Gross to Net
Market Access White Paper –
Product Case Studies

June 2021

What is US gross-to-net?

Gross / List Price
At ex-manufacturing / WAC level*

Net Price 1

Net Price Definition may vary between manufacturers depending on cost centres (Cost of Sales or Rebates)

Net Price 2

TOP SECRET

- *Commercial Payor Discounts, Rebates and Charge Backs*
- *Medicaid discounts and others (e.g. US Dept. of Vet. Affairs) –not confidential, 23.1%*

- *Patient Access Programs / Coupons*
- *Patient Access Services*

TOP SECRET

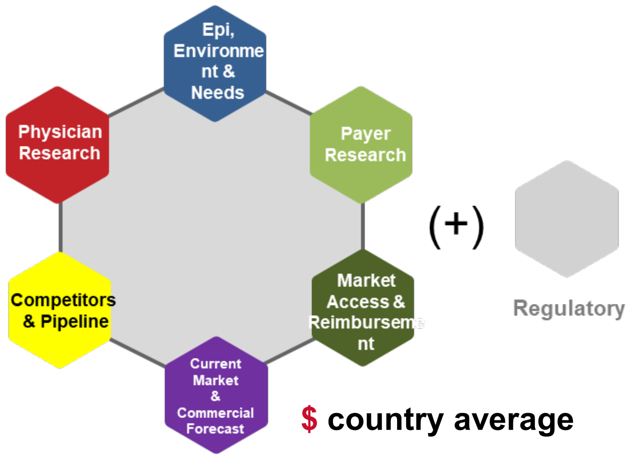
Gross prices displayed initially by manufacturers or reported by market audit data are not the same as the **negotiated net prices** paid in the end by insurers, employers or PBMs on behalf of patients.

Manufacturers at present only publish aggregate gross to net discounts across the entire portfolio.

Source: groupH research & analysis

Early-stage is different to working at late-stage: reliable US net-prices estimates are needed

Early Stage



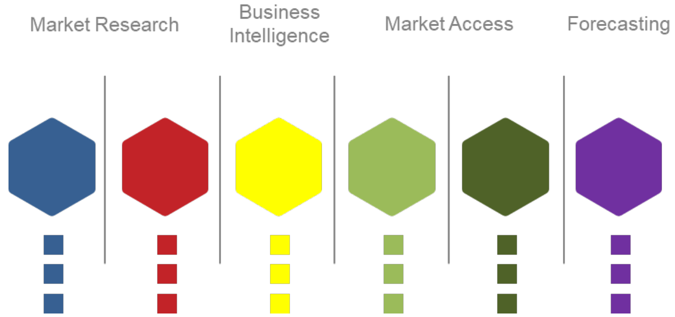
$ country average

Decision Points / Toll Gates + Optimisation

VS.

Later Stage

Departmental + Functional Silos



$ by account

Brand & Marketing Management

Further Refinement + Phase 3 or Launch Prep

What were the project objectives?

1

To understand payer thinking behind contracting and to develop a conceptual US gross-to-net model

2

To hopefully validate the model through real-life product case studies

3

To capture high-level US payer contracting trends

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Which overall approach did we take and who did we interview?

Step 1

Objectives

Approach

Discussion Guide

Product Case Studies

Pilot interview

Step 2

Secondary Research and Analysis
- Product Case Studies
- Pricing Research

Part 1 - Primary Research and Analysis
- 4 WATI 60 minutes Telephone Discussions following a DG and stimulus

Part 2 - Primary Research and Analysis
- 6 WATI 60 minutes Telephone Discussions following a DG and stimulus

Respondent Profiles
- 10 US senior payers with ~19 years experience
- Mix of National Payers, Regional Payers, PBMs and HIS
- Pharmacy Directors and Medical Directors
- All 10 payers covering 213m lives under Commercial, Medicare, Medicare Advantage and Managed Medicaid

Step 3

Analysis and Consolidation of Results

'Rough & Dirty' Conceptual Model

Documentation

We chose 10 product case studies covering a broad range of clinical and competitive settings

Case Study	Product	API	Administration	Manufacturer	Class	Main Indication	US approval year	OoE in class
1	Emgality	galcanezumab	SQ depot, syringe	Lilly	anti-CGRPs	Migraine Prevention	2018	3rd
2	OFEV	nintedanib	Oral capsules	BI	Multikinase inhibitor	Idiopathic Pulmonary Fibrosis (IPF)	2014	1st
3	Cosentyx	secukinumab	SQ, syringe or pen	Novartis	anti-IL-17s	Plaque Psoriasis (PsO)	2015	1st
4	ORKAMBI	Lumacaftor, ivacaftor	Oral tablets or granules	Vertex	CFTR modulator	Cystic Fibrosis (subset)	2015	2nd
5	zolgensma	onasemnogene abeparvovec-xioi	IV injection	Novartis / AveXis	AAV-based SMN gene therapy	Spinal Muscular Atrophy (SMA)	2019	1st
6	TRELEGY ELLIPTA	umeclidinium, vilanterol, fluticasone	Powder, inhaler	GSK	'closed triple' inhaler	COPD	2017	1st
7	PERSERIS (risperidone)	risperidone	SQ depot, syringe	Indivior	LAI with 2nd gen antipsychotic	Schizophrenia	2018	~7th
8	Trintellix	vortioxetine	Oral tablets	Lundbeck / Takeda	Serotonin modulator	Major Depressive Disorder (MDD)	2013	4th
9	Steglatro (ertugliflozin)	ertugliflozin	Oral tablets	MSD	SGLT-2i	Type 2 Diabetes (T2D)	2017	4th
10	KEYTRUDA	pembrolizumab	IV injection	MSD	anti-PD-1	Oncology (many indications)	2014	1st

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We gathered sales and pricing data from various sources and calculated gross-to-net discounts in two alternative ways

Case Study	Product	Manufacturer US Net Sales 2020 ($mn)		WAC per Unit and Unit Volume 2020			Gross to Net Discount Calculations	
		CR: Company reported **AE:** Analyst estimate (Vendor 1, ded except CR)	Manufacturer Sales calculated indirectly (Vendor 2, rounded)	**WAC per Unit** (calculated from RED BOOK) IBM Micromedex®	**Unit Average Price** (Vendor 2, rounded)	**Unit Volume** (Vendor 2, rounded)	**WAC per Unit** (RED BOOK 2021) vs. **Unit Average Price** (Vendor 2)	**WAC per UN** (RedBook 2021) * **Unit Volume** (Vendor 2) vs. **Manufacturer Net Sales** (Vendor 1)
1	Emgality	CR: 325	900	592	530	1,700,000	11%	68%
2	OFEV®	AE: 1,150	1,400	185	170	8,500,000	9%	27%
3	Cosentyx®	AE: 2,500	4,300	4,447	3,500	1,600,000	21%	52%
4	ORKAMBI	AE: 250	110	280	240	550,000	16%	- 87%
5	zolgensma®	*no data*	*no data*	2,125,000	*no data*	*no data*	-	-
6	TRELEGY ELLIPTA	AE: 700	2,000	20.05	18.00	110,000,000	13%	36%
7	PERSERIS® (risperidone)	CR: 14	20	2,199	2,000	9,500	10%	35%
8	Trintellix	AE: 650	1,150	14.10	13.00	94,000,000	11%	51%
9	Steglatro® (ertugliflozin)	AE: 60	230	8.85	9.00	25,000,000	14%	75%
10	KEYTRUDA	AE: 8,300	8,100	5,033	4,000	1,900,000	17%	15%

Sources: Vendor 1, Vendor 2, IBM Micromedex RED BOOK, Note: exchange rate variations possible in company reported sales for non-US based manufacturers

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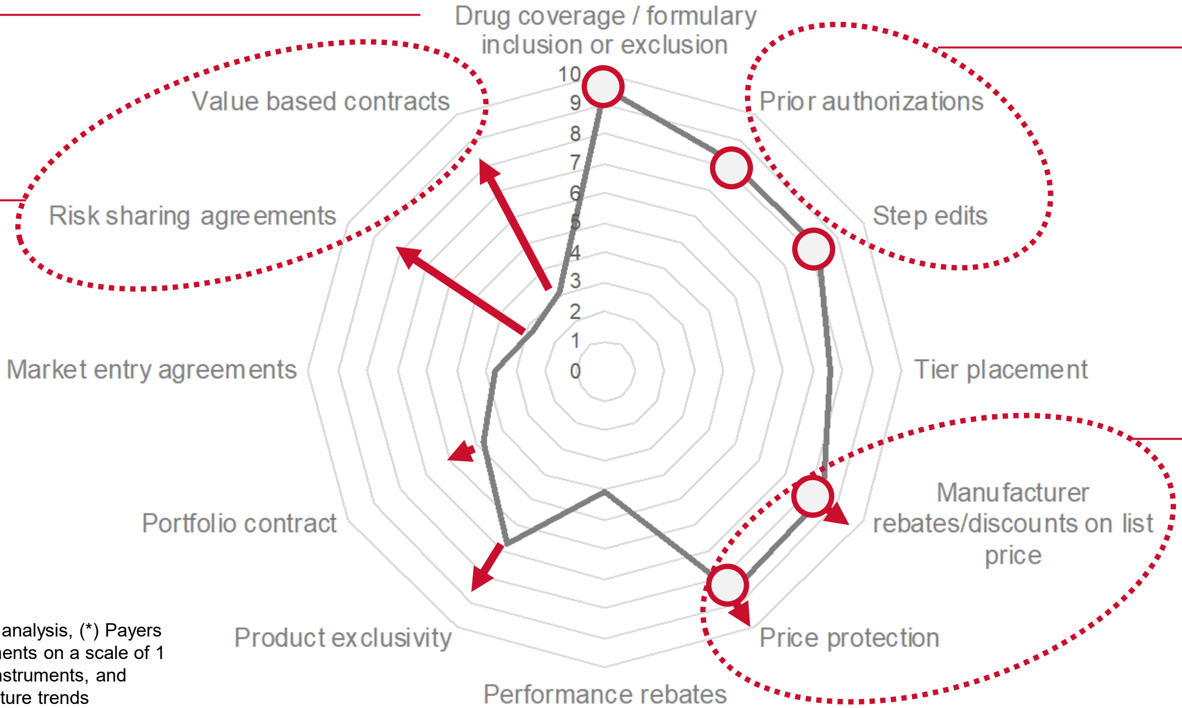
Primary Research: Current and future importance of selected instruments to control use and/or costs of medications*

Expected to be increasingly used also for oncology, HIV, rare diseases, etc.

Expected to become risk mitigation instruments for gene and cell therapies at launch

Typically used to manage classes rather than individual products

Typically linked; Expected to be increasingly used also for oncology, HIV, rare diseases, etc.



	Average Rating
	Highlighted top 5
	Future trend

Source: groupH primary research and analysis, (*) Payers (n=10) rated the importance of instruments on a scale of 1 (min) to 10 (max), named their top 5 instruments, and described their expectations around future trends

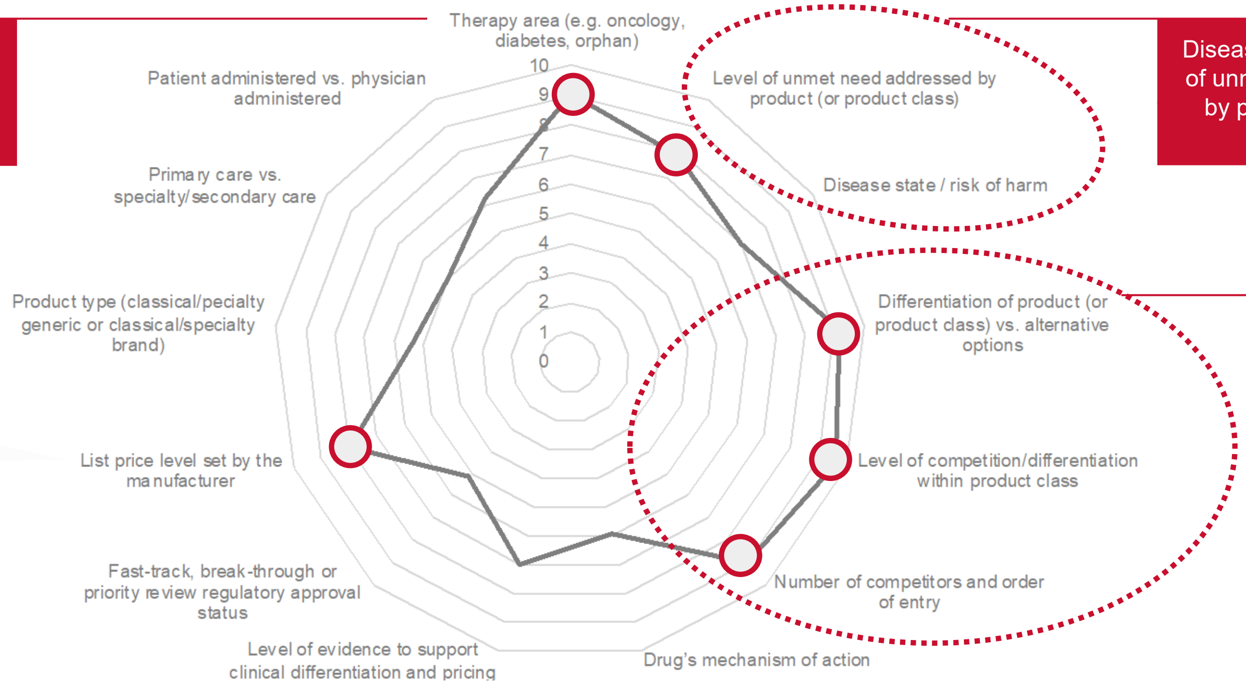
Primary Research: Drivers for rebates/discounts when contracting with manufacturers*

Defines level playing field, overall range of discounts

Disease severity and level of unmet need addressed by product (or product class)

Differentiation vs. alternatives and order of entry

Lower importance when using relevant comparators as analogue



Source: groupH primary research and analysis: (*) Payers (n=10) rated the importance of aspects on a scale of 1 (min) to 10 (max), and named their top 5 aspects

How to derive manufacturer net price assumptions for a new product X, based on comparator list price

groupH Gross-to-Net FAST TOOL

List price of relevant comparator

STEP1	***Q: At high level, what is the overall range of discounts for this type of product?***	*Example: Oncology (typically lower discounts, narrow range) vs. primary care (typically higher discounts wider range)*	**Determine overall discount range in product category** based on research with payers
STEP2	***Q: Within that high level overall range, most likely to be upper end, lower end, or in the middle?***	*Example: Within the oncology space, how does the product compare in terms of benefits it brings and the availability of alternatives?*	**Rating of project within product category** using 'Grid' → determine 'expected' discount rate
STEP3	***Q: Are there important differences vs the 'average' in the product category needing to be considered?***	*Examples: Pronounced high price / low volume OR low price high / volume strategy? Seeking 'very preferred' status by payers against additional discounts?*	**Apply correction factor** as needed

Expected Gross-to-Net product X

5 x 5 Grid for STEP 2

Differentiation vs. alternatives and OoE	Very Low	Low	Medium	High	Very High
Very High	%	%	%	%	*Abs Min %*
High	%	%	%	*Avg Min %*	%
Medium	%	%	*Avg Avg %*	%	%
Low	%	*Avg Max %*	%	%	%
Very Low	*Abs Max %*	%	%	%	%

Disease severity & level of unmet need addressed

Current Ranges of Gross-to-Net Discounts for Selected Therapy Areas / Product Types

Raw Data for STEP 1

Therapy Area / Product Type	Abs Min*	Avg Min**	Avg Avg***	Avg Max**	Abs Max*
Overall	0%		28%		70%
Primary Care overall	20%	26%	39%	48%	70%
Primary care low prevalence/budget impact	10%	Detailed data set is in the appendix			50%
Primary care high prevalence/budget impact	23%				50%
Specialty/secondary care overall	0%				70%
Specialty / secondary care low prevalence / budget impact	0%				50%
Specialty / secondary care high prevalence / budget impact	10%				50%
Oncology	0%				20%
HIV	0%				15%
Orphan and rare disease	0%				20%

Therapy Area / Product Type	Abs Min*	Avg Min**	Avg Avg***	Avg Max**	Abs Max*
Diabetes	15%				60%
Inflammation / Autoimmune	10%				70%
Cardiovascular	10%				50%
Asthma	5%				50%
MS	10%				40%
Mental disorders	5%				25%
Classical Generics	0%				90%
Specialty Generics	0%				30%
Biosimilars	10%				40%
Specialty Brand	5%				50%

Source: groupH primary research and analysis: Payers (n=10) gave their estimates on range and average of Gross-to-Net discounts by category; (*) Abs Min and Abs Max = lowest and highest individual estimate; (**) Avg Min and Avg Max = average of minimum estimates and maximum estimates; (***) average of average estimates

'Quick & Dirty' FAST TOOL for STEP1 and STEP2

Example: Gross-to-Net ranges for Primary Care

STEP 1: Gross-to-Net range for chosen category

Abs Min	Avg Min	Avg Avg	Avg Max	Abs Max
20%	26%	39%	48%	70%

STEP 2: Scoring within category

SCORE B: Differentiation vs. alternatives and OoE

	very low	low	medium	high	very high
very high	39%	33%	28%	23%	20%
high	45%	38%	33%	26%	23%
medium	51%	44%	39%	33%	28%
low	59%	48%	44%	38%	33%
very low	70%	59%	51%	45%	39%

SCORE A: Severity of disease and unmet need addressed

How to use

STEP 1: Choose product category with pre-populated discount ranges based on payer feedback

STEP 2: Rate product by SCORE A & B and thereby determine 'expected' discount rate

Grid for STEP 2

5 x 5 grid calculating 'expected' discount, based on:

- Discount ranges for product category from STEP 1 (Abs Min, Avg Min, Avg Avg, Avg Max, Abs Max)
- Scoring of product for SCORE A & B

Grid structure

- 'Inner' 3 x 3 grid covers **low, med, high** scoring and covers Avg Low, Avg Avg, Avg Max
- Outer additional layer also covers **very low** and **very high** scoring and extends range of discounts to Abs Min and Abs Max

Gross-to-Net with FAST TOOL vs. Best Available Evidence* (Case Studies)

Case Study	Product	STEP1: Product category		STEP2: Scoring within category		STEP3: Correction Factor	Gross-to-Net	
		Therapy Area / Product Type	Range Min Avg - Max Avg	SCORE A: Disease severity and unmet need addressed	SCORE B: Differentiation vs. alternatives and OoE		FAST TOOL	Best Available Evidence*
1	Emgality	Primary care	9 – 55%	Low	Low	-	48%	68%
2	OFEV	Specialty care	8 – 38%	High	Medium	-	15%	26%
3	Cosentyx	Specialty care	8 – 38%	Low	Low	-	38%	52%
4	ORKAMBI	Orphan and rare disease	0 – 10%	High	High	-	0%	n.a.
5	zolgensma	Orphan and rare disease	0 – 10%	High	High	-	0%	n.a.
6	TRELEGY ELLIPTA	Primary care	9 – 55%	Low	Medium	-	44%	36%
7	PERSERIS (risperidone)	Mental disorders	8 – 22%	Low	Very Low	-	24%	35%
8	Trintellix	Mental disorders	8 – 22%	Low	Very Low	-	24%	50%
9	Steglatro (ertugliflozin)	Diabetes	23 – 43%	Low	Very Low	-	52%	75%
10	KEYTRUDA	Oncology	3 – 15%	High	Medium	-	6%	14%
						Average	31%	44%

Pre - Payer Mix Considerations

* Vendor 2 units in US x RedBook US WAC per unit / US Net Sales from Vendor 1

6 Take-Aways and Learnings

1. Understand the strengths and weaknesses of your pricing data sources

2. Always use >1 approach and different sources and settle for the most plausible net-price

3. It may not be possible to reconcile different sources at times! – even with much effort

4. A calculated average for planning will almost inevitably differ from your own product gross-to-net

5. Conceptualising the dynamics of contracting negotiations seems possible for gross-to-net

6. Every tool has caveats: pharmacy benefit vs. medical benefit and current exclusion of government payers

next steps

- Tool refinement
- Include payer mix scenarios

Discussion within Forum / Q&A

Discussion

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COMMERCIAL ASSESSMENTS

STRATEGY WORKSHOPS

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