Pharmacy Benefit Management

Biosimilars and Gene/Cell Therapy

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3 Key Objectives

- Understand what biosimilars are
- Formulary placement of biosimilars in the U.S. and the market forces impacting biosimilars
- Understand cell & gene therapy

Misaligned Incentives

Manufacturer
Increase prices at their discretion
Higher drug costs = Higher profits

Wholesaler
Paid as a percent of drug costs
Higher drug costs = Higher profits

PBM
In control of formulary, contract language, manufacturer revenue
Higher drug costs = Higher profits

Employers & Public Purchasers
Lack of control
Higher drug costs = Lower profits

Let's Get Vertical: Looking at the Market
Insurer + PBM + Specialty Pharmacy + Provider

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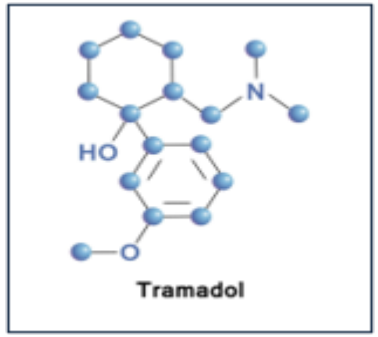
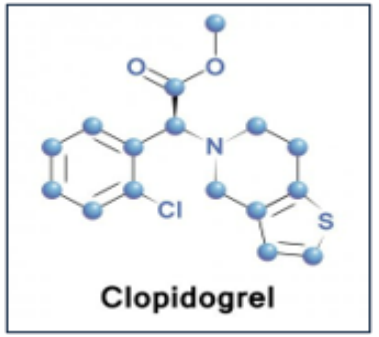
Industry consolidation leads to diminishing transparency and high cost of care.

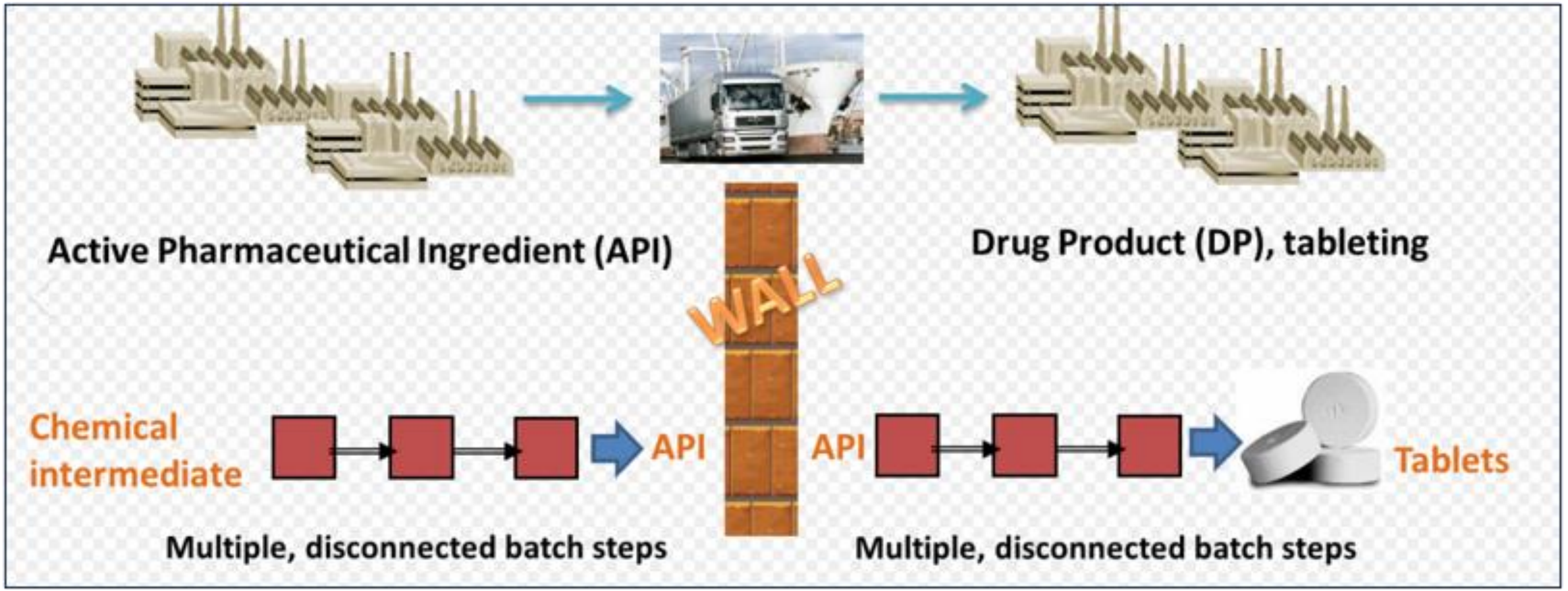
1. Since 2021, Prime's Blue Cross and Blue Shield plans have had the option to use Express Scripts or AllianceRx Walgreens Pharmacy for mail/specialty pharmacy services. IN Dec. 2021, Walgreens purchased Prime Therapeutics' 45% ownership interest, so this business had no PBM ownership as of 2022. Effective June 2022, the company was rebranded as AllianceRx Walgreens Pharmacy.
2. Centene has announced that it would outsource its PBM operations to Express Scripts in 2024. In 2023, Centene rebranded its pharmacy benefit subsidiary as Centene Pharmacy Sevrices.
3. In 2021, Centene sold a majority stake in its U.S. Medical Management to a group of private equity firms.
4. Since 2020, Prime has sourced formulary rebates via Ascent Health Services. In 2021, Humana began sourcing formulary rebates via Ascent Health Services for its commercial plans.
5. Previously known as Evernorth Care Group and Cigna Medical Group.
6. In 2021, Cigna's Evernorth business acquired MDLive.
7. In 2022, Cigna invested $2.7 billion for an estimated 14% ownership stake in VillageMD. Walgreens owns a majority of VillageMD.
8. In September 2022, CVS Health announced its acquisition of Signify Health. In February 2023, CVS announced its acquisition of Oak Street Health. Both transactions closed in 2023.
9. Previously known as IngenioRx.
10. In 2021, Partners in Primary Care and Family Physicians Group businesses were rebranded as Centerwell Senior Primary Care.
11. In 2022, Kindred at Home was rebranded as CenterWell Home Health. In 2022, Humana announced an agreement to divest its majority interest in Kindred at Home's Hospice and Personal Care Divisions to Clayton, Dubilier & Rice. Humana also announced plans to close a majority of its SeniorBridge home care locations.
Source: The 2023 Economic Report on U.S. Pharmacies and Pharmacy Benefit Managers, Exhibit 234. Companies are listed alphabetically by corporate name.

Small Molecule (Brand/Generic Drugs)





Small Molecular Manufacturing Process



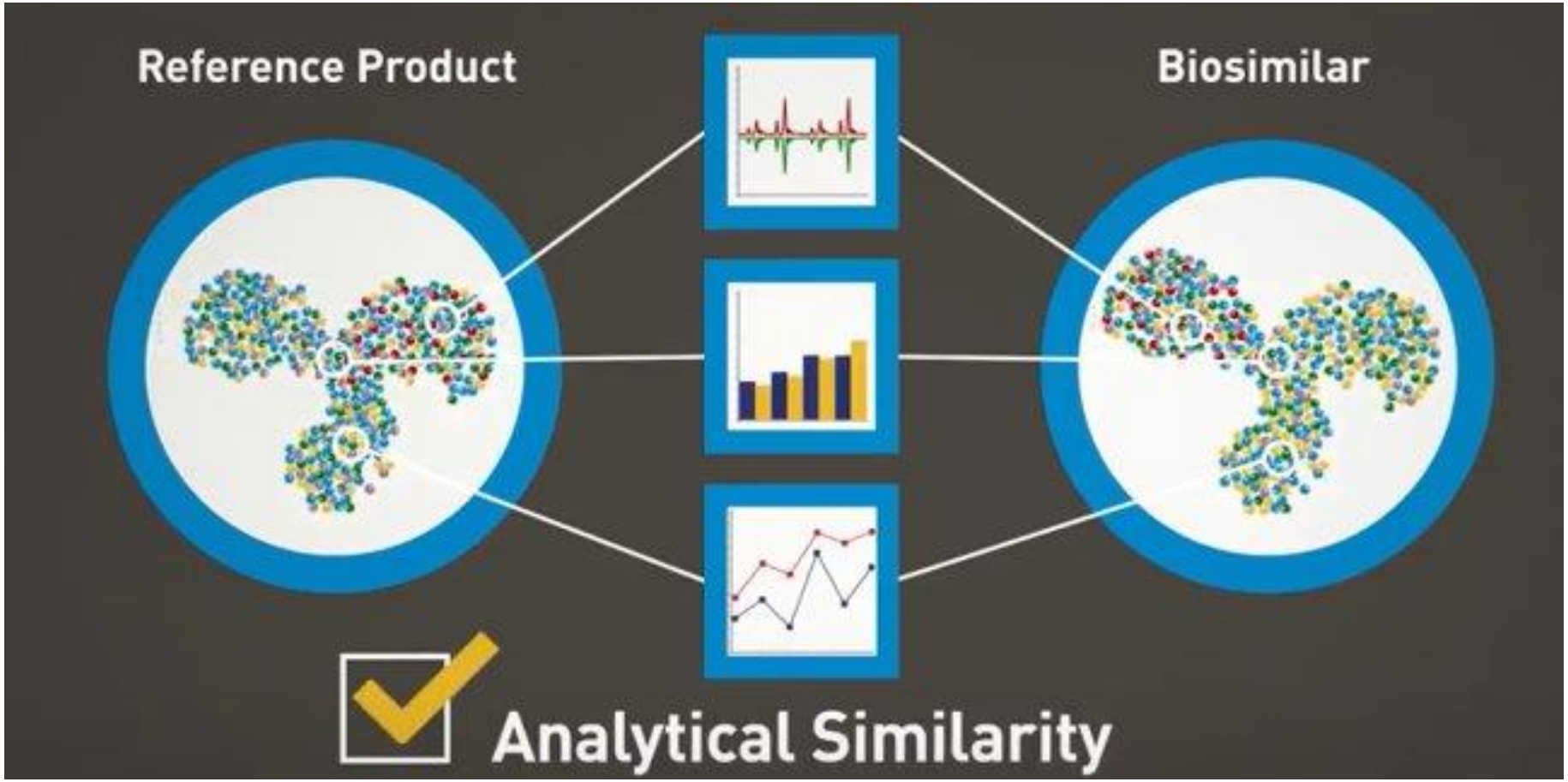
Molecular Sizes (Trying Not To Be Too Geeky!)

Aspirin Molecule
180 Daltons

Human Growth Hormone
849 Daltons

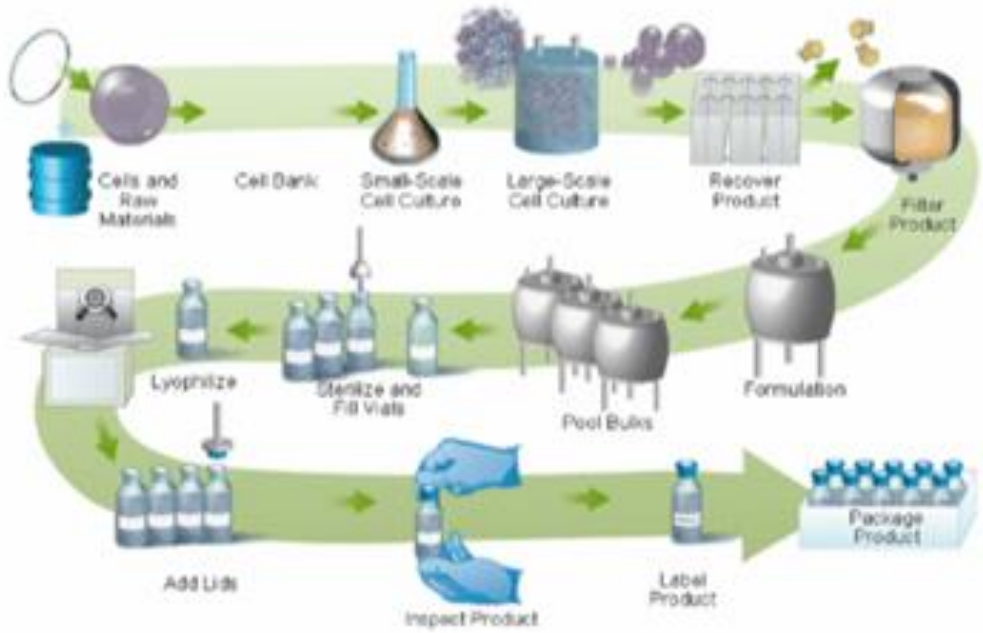
Monocional Antibody
150,000 Daltons

Reference Product vs. Biosimilar



Biopharmaceutical Manufacturing

Biopharmaceutical Manufacturing Is Inherently Complex



Allston Landing Facility

- Perfusion, microcarrier processes, 40-110 days in duration
- 22,000 line items to make one vial of Cerezyme
- >2,000 site procedures
- 8,500 discrete I/O points

genzyme

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Biosimilars in the US versus Europe

US	**41 biosimilars approved** **4% total spend** **90+ biosimilars in progress with the FDA**
Europe	**94 biosimilars approved** **34% total spend**

Cordavis, a CVS company

CVS launched a biosimilar company – another shell company

cordavis™

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Who we are

Cordavis is a wholly owned subsidiary of CVS Health® that works directly with manufacturers to bring biosimilar products *(a biologic medication that is highly similar to, and has no clinically meaningful differences from the reference product)* to the U.S. market. Cordavis will work with manufacturers to co-produce FDA-approved, high-quality products that are affordable and easy for patients to use. By focusing on these objectives, Cordavis aims to support a vibrant and competitive biosimilar market in the U.S. and drive sustainable cost savings for consumers well into the future.

cordavis™

Who we are About us Careers Contact us

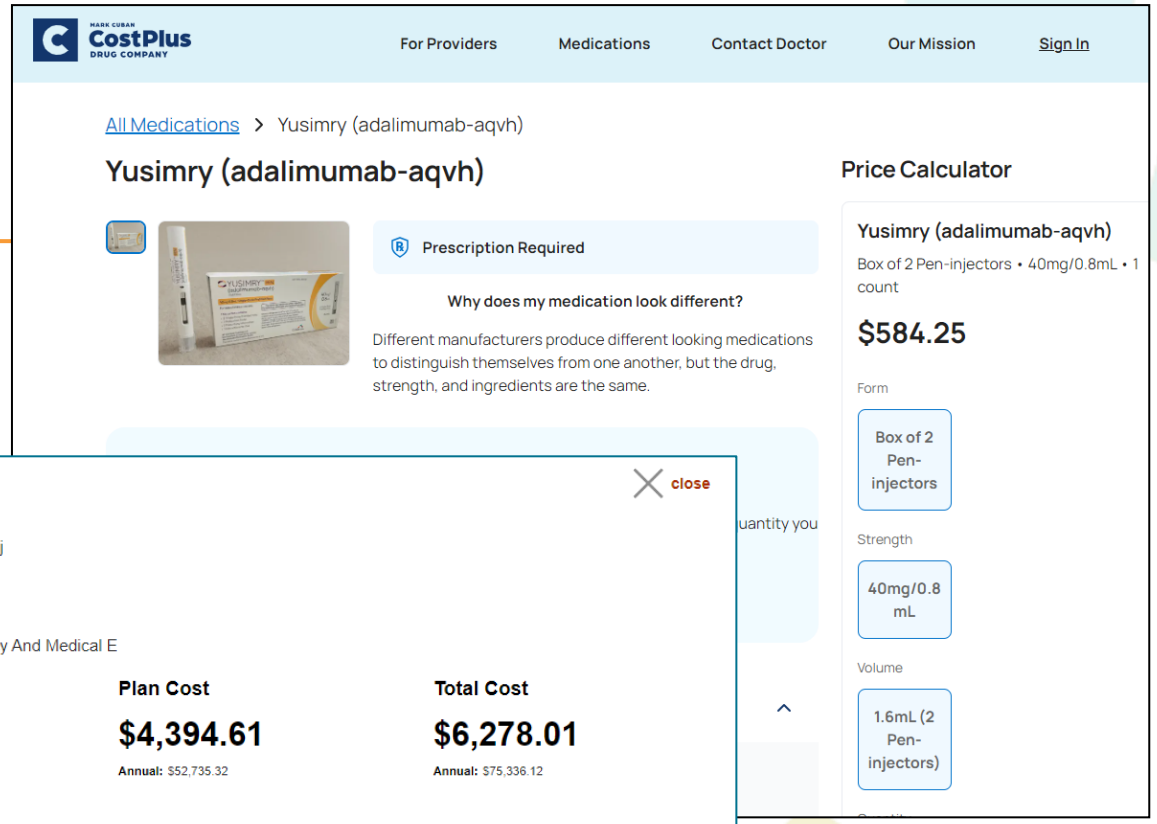
About us

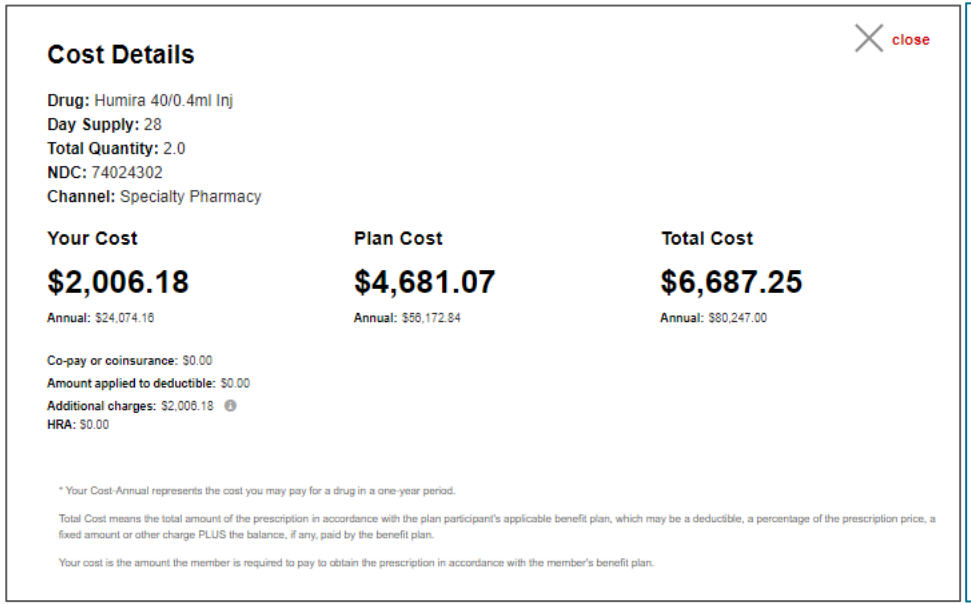
Every day, we work to build an innovative, diverse and world-class team. Based in Dublin, Ireland, we promote collaboration and stand by our commitments to our customers and patients.

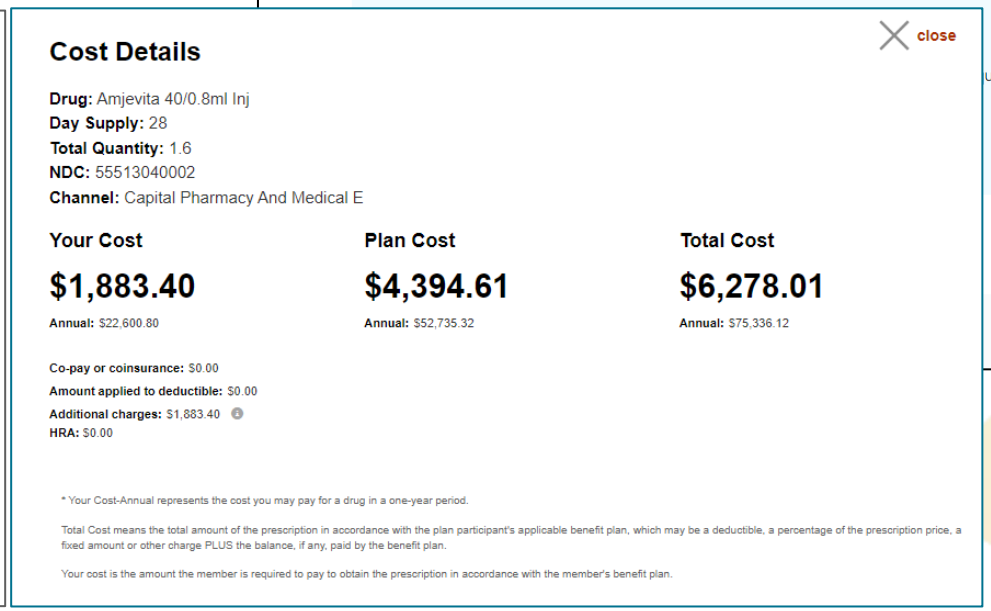
https://www.cvshealth.com/news/pbm/cvs-health-launches-cordavis.html

Humira biosimilars

Humira – 9 biosimilars with 8 launches in the US







Source: KEHP CVS Caremark Drug Pricing Tool and CostPlusDrugs.com

Humira biosimilars

Products that are approved and most-used on PBM formularies - are all high WAC

HUMIRA & ITS BIOSIMILARS, JULY 2023

Product name	Manufacturer	WAC	WAC vs. Humira
Humira	AbbVie	$6,922	n.a.
Amjevita (High WAC)	Amgen	$6,576	-5%
Amjevita (Low WAC)	Amgen	$3,115	-55%
Hulio	Biocon Biologics	$6,576	-5%
adalimumab-fkjp	Biocon Biologics	$995	-86%
Cyltezo	Boehringer Ingelheim	$6,576	-5%
Yuflyma*	Celltrion	$6,576	-5%
Yusimry	Coherus	$995	-86%
Idacio	Fresenius Kabi	$6,576	-5%
Hadlima*	Samsung Bioepis/Organon	$1,038	-85%
Hyrimoz*	Sandoz	$6,576	-5%
adalimumab-adaz*	Sandoz	$1,315	-81%

WAC = wholesale acquisition cost
* Indicates product is available in high concentration formulation
Source: Drug Channels Institute research

Published on *Drug Channels* (www.DrugChannels.net) on July 18, 2023.

DRUG CHANNELS INSTITUTE

Biosimilar – Sometimes They Count…

Rebate Language

1.3. EXCLUSIONS

Member Submitted Claims, Subrogation Claims, coordination of benefits claims, biosimilar products, vaccines, OTC products, U&C, claims older than 180 days, claims through Sponsor-owned, in-house or on-site pharmacies, Specialty Products, 340b pharmacies, and claims pursuant to a 100% Member Copayment plan are not eligible for the guaranteed Rebate amounts set forth in Section 1.1 above.

2. SPECIALTY REBATE AMOUNTS

Pricing Guarantee Language

"Specialty Products" means those injectable and non-injectable drugs on the Specialty Product List. Specialty Products, which may be administered by any route of administration, are typically used to treat chronic or complex conditions, and typically have one or more of several key characteristics, including frequent dosing adjustments and intensive clinical monitoring to decrease the potential for drug toxicity and increase the probability for beneficial treatment outcomes; patient training and compliance assistance to facilitate therapeutic goals; limited or exclusive product availability and distribution (if a drug is only available through limited specialty pharmacy distribution it is always considered a Specialty Product); specialized product handling and/or administration requirements. In addition, a biosimilar or generic product will be considered a Specialty Drug if the innovator drug is a Specialty Drug.

What are cell and gene therapies?

- Cell therapies transfer live cells into a patient to treat or cure a condition
  - Transferred cells are collected from the patient or a donor
- Gene therapies modify a person's genes to treat or cure a condition
  - This could be replacing, inactivating or introducing a new or modified gene
- FDA has approved (29) cell and gene therapies as of 5/19/23
  - The pipeline is quite full—with more than 1,000 gene, cell and tissue-based therapies currently in development globally
  - By 2025, the FDA expects to be approving 10 to 20 annually
- Familiar examples include:
  - Zolgensma – gene therapy treating spinal muscular atrophy (SMA) - $2.125M (1x, curative)
  - Luxterna – gene therapy treating an inherited retinal disease - $850K (1x, curative)
  - Hemgenix – gene therapy for Hemophilia B (Factor IX deficient) - $3.5M (1x, curative)

Gene Therapy Pipeline Projections

Based on the current pipeline, TMHCC projects the cost of cell and gene therapies in 2023 could be **more than four times** the cost in 2022 on a Per Employee Per Month (PEPM) basis.

-TMHCC 2022 Annual Market Report

Sources: https://www.tmhcc.com/en-us/-/media/TMHCC/Stop-Loss-Group/2022-Annual-Market-Report.pdf

Gene Therapy Pipeline Projections

Name	Manufacturer	Route	Status	Condition
Exa-cel (Exagamglogene Autotemcel)	CRISPR Therapeutics Vertex	Intravenous	FDA Review (BsUFA - 12/08/2023)	Sickle cell disease and beta thalassemia
Lovo-cel (Lovotibeglogene Autotemcel)	bluebird bio	Intravenous	FDA Review (BsUFA - 12/20/2023)	Sickle cell disease
OTL-200 (Atidarsagene Autotemcel)	Orchard Therapeutics GSK	Intravenous	FDA Review (BsUFA - 1Q 2024)	Metachromatic leukodystrophy
PF-06838435 (Fidanacogene Elaparvovec)	Spark Therapeutics Pfizer Roche	Intravenous	FDA Review (BsUFA - 2Q 2024)	Hemophilia B
Generxx (Alferminogene Tadenovec)	Angionetics Gene Biotherapeutics	Other	Phase III	Angina pectoris
AAV2-REP1 (Timrepigene Emparvovec)	Nightstar Therapeutics Biogen	Intravitreal	Phase III	Choroideremia (CHM)
Invossa (Tonogenchoncel-L)	Kolon TissueGene	Injectable	Phase III	Chronic degenerative joint disease
Engensis (Donaperminogene Seltoplasmid)	ViroMed Helixmith	Intramuscular	Phase III	Chronic diabetic foot ulcers Diabetic neuropathy
RGX-314	Regenxbio AbbVie	Ophthalmic	Phase III	Diabetic retinopathy
PF-06939926 (Fordadistrogene Movaparvovec)	Pfizer	Intravenous	Phase III	Duchenne muscular dystrophy (DMD)
D-Fi (Dabocemagene Autoficel)	Castle Creek Biosciences Paragon Biosciences Fibrocell Technologies Intrexon	Injectable	Phase III	Epidermolysis
AVR-RD-02	AvroBio	Intravenous	Phase III	Gaucher disease
SB-525 (Giroctocogene Fitelparvovec)	Sangamo Therapeutics Pfizer	Intravenous	Phasev III	Hemophilia A
GS010 (Lenadogene Nolparvovec)	GenSight Biologics Genethon	Ophthalmic	Phase III	Leber's hereditary optic neuropathy
RGX-121	Regenxbio	Injectable	Phase III	Mucopolysaccharidosis Type 2
Generx (Alferminogene Tadenovec)	Angionetics Gene Biotherapeutics	Other	Phase III	Myocardial ischemia and refractory angina due to coronary artery disease (CAD)

Name	Manufacturer	Route	Status	Condition
GALGT2	Sarepta Therapeutics	Injectable	Phase II	Duchenne muscular dystrophy
4D-310	4D Molecular Therapeutics	Intravenous	Phase II	Fabry disease
RP-L102	Rocket Pharma	Intravenous	Phase II	Fanconi Anemia
GBA1	Regenxbio Prevail Therapeutics Eli Lilly	Injectable Intravenous	Phase II	Gaucher disease
AXO-AAV-GM1	Axovant Sio	Intrathecal	Phase II	GM1 gangliosidosis
LYS-GM101	Lysogene	Oral Other Intravenous	Phase II	GM1 gangliosidosis
AXO-AAV-GM2	Ultragenyx	TBD	Phase II	GM2 gangliosidosis (Tay-Sachs and Sandhoff disease)
SPK-8011 (Dirloctocogene Samoparvovec)	Spark Therapeutics Roche	Intravenous	Phase II	Hemophilia A
DTX201	Dimension Therapeutics Bayer Ultragenyx	Intravenous	Phase II	Hemophilia A
SB-FIX	Sangamo Therapeutics	Intravenous	Phase II	Hemophilia B
FLT180a (Verbrinacogene Setparvovec)	Freeline Therapeutics	Injectable	Phase II	Hemophilia B
AskBio009	Baxalta Shire Takeda	Intravenous	Phase II	Hemophilia B
AMT-060	uniQure	Intravenous	Phase II	Hemophilia B
SB-728-T	Sangamo Therapeutics	Intravenous	Phase II	Human immunodeficiency virus (HIV)
SB-728-HSPC	Sangamo Therapeutics	Intravenous	Phase II	Human immunodeficiency virus (HIV)
AMT-130	uniQure	Injectable	Phase II	Huntington's disease
KB105	Krystal Biotech	Topical	Phase II	Ichthyosis
SAR439483	Atsena Therapeutics	Other Intravitreal	Phase II	Leber congenital amaurosis
RP-L201	Rocket Pharma	Intravenous	Phase II	Leukocyte Adhesion Defect Type 1
pIL-12 (Tavokinogene Telseplasmid)	OncoSec	Other	Phase II	Metastatic melanoma
RGX-111	Regenxbio	Injectable	Phase II	Mucopolysaccharidosis Type I

Name	Manufacturer	Route	Status	Condition
Reqorsa Quaratusugene Ozeplasmid	Genprex	Injectable	Phase II	Non-small cell lung cancer
XT-150	Xalud Therapeutics	Injectable	Phase II	Osteoarthritis
OXB-102	Axovant Sio Oxford Biomedica	Injectable	Phase II	Parkinson's disease
BMN 307	BioMarin	Intravenous	Phase II	Phenylketonuria
SPK-3006	Spark Therapeutics Roche	Intravenous	Phase II	Pompe disease
VCTX211	CRISPR Therapeutics Vertex	Implant	Phase II	Type 1 diabetes
ST-920 Isaralgagene Civaparvovec	Sangamo Therapeutics	Injectable	Phase II	Fabry disease

Gene Therapies

Though the range of predictions varies significantly, there is **overwhelming agreement** that spend on gene therapies will increase significantly in the near term

Probability of at Least One Gene Therapy Claim in Plan Year:						
# of Members	2024	2025	2026	2027	2028	2029
500	0.2%	0.4%	0.6%	1.2%	1.6%	2.0%
1,000	0.5%	0.7%	1.3%	2.4%	3.2%	3.9%
2,500	1.2%	1.8%	3.2%	5.8%	7.9%	9.4%
5,000	2.4%	3.6%	6.7%	11.3%	15.1%	18.0%
7,500	3.6%	5.4%	9.2%	16.4%	21.8%	25.7%
10,000	4.8%	7.1%	12.1%	21.2%	27.9%	32.7%
20,000	9.4%	13.7%	22.7%	38.0%	48.1%	54.7%

Sources: Brown & Brown Q1 2023 Market Trend Report – reference to Optum

About 1 in **100**

About 1 in **10**

Gene Therapies

Who is paying for them, and how?

- **Usually Carrier (Fully Insured) or Stop Loss (Self-Funded)**
- **Emerging funding models are changing this paradigm, as more and more expensive therapies are approved and released**
  - **Stop loss-type:** PEPM/PMPM fee to cover specific gene therapy treatments – subject to deductible
  - **Full carve-out:** PEPM/PMPM fee for full financial risk transfer – no deductible to satisfy
  - **Payment plans:** Ability to amortize full cost of the drug over a number of years into the future

What did you learn today?

- Understand what biosimilars are
- Formulary placement of biosimilars in the U.S. and the market forces impacting biosimilars
- Understand cell & gene therapy

INSPIRE

companies
healthcare
community

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PBGH '23
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