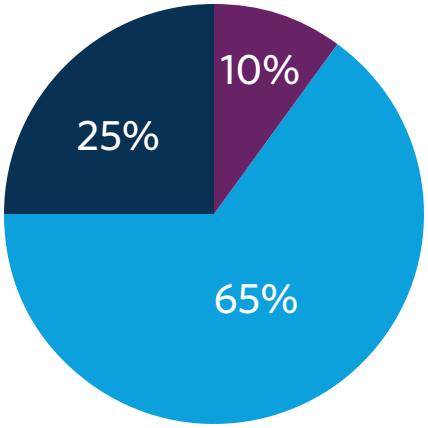
Payers represent 80% of the sample, while the employer community represent 20%. Of the total covered lives represented by payers sampled, 65% represented commercial, 25% Medicare, and 10% Medicaid. **(Figure 1)**.

In the payer-only sample, national payers comprise 29%, regional payers, 42%, Medicaid managed care plans, 12%, and pharmacy benefit managers (PBMs), 17% **(Figure 2)**. In the employer-only sample, employer benefits consultants (EBCs) comprise 50%, employers, 33%, and employer coalition stakeholders, 17% **(Figure 3)**.

In the plans sampled, the majority of commercial plan spend in rare and specialty is in the pharmacy benefit (56% of spend) compared to the medical benefit (44% of spend); the majority of Medicaid plan spend is in medical benefit (53% of spend) compared to pharmacy benefit (47% of spend); and the Medicare plan spend is equal (50% of medical and 50% of pharmacy spend) **(Figure 4)**. Differentiation between pharmacy versus medical spend for Commercial, Medicare, and Medicaid depend on the inclusion of specialty pharmacy networks. Those who have integrated specialty pharmacies tend toward covering a therapy under pharmacy rather than medical where the option is available.

*FIGURE 1:* **MANAGEMENT BY BOOK OF BUSINESS**

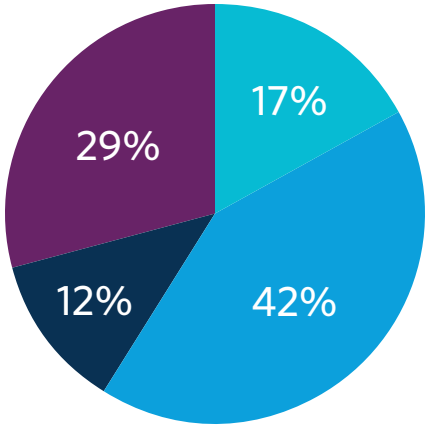
*PRESENTED AS % COVERED LIVES; N=24 PAYERS*




- Commercial
- Medicare
- Medicaid

*FIGURE 2:* **PAYER RESEARCH SAMPLE MIX**

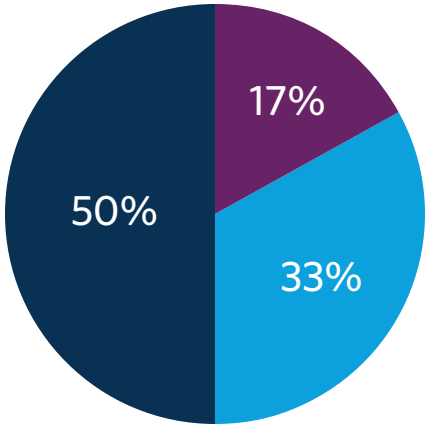
*PRESENTED AS % PAYER SAMPLE; N=24 PAYERS*




- Regional
- Managed Medicaid
- National
- PBM

*FIGURE 3:* **EMPLOYER RESEARCH SAMPLE MIX**

*PRESENTED AS % EMPLOYER SAMPLE; N=6 EMPLOYER STAKEHOLDERS*




- Self-Funded Employer
- Employer Benefits Consultant
- Employer Coalition

**THE EMPLOYER SAMPLE INCLUDES KEY ACCESS INFLUENCERS FROM SELF-FUNDED EMPLOYERS, EBCS, AND EMPLOYER COALITIONS. AMONG THESE ARE LARGE EMPLOYERS REPRESENTING A TOTAL OF OVER 100,000 LIVES, A LEADING EBC, AND A MEMBER OF THE NATIONAL ALLIANCE OF HEALTHCARE PURCHASER COALITIONS.**

*FIGURE 4:* **PAYER MIX & SPEND BY BoB** *PRESENTED AS AVERAGE % ACROSS PAYER SAMPLE BOOKS OF BUSINESS; N=24 PAYERS*

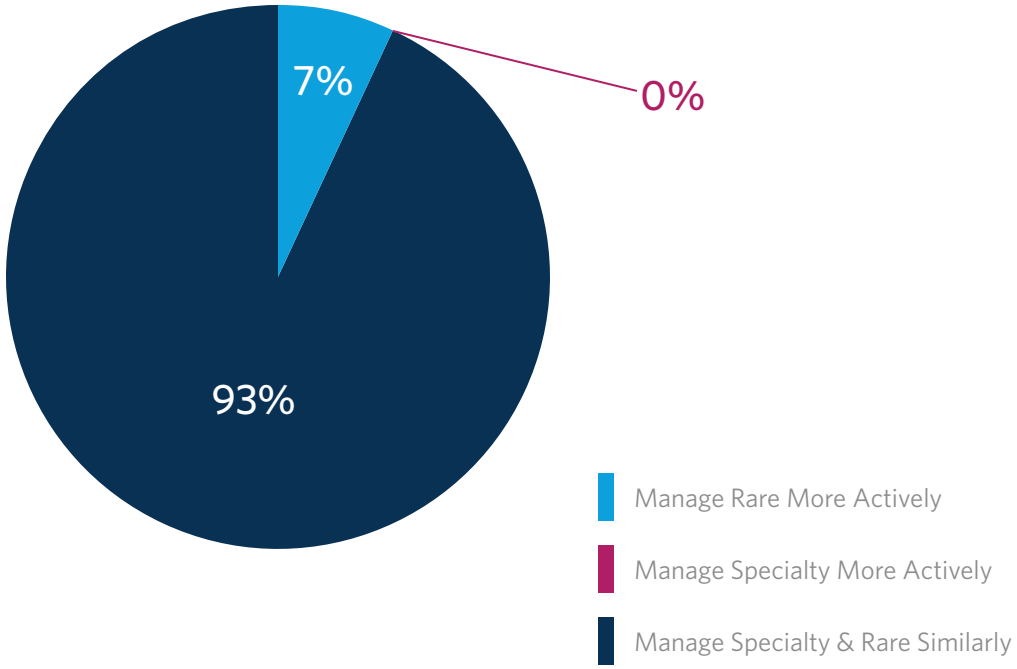
# RARE & SPECIALTY LANDSCAPE

With rapidly growing pipelines, the management of high-cost therapeutics continues to be a priority for payers. As they navigate the complex treatment landscape, payers largely consider specialty to include rare disease products. Generally, payers tend to label rare diseases as patient populations less than 200,000, as per the U.S. Food and Drug Administration (FDA) definition. Specialty is a broader category encompassing high-cost therapeutics or those requiring special handling or administration.

Unlike Medicare, which has established cost thresholds for specialty therapies (e.g., a cost of $830/month), commercial plans tend to have less standardized criteria on what "specialty" may mean. While payers differentiate rare and specialty products by definition, 93% of payers do not use differential management approaches for coverage and reimbursement decisions based on these classifications **(Figure 5)**. Instead, most payers report implementing specific management tactics based on competitive dynamics in each market. For example, products with limited competition in high unmet need areas, often a dynamic seen in rare, can face prior authorization restrictions beyond the labeled indication. Applying stricter, trial-based inclusion and exclusion criteria in these cases enables payers to align resources with the positive patient outcomes in clinical results, while managing the high costs of rare and specialty therapies. Meanwhile, payers may use other techniques for specialty products launching in competitive markets with multiple products and minimal differentiation. Tactics such as step therapy, which were once very uncommon in rare, are now seen as standard practice as competition increases across therapeutic areas. Many payers have considered or implemented step therapy requirements as competitive agents flood these classes.

*FIGURE 5:* **DIFFERENTIATION OF UTILIZATION MANAGEMENT TECHNIQUES FOR RARE VS. SPECIALTY**

*PRESENTED AS % TOTAL PAYER COVERED LIVES; N=24 PAYERS*



Similar to the management of rare vs. ultra-rare in 2022, payers reported consistency in the management approach for rare and specialty products in 2023. The implementation of traditional utilization management techniques, such as prior authorizations, step therapy, and detailed inclusion and exclusion criteria, do not differ significantly based on the product category.

However, some exceptions exist to the status quo of strict utilization management, largely due to federal and state mandates among Medicare and Medicaid plans. These may require specific inclusion and/or exclusion criteria be applied to certain products for patients in protected classes or due to state-mandated unified formularies (Medicaid). Demographic considerations also may factor into the criteria.

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

Previous editions of the report explored the effect of budget pressures on the desire for innovative, aggressive approaches to management vs. the investment and practicality of implementation. In each edition, payers continued to prioritize patient outcomes over financial burdens, while understanding that eventually more high-cost therapies would enter the market. Even now, as more high-cost products are set to launch in the near term, payers remain committed to finding and maintaining that delicate balance. As seen previously, despite economic pressures, clinical efficacy remains the top priority for payers. For manufacturers, this signals a continued interest and willingness among payers to support proven innovations for rare and specialty **(Figure 6)**.

However, payers indicated some significant shifts in value drivers. After climbing in importance over the past three reports, unmet need decreased in priority from third-highest last year to fourth-highest in the 2023 report, behind net price.

Meanwhile, due to the high costs and significant expansion of rare and specialty therapies as a whole, payers ranked economic and contracting priorities among four of the nine highest-value drivers in the pharmacy and therapeutics (P&T) review process in 2023. By comparison, in 2022, economic and contracting priorities only accounted for two of the most significant factors, with budget impact and cost-effectiveness ranking sixth-highest and seventh-highest, respectively.

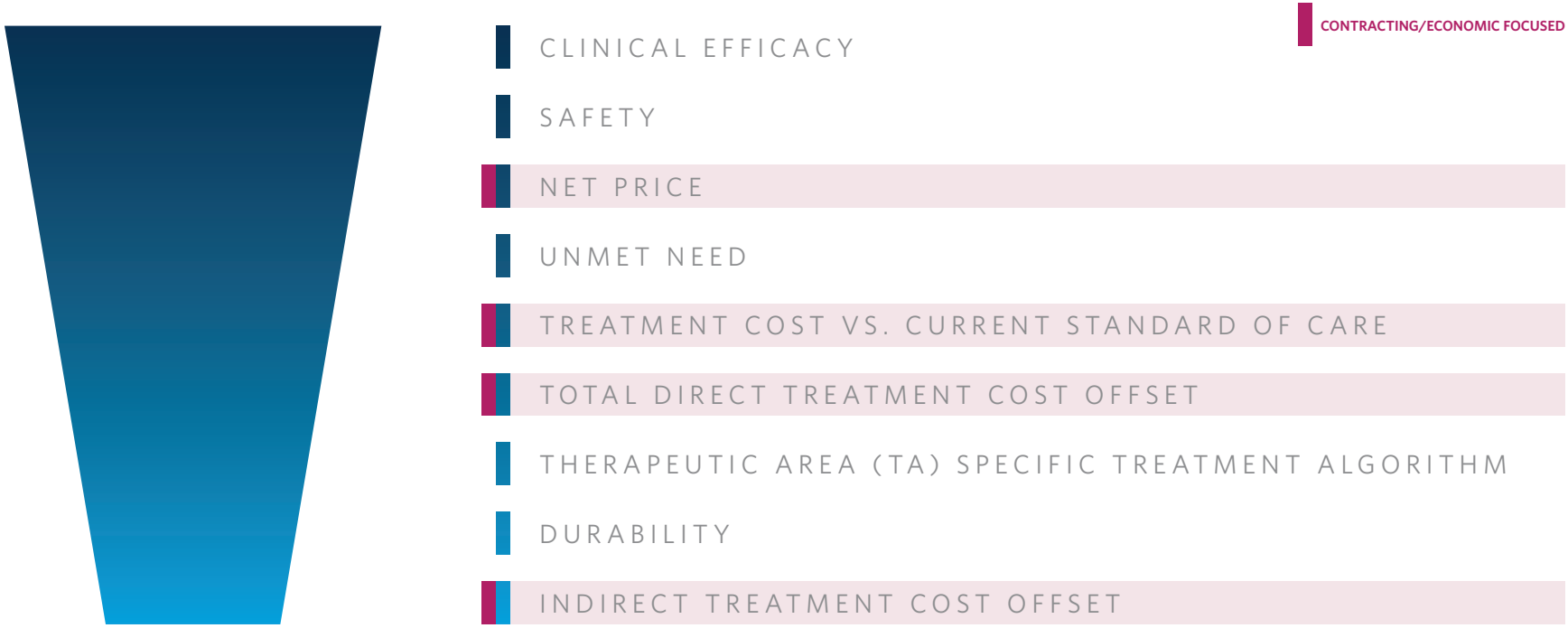
In this edition of the survey where value drivers were ranked across rare and specialty, net price rose to the third-highest value driver across all covered lives, largely driven by national payer and pharmacy benefit manager (PBM) priorities. PBMs are focusing on net price relative to wholesale acquisition cost (WAC), highlighting the continued impact of traditional rebate-based contracting in PBM management of rare and specialty therapies. Payers will continue to value the final contracted price above all other economic factors. Additional top-ranking economic and contracting value drivers in 2023 are treatment cost vs. standard of care (fifth), total direct treatment cost offset (sixth), and budget impact (eighth). In contrast to previous years, this year's rare and specialty survey results show a declining impact of unmet need and an increased focus on comparison to existing standard of care.

Real-world evidence (RWE) continues to factor little into coverage and reimbursement decisions, as it remains heavily dependent on availability, quality, and study design. Still, RWE previously rose in importance year over year, peaking at fifth-highest in 2022. In the 2023 report, however, it fell off the overall list of top value drivers across rare and specialty. Payers indicated they tend to consider RWE in their decision-making as a "nice to have" for follow-up class reviews after launch.

Despite overall trends where large PBMs and national payers tend to be proportionately represented due to their volume of covered lives, several value driver differences exist across payer types. Regional payers, for example, emphasize the total cost of care as their integration often gives them more visibility across pharmacy and medical. In addition, as smaller entities, regional payers are more impacted by their close relationships with employer groups and the priorities of these stakeholders. They were the only group to rank economic burden to employer groups as a top value driver, marking it as their fifth-highest, likely due to the direct impact that employers face with high-cost therapeutics. For another example, Managed Medicaid payers see regulations and cost pressures at a state-by-state level, highlighting the importance of economic-focused value drivers such as traditional contracting where applicable.

*FIGURE 6:* **VALUE DRIVER IMPACT ON ACCESS DECISION-MAKING FOR RARE & SPECIALTY DISEASE**

*WEIGHTED AVERAGE RANKING BASED ON TOTAL PAYER COVERED LIVES; N=24 PAYERS*



## UTILIZATION OF GUIDELINES

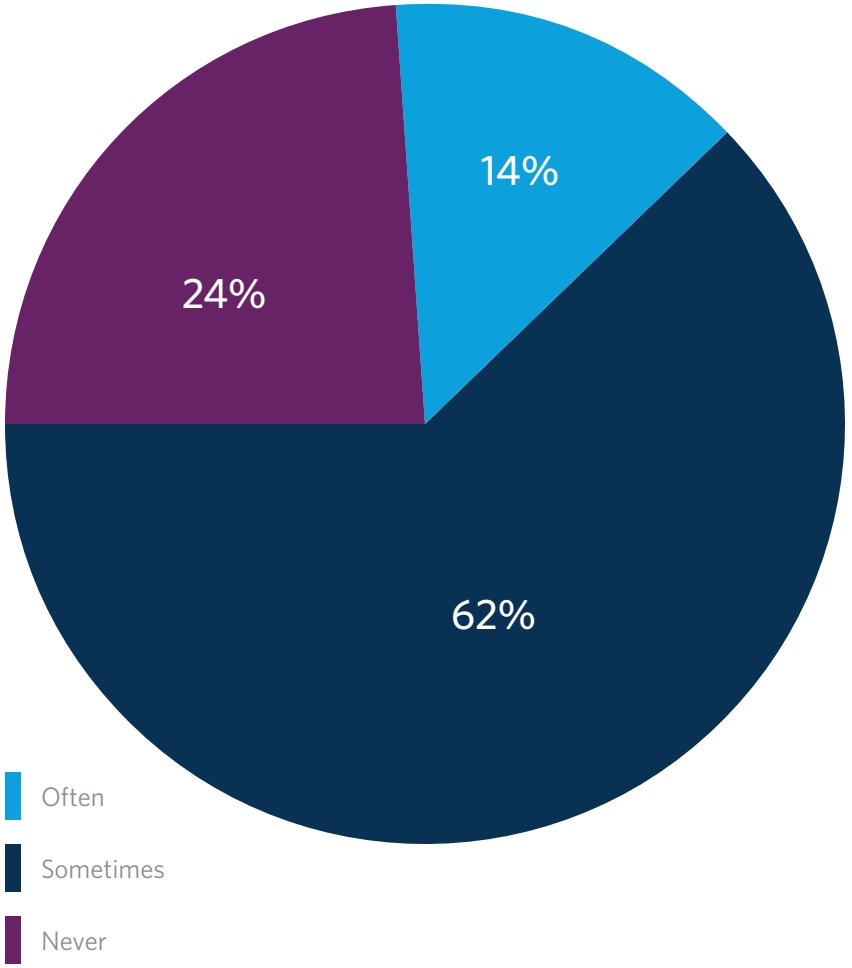
The majority of payers prioritize U.S. professional society guidelines (e.g., the American Society of Hematology) over those from outside the United States (e.g., the European Hematology Association). Payers prefer U.S. guidelines because they are more applicable to the U.S. health system. Payers generally reference global standards "sometimes" — particularly where U.S. guidelines are limited or unavailable **(Figure 7)** — as a way to inform decision-making. Namely, payers consult guidelines from outside the United States to support clinical assessment and management decision-making for therapeutic areas with significant unmet need, as well as for areas with limited or insufficient U.S. representation or consensus. In these cases, they prefer global guidelines that, where possible, incorporate or include the U.S. perspective, such as from the World Health Organization (WHO).

## OFF-LABEL USE

Off-label use is becoming more prevalent among rare disease therapeutics and other high-cost drugs for conditions in which there are too few cases for comprehensive study. For these situations, payers research off-label use of a particular drug on a case-by-case basis, such as when a patient has limited treatment options or compelling evidence exists to support off-label use of a particular product as determined by their health care provider. Similar to the 2022 report findings, several payers in 2023 report using the NCCN Compendium® from the National Comprehensive Cancer Network as evidence for the appropriate use of off-label therapies in cancer, and peer-reviewed literature for non-oncology therapeutic areas. In these cases, payers submit documentation and detailed rationale for coverage of the off-label product for a particular patient.

*FIGURE 7:* **U.S. PAYER UTILIZATION OF NON-U.S. GUIDELINES FOR DECISION-MAKING IN RARE & SPECIALTY**

*PRESENTED AS % COVERED LIVES; N=24 PAYERS*



## IMPACT OF HEALTH TECHNOLOGY ASSESSMENTS (HTA)

In keeping with the 2022 findings, payers indicated moderate use of external HTA reports for rare and specialty products and continue to expect little change with this approach in the coming years. Specifically, 60% of payers reported a moderate influence of external HTA reports, with a slight increase to 70% moderate influence in 3–5 years **(Figures 8 & 9)**. This is likely due to the impact of published studies in management to date and internal analysis. Payers indicated that HTA and Institute for the Clinical and Economic Review (ICER) findings are most relevant for pricing and contracting discussions, but mainly use these as "nice to haves" for confirming internal processes and conclusions surrounding a given therapy. Typically, regional organizations use HTAs to make decisions, while national organizations use HTAs to inform or reinforce current policy or decision-making.

*FIGURE 8:* **USE OF EXTERNAL HTA REPORTS (CURRENT)**

*PRESENTED AS % COVERED LIVES; N=24 PAYERS*

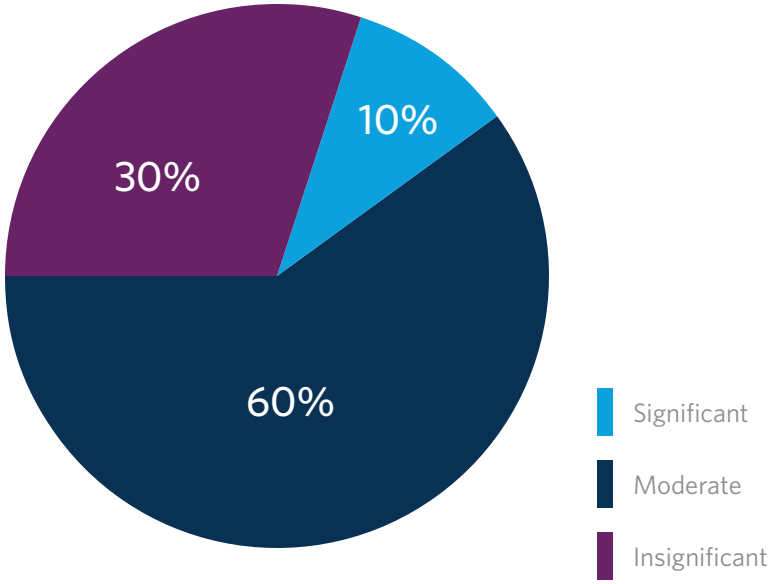
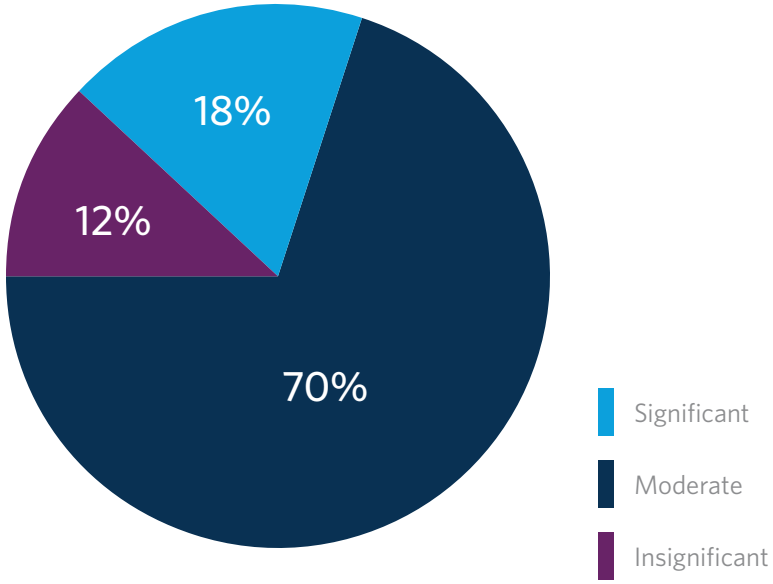



*FIGURE 9:* **USE OF EXTERNAL HTA REPORTS (NEXT 3-5 YEARS)**

*PRESENTED AS % COVERED LIVES; N=24 PAYERS*



# RARE & SPECIALTY MANAGEMENT PROCESSES

## SUBCOMMITTEES

Payers increasingly considered establishing subcommittees in recent years to address the complexities of rare and specialty management. In the 2020 trend report, 25% of survey respondents anticipated creating subcommittees focused on rare disease management within the next five years. However, in the 2021 and 2022 trend reports, the prevalence of subcommittees did not grow as anticipated, likely due to COVID-19 pandemic-related delays as payer priorities shifted. In 2023, subcommittees in rare and specialty remain limited to the largest payers. Survey results show 60% of surveyed national plans currently have a subcommittee dedicated to rare and/or specialty drug evaluation and coverage. This growth in subcommittees among national plans is likely due to the number of rare and specialty drugs entering the market, coupled with the broad organizational commitment to keeping up with new products and providing patients with access.

## MEDICAL VS. PHARMACY BENEFIT MANAGEMENT

Similar to the 2021 and 2022 report findings, payers surveyed in 2023 also prefer pharmacy benefit over medical benefit. Overall, payers stated the pharmacy benefit allows them to predict costs and manage products through traditional utilization management techniques more accurately than the medical side. For example, the pharmacy benefit provides payers with greater control over strict prior authorization criteria, step edits, and site of care and specialty product mandates.

Despite this preference for pharmacy benefit management, significant variability continues to exist among payers' ability and willingness to effectively manage across benefits. In 2023, 79% of survey respondents reported they successfully manage across benefits **(Figure 10)**. However, while payers representing the majority of covered lives report "success in cross-benefit management," this is limited to the visibility that each payer has across benefits. In short, cross-benefit management can only be effectively operationalized in instances where patients use that particular payer for both pharmacy and medical benefit coverage. For example, some payers (such as PBMs) may only have visibility into pharmacy benefit coverage for any given patient, as medical can be covered under another plan.

In survey responses, some integrated delivery networks (IDNs) and regional payers reported having visibility into both pharmacy and medical claims across their covered lives, while national payers and pharmacy benefit managers continue to face challenges successfully managing across

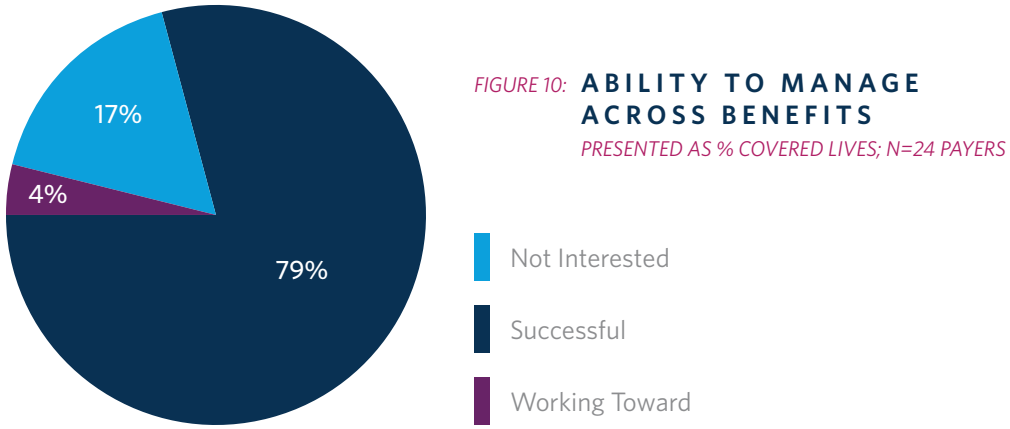



*FIGURE 10:* **ABILITY TO MANAGE ACROSS BENEFITS**
*PRESENTED AS % COVERED LIVES; N=24 PAYERS*

medical and pharmacy benefits. Those able to operationalize cross-benefit management are doing so through prior authorization criteria. In these cases, payers usually require physician attestation of trial and failure of a pharmacy product before the approval of a medical product. These health systems are instituting these policies in competitive markets, such as cardiology.

Meanwhile, management that "prefers" medical products over pharmacy products remains rare, as payers stated they usually have more control and tactical strategies available on the pharmacy benefit.

## VERTICAL INTEGRATION

Payers use different definitions to describe what "integration" means for their organization. Many large national payers indicated their integrated pharmacy benefit managers and specialty pharmacy branches provide cost-savings through site of care and specialty product mandates. Regional payers and IDNs largely indicated they clinically integrate, giving them the visibility needed to effectively manage across pharmacy and medical benefits. Overall, payers recognize that vertical integration improves network visibility, data capabilities, and offerings for both customers and manufacturer partners.

"We are working toward more integration beyond just clinical delivery in hospitals and outpatient sites, but there is a lot of resistance from companies. There also are governance and financial implications of integration that we aren't ready for yet."

– Regional Medical Director

Specialty pharmacy integration remains a priority for payers as they look for ways to mitigate and control high pharmacy spend. Payers with specialty pharmacy services reported their direct involvement in the product journey results in more cost-effective and efficient care. Among those surveyed, pharmacy benefit managers, national payers, and regional payers reported being vertically integrated with a specialty pharmacy. Many IDNs also integrate specialty pharmacies to save costs through programs such as the 340B Drug Pricing Program.

Each of the payer types surveyed recognize the benefit of specialty pharmacy integration on internal control and management. However, many expressed their dislike of closed manufacturer distribution networks, because closed networks restrict the availability of certain drugs to a limited number of distributors or pharmacies. This limitation can make it difficult for payers to provide a full range of options (e.g., specialty pharmacy savings) to their customers. It also adds complexity to their supply chain. Payers indicated they hope for more open networks in upcoming plan years to enable them to capitalize on the cost savings associated with internal specialty pharmacy procurement. Despite these limitations, payers also stated they understand why manufacturers prefer closed networks, which is, namely, these networks offer more control over data and more stability. With these considerations in mind, the use of open distribution networks in rare and specialty therapies remains unlikely. As such, payers are working with manufacturers to incorporate their specialty pharmacy into existing closed networks wherever possible.

As another spend management strategy, payers are increasingly creating networks for cell and gene therapies through centers of excellence. These networks provide payers with quality assurance, care coordination, cost predictability and risk management, patient support services, and access to outcomes data for value-based arrangements.

"We are working toward more integration beyond just clinical delivery in hospitals and outpatient sites, but there is a lot of resistance from companies. There also are governance and financial implications of integration that we aren't ready for yet."

– Regional Medical Director

# PAYER ECONOMICS

## RISK MANAGEMENT OF HIGH-COST THERAPIES

As more high-cost, one-time therapies ("lightning strikes") enter the market, payers are expanding their focus on future preparedness for their organizations. In the past, payers predominantly targeted highly controlled management strategies on mitigating the catastrophic-cost risks associated with cell and gene therapies **(Figure 12)**. But they are increasingly deploying such techniques in specialty categories with higher prevalence rates (e.g., oncology and cardiology). In many cases, these strategies involve internally facing techniques, such as site of care and specialty pharmacy mandates, as many payers find these tools easier to control.

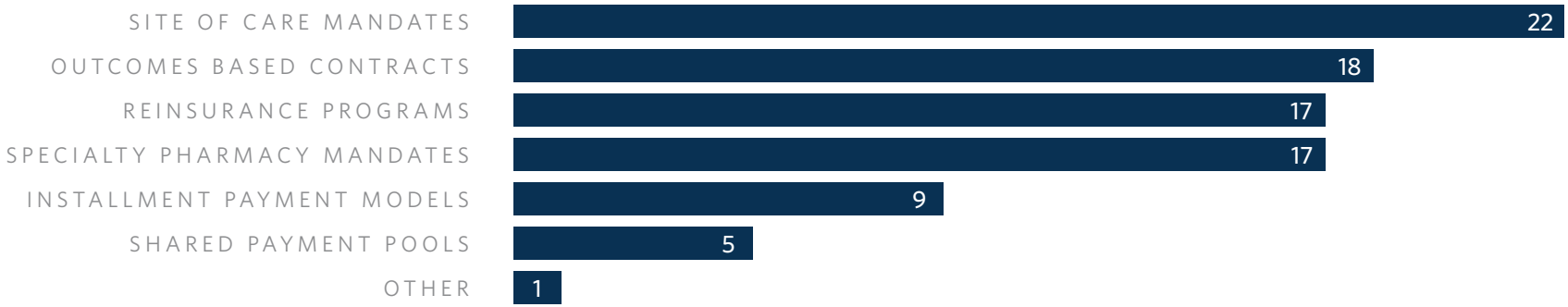
Payers surveyed in 2023 reported these internal strategies help drive effective utilization management and appropriate use across products and treatment locations. They also are leveraging reinsurance programs and shared payment pools. All of these strategies are helping payers mitigate financial risks for their own organizations and for the employers relying on the health plans.

In addition, payers are increasingly seeking outcomes-based contracting and installment-based payment agreements with manufacturers. Momentum is expected to grow for these types of arrangements, even as some payers question whether they effectively address their financial risks.

Meanwhile, payers surveyed in 2023 all agreed they would support outcomes-based contracts for rare and specialty products in which a manufacturer provides a significant rebate in the event a one-time-use drug failed to show efficacy across patient outcomes. To this point, payers noted all involved parties should share the risk equitably for a mitigation strategy to be mutually beneficial and successful. In order to effectively execute these types of arrangements, manufacturers would likely need to assume a greater portion of risk than previously seen in outcomes-based arrangements.

*FIGURE 12:* **RISK MANAGEMENT TECHNIQUES FOR ONE-TIME CELL & GENE THERAPIES**

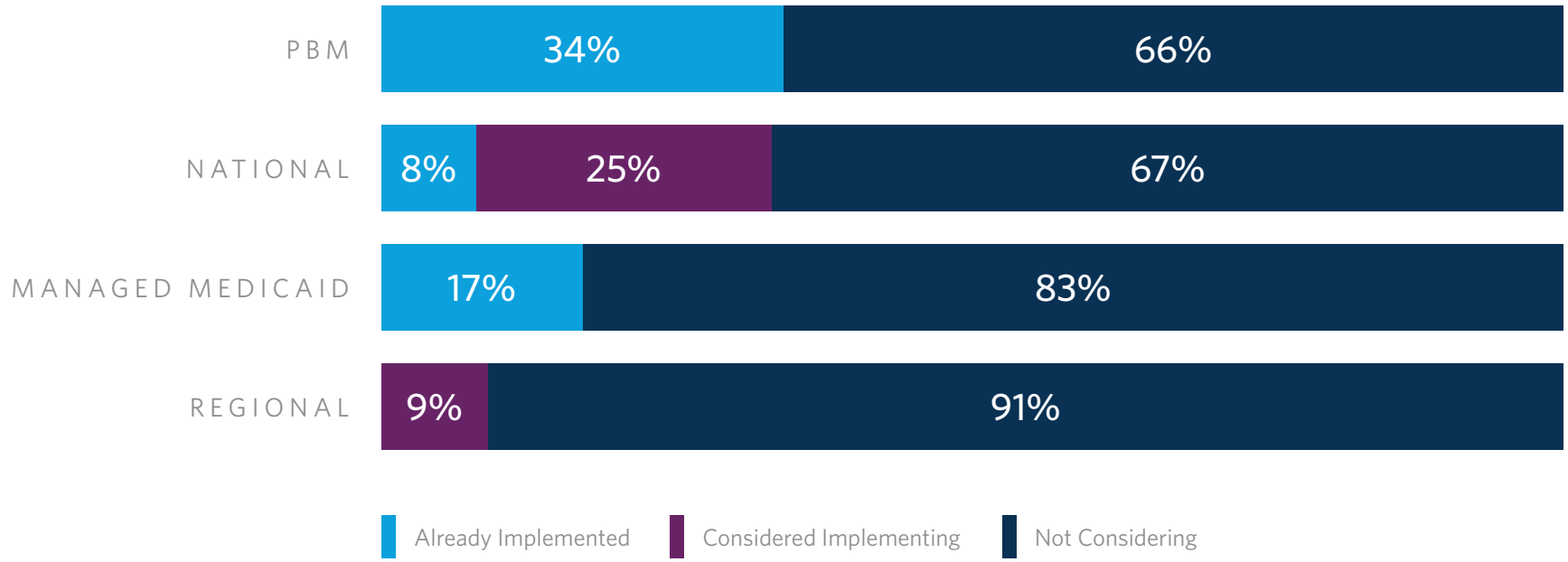
*PRESENTED AS COUNT - MULTIPLE SELECT (NOT MUTUALLY EXCLUSIVE); N=24 PAYERS*



## STRATEGIC FINANCING

Historically, payers relied on strategic financing techniques — including bundled payment strategies, annuities, and shared risk — as risk mitigation options to deliberately control traditional costs within their organization. However, some payers, particularly large-scale pharmacy benefit managers (PBMs) and national health plans, are beginning to use these techniques to manage the financial impacts of discount channels and expanding policies for 340B Drug Pricing Programs, patient assistance programs, inflation rebates, and other programs and policies. Survey responses in 2023 showed 34% of PBMs and 8% of national payers are implementing strategic financing techniques, while 25% of national and 9% of regional payers are considering the same **(Figure 13)**. Meanwhile, with uncertainty surrounding how forthcoming and potential policy changes will affect the industry, many payers, particularly regional ones, remain reluctant to alter their strategic financing plans until more is known about the tactical implications of these macro changes.

*FIGURE 13:* **CURRENT IMPLEMENTATION OF STRATEGIC FINANCING IN RESPONSE TO POLICY CHANGES**
*PRESENTED AS % COVERED LIVES; N=24 PAYERS*



## 340B TRENDS

Section 340B of the Public Health Service Act requires pharmaceutical manufacturers participating in Medicaid to provide outpatient drugs at discounted prices to eligible healthcare organizations that treat people who do not have insurance or who are experiencing financial hardship. The 340B drug discount program was created to protect such organizations from increasing drug costs and support access to care for these patients.

Since the program's inception, the number of hospitals participating in the 340B Drug Discount Program has dramatically increased — from fewer than 1,300 340B contract pharmacies in 2010 to more than 33,000 as of mid-2023.[2] With the rapid growth came increased attention among stakeholders and public scrutiny.

Payers surveyed in the 2023 report support the program in principle, but question its sustainability given recent controversies around transparency for eligible healthcare organizations. For instance, most payers remain skeptical of the dramatic increase in the number of participating organizations in recent years. They believe many pharmacies and hospitals are "buying low, selling high," and thus benefiting from the discounted prices without passing any savings along to patients and insurers. However, despite this perception, there was no evidence of widespread misuse or wrongdoing, as of the publication of the 2023 report.

In addition to uncertainties surrounding transparency and motive, payers surveyed expressed concern that 340B may be driving up overall healthcare costs for patients, payers, and health systems. They stated prices for therapies not included in the program may be raised over time to offset the discount profit losses.

While updates to the program have been made and are being proposed via legislative and regulatory mechanisms, payers surveyed echoed the general industry sentiment that exceptions are commonly found for every rule put in place. Because of these concerns, many payers continue to call for significant 340B program reforms.

"My concern with 340B is we are just squeezing the balloon on one end and everything that isn't regulated gets inflated."

– Regional Payer

"Payers are annoyed that health system pharmacies can get one drug for cheap and bill for much higher, but then complain about the rates for other products. It seems like a lifeline and how some pharmacies are staying afloat. 340B is overdue for significant reform and manufacturers are ready for this, too."

– National Payer

## INNOVATIVE CONTRACTING

As in the 2021 and 2022 trend report findings, payers again indicated interest in outcomes-based contracting and expect such risk-sharing agreements with manufacturers to grow over the next few plan years **(Figure 14)**.

In previous years, payers debated who should be responsible for the risk of a covered life if a member changes commercial plans. However, this point of contention is gradually softening, particularly among large payers. In the 2023 survey responses, payers recognized that individuals often move from one commercial insurer to another, while also noting gaining a member is as likely as losing one. This mindset shift may signal growing consensus that it is in everyone's best interest to give members access to appropriate and necessary treatment sooner.

"The number one concern we discuss is there are some groups who say it's for a greater good, and we will lose some people and gain others. However, others say we don't want to pay for someone else to have healthy members. Generally, we feel like accepting some patients will shift across plans is best for everyone. We believe this approach is for the greater good."

– Regional Payer

However, payers cited some of the same critical barriers to outcomes-based contracting as in previous reports. Namely, they still find it difficult to agree on endpoints and define clinical meaningfulness with manufacturers. This creates significant obstacles to aligning on contracting priorities for specific drug classes. In addition, payers surveyed indicated outcomes-based contracting discussions and negotiations historically have left payers disproportionately exposed to risk, compared to manufacturers. So, although many payers are interested in participating in outcomes-based contracts, they generally are reluctant to invest the time and resources into pursuing and executing them, until and unless manufacturers show willingness to adequately balance the risk. In the meantime, payers continue to turn to rebate models, saying these provide predictability and revenue.

## SITE OF CARE POLICIES

Similar to the 2021 and 2022 trend report findings, the use of site of care policies for the administration of rare and specialty therapies continues to increase. Implementing these policies often provides improved patient convenience and access to effective and affordable treatment options, while allowing payers to reduce cost and improve overall operations. As the use of specialty pharmacies increases, so will the administration of specialty products outside the conventional hospital setting. In the 2023 report, payers indicated they plan to keep giving patients access to centers of excellence, home care, and hospital outpatient sites. Payers who use site of care mandates reported a strong preference for ambulatory sites of care over costly hospital fees. However, they indicated these sites of care often are authorized when justified based on patient need and clinical rationale.

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

*PRESENTED AS COUNT - MULTIPLE SELECT (NOT MUTUALLY EXCLUSIVE); N=24 PAYERS*

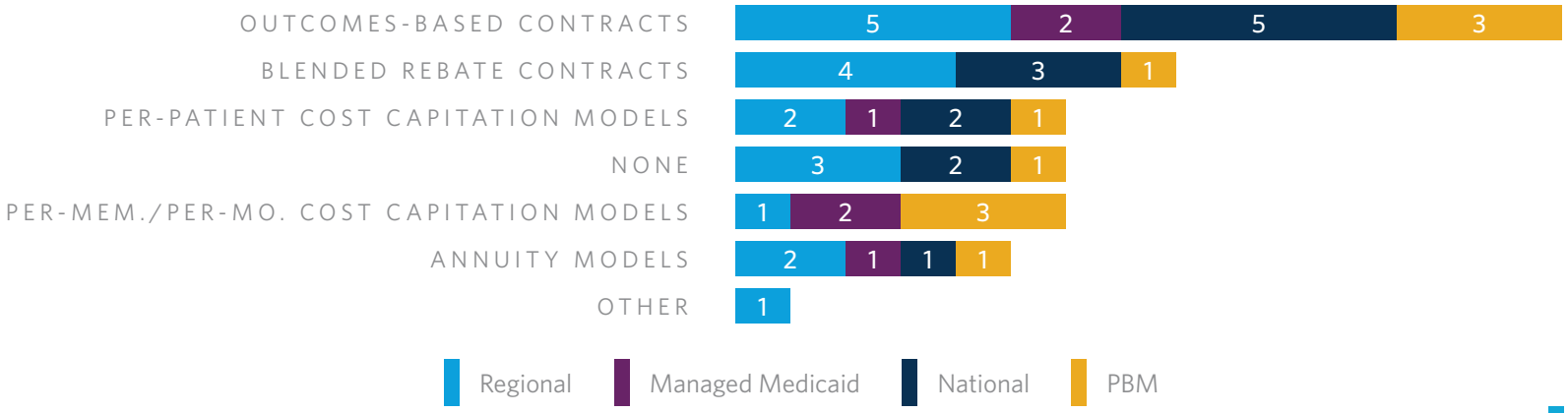
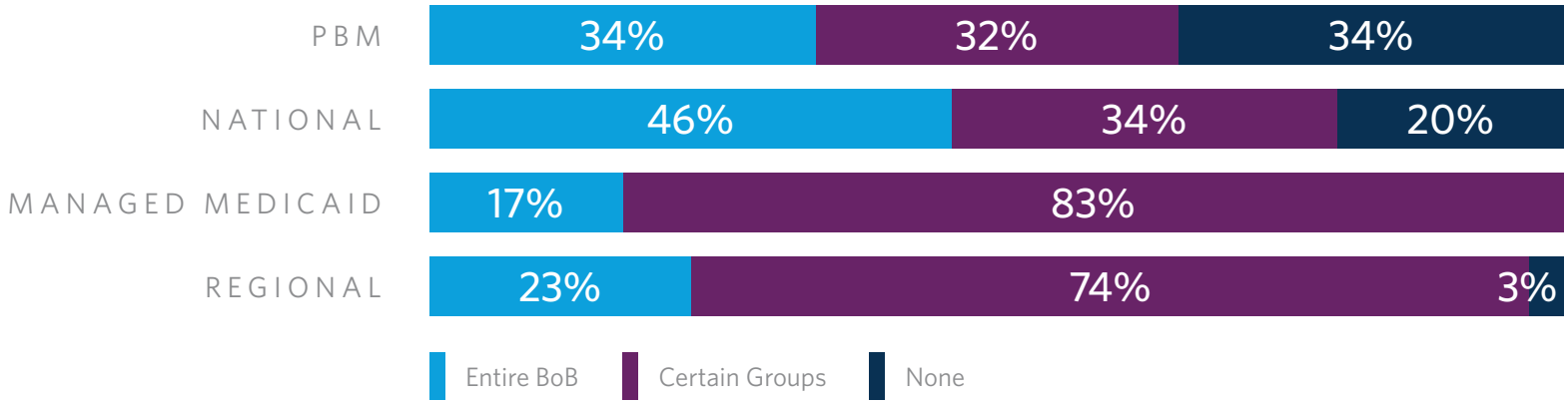



*FIGURE 15:* **UTILIZATION OF SITE OF CARE MANDATES**

*PRESENTED AS % COVERED LIVES; N=24 PAYERS*



# EMPLOYER PERSPECTIVE & ECONOMICS

## EMPLOYER INFLUENCE & INVOLVEMENT

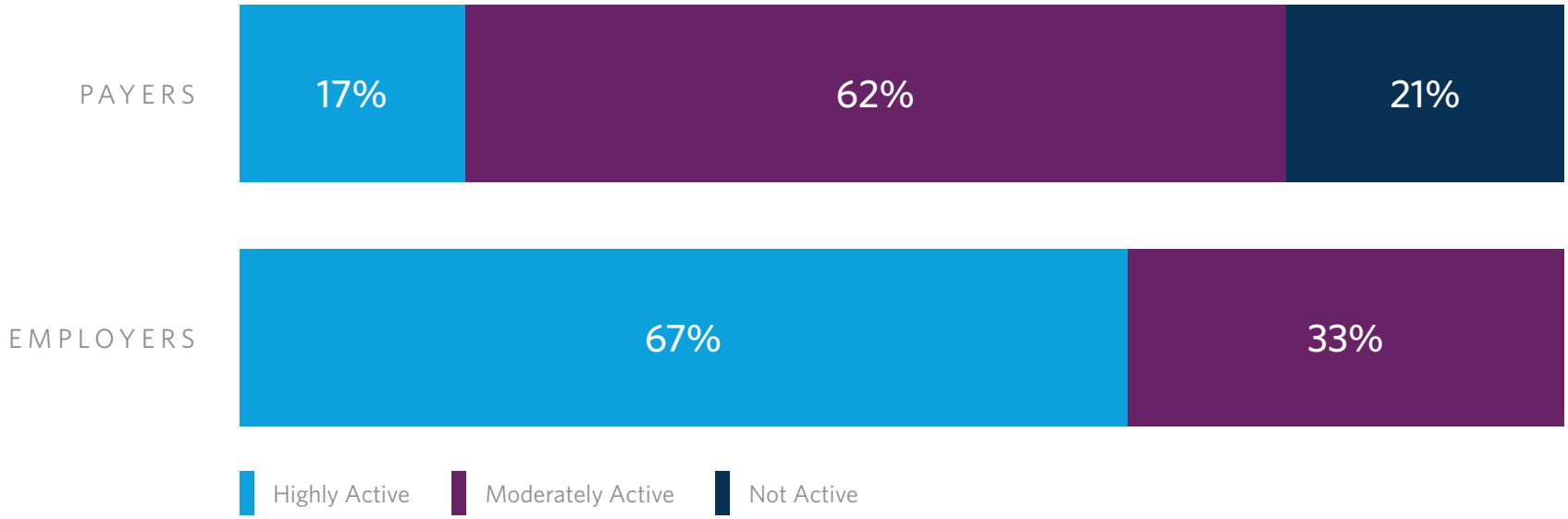
Many more employers are actively seeking solutions to offset the increasing likelihood of catastrophic claims than payers perceived. Specifically, 67% of employers surveyed in 2023 reported being highly active in looking for strategies to maintain their benefit plans, as more high-cost, one time therapies become available and increase the likelihood of a "lightning strike" claim. In the process, employers are considering ways to mitigate the risk to their plans, including in some cases by attempting to exclude certain therapy areas or products.

"[Employers] are getting more and more involved, especially in more rare products. Large buyers will come to us and say don't cover gene therapy, it is too expensive and there's other meds out there."

– Regional Medical Director

*FIGURE 16:* **PAYER & EMPLOYER PERCEPTIONS OF EMPLOYER INVOLVEMENT IN BENEFIT DESIGN**

*PRESENTED AS % OF TOTAL RESPECTIVE STAKEHOLDER MIX; N=24 PAYERS, N=6 EMPLOYERS*



While employers of all sizes are prioritizing risk mitigation strategies, smaller employers with their relatively smaller budgets likely face a greater challenge in overcoming a high-cost drug therapy claim. Even though the specialty category reaches a far broader market, employers reported a slightly higher focus on rare therapeutics. They indicated this is due to the unpredictable implications of rare disease therapies, especially as compared to more predictable specialty products, such as for cardiovascular and oncology. Rare therapeutics usually have little to no competition and, as such, tend to pose a greater catastrophic financial risk, whereas specialty therapies tend to have more competing products and lower-cost options.

Additionally, 2023 report findings indicated differing involvement between self-funded and fully insured employers. Because self-funded employers pay directly for the benefits they offer, they exercise more control over what they offer vs. fully insured employers that opt into largely predetermined plans. As such, with more opportunity to customize their benefits based on their own member needs, self-insured employers seek to design and tailor plans that provide access and financial sustainability. Self-insured employers also have more plan design leeway from a regulatory perspective because they are not bound by state insurance regulations, per the U.S. Employee Retirement Income Security Act (ERISA) law. In contrast, fully insured employers pay health plans and pharmacy benefit managers (PBMs) for standardized benefits packages. In these cases, the health plans and PBMs set the terms, manage the plan, and assume the overall financial risk.

## EMPLOYER RISK MANAGEMENT & BENEFIT DESIGN OPTIONS

While employers are increasingly seeking innovative financial risk mitigation strategies for high-cost therapeutics, they struggle to reach consensus with payers and thus keep relying on traditional approaches. To this end, employers surveyed expressed frustration with what they called a lack of transparency and urgency among payers to find risk management solutions. Meanwhile, employers, especially smaller ones, are looking into known cost-management techniques to make costs more predictable. For example, they are turning more to carve outs for rare and specialty products. Historically, carve outs have largely been used for single-treatment rare drugs like gene therapies. Payers and PBMs prefer not to expand the use of carve outs, which would give niche vendors the market advantage. Rather, payers and PBMs want to find ways to manage rare and specialty therapeutics within their own plans. Beyond market share, doing so also would give payers and PBMs more visibility into access needs of their populations and increased control over their benefit designs. However, until payers and PBMs innovate in their existing strategies for employers, employers indicated they expect to continue using carve outs for these purposes.

Optional riders — i.e., extra provisions for additional coverage, standard benefits like critical illness insurance, as well as clauses that allow employees to waive coverage components — are another financial risk mitigation technique employers reported using. According to the 2023 trend report findings, 73% of employers utilized riders in some capacity. Optional riders usually include some form of compensation to employees who opt out of the health plan, such as those who can access a different plan through a spouse or parent. Employers can save on premium costs when an employee opts out. As employers have fewer strategies to utilize for risk mitigation than payers do, any leverage point that can save on premiums will be a viable option.

## LEVERAGING EMPLOYER BENEFIT CONSULTANTS & COALITIONS

Employers often will turn to employer coalitions and employer benefit consultants for strategic guidance on navigating the complexities of health plans.

As a group, employers wield more collective influence and bargaining power. Together, they unite to enlist an employee coalition to advocate on their behalf and broker and negotiate contracts with manufacturers, payers, and policymakers. These coalitions also provide a platform for employers to share experiences and best practices.

"We have not joined a coalition yet, but that could come down the line. There's the ability to continue to negotiate to drive costs down. I don't know if any coalition has negotiated directly with pharma, [Coalitions] are currently sharing best practices and group negotiations around steerage."

– Large Self-Funded Employer

"As an employer, consultants will look at companies to assess what is going on. They help us navigate all of this."

– Large Self-Funded Employer

Employer benefits consultants help employers navigate the insurance market, comply with regulatory requirements, and institute benefit design best practices. Additionally, they provide insights and expertise on payer management practices to help employers build the best plans possible. Employee benefits consultants typically work more with self-funded employers that need individualized plans than fully insured employers that procure predefined plans. But both self-funded and fully insured employer groups leverage these consultants for data analysis to forecast expected healthcare usage and costs. Some employer benefits consultants use a claims data mining system that proactively assesses and plans for high-cost therapies. Although they consider this to be a helpful resource for future cost planning, some employer benefits consultants stated there are many limitations that make it difficult to plan accurately. Some of these limitations include using claims data inconsistencies, use of outside gene therapy programs, use of reinsurance programs, and the use of rebates for certain products. In addition to these assessments, employer benefits consultants and coalitions still heavily rely on PBM data and insights to gain a comprehensive understanding of the landscape and evolving trends.

# FUTURE RARE & SPECIALTY TRENDS

## CATASTROPHIC IMPLICATIONS

Considering the expanding high-cost drug market, payers are placing more emphasis on the importance of risk mitigation for these products, especially in the cell and gene therapy space. Namely, payers are preparing for the unlikely — but increasingly probable — "lighting strike" financial impact that high-cost, one-time therapies may have on their plan. Of the sample surveyed in 2023, payers representing 45% of covered lives indicated they have taken steps to mitigate the risks associated with these products **(Figure 18)**. The tools often used include value-based contracting, reinsurance models, and annuities.

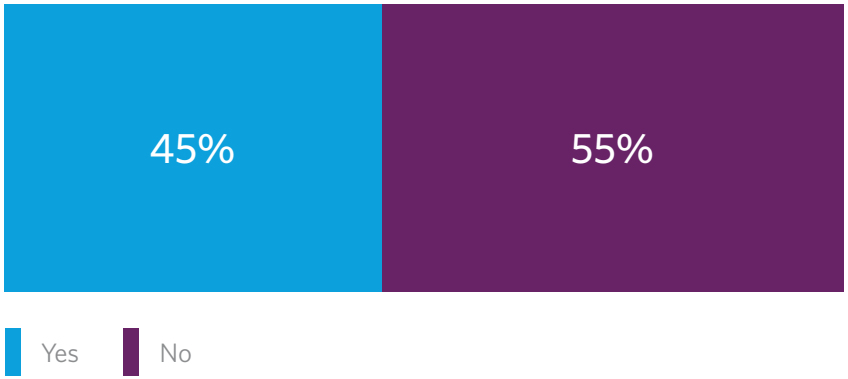
Interest in value-based contracting has increased compared to recent years, particularly in the one-time therapy space. However, payers continue to view these types of contracts as unreliable and difficult to implement, citing the challenges of agreeing on endpoints with manufacturers and of determining responsibility for risk when a covered member changes plans. As such, many payers prefer to utilize last-line management tools or stop-loss coverage for risk mitigation, which they consider to be more effective and easier to implement than value-based contracting. Other payers, pharmacy benefit managers (PBMs) in particular, reported turning to reinsurance and annuity models, even though it remains unclear if these models can effectively mitigate "lightning strike" financial risks.

## EXPANSION INTO ADDITIONAL INDICATIONS

While the 2023 trend report results have largely focused on the growth of rare and specialty therapeutics, payers also expressed concern over the potential impact of label expansions. Regardless of clinical positioning relative to each indication, label expansions for existing products increase payers' financial risk and add pressure to reduce costs through

*FIGURE 17:* **ACTIVELY TAKING STEPS TO MITIGATE "LIGHTNING STRIKES"**

*PRESENTED AS % TOTAL COVERED LIVES; N=24 PAYERS*



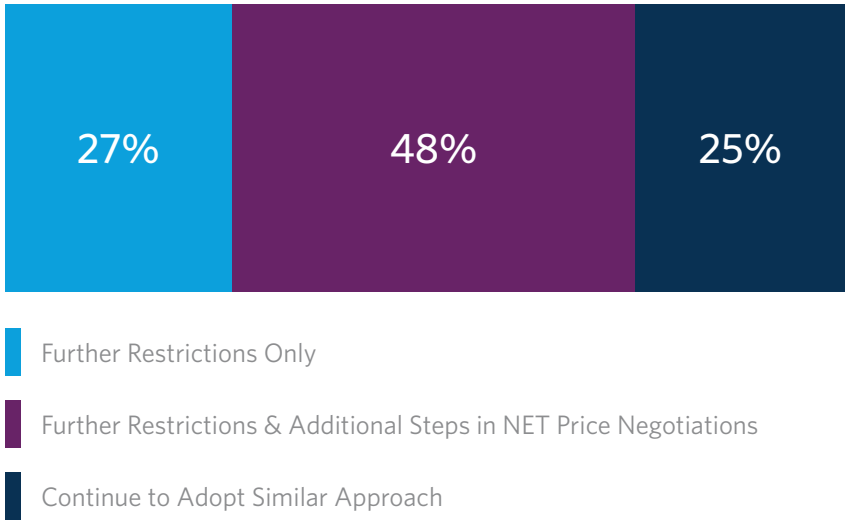

contracting. Payers surveyed indicated when a label is expanded, a product goes through the same pharmacy and therapeutics (P&T) review process as a new-to-market product. As with new products, any indication expansion reviews remain on hold until the product receives FDA approval. Additionally, indication expansions from "more rare" to "less rare" populations tend to be anchored to the price of the original indication. This provides a predicament for payers assessing indication expansions and budget impact, as payers do not often have the infrastructure, capabilities, or desire for indication-based management. Furthermore, in these cases, mitigation strategies for payers are limited. While prior authorizations can have specific requirements by indication, some payers stated they will manage these expansions directly with the manufacturer via price negotiations. Others simply expressed hope that manufacturers will create indication-based pricing on their own. On the employer side, payer and employee benefits consultant analysts actively take indication expansions into account to actuarially forecast potential impact and inform decision making for employer customers.

## FUTURE POLICY CHANGES & IMPLICATIONS

Similar to the perspectives provided in the 2022 trend report, payers are largely taking a "wait and see" approach to recent policy changes and their future implications, including for the Inflation Reduction Act (IRA), Medicaid AMP rebate cap removal, and legislative efforts to reform pharmacy benefit management. When discussing these topics, most payers indicated they typically take a reactive approach since many bills get introduced, changed through the committee process, and/or never become law. Accordingly, they wait for final outcomes before investing crucial resources into deploying risk mitigation techniques or associated policy changes.

*FIGURE 18:* **ACTIONS CURRENTLY TAKEN IN RESPONSE TO INDICATION EXPANSIONS**

*PRESENTED AS % TOTAL COVERED LIVES; N=24 PAYERS*



## INFLATION REDUCTION ACT

Regarding market events, payers noted the Inflation Reduction Act (IRA) as most top of mind, since it impacts several pharmaceutical payment and distribution areas, including: **1)** Medicare price negotiations of certain drugs, **2)** mandatory rebates manufacturers pay for price increases that surpass inflation, **3)** delays to the Trump administration's rebate rule, **4)** a temporary increase in biosimilar reimbursement, and **5)** Medicare Part D benefit redesign. Of those areas, payers indicated the Part D redesign will likely have the biggest impact. Part D changes increase plan liability in the catastrophic phase of coverage, resulting in more payer financial liability for high-cost patients. It also spreads out and caps patient out-of-pocket costs. As a result, especially for a heavily used high-cost therapy, payers will need to carry and sustain a longer, more pronounced financial burden, as incremental out-of-pocket payments trickle in. To offset this risk, payers are expected to increase utilization management efforts for these agents.

Payers surveyed in 2023 also indicated uncertainty about which strategies should be implemented to offset the potential impacts of the various policy changes. Despite speculation anticipating payers will increase formulary restrictions and pressure to negotiate contracts, most payers indicated they are holding off on taking any significant actions until they see what first-movers do. In the interim, they are fine tuning step edits and/or seeking additional rebates. As they consider their options, payers reported they continue to seek a balance between addressing the potential impact of policy changes and providing access to high-cost therapies.

"We're taking a 'wait and see approach' when it comes to IRA. Right now, I am not doing much on the pharmacy side because I am waiting for folks on the regulatory side to say what is needed to implement."

– Regional Payer

"We have not yet developed any specific policies because we have not gone to our state regulators yet to understand what we can and can't implement."

– Regional Payer

"We have to implement something with Medicare, and it may bubble over to commercial. We are focusing effort on drugs that will push people into catastrophe, like immunology, by implementing more steps and demanding more rebates. Negotiating oncology drugs is also where there will be a big impact."

– PBM

## MEDICAID AMP CAP REMOVAL

As designed, the Medicaid AMP cap removal could greatly reduce a drug manufacturer's potential profits, since it eliminates the limit on rebates manufacturers pay Medicaid if a drug's price increase outpaces the inflation rate. Previously set at 100% of the average manufacturer price (AMP), the cap removal substantially increases a manufacturer's Medicaid rebate liability, especially for mature brands with significant drug price increases since launch. These manufacturers are subject to paying inflationary penalties. In turn, payers expressed concern these penalties may also impact them, but plan to hold off on taking any action until the concrete impact is known.

## INCREASE OF PBM TRANSPARENCY

Payers surveyed in 2023 expressed support for legislation aimed at creating more transparency on the part of pharmacy benefit managers (PBMs) around their drug pricing agreements and disclosure requirements for rebates or other discounts with manufacturers. Congress is actively considering legislation to increase PBM transparency and address PBM related fees, but payers are not taking proactive steps until legislation is passed. Still, there is a lot of industry speculation about the potential impact of such legislation, if eventually approved, on payers. This speculation concerns what the recently established innovative models may signal for future plans and other stakeholders. For example, Blue Shield of California stepped back from its partnership with CVS Caremark across broader pharmacy and, with the goal of increasing transparency, shifted to a carve-out approach in which several companies manage their PBM needs rather than one. Payers broadly are aware of these trends and are paying attention more out of curiosity than interest in changing their strategy in the short term to follow suit. Other recent advancements have also been seen with PBMs implementing new offerings (e.g., Express Scripts ClearNetwork℠, CVS "TrueCost" and "CostVantage") to allow employers, government organizations, and health plans access to estimated acquisition costs for medications.

## PRESSURE ON PROTECTED CLASSES

The recent influx of approved products within Medicare's six protected classes (immunosuppressants, antidepressants, antipsychotics, anticonvulsants, antineoplastics, and antiretrovirals) creates further pressure on payers to carefully consider how to balance their risk mitigation and access strategies. Further compounding the challenge, Part D prohibits plans from applying utilization management tactics to antiretrovirals. For reference, such management techniques have led to differences in out-of-pocket costs for patients, prior authorization restrictions, and even step therapy for certain drugs. Additionally, Medicare requires Part D plans to cover nearly all drugs in these classes. Medicare formularies plan to continue using preferred agents within these protected classes where possible to spur competition among manufacturers interested in capturing market share. In response, payers surveyed in 2023 indicated they will continue assessing the situation and considering how to proceed with prudence.

> "Protected products are protected for a reason. Typically, if it is mandated, those are going to be kept. Also, there can absolutely be competition in rare and specialty, but there is a distinction to be made between these and protected classes."
>
> – Managed Medicaid Pharmacy Director

# CONCLUSIONS

The research for the fourth annual Alnylam Rare and Specialty Trend report was conducted in September and October of 2023. While past reports were focused on rare disease management and trends, this year's report focused on the management strategies and potential impact of market dynamics across high-cost therapeutics regardless of disease prevalence. In addition, this year's report brought in perspective from employers as another crucial and influential risk-bearing entity.

Similar to previous reports, payer survey findings show that clinical efficacy and safety remain top value drivers for evaluating rare and specialty therapies. However, this year, both payers and employers prioritized several contracting- and economic-focused value drivers (net price, treatment cost vs. current standard of care, total direct treatment cost offset, and indirect treatment cost offset). This signifies their increasing focus on the economic pressures driving decision-making across both rare and specialty.

This report also explores the ways in which payers and employers alike are simultaneously thinking through strategies to mitigate high costs, establish predictability in an otherwise unpredictable healthcare environment, and do their best to ensure the people who rely on them can.

The Rare and Specialty Trend Report is designed to help U.S. payers, employers, and manufacturers in understanding key trends and by benchmarking rare and specialty drug management practices against industry peers. In addition to promoting mutual understanding and awareness, the aim of publishing the annual trend report is to foster collaboration to help create a better healthcare system for all.

In the next issue, the report will track the urgent and emerging economic and administrative challenges payers and employers face and must address, as the rare and specialty pipeline rapidly evolves, market dynamics and legislative policies shift, and patient access needs swell. Potential topics may include the evolution of price transparency, evolving 340B program trends, the impression of merger & acquisition activity, the impact of state-sponsored Prescription Drug Advisory Boards, IRA policy updates and implications, and the impact of social determinants of health on access and coverage.

## SECONDARY SOURCES


1. https://payorsolutions.cvshealth.com/insights/next-in-gene-therapy-2024-roundup

2. https://www.drugchannels.net/2023/07/exclusive-for-2023-five-for-profit.html#:~:text=As%20of%20mid%2D2023%2C%20DCI,1%2C100%20locations%20(%2B3%25)

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