

Key Trends in US Specialty Pharmacy



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We would like to acknowledge the research of Maximilian Vargas, PhD MBA.

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Research Methodology

- Using Certara’s Compass research network, we conducted an online survey among active voting members of P&T committees in US managed care organizations (MCOs), followed by a set of semi-structured interviews for further interpretation and probing of key trends. In-depth interviews often help to clarify the gap between expressions in survey research and reality on the ground.
- A targeted literature review was conducted to contextualize the research in the current landscape of the specialty pharmacy category.
- Of 31 respondents, 19 were pharmacy directors and 12 were medical directors. These payers represent a total of 198.8M US lives (169.6M Commercial and 29.2M Medicare lives). All 31 respondents were responsible for Commercial lives and 25 of the 31 responsible for Medicare as well.
- Respondents were comprised of national (n=17) and regional health plans (n=14), pharmacy benefit managers (PBMs; n=7) and integrated delivery networks (IDNs; n=6).
- MCOs were also categorized by size, based on the number of covered lives, into large, mid-sized and small health plans
 - Small plans: <920,000 lives; n=7 plans
 - Mid-sized/medium plans: (≥920,000 lives and <3.4M lives) (n=8 plans)
 - Large plans: (≥3.4M lives) (n=11 plans)
- PBMs: 59.5M lives (6 unique organizations)
- IDNs: 24.4M lives (6 unique organizations)
- Small plans: 3.4M lives (7 unique plans; includes PBMs and IDNs)
- Mid-sized/medium plans: 13.5M lives (8 unique plans; includes PBMs and IDNs)
- Large plans: 182M lives (11 unique plans; includes PBMs and IDNs).
- Parts of the analysis presented in this report have been accepted for publication as posters by the American Academy of Managed Care Pharmacy (AMCP) in 2020, one of which has been awarded a prestigious gold ribbon in professional review.^{1,2}

Guidance on Document Use, Important Terms, and Abbreviations

LIST OF ABBREVIATIONS

ACO Accountable care organization	MCO Managed care organization
AMA American Medical Association	OBA Outcomes-based agreements
AAFP American Academy of Family Physicians	OIG Office of Inspector General
AMCP Academy of Managed Care Pharmacy	OMB Office of Management and Budget
CMS Center for Medicare and Medicaid Services	P&T Pharmacy & Therapeutics
ESI Express Scripts	PA Prior authorization
FDA Food and Drug Administration	PBM Pharmacy benefit manager
HHS Department of Health and Human Services	Rx Prescription
ICER Institute for Clinical and Economic Review	SME Small molecular entities
IDN Integrated delivery network	SPP Specialty pharmacy provider
MAPD Medicare Advantage plan	UM Utilization management
	US United States

Limitations

The estimates and findings in this report are based on a qualitative research methodology. Throughout this report, the numbers of covered Commercial and Medicare lives per health plan type are reported to illustrate and provide a deeper understanding of the research findings. The numbers of reported lives are approximations provided by research respondents.

Certara has not accounted for any overlap in covered lives between health plans. As such, findings on the trends we document should be considered indicative rather than conclusive.

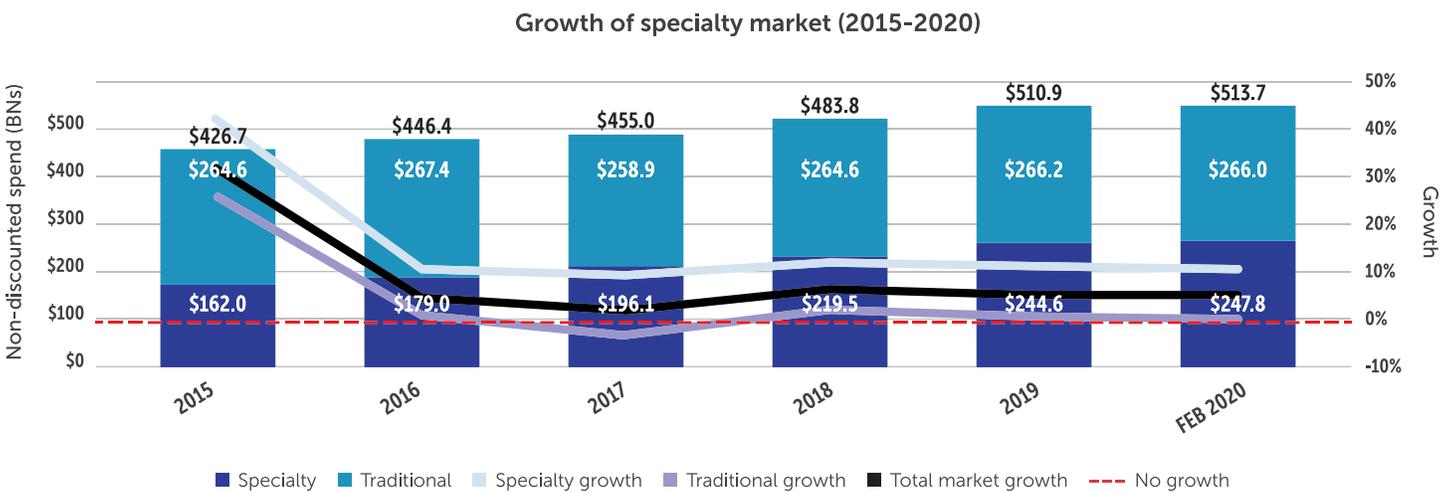
Research Methodology

Market Context

- No universally accepted definition exists for specialty pharmaceuticals. Most refer to high-cost^a complex therapies often used for chronic conditions which require special monitoring, dose adjustments, special distribution and administration (self- or physician-administered injectables) practices.
- While larger, injectable, protein-based molecules (known as biologics) are most likely going to be specialty drugs, we note that roughly half of all specialty sales are still small molecular entities.⁴
- Covering the range of \$10,000 to \$7,000,000 per patient annually, specialty drugs are understood to be higher priced therapies accounting for half of all US pharmaceutical spending roughly evenly split between the medical and the pharmacy benefit categories.^{5,6}
- The FDA has approved over 140 new specialty drugs since 2013 and approximately two-thirds of the 48 novel therapies approved in 2019 were specialty drugs.^{7,8} About 60% of new molecular entities awaiting FDA approval through 2021 can be classified as specialty pharmaceuticals⁹ as late stage pipelines are dominated by specialty therapies led by oncology indications and niche products across a range of classes.

Figure 1.

Pharmaceutical spending since 2015



Source: IQVIA, National Sales Perspectives, February 2020

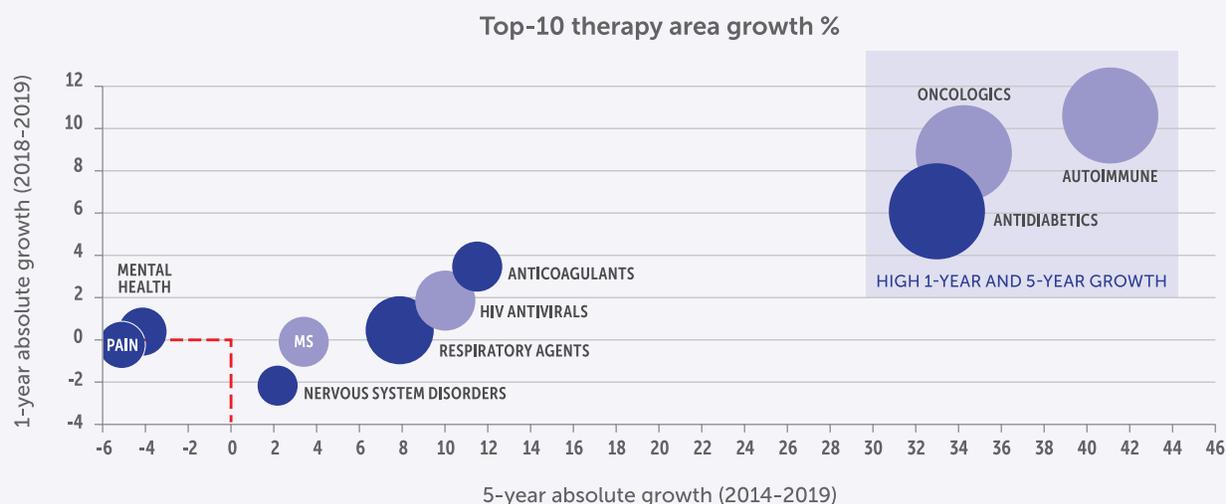
^a >\$670 sponsor-negotiated price per Medicare standards for 2019³

Market Context

- US specialty drug spending saw a modest annual growth of 3% from 44.7% in 2018 to 47.7% in 2019 per ESI.¹⁰ On the basis of non-discounted spending, specialty growth has been outpacing traditional product growth with a 10% to 0.3% dollar volume increase, per IQVIA.
- The two drivers of growing spending on specialty drugs are an increase in unit cost and increased utilization. Specialty utilization increased by 8% year-over-year (YOY) from 2017 to 2018.¹¹
- In 2018, the top ten specialty categories represented 87% of total specialty spend, with oncology, inflammatory diseases and multiple sclerosis as the leading categories.¹² Prescription utilization across commercial plans for oncology and inflammatory conditions increased 4.4% and 3.6% and unit cost rose 13.7% and 10.5%, respectively.¹³ Notable drugs from these classes include Keytruda (pembrolizumab), Humira (adalimumab), and Enbrel (etanercept).

Figure 2.

Three therapy areas responsible for 2/3 of historic (5-year) sales growth and are dominating growth in recent (1-year) launches



Bubble size = Total market size

Source: IQVIA, National Sales Perspectives, February 2020

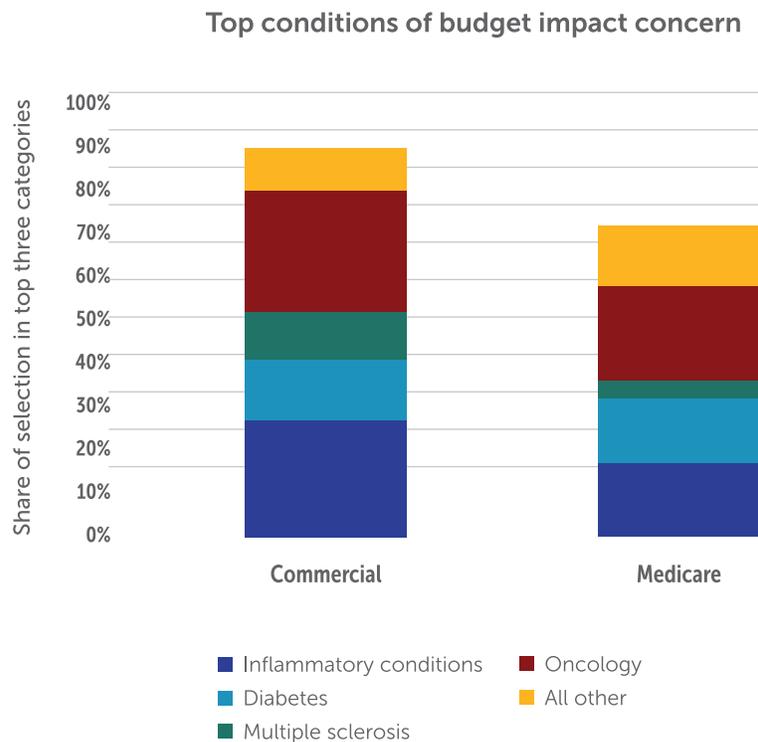
• Specialty • Traditional --- No growth

Key Market Trends

- Our survey confirms that inflammatory conditions, oncology and diabetes remain the top three categories of budgetary concern for Commercial and Medicare payers.^b They are responsible for two thirds of the absolute budgetary growth and dominate new launches. Budget impact is attributable to the combination of high priced therapies and a high number of patients in these categories.
- Payers are concerned that the growth of specialty drug costs is outpacing that of non-specialty drugs pointing to new approvals, strong research pipelines, limited competition and increased utilization among a growing number of patients.
- Our interviews confirmed the payer view that the slow introduction and uptake of biosimilars into the market has hindered potential cost savings.¹⁴ Payers express hope that over the next decade, biosimilar introductions could lead to costs savings in the range of \$25B to \$44B.¹⁵

Figure 3.

Leading conditions of budget impact concern



With respect to their management of the specialty category, the top 3 challenges noted by payers outside of rising cost are:

CHALLENGE 1

The increased utilization and expanded indications of drugs (cited by 15%)

- Payers mention that utilization surges can add the challenge of actuarial unpredictability since only about 5% of patients may account for half of a payer’s entire budget.
- Expanded indications, from original rare disease patient groups at launch to broader populations later on, make historic launch pricing untenable given considerable volume increases.

CHALLENGE 2

A large number of rare disease products (13%)

- It is estimated that 25-30M Americans live with a rare disease. 65% of new drug approvals in the next 3 years will fall into the rare disease and cancer categories, often for targeted therapies. In the aggregate, payers are concerned about the rising median cost per orphan drug patient.¹⁶

CHALLENGE 3

Entry of one-time treatments such as gene therapies (12%)

- As of 2020, there are four gene therapies approved by the FDA with more than 900 INDs in clinical trials.¹⁷ The cumulative effect of curative therapies across multiple conditions is expected to put increasing strains on current ‘pay-as-you-go’ payment systems.
- Collapsing decades worth of potential cost-offsets into the single, one-time administration of a drug produces extraordinary up-front budget pressures on payers.

With respect to their management of the specialty category, payers also see these top three opportunities:



The increased utilization and expanded indications of drugs (cited by 15%)

- Traditionally, there has been little to no contracting for medical benefit products but that may be changing as systems evolve to incorporate pharmacy benefit strategies.
- As more clinically undifferentiated products (like biosimilars) enter a category, there are more opportunities to contract for preferred access.



A large number of rare disease products (13%)

- Utilization management tactics remain the focal point for payers in managing spend in the specialty category and are expanding in most areas.
- Payers are determined to become more restrictive across the board with different tactics to contain costs.



Entry of one-time treatments such as gene therapies (12%)

- Payers express a strong desire to manage the medical benefit like the pharmacy benefit and increasingly integrate coverage decisions across both categories. In shifting the medical benefit to parity with the pharmacy benefit, they hope to draw more heavily on UM tactics such as product exclusions and preferred products.
- No longer protected from cost containment, the medical benefit is now subject to the type of restrictions once limited to pharmacy benefit drugs.¹⁸ Payers reiterate that a key medical management objective is to move specialty infusions towards the lowest cost site of service.¹⁹



Managed market success requires the tactical employment of a growing set of commercial partners. In today's market, patient access and therapy use become a product of comprehensive employment of hubs, 'wrap-around' services, patient assistance and 'quick-start' programs. Interestingly, those are moving from specialty and orphan drugs to increasingly 'hub'-lite areas like chronic care.



– **PAUL GALLAGHER,**
Vice President, US Access Strategy, Certara

Patient cost-sharing as leading response strategy

- Payers listed “increased cost-sharing” as the leading strategy to finance specialty therapeutics across 50% of Commercial and 30% of Medicare lives overall.
- 42% of respondents^c have currently implemented cost-sharing for greater than 70% of covered Commercial lives. For the future, 67%^d of payers report they are likely to have implemented a cost-sharing strategy across Commercial lives.
- On the Medicare side, 35%^e of respondents have currently implemented cost-sharing for greater than 70% of covered lives. In the future, 48%^f are likely to use cost-sharing.
- Mid-sized plans (≥920,000 and <3.4M covered lives) draw on increased costsharing for 70-90% of Commercial lives while regional plans are nearly twice as likely as larger, national plans to expand it further. On the Medicare side, regional plans are four times more likely to utilize cost-sharing than national plans.



^c n=13; representing 49.7M Commercial lives
^d n=21 representing 107.4M Commercial lives

^e n=11 representing 3.2M Medicare lives
^f n=15, representing 9M Medicare lives

- Data from IQVIA shows that the growing shift towards higher deductibles and coinsurance (Figure 4) comes with tradeoffs as it can have a significant impact on patient’s medication compliance and drug waste. Patients generally show high sensitivity to higher out-of-pocket costs. As cost exposures are increased, the rate of prescription abandonment accelerates to over 60% at \$250 monthly patient out of pocket costs.

Patient out-of-pocket cost by type of cost-sharing

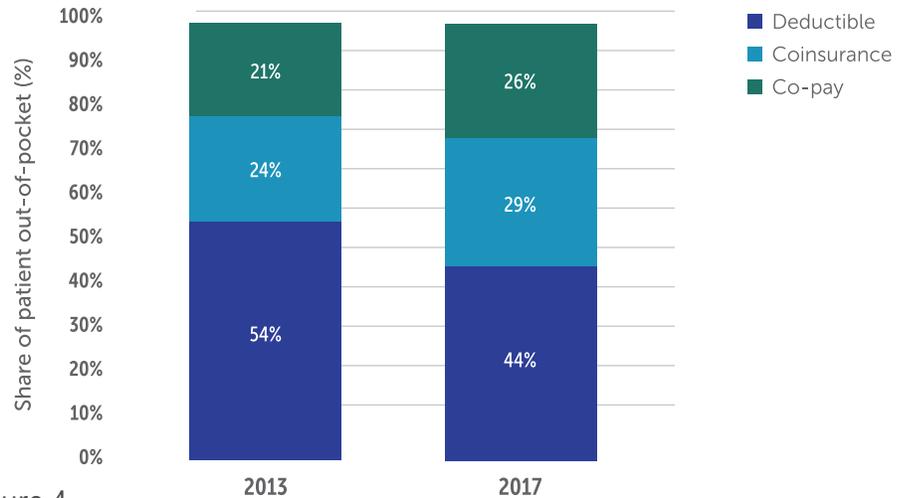


Figure 4.

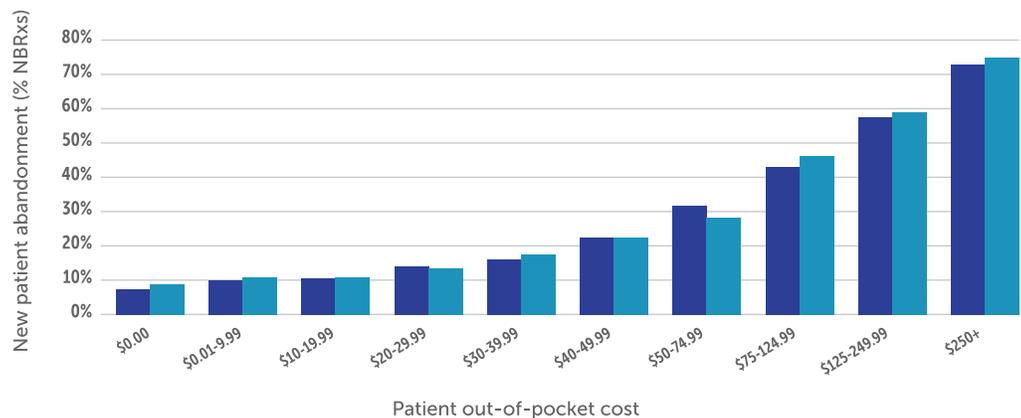
Rising patient cost share of deductibles and coinsurance (Commercial) Source: IQVIA Rx Benefit Design; IQVIA analysis

Figure 5.

Increasing abandonment with level of patient cost exposure Source: IQVIA Formulary Impact Analyzer; IQVIA Analysis, Dec 2018

■ Commercial
■ Medicare

30-day new-to-brand abandonment by patient out-of-pocket cost in 2018 (top brands)



Case Example

Hemophilia has traditionally been an indication with treatments managed under the medical benefit; however, as the category expands, new options have entered such as self-administered Hemlibra. A client approached Certara to better understand utilization management around hemophilia treatments and what restrictions are in place for these products. Certara

conducted qualitative research to validate the hypothesis that payers have started to implement utilization management criteria seen with pharmacy benefit drugs in indications with drugs predominantly covered under the medical benefit, like hemophilia. Among national and regional payers and PBMs, Certara confirmed that most treatments across all four hemophilia indications

are covered with a PA to the FDA-label or PA beyond the label tied to clinical trial design. The restrictions in this setting mimic those traditionally seen in categories managed under the pharmacy benefit. As Certara hypothesized, payers are becoming more stringent in the management of indications with largely infusible drugs, like hemophilia, in an attempt to manage high costs.

KEY TRENDS WITH RESPECT TO UTILIZATION MANAGEMENT (UM) REACH ACROSS EIGHT AREAS

TREND 1 Prior authorizations limiting to populations narrower than label approved indication

TREND 2 Reauthorization criteria based on improved clinical response to drug

TREND 3 Designate preferred medical benefit specialty products

TREND 4 Medical benefit products excluded

TREND 5 Split-fill program

TREND 6 Evidence-based pathways promoted to specify drug use

TREND 7 Quantity restrictions

TREND 8 "Brand A before Brand B" step edits expanded

Average level of utilization management among payers, ranked by level of current implementation

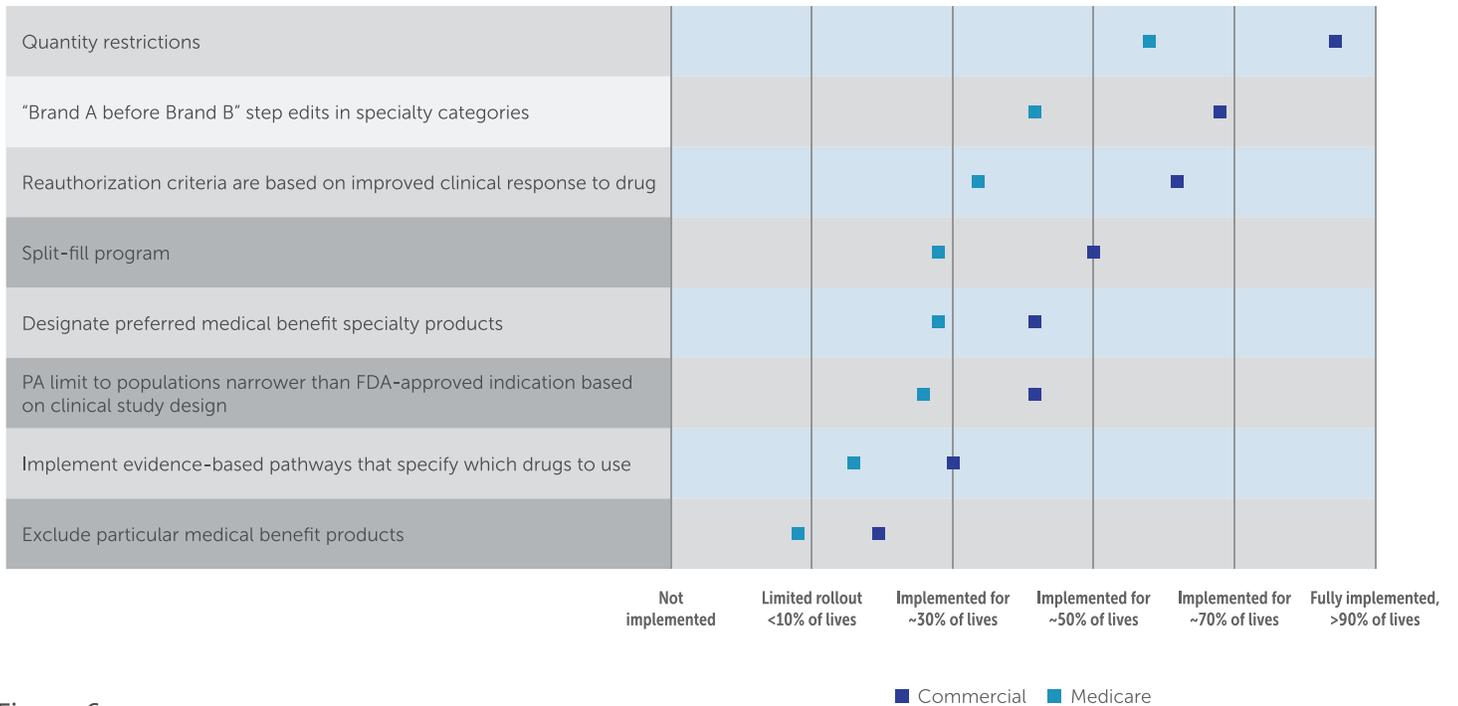


Figure 6.

Average level of UM tactics in 2020, as estimated by Commercial and Medicare payers

TREND 1 TREND 2

Prior authorizations and reauthorizations

- Payers limit drug utilization to populations narrower than the FDA approved indication based on clinical study design. Restrictions beyond the FDA label make the PA process more rigorous and limit use of specialty medications.
- Payers require confirmation of clinical response to drug as renewal criteria. These reauthorization criteria are used by payers to ensure that continued use of a product is warranted. Evidence of clinical response to treatments is often required at annual or six-month intervals.

Current State

- 55% of surveyed payers^g utilize PAs beyond the label for an estimated 70% or more of their Commercial and Medicare lives.
- 70% of payers from PBMsh and 50% of IDNs^h implement PAs beyond the label for at least 70% covered Commercial lives.
- According to the Kaiser Family Foundation, 72% of beneficiaries with Medicare Advantage require a prior authorization for Part B drugs.²⁰ We find that 35% of payers are implementing a narrow PA for 70% (or more) Medicare lives.
- Two-thirds of payersⁱ utilize reauthorization criteria based on improved clinical response to drug for at least 70% of Commercial lives including 86% of PBMsk, 80% of small and mid-sized plans^l, 66% of IDNsm, and 56% of larger MCO plans.

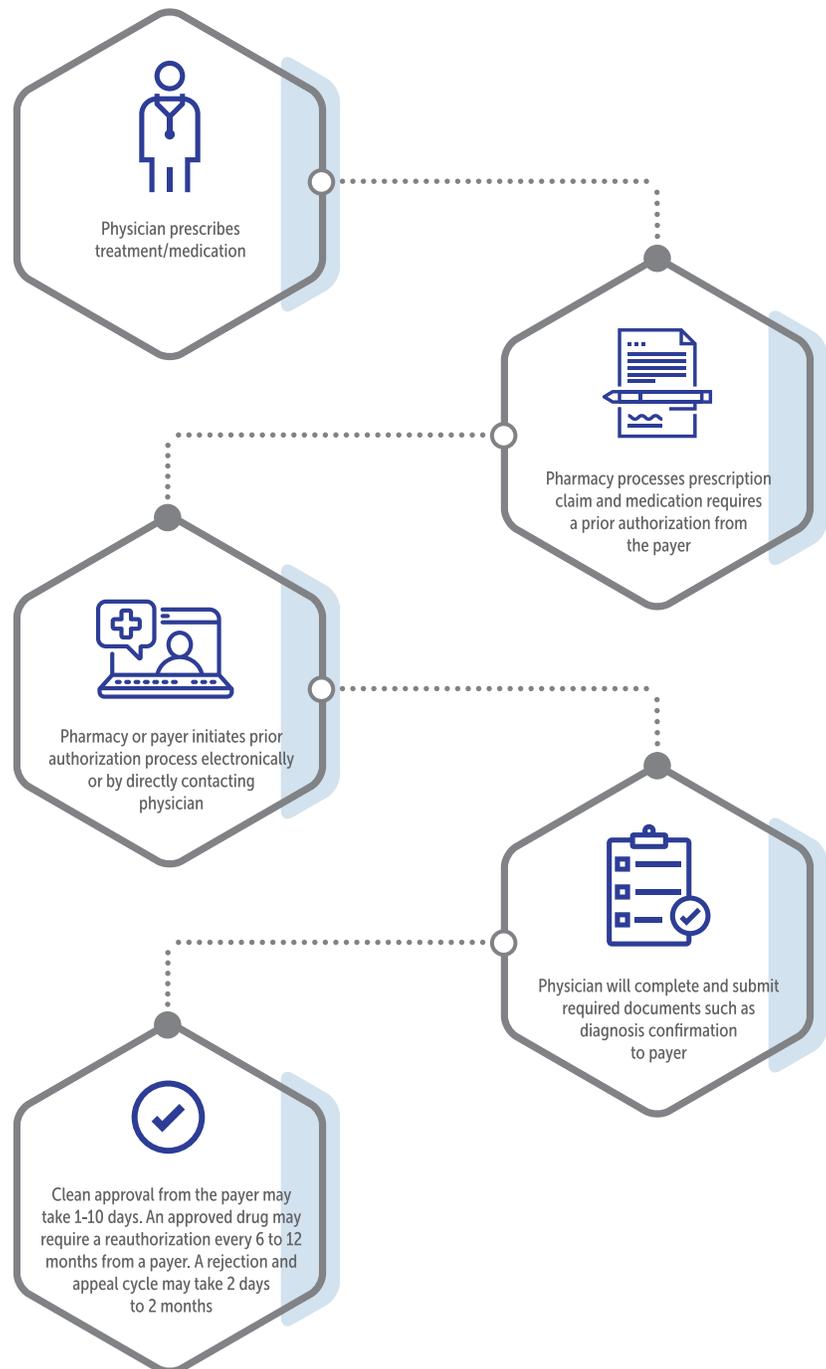


Figure 7.
Customary steps in the prior authorization 21

^g n=17, representing 34.3M Commercial lives

^h n=5, representing 24.8M Commercial lives

ⁱ n=3, representing 1.1M Commercial lives

^j n=21, representing 145.4M Commercial lives

^k n=7, representing 57.3M Commercial lives

^l n=15, representing 10.9M Commercial lives

^m n=6, representing 5.1M Commercial lives

ⁿ n=9, representing 135.5M Commercial lives

FUTURE EXPECTATION

- All commercial payers plan to expand the use of more stringent PA criteria for specialty medications. All PBM respondents and nearly eight in ten IDNs are likely to expand implementation of narrow PA in the future.
- We should note that US payers understand this to be a response mechanism, not a fait accompli. They use more stringent PA criteria in reaction to a certain pricing level. Certara’s price testing research routinely probes for price points at which payers are open to remove additional restrictions.
- 80% of smaller and mid-sized plans^o are more likely to embrace this approach than are large payers.
- Based on survey results, payers are expected to maintain status quo on the Medicare side, not aiming to expand PA beyond the label.

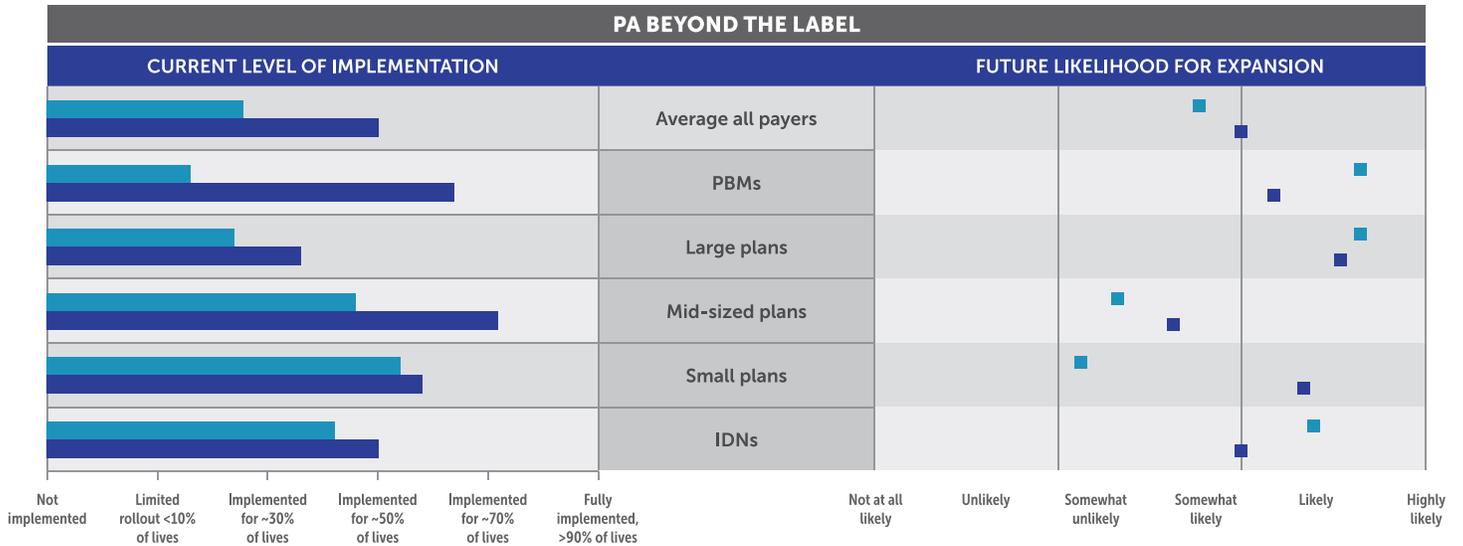
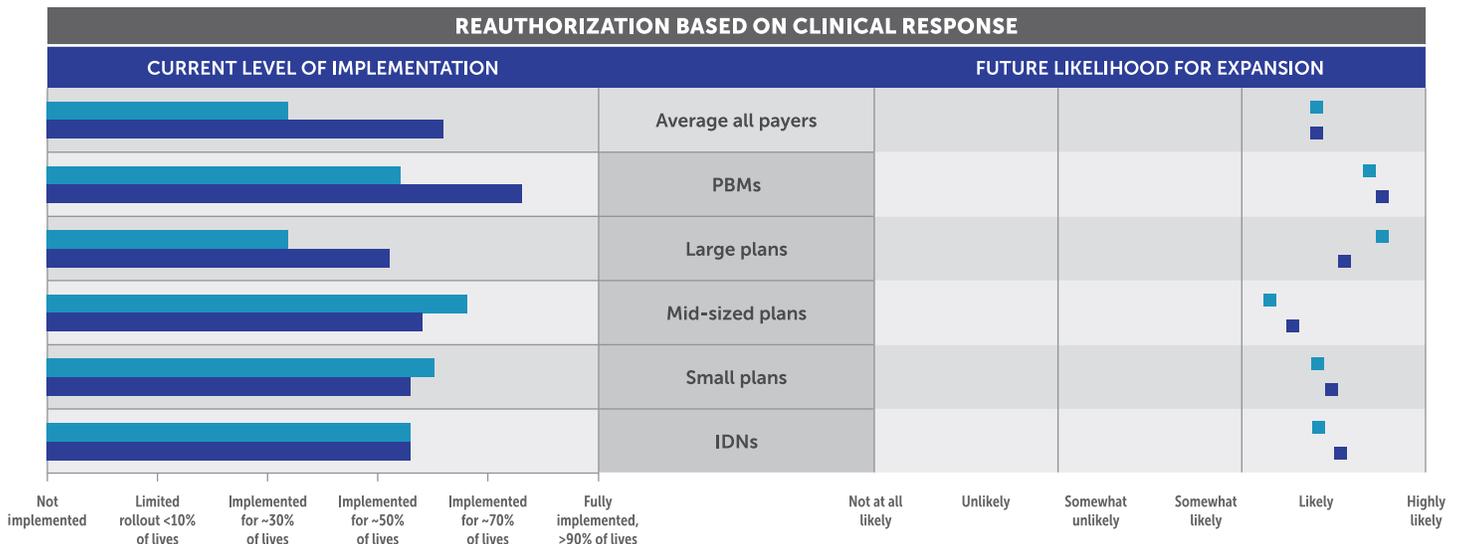


Figure 8.
PA to populations narrower than the FDA approved indication

Figure 9.
Reauthorization criteria based on improved clinical response to drug



^o n=12, representing 11.6M Commercial lives

- There will be a 62% increase in the number of payers using reauthorization criteria for Medicare lives, up from 42% to 68% of payers.
- Nearly 9 in 10 commercial payers are likely to expand future use of reauthorization criteria as a means for cost containment.
- While PAs and reauthorizations are seen as an effective means for cost containment and reduction of drug waste from the payer perspective, they do increase the treatment burden for patients, providers and developers from an access perspective.

Provider burden

- According to the American Medical Association (AMA), 9 in 10 physicians find that prior authorizations have a

negative impact on patient outcomes and believe the burden associated with PAs has increased over the past 5 years.²³ 79% of physicians report that they sometimes, often or always have to submit medication reauthorizations when a patient with a chronic condition is stabilized.²⁴

- Most of Certara’s physician research engagements are aimed to give a nuanced perspective on the level of disruption or burden of the administrative procedure that is associated with PA. It depends on various factors such as provider type, indication, type (e.g. soft, or requiring lab values etc.) and associated requirements (e.g. step edits).

Patient burden

- Nearly 8 in 10 physicians find that PAs may result in patients stopping treatment and sometimes lead to treatment abandonment.²⁵
- 9 in 10 physicians report that PAs cause delays in patient care.^{26,27}
- PAs also impact therapeutic areas with recognized need of treatment personalization. According to a survey among cancer radiologists, 73% report their cancer patients regularly express concern about the delay caused by prior authorizations, forcing a third of doctors to pursue different treatments than the ones indicated just to avoid such delays.²⁸

“

The prior authorization process is out of control. It is increasing and rather than a tool for preventing unnecessary or expensive care, prior authorizations negatively impact my patients’ health and is a significant cause for family physician burnout and the closure of small private practices.

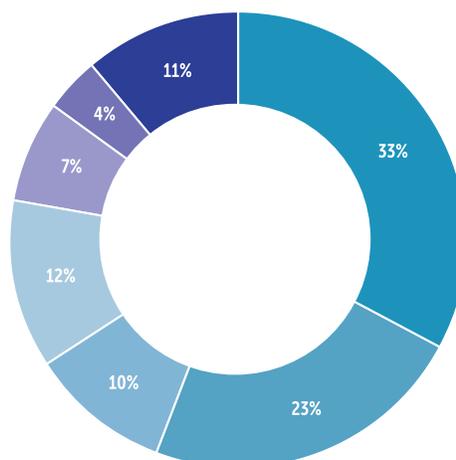
”

– DR. JOHN CULLEN

American Academy of Family Physicians (AAFP)²²

Opportunities in specialty category

23%
OF SURVEY
RESPONDENTS FIND
MORE AGGRESSIVE
UM AN OPPORTUNITY
IN MANAGING THE
SPECIALTY CATEGORY



- Additional contracting opportunities
- More aggressive UM
- Encourage biosimilar and generic utilization
- More restrictive benefit designs
- Changes to physician drug reimbursement
- Stakeholder education
- Other

Figure 10.

Payer noted opportunities in the specialty category

“

Restrictive prior authorization practices can cause unnecessary, stressful and potentially life-threatening delays for cancer patients. ... In its current form, prior authorization causes immense anxiety and wastes precious time for cancer patients.

”

– PROF. PAUL HARARI, MD, FASTRO
Chairman of Human Oncology, University of Wisconsin-Madison³⁰

Case Example

- A manufacturer in early Phase 3 planning to launch a second-to-market product for a rare disease wanted to assess the current level of management and access in the category.
- Certara conducted MCO payer interviews covering a total of 73M lives. Almost ¾ of commercial payers were managing the category with a prior authorization going beyond the FDA label. Payers anticipated similar coverage for new category entrants and criteria beyond the label most often aligned with clinical trial criteria. Certara, together with the commercial team, engaged the clinical team to clarify how the clinical trial design would impact access, and, as a result, commercial forecasts and product revenue, if based on a broad indication.
- In such instances, tighter integration across manufacturers between clinical and commercial teams especially at earlier stages, is warranted. Incorporating payer feedback early in the development process can align commercial forecasts with clinical development to ensure maximized revenue and access.

Product PA status across payers

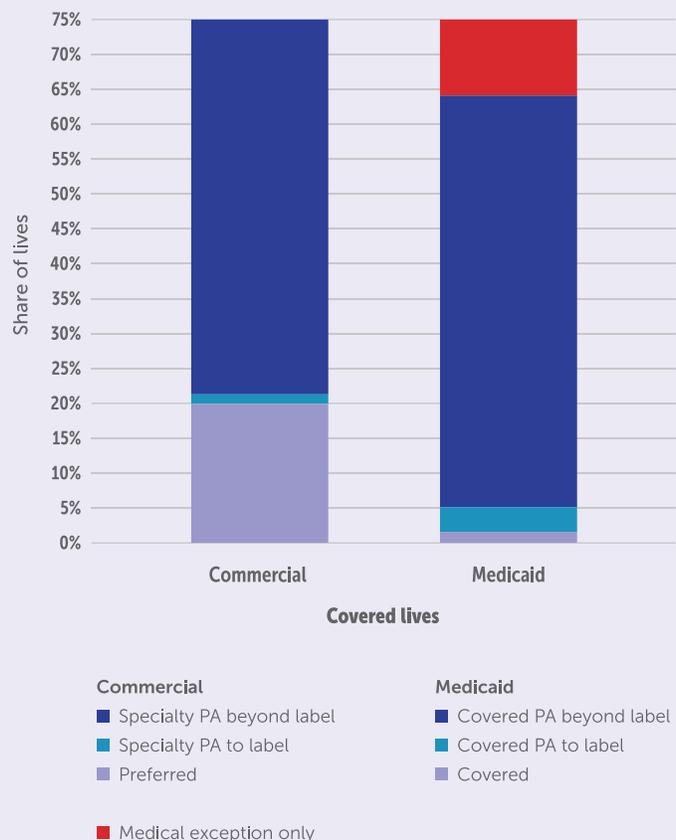


Figure 11.

Prior authorization criteria for a rare disease product

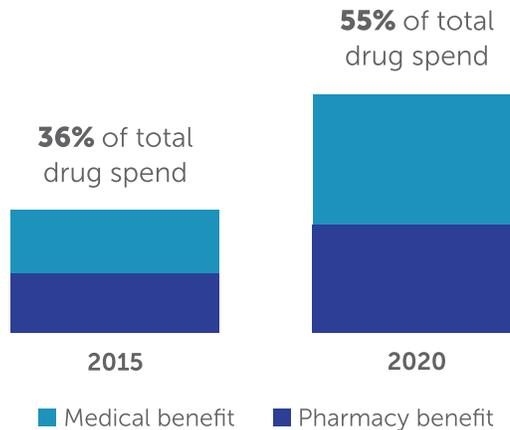
Designating Preferred Specialty Products on the Medical Benefit

- Compared to treatments on the medical benefit, medications covered on the pharmacy benefit traditionally allow payers to have more control on management and utilization.
- Specialty drugs covered on the medical benefit (physician administered) are no longer immune to UM tactics such as product exclusions and designated preferred products as payers try to integrate medical and pharmacy benefits.
- According to Express Scripts data, up to 15% of the specialty spend could be reduced by health plans implementing medical benefit management services.³¹

Figure 12.

Total specialty spend between benefit type

Data source: Medicines Use and Spending in the US IMS, April 2016. NHE, Artemetrix, CVS Health Internal Analysis, 2016.



“US health plan sponsors are projected to waste more than \$9 billion, or 49% of their total pharmacy spend on specialty medication services that provide no additional value. This wasteful spending could be recovered if payers applied the same cost-saving techniques from the pharmacy benefit on medications that are administered through the medical benefit.”

– BRIAN SEIZ
PharmD, President
Pharmacy at Express
Scripts³²

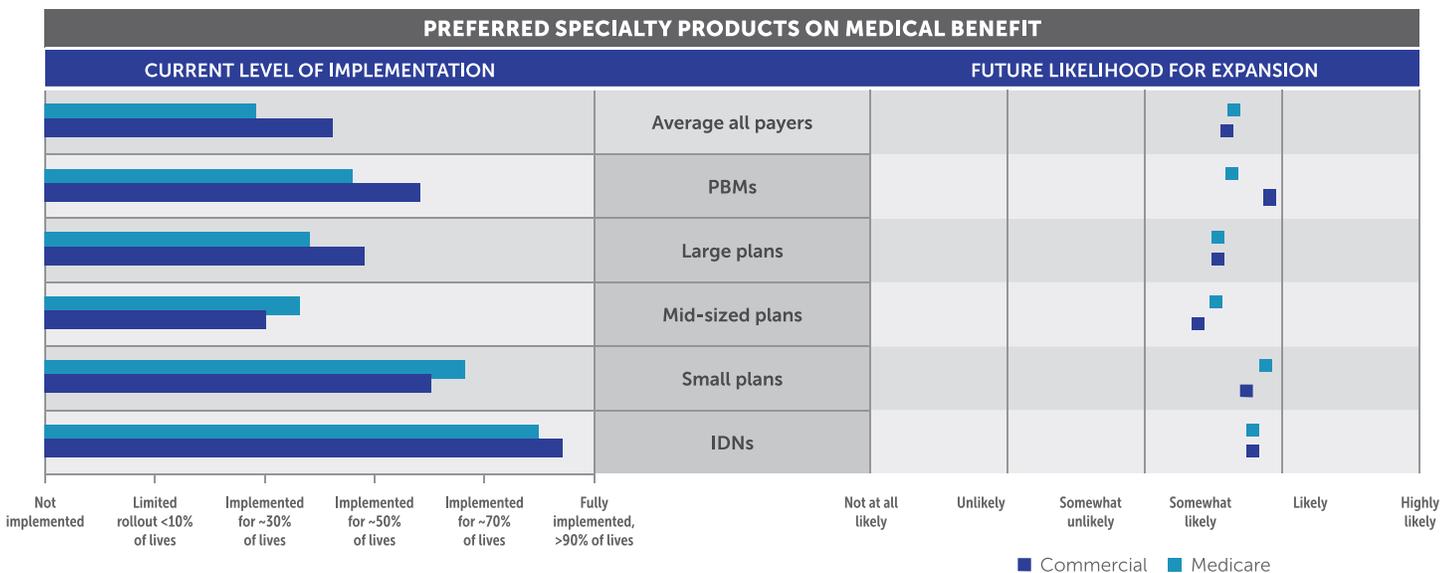
CURRENT STATE

- All surveyed^p IDNs currently implement preferred medical products for 70% or more lives.
- One in two MCO plans^q, regardless of plan size, implements this UM tactic for medical benefit drugs.

FUTURE EXPECTATION

- Going forward all payers will likely expand, or in the case of IDNs continue, this model of preferred medical treatments.
- Based on the status quo, we may see more preferred products on PBM and MCO formularies in the coming years.

Figure 13.
Designating preferred specialty products



^p n=6, representing 18.6M Commercial lives

^q n=18

Increasing Product Exclusions of Specialty Drugs

- The concept of product exclusions traditionally applied to small-molecule drugs on the pharmacy benefit.
- Payers started introducing product exclusion lists as another UM tool and cost containment strategy. While traditional drug classes see this more than specialty drugs, specialty drugs in rare diseases and on the medical benefit are no longer immune to exclusions.
- The first exclusion list, released by CVS in 2012, only applied to small-molecule non-specialty drugs. In 2017, CVS also began excluding products for rare diseases such as Gleevec and Tasigna for chronic myeloid leukemia (CML), though still on the pharmacy benefit.^{33,34}
- In 2014, ESI started excluding certain specialty products like biologics Cimzia, Simponi, Stelara, Xeljanz for inflammatory indications.³⁵ In 2019, 50 new drugs were excluded including specialty products like Onpattro for polyneuropathy of hereditary transthyretin-mediated amyloidosis. In 2020, ESI is excluding 32 new drugs from its national formulary including specialty products like Factor VIII recombinant products for hemophilia and granulocyte stimulating agents.³⁶
- Other important payers such as Cigna, Aetna, Optum, and Prime Therapeutics also began product exclusions since 2016.³⁷

CURRENT STATE

- We find that there is still overall limited implementation of product exclusions across all payers today with only a quarter of payers' excluding particular specialty products covered on the medical benefit 70% or greater covered Commercial lives.
- 12% of survey respondents consider more restrictive benefit designs a key opportunity in managing specialty pharmaceuticals.

FUTURE EXPECTATION

- All payer archetypes anticipate to expand use of this tactic to more covered Commercial lives in the next few years with more than two-thirds of the 31 payer respondents likely to begin excluding particular medical benefit products.

Figure 14.

Number of brand exclusions from PBM formularies

Source: Drug Channels Institute. Numbers of Products on PBM Formulary Exclusion Lists, 2012 To 2019.; 2018. <https://www.drugchannels.net/2018/08/2019-expressscripts-formula>. Accessed April 16, 2020.

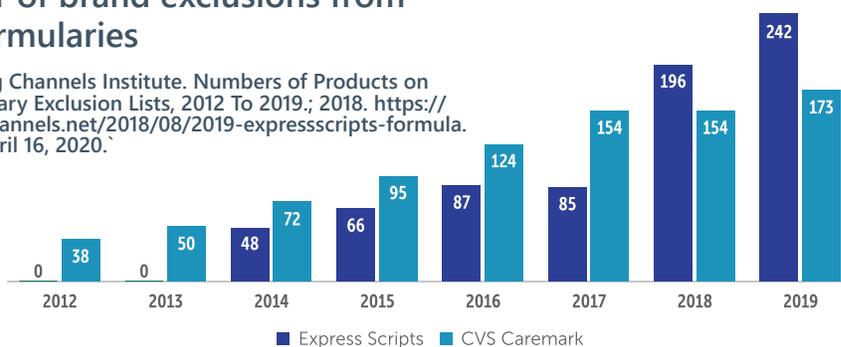
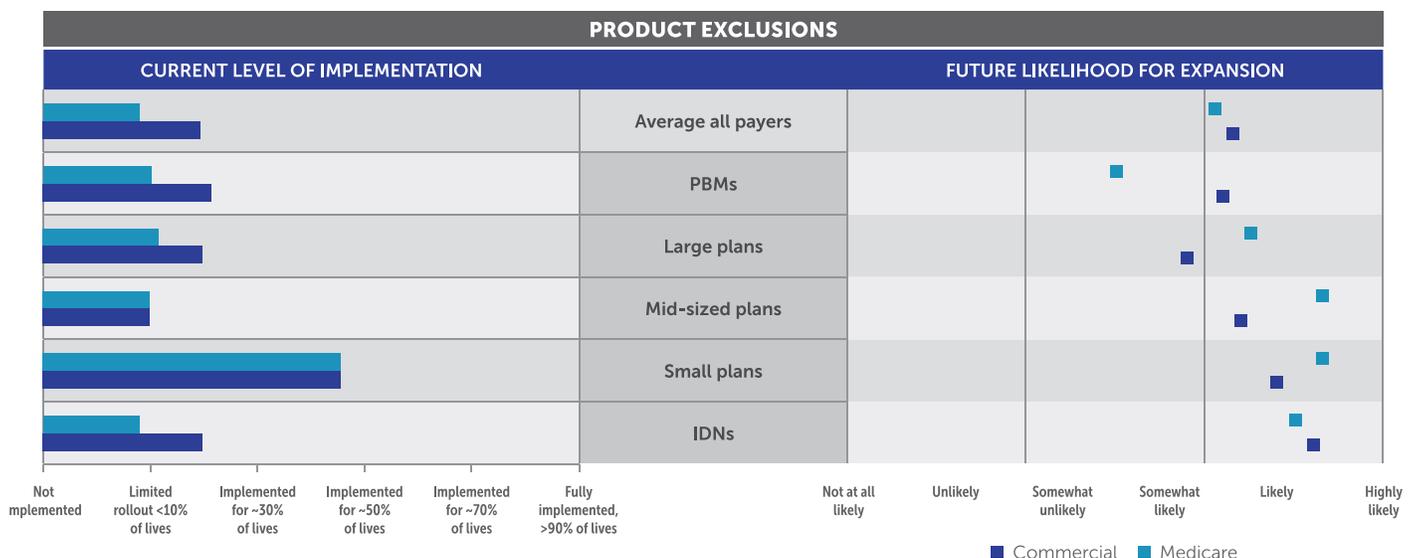


Figure 15.

Exclude particular medical benefit products



¹ n=8, representing 47.2M Commercial lives s n=21, representing 77.1M Commercial lives

Split-fill Programs

- Split-fill (also known as partial fill) programs for oral medications allow payers to reduce medication waste, improve medication adherence and consequently drive down costs.

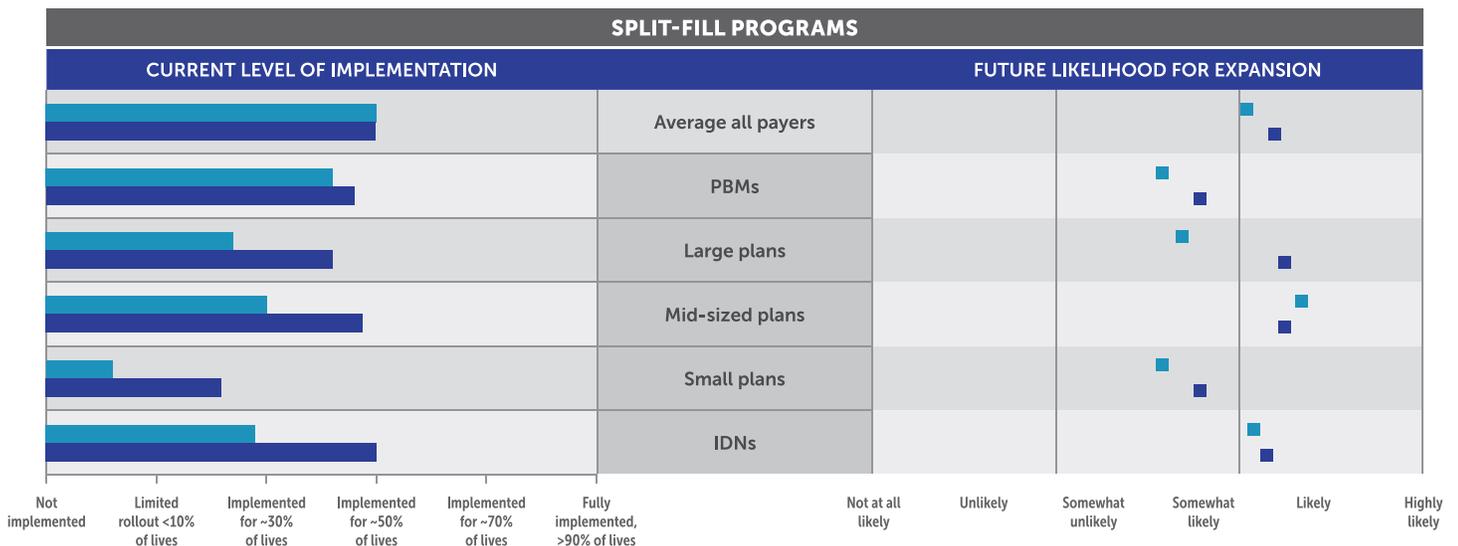
CURRENT STATE

- AllianceRx Walgreens Prime research found that within the first 3 months of implementing a split-fill program, payers would see savings of \$2,724 per month on average for one oral oncology medication. Within the first month, split-fill was associated with a \$132.50 lower copay than non-split fills (p<0.007).³⁸
- Split-fill programs showed lower discontinuation rates, pharmacy costs and potential wastage as demonstrated by a study of an oral oncology split fill program in a national specialty pharmacy. Within six months, the Walgreens program saved \$2,646.74 monthly in medication wastage.³⁹
- Only about 30% of all payers[†] have not implemented any split-fill programs for specialty products within their organizations--half of them PBM and IDN payers.

Non-split fill cost difference from split-fill (Walgreens' study for oral oncolytics) ³⁹	
Month filled	AWP \$*
1	3,118.90
2	2,259.80
3	2,796.20
3-month average	2,714.97

Figure 16.
Monthly mean differences in cost between split-fill and nonsplit-fill

Figure 17.
Split-fill Programs



[†] n=10, representing 48.8M Commercial lives

FUTURE STATE

- In the future, the utilization of split-fills is likely to remain relatively stagnant with 75% of payers^u continuing use. Oncology, inflammatory conditions and MS are the top indications in which payers implement split-fills, though split-fill is present in other indications like diabetes, asthma and hypercholesterolemia.

Categories with split-fill programs	Number of mentions (total=30)
Oncology	17
Inflammatory conditions	5
Multiple sclerosis	5
High cholesterol	2
Attention deficit disorders	1

Figure 18.
Indications with most split-fill use

“

We continue to expand the number of medications available under our split-fill program to support patients and maximize the investments health plans make in their patients.

”

– RICK MILLER

VP, Clinical and Professional Services AllianceRx Walgreens Prime⁴⁰



Evidence-based Pathways: Increased use to Manage Specialty Drugs

- Treatment guidelines like the National Comprehensive Cancer Network (NCCN) and supporting literature have been used by payers to provide evidence-based care.
- Payers are able to standardize care and maintain indication costs by covering specific products recommended per evidence-based pathways.
- In 2019, ESI estimated that \$1.3B could be saved annually in specialty costs by implementing evidence-based UM policies for medical benefit drugs similar to those done for the pharmacy benefit.⁴¹
- ESI reports that 15-20% of current drug claims do not follow treatment guidelines.⁴²

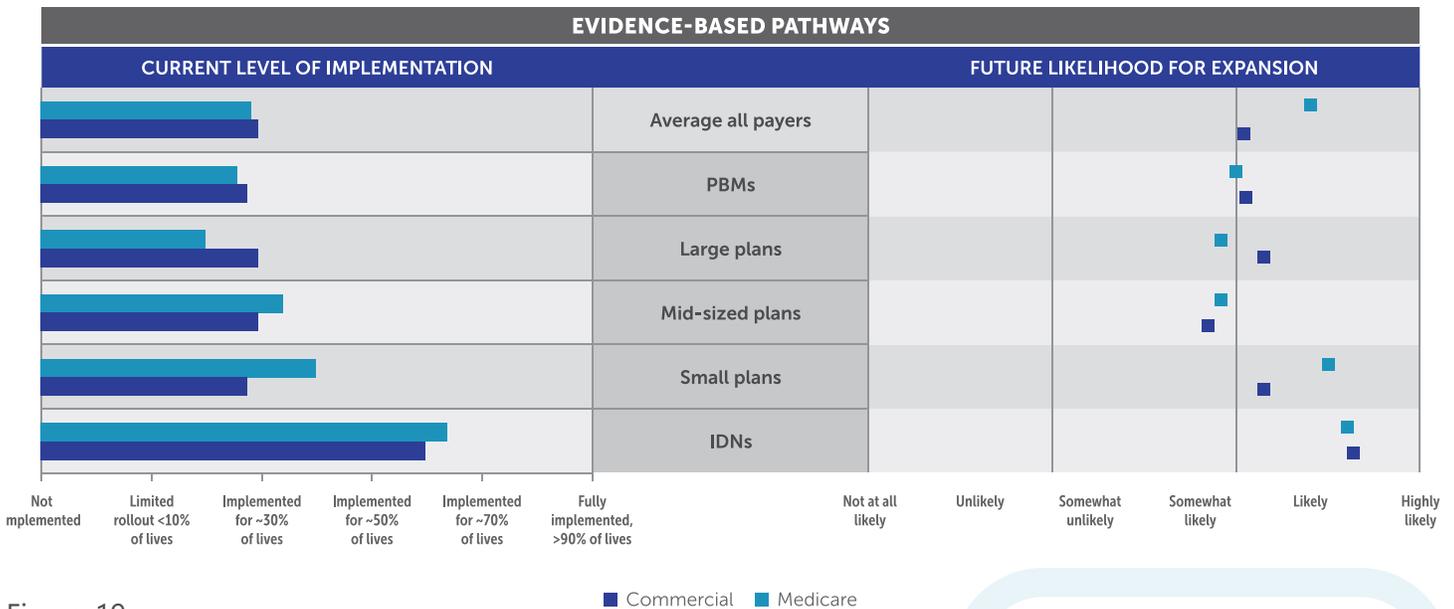


Figure 19. Level of implementation of evidence-based pathways for drug use



CURRENT STATE

- In our analysis, PBMs and IDNs^v see the highest level of implementation of evidence-based pathways, as well as the highest expressed interest to expand them further.
- Rheumatology, cardiology, diabetes and MS are found to have the most uptake of evidence-based pathways outside of oncology. Clinical guidelines and randomized controlled trials are the most common sources for evidence-pathway development⁴³ (Figure 20).

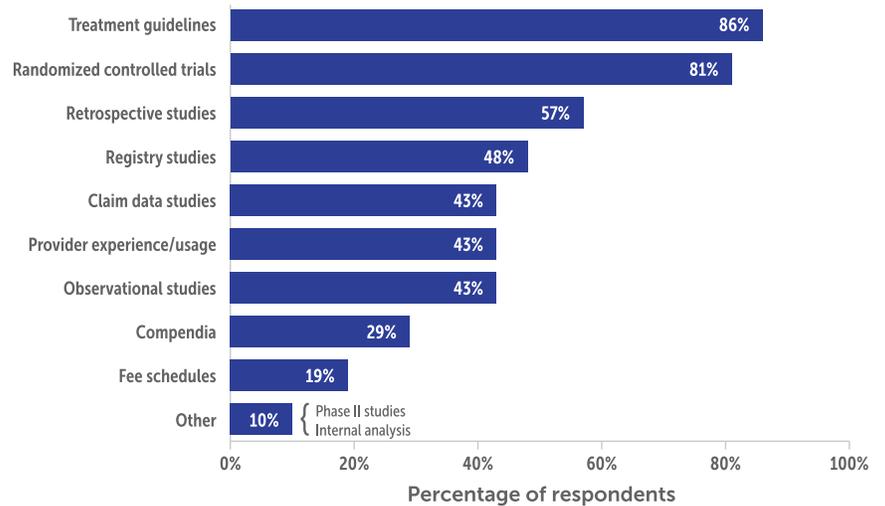


Figure 20.

Top sources of data for development of evidence-based pathways

FUTURE EXPECTATION

- 60% of payers^w of which half are large health plans, are likely to implement evidence-based pathways that specify which drugs to use in the near future; this is an almost 4-fold increase from the status quo of payers fully utilizing evidence-based pathways for Commercial lives. As larger plans are more likely to adopt evidence-based pathways, smaller and mid-sized plans may follow suit.
- We find that the expected increase in providing evidence-based care will come largely from IDNs and MCOs as opposed to PBMs.
- Certara research indicates that oncology, diabetes, and MS are key therapeutic areas where payers rely on evidenced-based pathways in formulary decision-making processes.
- In oncology, a pathway is typically developed for first-line treatments and not later lines. Payers develop these pathways to specify which drugs should be used first and while physicians are not required to follow the guidance, they are incented to do so, usually by a monetary incentive.

^v n=9, representing 40.5M Commercial lives ^w n=10, representing 76.6M Commercial lives

Quantity Restrictions and Step Edits

- Quantity limits and step edits have been cited as two of the most common restrictions payers use in drug management.⁴⁴
- Our research confirms that quantity restrictions and step edits are the most implemented UM tactics with the latter seeing further expansion across all payer types in the future.

Figure 21.
Current and future utilization of quantity limits

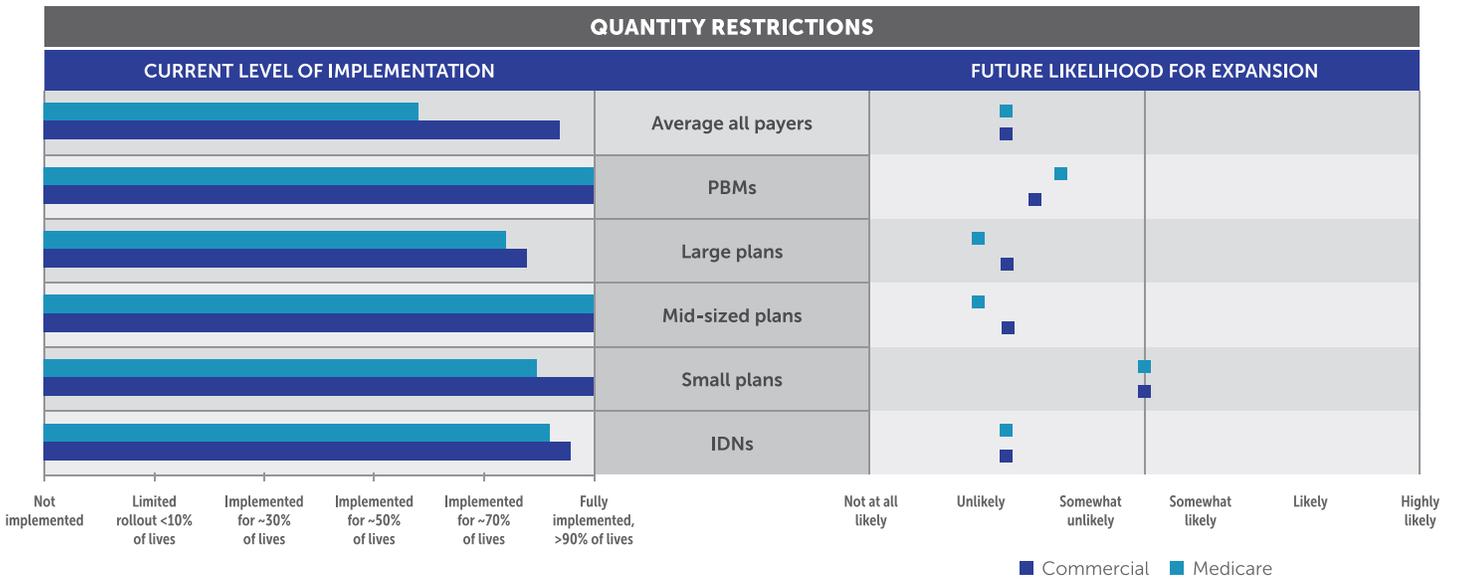
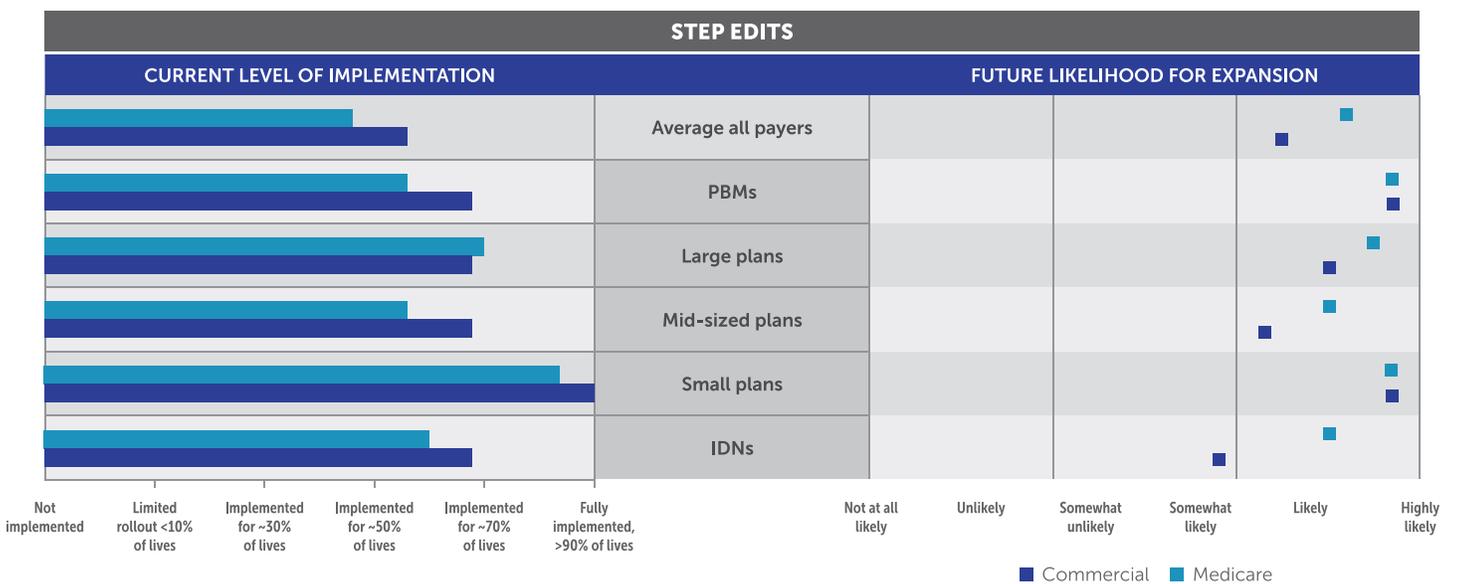


Figure 22.
Current and future utilization of Brand A before B step edits



DEVELOPER TAKEAWAYS

- Clinical trial designs are subject to scrutiny as a means to limit product use with a narrower PA than the FDA label.
- Developers of specialty pharmaceuticals will be subject to more stringent reauthorization criteria which will likely align with clinical response.
- Strong engagement with payers via advisory board and primary research provides vital insight on PA management and criteria that may be included in PAs.
- Developers must be proactive with payer engagement to understand the current reauthorization environment for their product's respective indication and competition.
- Developers should educate payers on clinical endpoints/responses that are most relevant for their product.
- A robust assessment of clinical trial designs through the payer perspective early on in the clinical development phases is warranted to ensure the most appropriate and widest patient inclusion criteria are developed.
- An expanded use of product exclusions by payers suggests that payers are unable to distinguish value across products in crowded therapeutic areas.
- Payers may use product exclusions to negotiate deeper rebates with developers.
- Developers must leverage attributes of product value that may warrant a preferred product status outside of and beyond price.
- Key considerations for developers include:
 - *Will inclusion in certain guidelines or treatment protocols such as the NCCN allow for better access at the payer level?*
 - *Does the timing of inclusion vs. P&T review impact access?*
 - *Does use of evidence-based pathways vary across payer segments?*
 - *What can developers do to support physician use of evidence-based pathways?*



The definition of what constitutes “value” for healthcare interventions is an incredibly complex and hotly debated topic. However, regardless of the school of thought you come from, there is broad consensus that value assessment must take into consideration a multitude of factors beyond purely economic ones. Especially important in value assessment are factors such as unmet needs and disease severity, in particular this applies for rare diseases. Whether they are explicitly or implicitly captured in the assessment criteria, it is clear that healthcare decision-makers are indeed swayed by these factors, and as such it is critical for developers take a holistic approach to their evidence development and communication activities.

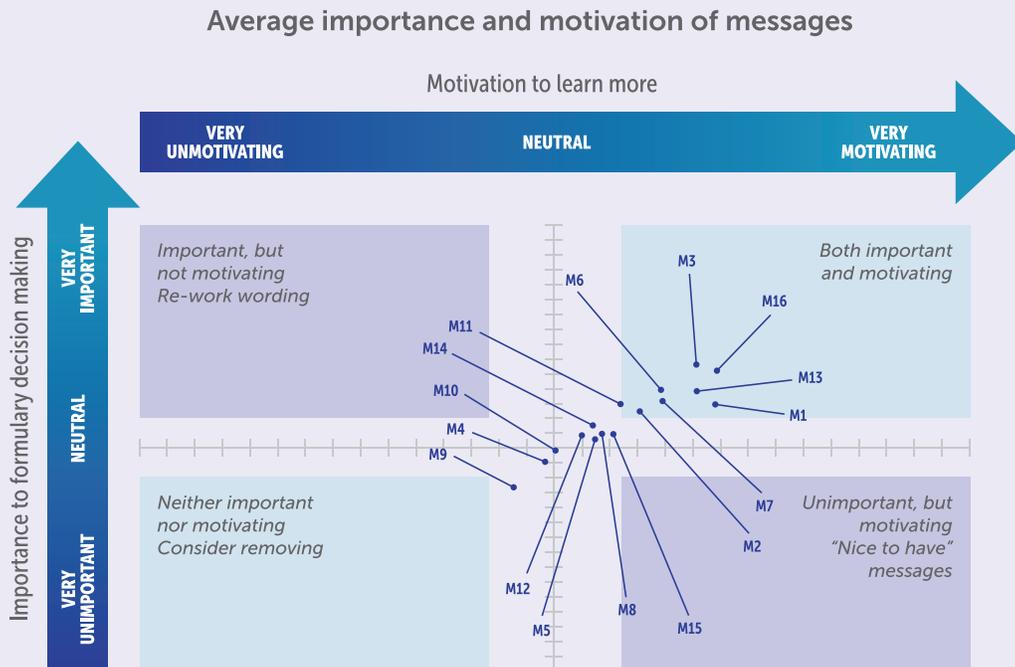


– ROMAN CASCIANO
General Manager and SVP, Certara Evidence & Access

Case Examples

- A manufacturer in a specialty category needed to test the brand messaging and determinants of value for its flagship product. Certara conducted an evidence based assessment of the product’s value story with 15 MCOs and GPO. Certara was able to identify key clinical and class elements important to payers which were likely to result in perceived meaningful differentiation.

Figure 23.
Payer assessment of key elements of product value



- A developer in the oncology space wanted to understand the impact inclusion in the NCCN guidelines has on formulary coverage when the FDA label is narrow. The developer was anticipating a narrow FDA label but inclusion in the NCCN guidelines for a broader indication. Certara’s initial hypothesis was that in oncology, payers rely heavily on evidence-

based pathways to guide formulary decisions. Through discussions with our proprietary payer network, Certara assessed the extent to which national and regional MCO payers align formulary coverage with NCCN guidelines and FDA labels. Certara was able to validate that a majority of payers will align coverage with broader NCCN guidelines over the

FDA label for product use. Certara advised the manufacturer to develop a strong key opinion leader (KOL) education and engagement strategy as an initial step to be positioned in clinical guidelines. We recommended that the developer conduct an advisory board to facilitate KOL engagement around product value.

Payers expect use of Product X in all eligible patients if recommended by the NCCN, otherwise will be consistent with trial inclusion/exclusion criteria or FDA-specific label.

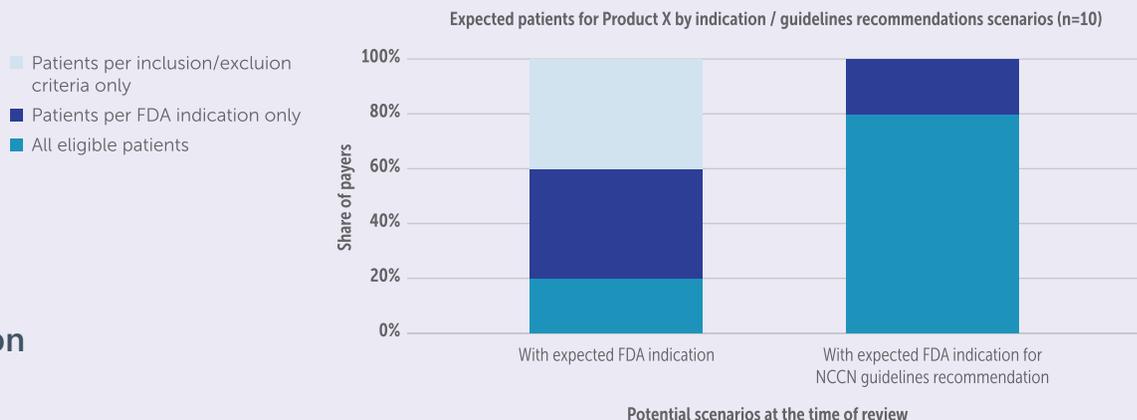


Figure 24.
Evidence-based pathways impact on access

Increase in Limited Distribution for Specialty Pharmaceuticals

- Payers’ preferred distribution channel for pharmacy benefit specialty medications are specialty pharmacies through a limited distribution network, which are owned today by various market entities. Approximately 80% of payers required certain specialty drugs to be dispensed through specialty pharmacies in 2018.⁴⁵
- Limited distribution networks can limit medication access for providers as HCPs and hospitals not part of a limited network may have to pay higher costs to obtain drugs.

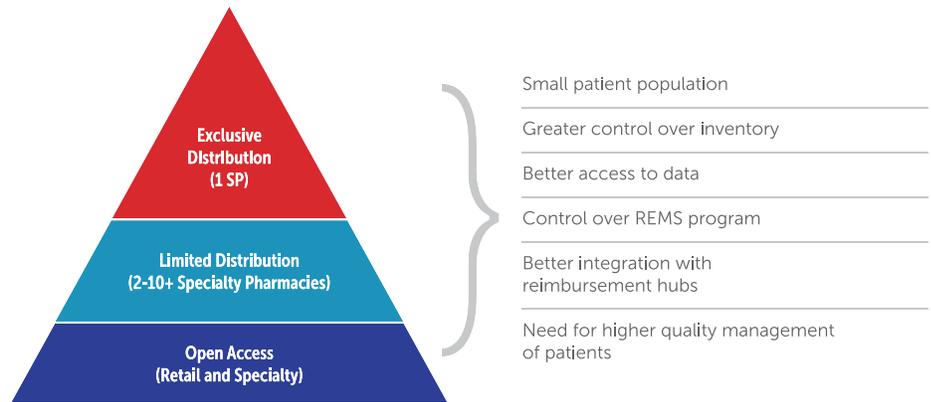


Figure 25. Distribution channels for specialty pharmaceuticals

Shifting away from ‘buy-and-bill’ on the medical benefit

- Specialty drugs are reimbursed through the supply chain as either a pharmacy benefit, or as a medical benefit, through the buy-and-bill model. Each channel receives different reimbursement and is subject to different management practices.
- Similar to utilization management, distribution on the pharmacy benefit allows payers to have more control and management over medication use as compared to buy-and-bill practices on the medical benefit. Payers leverage specialty pharmacies to provide cost management and coordinated patient care leading to better health outcomes.

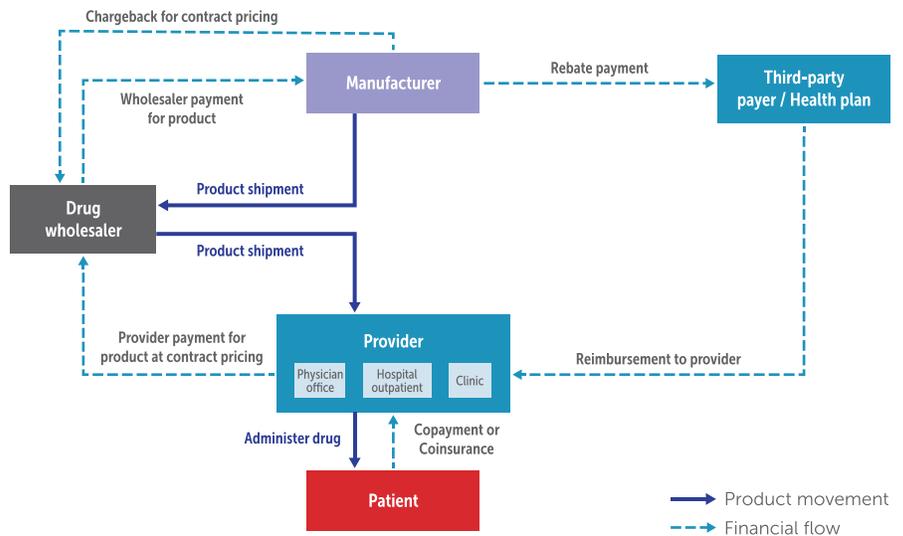


Figure 26. Flow of buy-and-bill distribution
Adapted from: Fein, Adam. J., The 2016–17 Economic Report on Pharmaceutical Wholesalers and Specialty Distributors, Drug Channels Institute, September 2016, Exhibit 28.

CURRENT STATE

- Today only about 30% of PBM respondents^x have fully implemented mandated use of specialty pharmacy ,and/or direct contracting to eliminate buy-and-bill across Commercial lives whereas 80% of IDNs^y have done so.
- 42% of large, mid-sized and small health plans^z have specialty pharmacy use and/or direct contracting implemented for 70%+ of Commercial lives.

FUTURE EXPECTATION

- Research shows an upwards trend in the mandated use of specialty pharmacy from payers. More than 75% of payers, including MCOs, IDNs and PBMs are likely to expand use of specialty pharmacy within the next three years.
- On the medical benefit side, the key trend being seen is an overall push away from the traditional buy-and-bill practices towards alternative distribution strategies that allow payers to have more control over drug use such as payers taking over distribution themselves.
- Across our survey respondents, about two-thirds have not increased physician reimbursement for lower cost options among specialty buy-and-bill products.

DISRUPTORS ON OUR RADAR

- High-cost, curative therapies bring significant challenges to the traditional buy-and-bill reimbursement model. As more one-time treatments like gene therapies enter the market, novel distribution alternatives are emerging.
- The 2020 initiative “Embarc Benefit Protection” establishes Cigna as an in-network gene therapy provider. Employers and plan sponsors will pay a \$12 per-member monthly fee for access to Luxturna and Zolgensma with a zero OOP. Eventually, Cigna plans to include more gene therapies like CAR-Ts, into the program.
- Through previous vertical integration and expansion, Cigna owns a specialty pharmacy network (Accredo), specialty pharmacy distributors (CursaScriptSD, ESI), a medical benefits management company (eviCore) and a PBM (ESI). Cigna can use this armamentarium to be an in-network gene therapy provider. The Embarc program increases Cigna’s position as it will serve as payer and distributor, the first time we have seen this level in a high-cost area.^{46,47}



Payers that participate with us will be getting the best price. They will be getting uniform utilization management.
STEVE MILLER, MD, Chief Clinical Officer, Cigna



**– STEVE MILLER, MD,
 Chief Clinical Officer, Cigna**

DISRUPTORS ON OUR RADAR

Amazon: PillPack

- Amazon’s acquisition of PillPack, the online pharmacy, is an enormous advance for the retailer within the drug distribution channel. PillPack brings economies of scale to the medication supply chain by coordinating, organizing, packaging and supplying presorted doses of medications directly to millions of patients.
- While still unclear how PillPack will play in the specialty category, PillPack could limit distribution through PBM-owned specialty pharmacies and provide an alternative avenue of distribution that developers and health plans directly contract or integrate with PillPack’s ecommerce model which can decrease the practice of polypharmacy.⁴⁸



*BCBS of Massachusetts has partnered with PillPack to integrate their pharmacy services into BCBS’s website and app concluding that “Members have reported higher satisfaction with PillPack than with other pharmacy options”.*⁴⁹



DEVELOPER TAKEAWAYS

- The shift away from buy-and-bill on the medical benefit side means that health plans are contracting more directly with developers as a means to achieve deeper discounts on products and avoid markups from provider facilities.⁵⁰
- Payers are taking on more distributor roles. The shift to alternative strategies such as direct contracting and clearbagging spurs payers’ more pro-active distribution management.⁵¹
- Consider direct purchasing such as when Harvard Pilgrim contracted directly to receive Luxturna from Spark Therapeutics rather than hospitals purchasing the product. Harvard Pilgrim supplies Luxturna to its contracted treatment centers, but it can avoid any additional markups

hospitals would have added to Luxturna.⁵²

- In such instances, payers can verify coverage before a drug is shipped/dispensed to patients, allowing for more management of utilization. Such a proactive approach allows payers to have similar influence in managing the medical benefit as they do pharmacy benefit. However, hospital purchasers (pharmacy directors) in Certara research have voiced their frustration with mandated buys from specialty pharmacies, leading many to open up their own specialty pharmacy, or in some instances push back to request buy-and-bill.
- As utilization moves away from buy and bill, patients may experience greater cost sharing as the product

is now paid out of their pharmacy benefit, providers may experience benefits related to inventory management and challenges related to reductions in revenue and additional access controls. Manufacturers may experience additional controls on utilization as authorization becomes even more proactive.

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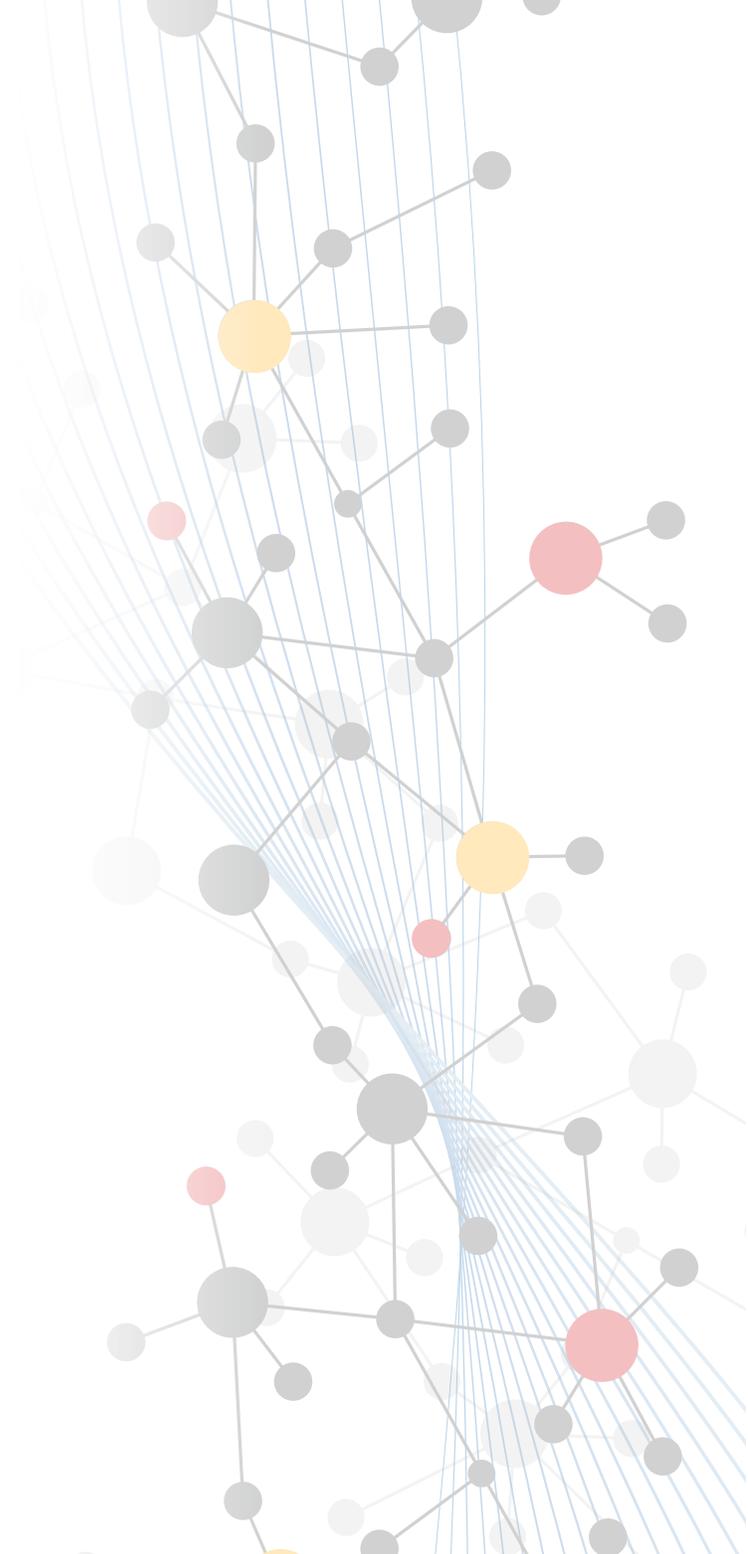
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About Certara

At Certara, we accelerate medicines to patients, partnering with life science innovators. Together with our partners, we use biosimulation and technology-enabled services to transform drug discovery and development.

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