EXECUTIVE INSIGHTS

Refining Gross-to-Net Expectations for Improved Strategic Planning

In today's U.S. pricing and access environment, biopharma manufacturers must carefully consider gross-to-net (GTN) dynamics early as they forecast and prepare commercial strategies, especially for a first launch. Representing the difference between gross price (typically, wholesale acquisition cost, or WAC) and manufacturers' realized net price, GTN is highly multifactorial, varies from product to product and can be a key determinant of commercial success. While some discounts, rebates and fees are mandatory, others are negotiated to drive optimal access for the product.

Across the industry, GTN continues to expand and evolve. While list prices continue to grow, net prices have been declining, generating a schism between the two.[1] The total estimated value of GTN deductions for brand-name drugs grew to between $220 billion and $260 billion in 2022, an approximate 33% increase from 2018.[2]

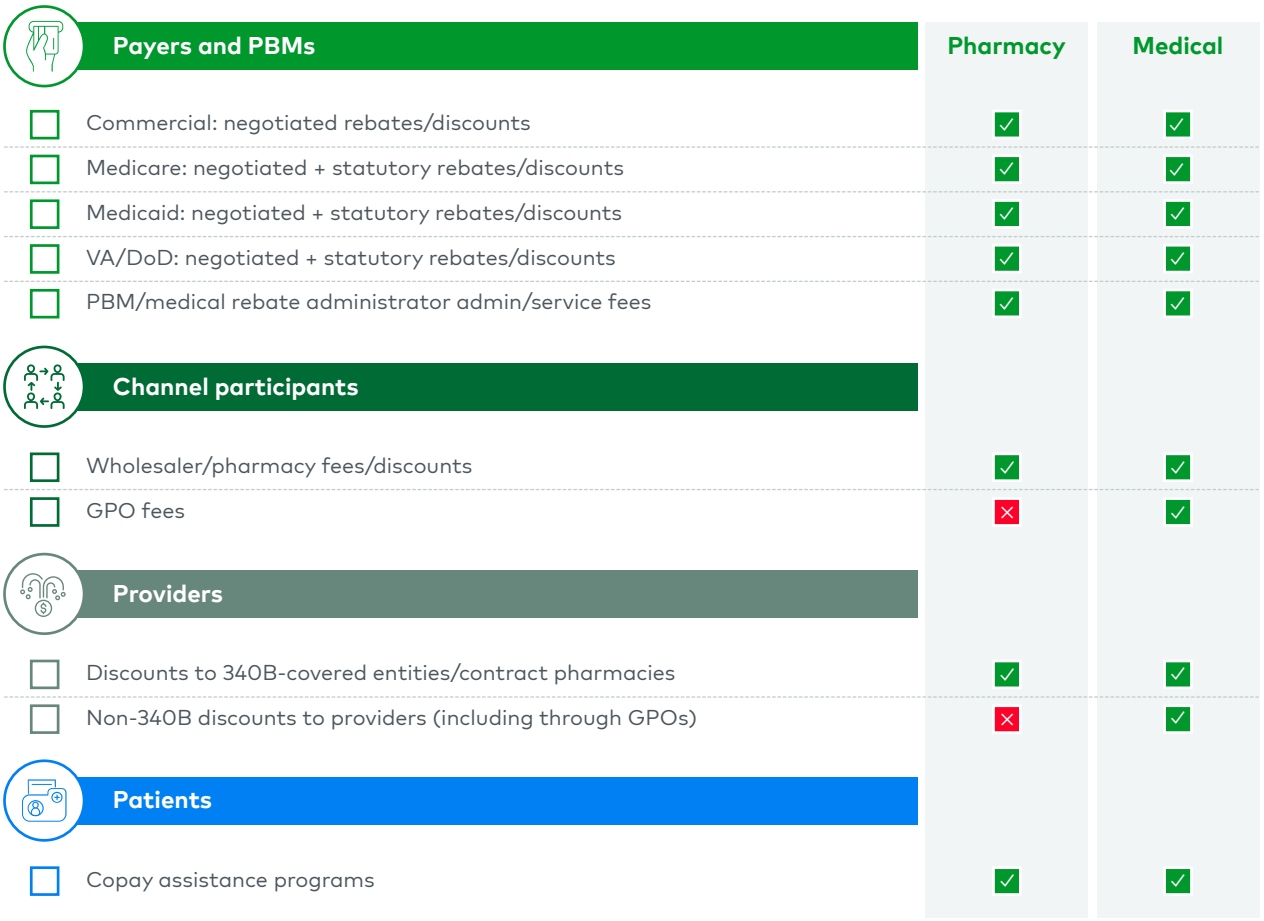
In this edition of L.E.K. Consulting's *Executive Insights*, we discuss the components and drivers of GTN, highlighting trends and implications for biopharmas.

GTN reflects a complex web of discounts, rebates and fees required to provide patients access to pharmaceuticals

There are several components of the gross-to-net calculation. Some of these require careful trade-offs and strategic decision-making, while others are unavoidable but need to be carefully considered. The majority of components are shared across medical and pharmacy benefit drugs (see Figure 1).

Figure 1

Components of GTN by stakeholder and benefit type



Not included in GTN: Cost of goods sold, enterprisewide costs (e.g., real estate, debt), royalty payments on assets/platforms, contributions to patient advocacy groups (including those with grant programs for treatment)
Note: GTN=gross-to-net; PBM=pharmacy benefit managers; VA=veterans affairs; DoD=Department of Defense; GPOs=group purchasing organizations
Source: L.E.K. research and analysis

Rebates to payers can often represent the single greatest portion of a drug's GTN discount and include both negotiated discounts (for all payers) and statutory discounts (for government payers).

Negotiated rebates are offered to secure formulary placement, reducing access restrictions and patient cost-sharing. A biopharma's contracting strategy — its posture toward providing rebates to payers to help secure broader access for patients — is one of the most critical components of overall market access strategy.

Statutory rebates have long been a key component of the Medicaid channel; Medicaid plans have access to biopharmas' best rebates offered in other channels. Crucially, they are becoming an increasingly important component of the Medicare channel in light of the Inflation Reduction Act (IRA), which introduced rebates for drug list price increases outpacing

inflation and increased manufacturers' liability for high-cost Part D drugs. Carefully managing rebate liability in these channels can have a large impact on a drug's overall net price.

Manufacturers also provide fees and discounts to various channel participants (e.g., wholesalers, group purchasing organizations). Depending on the distribution strategy, costs may vary and can exceed 10% of WAC.[3]

Among the provider-focused elements of GTN, 340B discounts represent the largest component. The 340B program has expanded significantly over the past decade, representing about $52 billion in 2022 (a 36% increase from 2018),[4] or roughly 20% of the total estimated manufacturer GTN. Exposure to 340B can vary significantly by product. Understanding 340B exposure requires detailed, local market-level analysis. Non-340B discounts may be more significant among more consolidated/integrated providers with greater leverage.

Patient assistance programs (e.g., copay assistance) are often implemented by manufacturers to offset commercial patient cost exposure. This could be a nontrivial expense, which requires thoughtful design considerations.

GTN varies significantly across markets

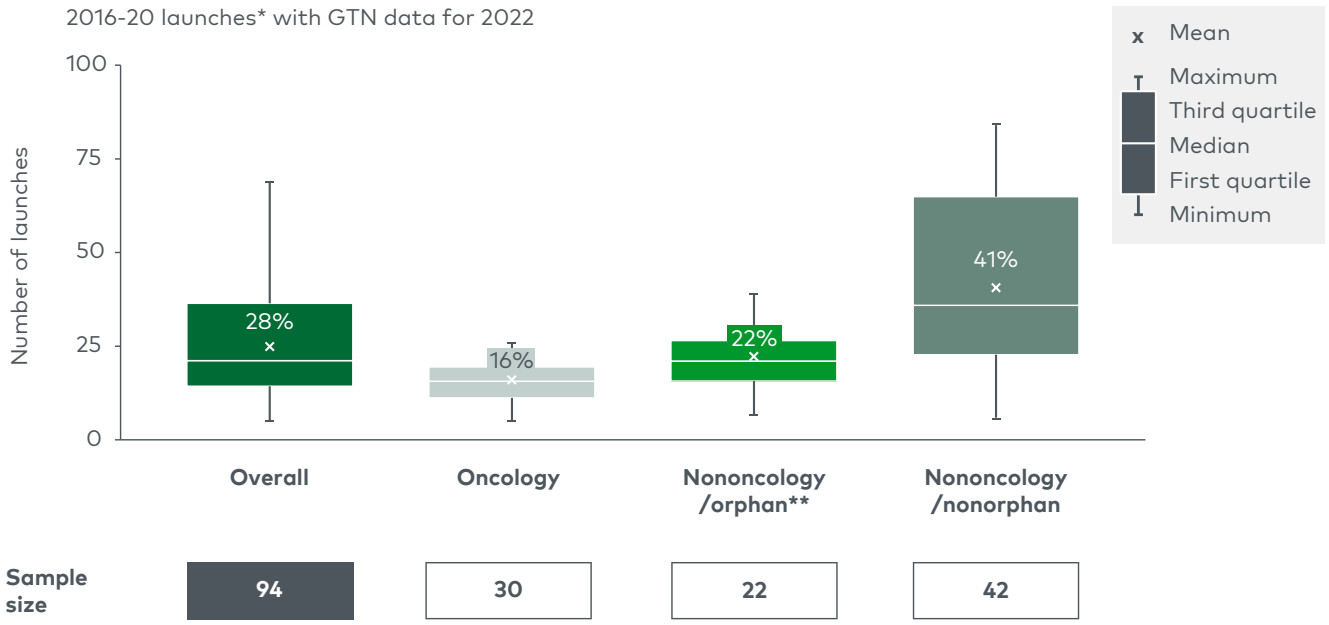
The magnitude of a product's total GTN and the contribution of the individual components are driven by a combination of factors that are either inherent to the product, disease or patient population (e.g., therapeutic area, site of care, supply chain, payer mix) or driven by external factors (e.g., competitors, payers, policymakers).

To understand trends in GTN, we leveraged SSR Health's dataset, focusing on assets mid-launch. We focused on 94 innovative assets the Food and Drug Administration (FDA) approved during 2016-20 with available 2022 GTN data, excluding approximately five likely data artifacts. This represents around 37% of the innovative FDA approvals during that time period.

Across these products, GTN was found to be lower (i.e., greater price retained) for oncology and nononcology/orphan indications than others (see Figure 2). The lower GTN in oncology largely reflects its clinical severity, unmet need and "protected class" status. Precision medicine approaches may also fragment patient populations and reduce head-to-head competition. No significant differences were seen between solid and liquid tumor types. These factors can diminish payers' motivation and leverage to negotiate for discounts. Many orphan diseases are also characterized by high unmet need, low levels of competition and low overall spend. Likewise, GTN for nononcology/orphan disease products is relatively similar to that of oncology.

Figure 2

GTN by therapeutic area group



*CDER NMEs and new therapeutic products and innovative biologic products from CBER, excluding vaccines
**Orphan designation upon first approval
Note: GTN=gross-to-net; CDER=Center for Drug Evaluation and Research; NMEs=new molecular entities; CBER=Center for Biologics Evaluation and Research
Source: L.E.K. research and analysis of SSR Health, Evaluate Pharma, Food & Drug Administration

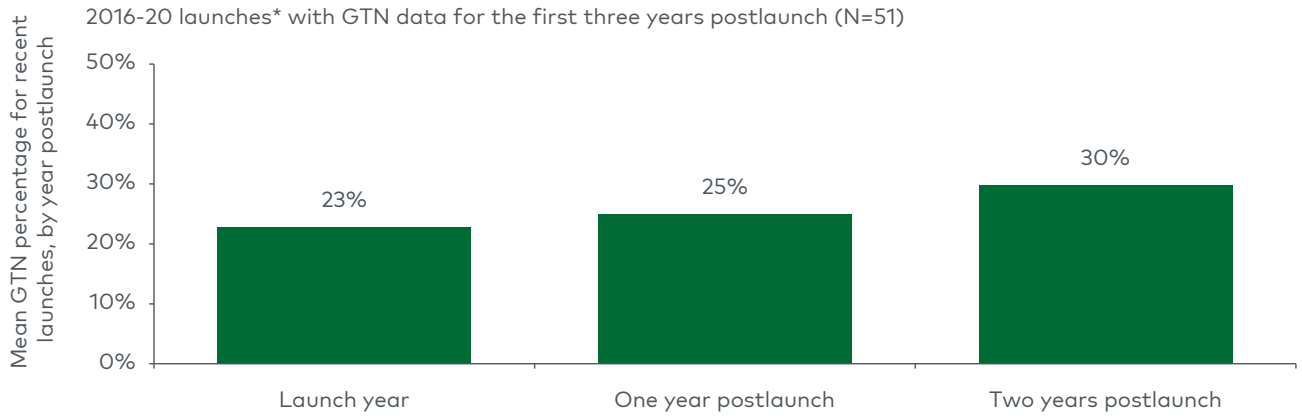
Outside oncology and orphan diseases, GTN trends steeper, with substantially higher variance. Breaking the 2022 data into more specific therapeutic areas (e.g., central nervous system, infectious disease) did not result in any clear GTN trends. This suggests that more-granular factors, specific to individual products and markets, drive GTN. These factors may include the site of care and insurance benefit (i.e., pharmacy vs. medical), payer mix and competitive landscape. Biopharmas will need to understand these dynamics and look for strong analogs to better gauge GTN expectations.

GTN evolves over the product life cycle

As manufacturers' market access and net price strategies are executed over the early years postlaunch, payer and distributor contracts are established across the country, driving GTN to steadily rise. As early demand is tested the first two years, manufacturers may be less aggressive in payer rebate/formulary negotiations. Once demand is established, manufacturers may become more aggressive to ensure volume is pulled through via broad, competitively favorable formulary placement. Looking at the 51 assets with GTN available for the first three years of launch shows this increase (see Figure 3).

Figure 3

GTN across early launch year



*CDER NMEs and new therapeutic products and innovative biologic products from CBER, excluding vaccines
Note: GTN=gross-to-net; CDER=Center for Drug Evaluation and Research; NMEs=new molecular entities; CBER=Center for Biologics Evaluation and Research
Source: L.E.K. research and analysis of SSR Health, Evaluate Pharma, Food & Drug Administration

In the early postlaunch years, investing in patient assistance programs can be effective to maximize uptake by capitalizing on early demand as broad payer coverage is being established. This can mean covering the full cost of the product for patients who are not yet covered, which comes with a notable up-front impact on net price per patient. However, satisfying early customer demand and reducing access barriers can steepen the uptake curve and foster positive sentiment among patients and prescribers. As patients are then converted to traditional coverage (if treated chronically), net price per patient can improve moving forward.

Once payer access and net price are established, it can remain stable until manufacturers choose to pivot in response to insufficient pull-through of demand, new competitive entrants or shifts in payer/public policy.

Biosimilar or generic competition can represent the ultimate threat to a product's GTN as significant net price competition ensues and payers drive use toward lower-cost options. However, in today's GTN environment, those who are already heavily discounting may be somewhat protected due to "rebate walls." On the other hand, products that have maintained modest GTN deductions are most susceptible to market share erosion upon biosimilar entry. A recent report[5] illustrates this dynamic well, clearly showing that oncology, the therapeutic area with the most modest GTN deductions, has been the most susceptible to market share and net price (average sales price) erosion from biosimilars.

New policies may have significant impacts on GTN

Upcoming policy changes, namely IRA, are a looming presence whose impact on GTN will be felt directly and indirectly, in some ways applying additional pressure and in other ways disincentivizing practices that have driven increasing GTN over time. We have been closely following the IRA and its potential impacts throughout the biopharma ecosystem.[6,7,8,9]

Most prominent is the Centers for Medicare & Medicaid Services (CMS) Maximum Fair Price negotiation after nine (small molecule) or 13 (biologic) years, which will affect products with >$200 million in gross Medicare spending.[10] For selected products, net price is likely to decline for the remaining years of patent life, though uncertainty around the magnitude of decline remains, as there is no "floor" for Maximum Fair Price. Life cycle evaluations and revenue expectations will now need to be viewed through the lens of both patent and CMS negotiation runways. The curtailed life cycle of branded drugs, and more so for small molecules, may place a greater emphasis on maintaining optimal margins early.

The Part D benefit redesign under the IRA introduces two key changes with implications for GTN. First, manufacturers will have direct liability in the coverage (10%) and catastrophic phases (20%) in lieu of coverage gap liability (70%). Second, plan sponsors, not CMS, will now face most of the liability in the catastrophic phase (60% vs. 15% pre-IRA).[11] This creates increased incentive for plans to implement utilization management controls for high-cost drugs, which may drive further discounts. Historically, patients who reached the catastrophic phase drove rebates to plan sponsors, while CMS faced the liability; plans' heightened liability in the catastrophic phase per the IRA may disincentivize high-list-price, high-rebate strategies.

The IRA also introduces new penalties in Medicare for list price increases that outpace inflation, disincentivizing postlaunch list price increases, even if those strategies maintain consistent net price. Finally, under the American Rescue Plan, the 100% "Average Manufacturer Price (AMP) cap" on Medicaid rebates has been removed,[12] which also disincentivizes high-list-price, high-rebate strategies that previously would have been triggered by this cap and protected GTN margin.

Outside the IRA, GTN dynamics may be impacted by a number of other market trends, including PBM legislation, 340B growth and hospital consolidation.

Biopharmas will need to consider several key GTN questions when strategically planning

- What is the expected magnitude of GTN for a drug's particular market situation?
- How sensitive are forecasts to GTN dynamics?
- How will GTN evolve over the product's life cycle?
- How will new policies, such as the IRA, impact GTN strategy?

Our Biopharma practice works with clients across a range of strategic issues, including pricing and access optimization, IRA preparation, and developing dynamic GTN forecasting. If you or your organization is interested in discussing the implications of the growing GTN bubble or the implications of IRA/PBM legislation for your future opportunities and optimal strategies to prepare, please reach out to us.

For more information, please contact **lifesciences@lek.com**.

We would like to thank **Adam O'Neil** for his contributions to this piece.

Endnotes

[1]Drugchannels.net, "Tales of the Unsurprised: U.S. Brand-Name Drug Prices Fell for an Unprecedented Sixth Consecutive Year (And Will Fall Further in 2024)." https://www.drugchannels.net/2024/01/tales-of-unsurprised-us-brand-name-drug.html

[2]Drugchannels.net, "Four Trends That Will Pop the $250 Billion Gross-to-Net Bubble—and Transform PBMs, Market Access, and Benefit Design." https://www.drugchannels.net/2023/04/four-trends-that-will-pop-250-billion.html

[3]Commonwealthfund.com, "The Impact of Pharmaceutical Wholesalers on U.S. Drug Spending." https://www.commonwealthfund.org/publications/issue-briefs/2022/jul/impact-pharmaceutical-wholesalers-drug-spending

[4]Drugchannels.net, "EXCLUSIVE: The 340B Program Reached $54 Billion in 2022—Up 22% vs. 2021." https://www.drugchannels.net/2023/09/exclusive-340b-program-reached-54.html

[5]Samsungbioepis.com, "FDA Approval and Launch Status of US Biosimilars." https://www.samsungbioepis.com/upload/attach/SB+Biosimilar+Market+Report+Q3+2023.pdf

[6]LEK.com, "How the Inflation Reduction Act Will Impact the Biopharmaceutical Industry." https://www.lek.com/insights/ei/how-inflation-reduction-act-will-impact-biopharmaceutical-industry

[7]LEK.com, "Initial Drugs Selected for Medicare Price Negotiation: Emerging Perspectives." https://www.lek.com/insights/hea/us/ei/initial-drugs-selected-medicare-price-negotiation-emerging-perspectives

[8]LEK.com, "The Inflation Reduction Act: Implications for Drug Delivery Innovation." https://www.lek.com/insights/hea/us/ei/inflation-reduction-act-implications-drug-delivery-innovation

[9]LEK.com, "Understanding the Inflation Reduction Act Negotiation Prices After the Dust Has Settled." https://www.lek.com/insights/hea/us/ei/understanding-inflation-reduction-act-negotiation-prices-after-dust-has-settled

[10]CMS.gov, "CENTER FOR MEDICARE." https://www.cms.gov/files/document/revised-medicare-drug-price-negotiation-program-guidance-june-2023.pdf

[11]KFF.com, "Changes to Medicare Part D in 2024 and 2025 Under the Inflation Reduction Act and How Enrollees Will Benefit." https://www.kff.org/medicare/issue-brief/changes-to-medicare-part-d-in-2024-and-2025-under-the-inflation-reduction-act-and-how-enrollees-will-benefit/

[12]KFF.com, "Costs and Savings under Federal Policy Approaches to Address Medicaid Prescription Drug Spending." https://www.kff.org/medicaid/issue-brief/costs-and-savings-under-federal-policy-approaches-to-address-medicaid-prescription-drug-spending/

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