



Privacy for the end user

groupH does not collect any personal data and no data from this tool is stored on our servers including product names or any selections in our tool.

Background

Published list prices of drugs at the WAC level ('Gross prices') in the US do not reflect the actual amount paid to the manufacturer after application of discounts, rebates and cash-backs as mandated by and/or negotiated with certain payer types in the US ('Net price'). The relative difference between the two is referred to as the Gross-to-Net (or GtN) discount rate. At present, some manufacturers do report aggregate average GtN discounts across their entire portfolio, but neither manufacturers nor payers do publish such information on a product level. Product-specific data on sales volumes, pricing, and manufacturer reported sales as offered by various vendors can in principle be analysed to calculate the GtN discount, but costs for such data sets can be considerable, data analysis is often complex, and results are often inconsistent when using different sources or approaches, and thus tend to have a low level of confidence. Dedicated payer primary research can help to generate more robust assumptions on product-specific GtN discount rates, but this is often beyond scope and/or budget. This tool is using identified market and product specific parameters driving GtN discounts in order to allow the calculation of good GtN estimates for planning purposes. This tool calculates potential payer rebates, it does not consider product-specific, manufacturer-internal costs for e.g. patient access programs and other internal costs sometimes included in the GtN discount.

Model Framework and Proof of Concept

With our Gross-to-Net Tool we aimed to develop a simple and straightforward but still meaningful model to estimate product-specific GtN discount rates in the US. Initially, we conducted a series of interviews with high profile US payers (n=10, >200m lives coverage) to derive a conceptual framework that reflects the key drivers for the GtN rate of a given product in the US. As a result of these interviews, we developed a two-step-approach that allows for a quick estimate of a product's GtN discount rate. Practically, in a STEP 1 the product is assigned to an indication area and/or product type for which we had gathered payer estimates on current GtN discount rates in the US. This defines the level playing field for that indication area or product type in form of a certain GtN discount range. STEP 2 then defines what specific GtN discount rate within that range can be reasonably be expected for the specific product. It is based on the rating of two aspects in a two-dimensional matrix, both of which are key aspects considered during discount negotiations with payers: Severity of disease and unmet need addressed by the product (SCORE A) and differentiation of the product vs alternatives and order of entry (SCORE B). A proof of concept study involving 10 selected products as case studies and a preliminary GtN discount data set supported this overall approach.

Optimization of Framework and Generation of Comprehensive Data Set

The tool was then optimized after conducting more payer PMR by further refining parameters such as the indication areas (expanded to a total of 11 to get sufficient resolution for commercially important indications) and product types (reduced to a total of 5 to avoid potential overlaps), each of which can be used alone or in combination. A summary plus some comments on the definitions of these final product categories is given in Table 1. In addition, we expanded the GtN discount data set to better reflect the complexity of the GtN discount ranges encountered in different key constellations in the US payer landscape (Payer Mix). To that end we considered four key settings for each of the indication areas and product types: Products covered under (i) pharmacy benefit in the context of commercial

payers, (ii) pharmacy benefit in the context of Medicare, (iii) pharmacy benefit in the context of Medicaid, as well as (iv) products covered under medical benefit with no breakdown by payer type. This data set was derived from 15 interviews with high profile US payers (1). The payers were asked to provide estimates on the GtN discount ranges (lower and upper end) and the average discount rates for each of the the indication areas and product types in context of the 4 key settings. Based on the 3 values per constellation obtained from individual payers we generated a comprehensive DISCOUNT RANGE data set consisting of 5 values per constellation (Min Abs, Min Avg, Avg, Max Avg, Max Abs). Min Abs and Max Abs correspond to the lowest and highest single individual estimate of the lower and higher end of the range, respectively. Min Avg, Avg, and Max Avg correspond to the mean of the complete set of multiple estimates of the lower end of the range, the average, and the higher end of the range, respectively. Furthermore, in order to calculate average GtN discount ranges on an US national level for each Payer Mix we also derived a data set addressing the US average benefit and Payer Mix for each of the indication areas and product types (details are available upon request). A summary of the conceptual framework with the data sets is summarized in Figure 1.

Indication Area Category		Comments	Product Type Category		Comments
1	Oncology		1	Generic (non-specialty)	Product type categories are intended to cover all indications
2	HIV		2	Specialty generic	'Specialty' brand or generic in this context means: <ul style="list-style-type: none"> Rx medications for more complex conditions, typically prescribed by secondary care / specialists rather than primary care / GPs May require special handling / administration May need closer patient monitoring by HCPs Often higher priced
3	Orphan and rare disease	Independent of indication area	3	Biosimilar	Biosimilars would typically be 'Specialty' type products
4	Diabetes		4	Brand (non-specialty)	
5	Inflammation / autoimmune / immunology	Complex/chronic conditions, independent of indications area, but not including simple anti-inflammatory agents such as for pain	5	Specialty brand	
6	Cardiovascular				
7	Respiratory asthma	Use in asthma (incl. use in asthma plus other indications, such as COPD)			
8	Respiratory other	Respiratory products not used in Asthma			
9	Multiple sclerosis				
10	Mental disorders	Schizophrenia, depression, etc.			
11	Neurology	Non-MS neurology, e.g. epilepsy, Parkinson's			

Table 1. Product categories comprising 11 indication areas and 5 product types

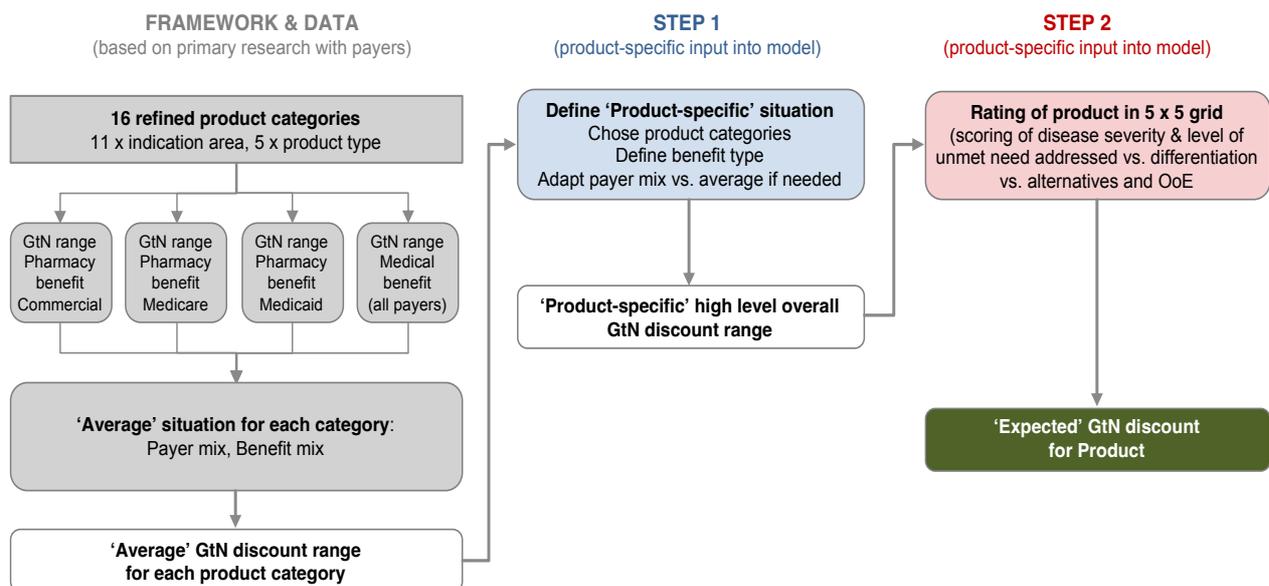


Figure 1. Conceptual framework and comprehensive data set

Calibration and Validation

The tool was calibrated by applying a correction factor to the data set generated from the primary research with payers, as preliminary calculations with case studies revealed evidence for a small but meaningful systematic underestimation of the GtN when comparing to best evidence on actual GtN. We believe that this underestimation was a consequence of a combination of factors (i) payer feedback reflecting averages of last few years rather than latest status, (ii) non-consideration in our simplified approach of 340B pricing as well as several federal programs that have the highest GtN discounts (the ‘Big 4’: Veterans Affairs, Department of Defence, Public Health Service, and the U.S. Coast Guard). After calibration, the tool was validated using 8 case studies covering a wide range of indications areas and product types. The calculated output of the tool was compared with best available evidence for the actual gross to net discount. For individual products, the absolute and relative difference between the calculated output and the best available evidence was in the range of 0-5% with a mean of 0.6% and in the range of 0-14% with a mean of 0.4%, respectively. A summary of the validation is presented in in Table 2 (details available upon request).

Case Study	Product	STEP1: Product categories, benefit type, and payer mix adaption		STEP2: Scoring within 5 x 5 matrix		Gross-to-Net			
		1. Therapy Area 2. Product Type	3. Benefit type 4. Payer Mix Adaption	SCORE A: Disease severity and unmet need addressed	SCORE B: Differentiation vs. alternatives and OoE	STEP 3: GtN Tool			Best Available Evidence*
						LOWER	EXPECTED	UPPER	
1		1. Other 2. Brand (non-specialty)	3. Pharmacy benefit 4. None	Low	Very Low	59%	68%	77%	68%
2		1. Respiratory other 2. Specialty Brand	3. Pharmacy benefit 4. None	High	Medium	14%	23%	31%	26%
3		1. Inflammation / Autoimmune/ immunology 2. Specialty Brand	3. Mixed/unknown 4. None	Low	Low	42%	48%	62%	52%
4		1. Respiratory other 2. Brand (non-specialty)	3. Pharmacy benefit 4. None	Low	High	30%	38%	46%	36%
5		1. Mental disorders 2. Specialty Brand	3. Medical benefit 4. None	Medium	Very Low	33%	39%	45%	35%
6		1. Mental disorders 2. Brand (non-specialty)	3. Pharmacy benefit 4. None	Low	Very Low	44%	49%	55%	50%
7		1. Diabetes 2. Brand (non-specialty)	3. Pharmacy benefit 4. None	Low	Very Low	60%	70%	79%	75%
8		1. Oncology 2. Specialty Brand	3. Medical benefit 4. None	High	Medium	11%	16%	21%	14%

Table 2. Summary of validation with 8 case studies (* Best Available Evidence = Units volume in US x RedBook US WAC per unit / Company reported Net Sales, details available upon request)

How to Use the Tool

STEP 1 – INPUTS to determine DISCOUNT RANGE

- **Enter the product name and chose product categories.** These are the INPUTS that drive the calculation of the DISCOUNT RANGE. Please enter the product name and then choose the product’s indication area and/or the product type. If both aspects are defined, the model calculates with an equally-weighted average. If you can or want to define only one of these aspects, then the calculation will be based on that aspect only.
- **Chose benefit type and optionally adapt payer mix.** Four options can be chosen, guiding the model to apply respective data sets for calculation of the DISCOUNT RANGE (*Unknown/mixed*, *Pharmacy benefit*, *Medical benefit*, or *Custom*). Drugs that are self-administered, including orals or self-injectables, are typically covered under *Pharmacy benefit*. Drugs that are injected or infused by a healthcare professional (HCP), which can also include out-patient clinics and infusion centers, are typically covered under *Medical benefit*. For some drugs that might not yet be defined or they

could be covered under both benefit types depending on the situation, then choose *Unknown/mixed*. Depending on your selected parameter, the model will assume typical relative proportions of the 4 key settings in the overall US market, e.g. % covered under (i) pharmacy benefit in the context of commercial payers, (ii) pharmacy benefit in the context of Medicare, (iii) pharmacy benefit in the context of Medicaid, as well as (iv) products covered under medical benefit with no breakdown by payer type. When choosing *Custom* you'll get the numbers for *unknown/mixed* as starting point with the option to manually override the benefit/payer mix default assumptions to account for certain product specifics. For example, if the product is expected to be used predominantly in employed and in under 65y old patients (increase 'Commercial'), or predominantly in the >65 (increase 'Medicare'), or predominantly in the socioeconomically weak (increase 'Medicaid').

- **DISCOUNT RANGE.** This is the calculated output of STEP 1 of the model in form of a set of 5 values (Min Abs, Min Avg, Avg, Max Avg, Max Abs). This defines the level playing field for the product, based on the INPUTS defining indication area, product type, and benefit/payer mix.

STEP 2 – Rating of product in PRODUCT SPECIFIC MARIX

- **PRODUCT SPECIFIC MATRIX.** This is to derive a product-specific EXPECTED GtN discount rate from the wider DISCOUNT RANGE obtained in STEP 1. The approach is based on a simple rating of the specific product according to two dimensions that represent key aspects considered during discount negotiations with payers: Severity of disease and unmet need addressed by the product (SCORE A) and differentiation of the product vs alternatives and order of entry (SCORE B). The product's SCORE A and B can be rated as 'Very High', 'High', 'Medium', 'Low', or 'Very Low', resulting in a 5 x 5 matrix with 25 cells. Each of these cells contain a specific % value, that is derived from the DISCOUNT RANGE by simple mathematical operation: The set of 5 values of the DISCOUNT RANGE creates the diagonal from the Very Low/Very Low cell to the Very High/Very High cell, and the other values are calculated as an average of adjacent cells. To rate your product, click on the respective cell in the PRODUCT SPECIFIC MATRIX. The chosen cell and the adjacent cells will be highlighted in green and light green, respectively, and deliver the values for the OUTPUT in STEP 3.

STEP 3 – OUTPUT

- **OUTPUT.** The scoring of the product according to the two dimensions results in the EXPECTED GtN discount rate for the product. The model also calculates a LOWER and a UPPER value, which represent the calculated average of the two lower values and the two higher values of the horizontally and vertically adjacent cells in the PRODUCT SPECIFIC MATRIX. These values are intended to give an idea on the potential increase or decrease of the EXPECTED GtN discount rate if one of the SCORES in STEP 2 was one step higher or lower.

Caveats and Limitations

Our data suggests that it is possible to conceptualise the negotiation of GtN discount rates and to use this simple tool to generate a quick view on the expected GtN for a given product in the US for planning purposes without need for extensive secondary data analysis or dedicated payer research. However, the model works with simplifications and calculated averages and therefore as such cannot reflect the complexity of all factors that might drive the actual GtN for individual products at a given moment in its lifecycle. Furthermore, real-life contracting situations have their own dynamics and individual outcomes may not be in line with our tool. Other variables that play a role are that payer organisations vary in size and vary from state to state and in the end 'payers are only humans too'. It is

also important to note that the actual GtN discount rate for any product will also depend on the product specific market access strategy which this tool does not reflect but which can be included as the next step after using this tool.

NOTES

(1) The payers had an average of 19 years of experience, included pharmacy directors and medical directors, covered a mix of national payers, regional payers, PBMs, and HIS, with a combined coverage of >200m lives under Commercial, Medicare, Medicare Advantage and Managed Medicaid.