Q4, December 2022

Market Access

Quarterly Advisor

IQVIA

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Quarterly overview

Hello everyone, and welcome to IQVIA's fourth quarter edition of the 2022 Market Access Quarterly Advisor.

Kicking off this issue, we will dive right into one of the hottest topics in the pharmaceutical industry today: the Inflation Reduction Act (IRA) of 2022. We will examine the dynamics of this significant legislation like a chessboard, and lay out the importance of contemplating the board, the pieces, and the players. As in chess, planning out both the short and long games will be key, and understanding the impact of each move, both large and small, as well as the points of risk, will be essential to being prepared for the inexorable change resulting from this legislation. As we move forward with subsequent editions of the Quarterly Advisor, we will provide more updates on the legislation; however, if you have questions in the meantime, we are here to help.

Also in this issue, we will examine the impact of pharmacy discount card utilization—where the cards are used the most, how they affect patient affordability and access, and what impact their use has on payer controls.

Next, we will continue our exploration of gross-to-net by introducing a three-episode podcast series that covers a broad range of topics, from a landscape overview to the use of sophisticated data and analytics for optimizing gross-to-net management.

We round out this edition with an article that takes a critical look at the increased use of external control arms ("ECAs") in Health Technology Assessment (HTA) submissions as a means of helping to satisfy requirements by HTA agencies and payers. The article questions the trend, asking how effective are ECAs, and how can they be designed to help optimize the success of an HTA submission?

While we are only able to scratch the surface of these subjects in this Quarterly Advisor, we have embedded links to additional publications and podcasts for you to explore these topics in greater detail. As always, please reach out to us if you have any questions or specific areas of focus you would like to discuss further. IQVIA is here to help!

Luke Greenwalt
VP, Market Access
Center of Excellence

See the whole board

THE INFLATION REDUCTION ACT OF 2022, AND THE COMPLEX CHESS GAME NOW IN PLAY FOR PHARMACEUTICAL MANUFACTURERS

By: Mason Tenaglia, VP, U.S. Thought Leadership, IQVIA
Luke Greenwalt, VP, Head U.S. Market Access Center of Excellence, IQVIA

Editor's note
At IQVIA, we have rallied a team of industry experts from across our organization — from policy and market access to brand strategy and financial planning — to establish the contours of the conversation and elucidate both short-term impact and long-term implications. As we learn more, and see more, our insights and analysis will evolve in kind.

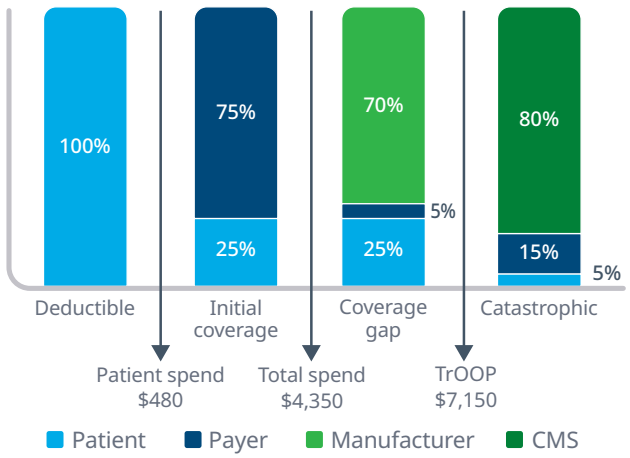
Changes to Medicare are complex and will play out over the next decade: Are you prepared?

The Inflation Reduction Act of 2022 is poised to be a watershed event for the U.S. healthcare system. The ripple effects of provisions designed to transform drug price negotiations, funding sources, and patient burden will be both swift and extensive. Inaction or avoidance will not be rewarded; organizations across the ecosystem will need to quickly separate theory from reality, and strategically prepare for significant change.

THE PIECES AND PLAYERS

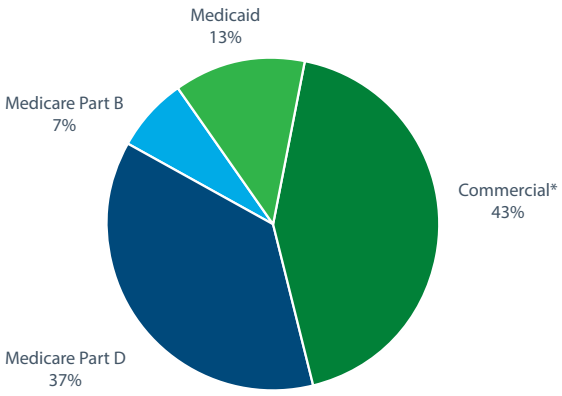
The dynamics at play in the U.S. healthcare system are not for the faint of heart. The relationships, influencers, and value exchange across an expanding set of stakeholders — each with their own priorities and incentives — creates nothing short of a multi-dimensional

Figure 2: Phases of Medicare liability, by stakeholder



Source: U.S. Market Access Strategy Consulting analysis, IQVIA

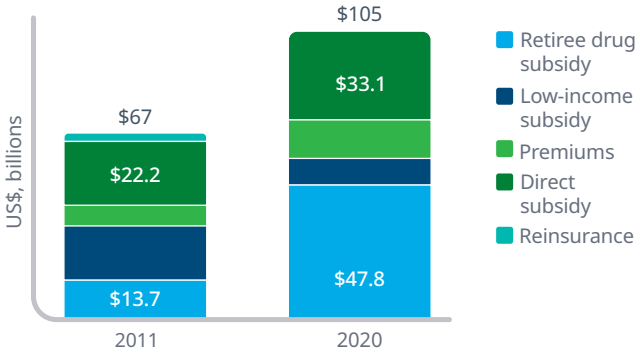
Figure 1: U.S. drug spend, 2020, % of total



*Commercial calculated in 2020 from NSP total drug sales by subtracting CMS-reported total spend in Medicare and Medicaid

Source: National Sales Perspective, IQVIA. Publicly available information, CMS: CMS Drug Spending Main | CMS

Figure 3: Aggregate CMS Part D reimbursement, 2011 v. 2020



Source: 2016-2021 Annual Report of the Boards of Trustees of the Federal Hospital Insurance and Federal Supplementary Medical Insurance Trust Funds, Table IV.B10, Kaiser Family Foundation, U.S. Market Access Strategy Consulting analysis, IQVIA

chessboard. A playing field where intense competition, oft-changing rules, and generation-level consequences on public health and system innovation is just the beginning. The sheer size and scope of the chessboard alone is remarkable; spending on medicines in the U.S. hit $589B in 2021.[1] But the intrigue is in the details. Most of this spend is subject to a complex juggernaut of negotiated discounts and rebates between the Centers for Medicare & Medicaid Services (CMS), payers, providers, and manufacturers. And, significantly, 40% happens to go through the Medicare program (Figure 1). Here, even small moves have outsized impact, and everyone is invested in ensuring a smooth and sustainable program that benefits patients. The bad news is that it's getting harder. And more expensive. For everyone. Specialty medicines, which routinely have a high list price, and which are disproportionately consumed by Medicare patients, now account for 55% of total spending, up 28% from 2011.[2] This will be the match to watch, for reasons that are about to become clear.

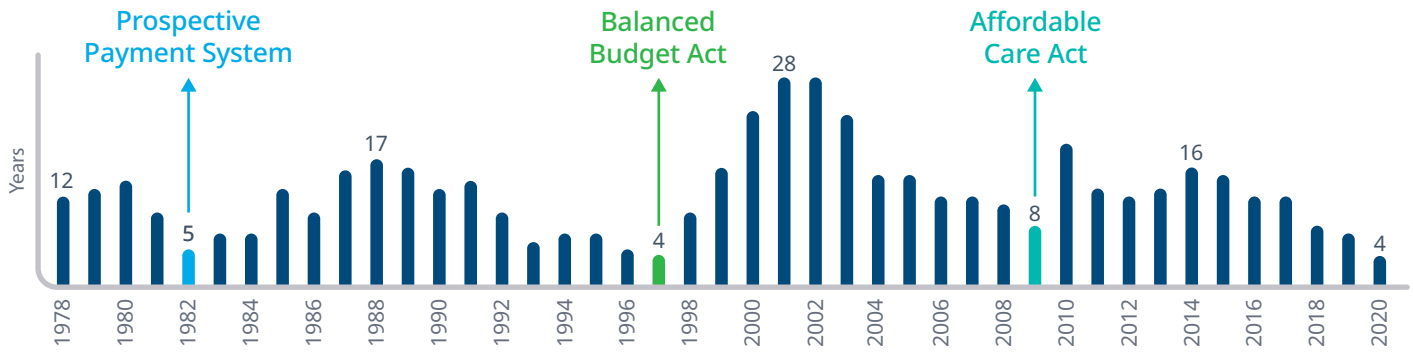
MEDICARE: A QUEEN AT RISK

Because of its stature, both financially and politically, CMS is a powerful player in the American healthcare system. As of May 2022, 58.5 million people in the United States are covered by Medicare[3], the significant majority of whom are covered by Medicare Part B and D. Between the two programs, America's most vulnerable populations — elderly, disabled, and those struggling with long-term illness — have access to necessary medicines and care. However, Medicare's importance is only matched by its vulnerability; it is the queen under constant peril on our chessboard.

This vulnerability has historically stemmed from two primary pressure points — catastrophic reinsurance and low-income subsidy (LIS) provisions. Catastrophic reinsurance represents coverage that triggers after an individual meets his/her out of pocket (OOP) maximum, having passed through the "donut hole" of coverage, also known as the Coverage Gap (Figure 2). The timing of the trigger matters — the sooner the patient moves through the donut hole, the greater the benefit to the patient (less time to incur costly expenses, greater chance of adherence), but the steeper the burden on CMS. The price of medicines also matters — the more expensive a single prescription is, the faster the patient moves through the phases of coverage. In fact, over the past decade, due in part to biomedical innovation (i.e., specialty drugs), what CMS has paid in catastrophic reinsurance has grown by over 240% — from $13.7B in 2011 to $47.8B in 2020 (Figure 3).

The LIS is a program designed to help Medicare beneficiaries with limited income pay their premiums, deductibles, and coinsurance. In 2021, 13 million Medicare beneficiaries received LIS support.[4] Any growth in LIS spend is notable for two reasons; first, it reflects the increasing and undeniable burden of certain disease areas, particularly chronic illnesses,

Figure 4: Reported years of Medicare solvency



Source: 2016-2021 Annual Report of the Boards of Trustees of the Federal Hospital Insurance and Federal Supplementary Medical Insurance Trust Funds, Table IV.B10; Kaiser Family Foundation; US Market Access Strategy Consulting, IQVIA

in historically under-served populations with both low access and low adherence. Second, if the baseline population definition were to expand (spoiler alert), more patients who often need the most help would benefit, but the pressure on the system would experience a multiplier effect (i.e., an increasingly expensive program would get bigger). The result of this, and of course many other factors, is a program that suffers through an ongoing ebb and flow of solvency, reaching a nadir approximately every decade that usually triggers watershed moments for the industry in the form of policy reform (Figure 4). But while the financial strain on Medicare threatens the program, it is the underlying human impact — the threatened ability to cover and care for a growing population — that creates the burning platform for change, and progress. Which brings us to today.

Click here to read more.

Pharmacy discount card utilization and impact

By: Nicholas Adolph, Associate Principal, U.S. Market Access Strategy Consulting, IQVIA
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Anjali Kokra, Associate, U.S. Market Access Strategy Consulting, IQVIA

Between 2017 and 2021, the proportion of prescriptions adjudicated with a discount card nearly doubled. By circumventing traditional insurance, discount cards allow patients additional flexibility in terms of how and where they can fill prescriptions. However, this benefit is not without costs. While discount cards can provide savings to patients, they are not a complete substitute for insurance. The average patient out-of-pocket cost through a discount card is usually higher than non-discount card out-of-pocket costs for patients with insurance; although, insured patients using pharmacy discount cards sometimes realize substantial savings compared to using their health insurance benefit. The discount card model continues to evolve, giving patients more options and transparency. More organizations, including Pharmacy Benefit Managers (PBMs), are exploring discount card options for their books of business. In this article, IQVIA leverages pharmacy claims data to investigate discount card utilization, patient affordability, and payer access challenges in order to provide a holistic picture around why patients use discount card programs and how they are impacted.

Overview

PHARMACY CARD DISCOUNT UTILIZATION

- Pharmacy discount cards accounted for 5.4% of all prescription adjudications in 2021, up from 3.3% in 2017.
- Discount cards are especially prevalent in generic medicines, accounting for 6% of claims vs. 2.9% in branded medicines.
- Large volume therapeutic areas with many generic options lead in terms of discount card volume despite lower utilization rates, such as 5.7% in the mental health area of anxiety and 4.7% in hypertension.

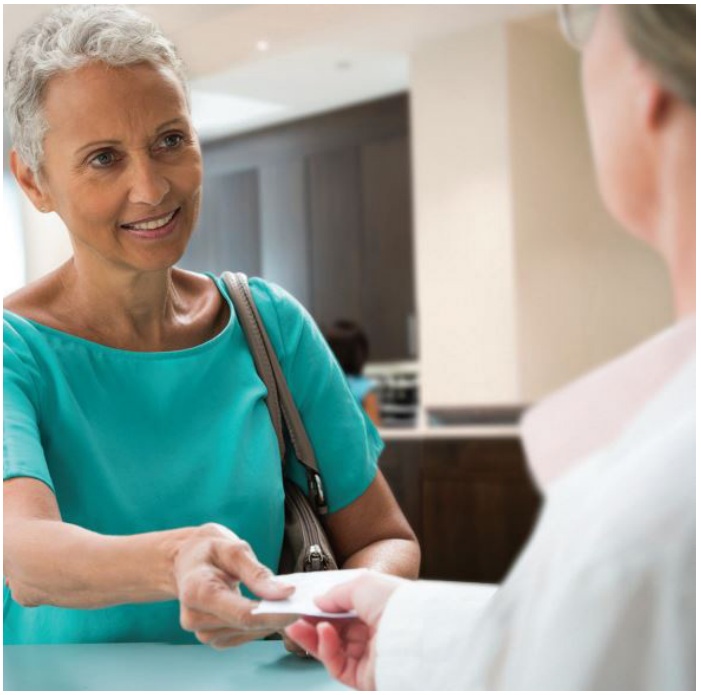
DISCOUNT CARDS AND PATIENT AFFORDABILITY

- While the proportion of pharmacy claims that are adjudicated with a discount card is low overall, nearly one in five patients use at least one discount card in a year.
- Other than cash-filling patients, those with commercial insurance and observed deductibles use discount cards most (24% of patients) – followed closely by standard eligible patients in Medicare Part D.

- Still, patient out-of-pocket costs are generally lower among non-discount card-using patients when they fill prescriptions through their benefit.
- The largest difference in patient out-of-pocket costs, and therefore greatest savings, are observed between cash and pharmacy discount card claims.

PAYER CONTROLS AND ACCESS HURDLES

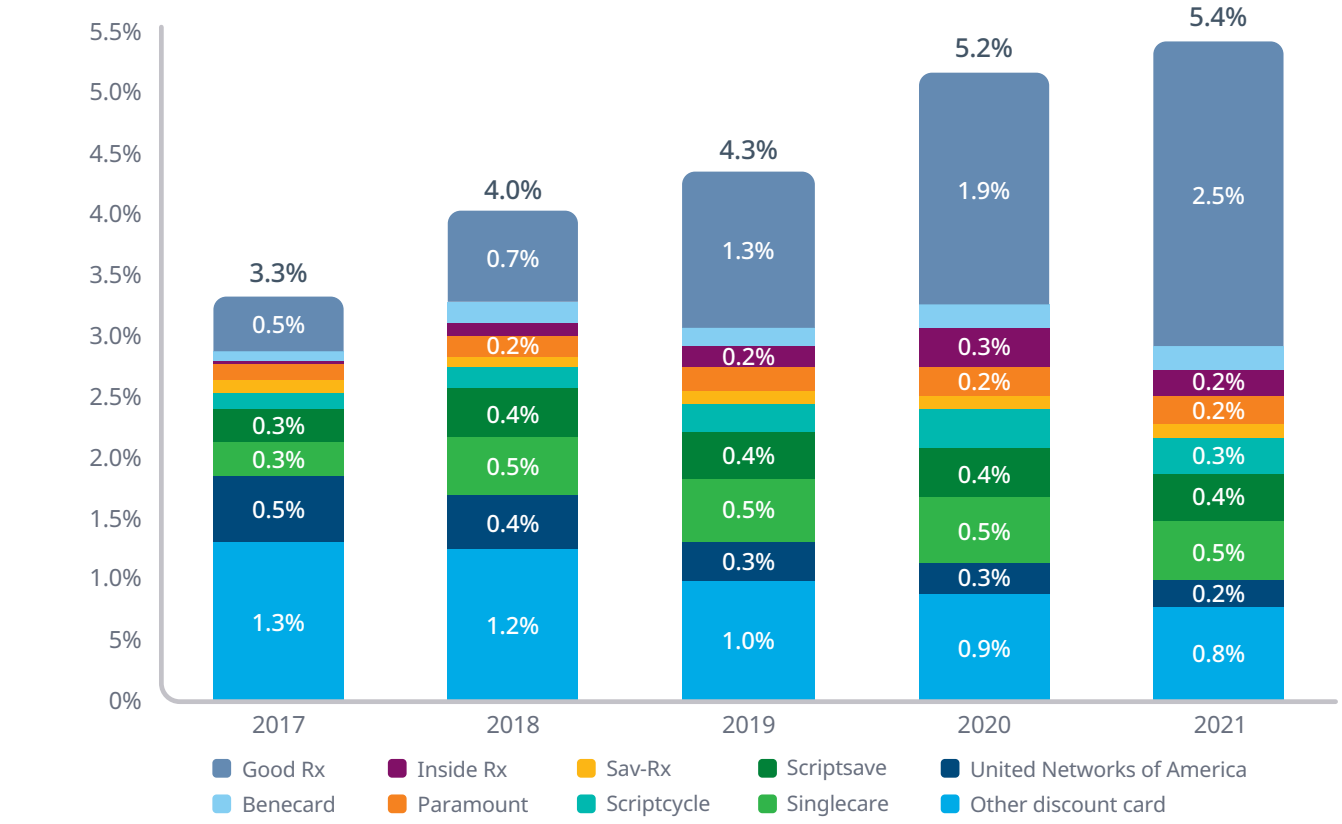
- More than half of first-time discount cards are utilized on the patient's first attempt.
- A quarter of first-time discount cards are preceded by a rejection; pre-discount rejections are highest in Medicaid (more than 50%) where out-of-pocket costs might be low, but payer restrictions are still an access barrier.
- Among patients who first abandon a prescription before filling with a pharmacy discount card, savings are mixed; approximately half see a reduction in out-of-pocket costs.



Pharmacy discount card utilization

Discount cards have grown in prevalence over time, reaching 5.4% of all pharmacy adjudications in 2021.

Pharmacy discount card utilization trend by top vendors, all payer channels



Source: U.S. Market Access Strategy Consulting analysis, IQVIA

- In the last five years, discount card utilization has increased by nearly 60%.
- Growth was driven primarily by GoodRx, which grew from 0.5% of all adjudications to 2.5% in the same time period.
- GoodRx is the largest vendor by volume and accounts for 46% of all discount card claims in 2021, up from 14% in 2017.
- Though largely concentrated, the discount card landscape is populated by dozens of vendors, including next-largest Singlecare and Scriptsave (<1% combined).

Click here to read more.

External control arms for HTA submissions: Great idea, but you've got to get it right

By: Leora Schiff, Principal, Value & Access Strategy Consulting, IQVIA

As biopharma companies have increasingly focused on developing drugs for rare and ultra-rare indications, they have often encountered challenges in generating compelling evidence that will satisfy HTA agencies and payers. This is particularly the case for single arm trials (SATs). Payers strongly prefer randomized controlled trials since they provide a comparator against which an investigational drug can be measured with statistical rigor. When faced with SATs, unless the effect size is large, payers may view the clinical meaningfulness of the investigational drug's efficacy as uncertain, particularly if the number of subjects in the pivotal study is extremely small.

As a means of addressing payer concerns, some companies have turned to real world evidence approaches to create external control arms (ECAs). These approaches use data from matched patient populations from sources such as registries, electronic health records, or other clinical studies. Study designs may be prospective and/or retrospective and may compare the investigative drug to standard of care drugs or placebo. Over time, statistical approaches have evolved to provide more rigorous comparisons using adjustment methodologies to improve the appropriateness of the external data for comparisons.

The use of ECAs has been growing. A recent study using IQVIA's HTA Accelerator database evaluated the use of ECAs in regulatory and HTA submissions for drugs and cellular therapies treating indications in hemato-oncology, a field with many rare and ultra-rare patient populations. Between January 2018 and April 2022, 51 EMA approvals were identified. Of these, 29% (15 indications across 11 drugs) relied exclusively on SAT-data.

Nine of the drugs were submitted to one or more of the following HTA agencies: NICE (England), G-BA (Germany), HAS (France), TLV (Sweden), and ZIN (the Netherlands). The total number of HTA submissions was 48 across 12 EMA-approved indications. Of the 48 HTA submissions presenting SAT data as the main type of evidence, 42/48 (88%) provided data from external control arms of which 35/42 (83%) were derived from real world data.

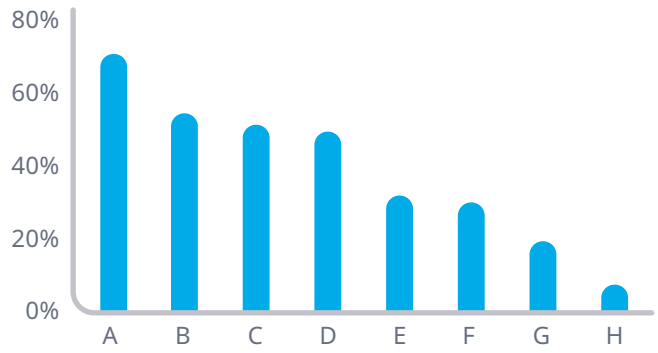
In looking at the HTA evaluations of the ECA data, the results were mixed. In only 8 out of the 42 submissions (19%) were the ECAs considered to be acceptable and were taken into consideration in the HTA decisions. Examples of submissions with acceptable ECAs that factored into positive HTA decisions include a 2019 NICE recommendation for a B-cell acute lymphoblastic leukemia indication expansion for

Blincyto (blinatumomab) for patients following their first recovery, and favorable 2021 HAS decisions to maintain Kymriah and Yescarta on the list of drugs approved for hospital use.

Of the remainder, 24/42 (57%) were deemed inappropriate/unusable for informing the HTA determination, and for 10/42 (24%) they were either considered uncertain or it was unclear whether they had an impact on the HTA decisions.

Why were only one fifth of the HTA submissions using ECAs considered appropriate? Out of the 42 submissions with ECAs, nearly 70% were faulted for using data from heterogeneous populations. About half of the ECAs were found to have non-justified or incorrect data adjustment, missing data and heterogeneity in study execution or operationalization of outcomes, while about 30% had limited or different follow-up and limited sample size.

HTA critiques of ECAs



A = heterogeneous populations; **B** = non-justified or incorrectly defined prognostic factors for adjustment; **C** = missing data to estimate comparability; **D** = heterogeneity in study execution or operationalization of outcomes; **E** = limited or different follow-up; **F** = limited sample size; **G** = uncertain clinical benefit; **H** = different doses

Given that close to 90% of the HTA submissions based on SATs included ECAs, companies clearly recognized the potential value of including ECAs in strengthening their evidence package to satisfy payers. However, as with all evidence submissions, the devil is in the details. For ECAs to succeed in providing an appropriate comparator for an investigative drug from an SAT, it is critical to conduct such a comparison with methodological rigor. Otherwise, it is a waste of time, money, and opportunity.

GETTING ECAS RIGHT – FOUR KEYS TO SUCCESS

In a recent IQVIA blog on ECA strategy, Project Management Director Dony Patel described a five-step strategic process in designing an external comparator study which includes selecting the right external comparator group and using the most appropriate methodology. Based on the evaluated HTA critiques, we have identified four keys to successfully implementing this process:

- Make sure the comparator population is not overly heterogeneous and is a good match for the patients in the investigative arm of the study
- Apply appropriate adjustments to the data based on sound methodology
- Prevent/minimize data gaps
- Be consistent in study execution

IQVIA has a dedicated team of experts with significant experience working with manufacturers to define the strategy and methodology for external comparators supporting submissions to regulators and HTA bodies.

ABOUT IQVIA'S HTA ACCELERATOR

IQVIA's HTA Accelerator tool contains over 34,000 HTA publications covering 41 countries and 100 HTA bodies published since 2011. Companies can review indication-specific, clinical evidence and comparators, economic analysis, HTA body critique and recommendations. It also features information about the use of RWE, the types of RWE used, the areas supported and the acceptance by HTA bodies. This enables a data-driven approach to your market access strategy and study design.

Sources:

Dijkhuis S., Patel D., Foster S., van Engen A., van Gils C. The use and acceptability of external comparator studies to support hemato-oncology single-arm trial submissions to health technology assessment bodies. Poster presented at: ISPOR Europe 2022; 2022 Nov 6-9; Vienna, Austria

Securing market access with single-arm trial data; What is the optimal external comparator strategy? Dony Patel, Director, IQVIA, Blog, Jun 10, 2021

Gross-to-Net—How to eat an elephant: An IQVIA podcast series

The elephant-sized topic of gross-to-net is broken into three digestible podcasts. Listen in as our team of experts; Luke Greenwalt, Cam Hall, Diane Weisbrod, Shiraz Hasan, and Heather Kenny break down the complexity of gross-to-net, talk about how it may be negatively affecting your business, and share insights into how you can improve the accuracy of your gross-to-net calculations.

Click here to access all episodes.

EPISODE 1

In episode one, we share information about the general environment around gross-to-net, the impact it has on your business, and how to help maximize it for organization efficiency and profitability. Plus, insights for collecting and integrating together all the necessary data.

EPISODE 2

During this episode, the team digs into the hot topic of 340B. For many organizations, 340B has a negative impact on their gross-to-net. Tune in and learn about the effect discount stacking has on product pricing and service fees that are paid to specialty pharmacies and wholesalers. All effect your gross-to-net profit and calculations.

EPISODE 3

Yes, gross-to-net is big! During this wrap-up session, we introduce rebate exclusions, anti-kickback statutes, and financial SOX compliance controls into the conversation. The team sheds light on data integration as critical in pulling all the data together and pushing the analytics to the right people across your organization. Plus a few thoughts on the future of gross-to-net and how leveraging newer technology will help to build an even clearer picture.

IQVIA discusses new GTN insights at Medicaid Drug Rebate Conference 2022

By: Diane Weisbrod, General Manager, Market Access Contract Performance Solutions, IQVIA

It was a pleasure seeing some our clients in person at the October 2022 MDRP Conference in Chicago. The agenda featured presentations on several key industry challenges around contract and revenue management, including a half-day update from a team of IQVIA subject matter experts regarding what we are seeing in the industry related to gross-to-net ("GTN"). Below is a summary of the IQVIA discussion.

Managing GTN in the new margin era

From a macro perspective, healthcare spend in the United States continues to increase, and in 2020 it accounted for almost 20% of GDP. Of the $4.1 billion in total national health expenditures, the total prescription drug costs accounted for less than 10% and are increasing at a much slower rate than total health expenses.[1] Although retail prescription drug costs make up a small amount of total U.S. healthcare spend, the government is presently very focused on this area.

When we analyze pharmaceutical costs, manufacturers' operating profit growth is being dwarfed by cost growth, seen particularly through rebates. Drug manufacturers continue to be squeezed on both the demand and margin side, but patients are not receiving the benefits. This new margin era is one in which, for the first-time, average net prices dipped below 50% of list prices for the top branded drug manufacturers, and over $200 billion dollars was paid in rebates and discounts in 2021 for brand name drugs.[2] To put that in perspective, the government spent $310 billion on *all* drugs in 2020 for Medicare Part D, Medicare Part B, and Medicaid Patients.[3]

The focus of our session was primarily on how manufacturers can start thinking about transformation in the new margin era. It is everyone's job to help protect margins so continued innovation investment is available to help patients. Some of the questions we posed for consideration included:

- How do you drive the right GTN insights to guide better commercial decisions, and will your strategy enable you to effectively measure and manage through all the changes that are coming?
- How do you obtain (or secure) more payment transparency, and how do you gain insights into the stacking of discounts?
- What GTN processes do you digitize, and how will you fund innovation?

We are surrounded by problems, but it takes proactive approaches to help solve them. One of the first steps is to assess your goals and the problems you want to solve. There are many approaches to assessments, but evaluating these complex processes requires structure to generate meaningful and actionable

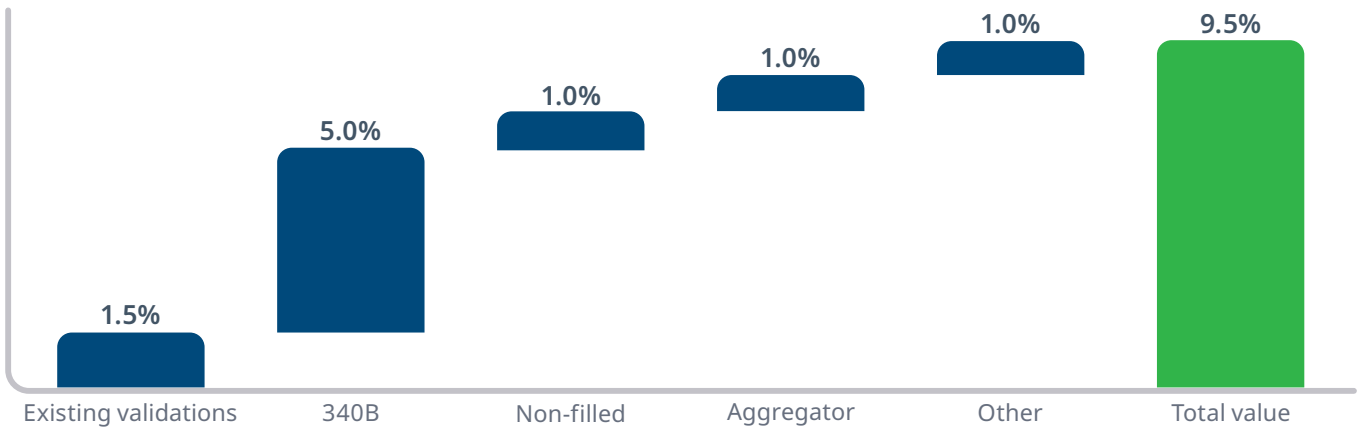
results. Gross-to-net is a massive topic with lots of challenges and it can be daunting, but by breaking it down into smaller hurdles or phases, you can extract insights and develop recommendations. Some of the key pain points the audience shared were: misalignment and lack of coordination and operations; data management and quality issues; disconnected and incomplete information; lack of timely, high-value insights; manual and cumbersome modeling processes; and, financial risk.

Organizational stakeholders may have different needs, but overall, they require support to increase efficiency, maximize time, and reduce risk by enabling them to make faster and evidence-based decisions and to better understand a product's financial health. Manufacturers are focused on several areas to help transform the way they address these and other challenges.

- **Digitized processes and resource optimization:** Organize and optimize processes, people, and assets through innovative technologies and services that provide client value, drive continuous growth, and improve financial outcomes.
- **Insights and analytics:** Enable connected intelligence across organizational personas through data acquisition, linking, and enrichment processes that provide advanced insights and identify gross-to-net value profiles across customers, products, programs, and geographies.
- **Process and communication:** Standardize processes to promote new cross-functional culture with reduced hand-offs, improved documentation and audit controls, and documented approval workflows.
- **Revenue and margin preservation:** Provide solutions that address revenue leakage, and help financial stakeholders make informed decisions that minimize financial exposure, helping to improve a product portfolio's financial health.

We have found that the easiest way to fund innovation in GTN is to find the funds by identifying and investing in new areas to shore up revenue leakage. One thing is certain — the industry lacks data transparency, which can stymie solution optimization. But IQVIA has been investing heavily in data and analytics, and has identified new areas to which you can hold your business partners more accountable in this new margin era. Some of these include identifying covered entity and contract pharmacy 340B claims; submitting rebates when the patient never received the drug; providing rebates when cash cards were used; and, being invoiced for medical and pharmacy claims. The diagram below illustrates the value that investing in these capabilities can add to a manufacturer's organization to help address GTN complexities and revenue leakage over the next decade.

Illustrative value

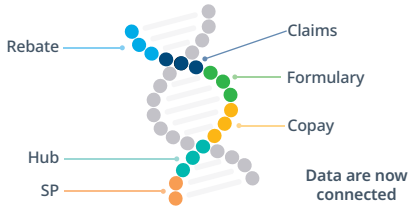


IQVIA has solutions to address your GTN needs:

Data as a service

Financial genome

Connecting financial data for clients

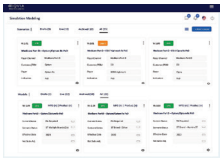


The Financial Genome Project

Software as a service

Gross-to-net workflow solutions tool kit

Providing next gen solutions to the finance, accounting, and managed care operation stakeholders



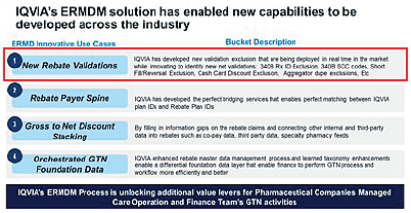
Data connectivity and enrichment hub

Forecasting and planning

Business process outsourcing

Payment transparency solutions

Providing and creating new opportunities for revenue leakage management



Assessment approach to generating greater efficiencies:

Stage 1: Current state process mapping — 1

Current state process mapping, gap analysis, quick win identification

1. **Mapping**–Current state processes, data, tools, and methodologies across contract analytics (pre-deal, scenario modeling, post-deal tracking)
2. **Roadmap development**–Identify/ prioritize the short-, mid-, and long-term solution needs to enhance capabilities

Stage 2: Quick wins and intermediary solutions — 2

Implementation of process/ data changes, integrate tools and models

1. **Integration**–Integration and development of contract pre-deal and scenario modeling tools to improve deal/no-deal analytics
2. **Enhancement**–Update data models across users as well as methodologies for comprehensive deal assessment

Stage 3: Long-term platform solution development — 3

Integrated platform development–fully integrated and component level (agile)

1. **Contract modeling/management (+)-** Platform capability development encompassing contract modeling, measurement, and additional GTN assessment capabilities
2. **Sustainable, cross-functional, capability development**

About the IQVIA U.S. Market Access Center of Excellence

Empowered by the IQVIA CORE, the IQVIA Market Access Center of Excellence (CoE) is a division built for purpose – delivering the speed to market insights and optimal gross-to-net value our clients seek from their market access investments. Our CoE is comprised of more than 1,100 professionals with expertise in all areas of market access, from strategy and analytics to operations. Our CoE is built by market access specialists for market specialists.

The IQVIA Market Access Center of Excellence engages in helping clients understand, plan, and navigate today's and tomorrow's challenges with our innovative and industry-leading solutions. We offer copay card design, optimization, and administration, full patient hub services, strategy consulting and analytics, gross-to-net strategy and operations, contract strategy and administration, revenue management implementation, and many other demand and margin tools. Our solutions are designed to ensure that our clients are operating at optimal efficiency and executing programs that maximize their investments and the value of their brand throughout the full lifecycle of their products. Quite simply – we will take your business further than you are able to do alone.

To learn more, "https://secure.constellation.iqvia.com/US-MarketAccess" contact us at the U.S. Market Access Center of Excellence.

Sources:

1. National Health Expenditures by type of service and source of funds, CY 1960 - 2020 Data from CMS.gov (https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/NationalHealthExpendData/NationalHealthAccountsHistorical) Retail prescription drug spending only increased 3.0% between 2019 to 2020 while total expenses increased 9.7%
2. Adam J Fein, Ph.D., Gross-to-Net Bubble update: 2021 Pricing Realities at 10 top drugmakers. May 10, 2022. and Warped Incentives Update: The Gross-to-Net Bubble Exceeded $200 Billion in 2021. March 22, 2022. https://www.drugchannels.net/
3. CMS Drug Spending, CMS.gov https://www.cms.gov/research-statistics-data-and-systems/statistics-trends-and-reports/information-on-prescription-drugs

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