Biosimilar is a Four Letter Word:

Making sense of the suffix

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The University of Toledo Medical Center

OPA Annual Conference & Trade Show
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OHIO PHARMACISTS ASSOCIATION

1 VOICE VISION TEAM

Disclosure Statement

- Meghan Fox, Sarah Lorenzen, Dana Ortiz, and Amanda Porter have no relevant financial relationship(s) with ineligible companies to disclose.

  and

- None of the planners for this activity have relevant financial relationships with ineligible companies to disclose.

Learning Objectives

At the completion of this activity, the participant will be able to:

Define	Describe	Explain	Identify	Summarize	Describe
Define what a biologic product is	Describe the difference between a generic and a biosimilar drug product	Explain the different regulatory approval pathways for reference products and biosimilars	Identify selected biosimilars, their associated nomenclatures, and the disease states for which they are indicated	Summarize patient assistance and copay card options for biosimilars	Describe managed care implications of biosimilar availability and the potential impact of such availability on patient care

UT Access Pharmacy

Biosimilars are the next chapter in our journey—ready or not, here they come!

Definitions

What is a Biologic?

Large, complex molecules that are made from living sources

- Bacteria
- Yeast
- Animal cells

More complex structures than those of other medications

- More complicated to purify, process, and manufacture

Contain many slight variations from batch to batch

Used to treat many illnesses

- Cancer
- Psoriasis
- Rheumatoid arthritis
- Inflammatory bowel disease (Crohn's and UC)

The Straightforward Generic

Generics are based on already marketed brand name drugs and are the same in terms of dosage form, safety, strengths, route of administration, quality, performance characteristics, and intended use

FDA: "a generic medicine works in the same way and provides the same clinical benefit as the brand-name medicine"

FDA Generic Drugs Program reviews generics to ensure standards are met and manufacturing process and post-market monitoring is consistent once product is on the market

What is a Biosimilar?

Biologic medication

Highly **similar** to the existing FDA-approved biologic

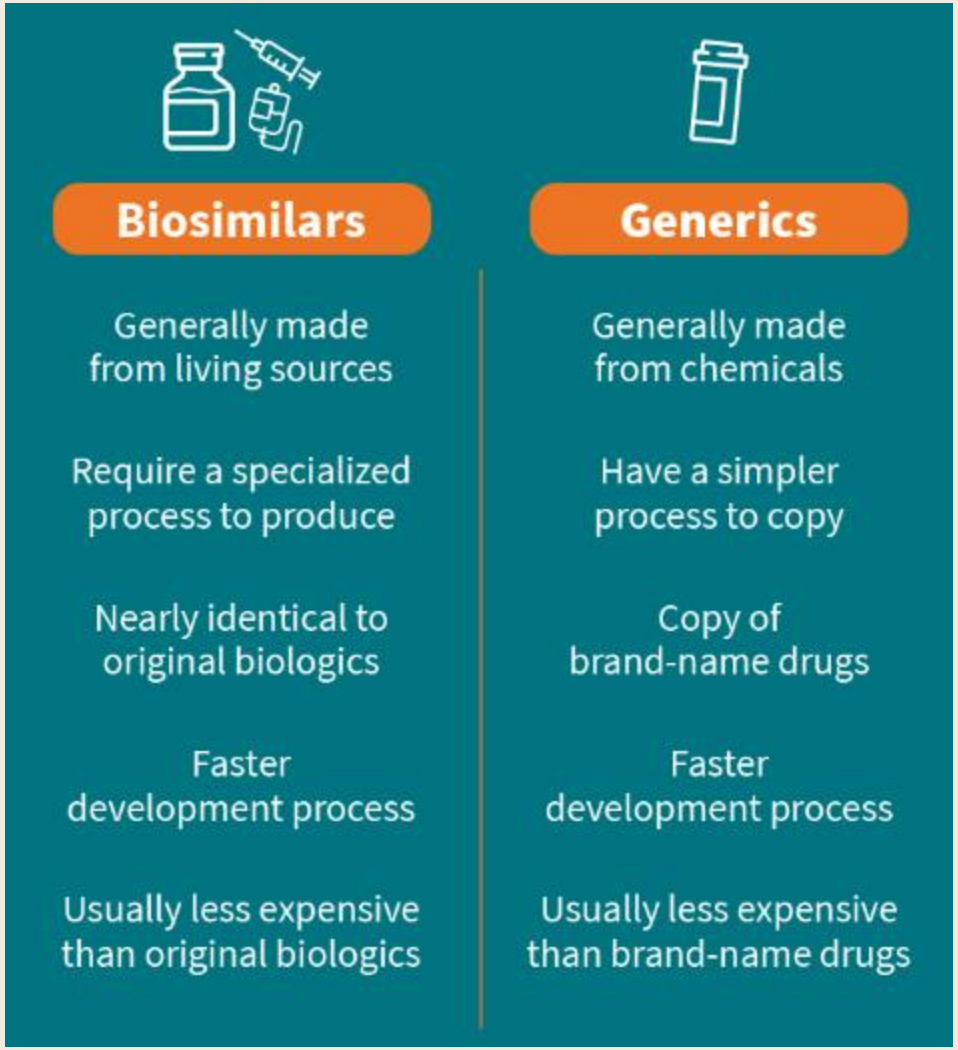
- No clinically meaningful differences

Existing FDA-approved biologic is the "reference product"

- Utilizes the same mechanism of action as the reference product
- Proposed labelling is the same as the reference product
- Has the same route of administration, dosage form, and strength as the reference product

Differences

Biosimilars vs. Generics



What is an interchangeable biosimilar product?

Biosimilar that meets additional requirements

May be substituted for the reference product at the pharmacy

- Without the intervention of the prescriber
  - Much like generic drugs substituted for brand-name drugs

May help increase patient access to biologics

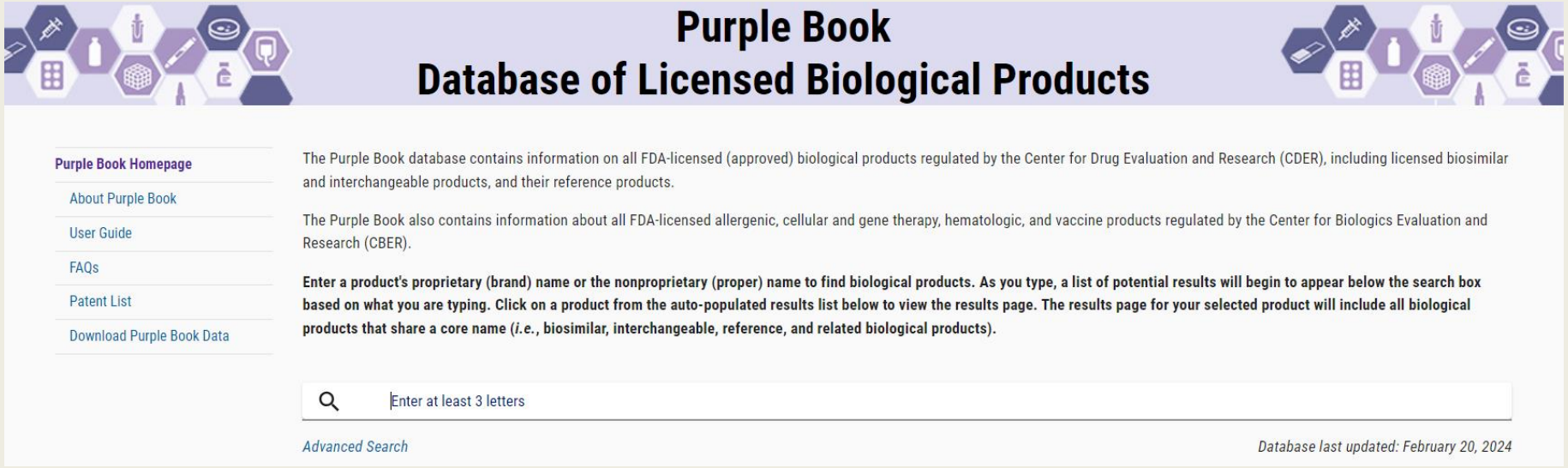
Not all biosimilars are interchangeable

- Companies must submit an application
- Must be adequate information to support an interchangeability

Purple book (https://purplebooksearch.fda.gov/)

Purple Book

https://purplebooksearch.fda.gov/



Interchangeable(s)

Proprietary Name
Abrilada

Proper Name
adalimumab-afzb

PRODUCT LABEL

Proprietary Name
Cyltezo

Proper Name
adalimumab-adbm

PRODUCT LABEL

Proprietary Name
Simlandi

Proper Name
adalimumab-ryvk

PRODUCT LABEL

Reference Product(s)

Proprietary Name
Humira

Proper Name
adalimumab

PRODUCT LABEL

Biosimilar(s)

Proprietary Name
Amjevita

Proper Name
adalimumab-atto

PRODUCT LABEL

Proprietary Name
Hadlima

Proper Name
adalimumab-bwwd

PRODUCT LABEL

Proprietary Name
Hulio

Proper Name
adalimumab-fkjp

PRODUCT LABEL

Proprietary Name
Hyrimoz

Proper Name
adalimumab-adaz

PRODUCT LABEL

Proprietary Name
Idacio

Proper Name
adalimumab-aacf

PRODUCT LABEL

Proprietary Name
Yuflyma

Proper Name
adalimumab-aaty

PRODUCT LABEL

Proprietary Name
Yusimry

Proper Name
adalimumab-aqvh

PRODUCT LABEL

Regulatory Pathways

Reference Product Approval Pathway

351(a) application

"Stand-alone"

- Manufacturer sponsoring the application must conduct sufficient clinical trials, including phase 3 trials, to prove efficacy, safety, tolerability, and purity
- Must independently demonstrate efficacy and safety for the full profile of the medication

Biosimilar Product Approval Pathway

351(k) application

Abbreviated licensure pathway

- Relies on FDA's previous finding regarding the reference product to support approval of the biosimilar product
- Application must prove the biosimilar product is highly ***similar*** to the reference product, with no clinically meaningful differences
- Allows for a potentially shorter and less costly drug development program

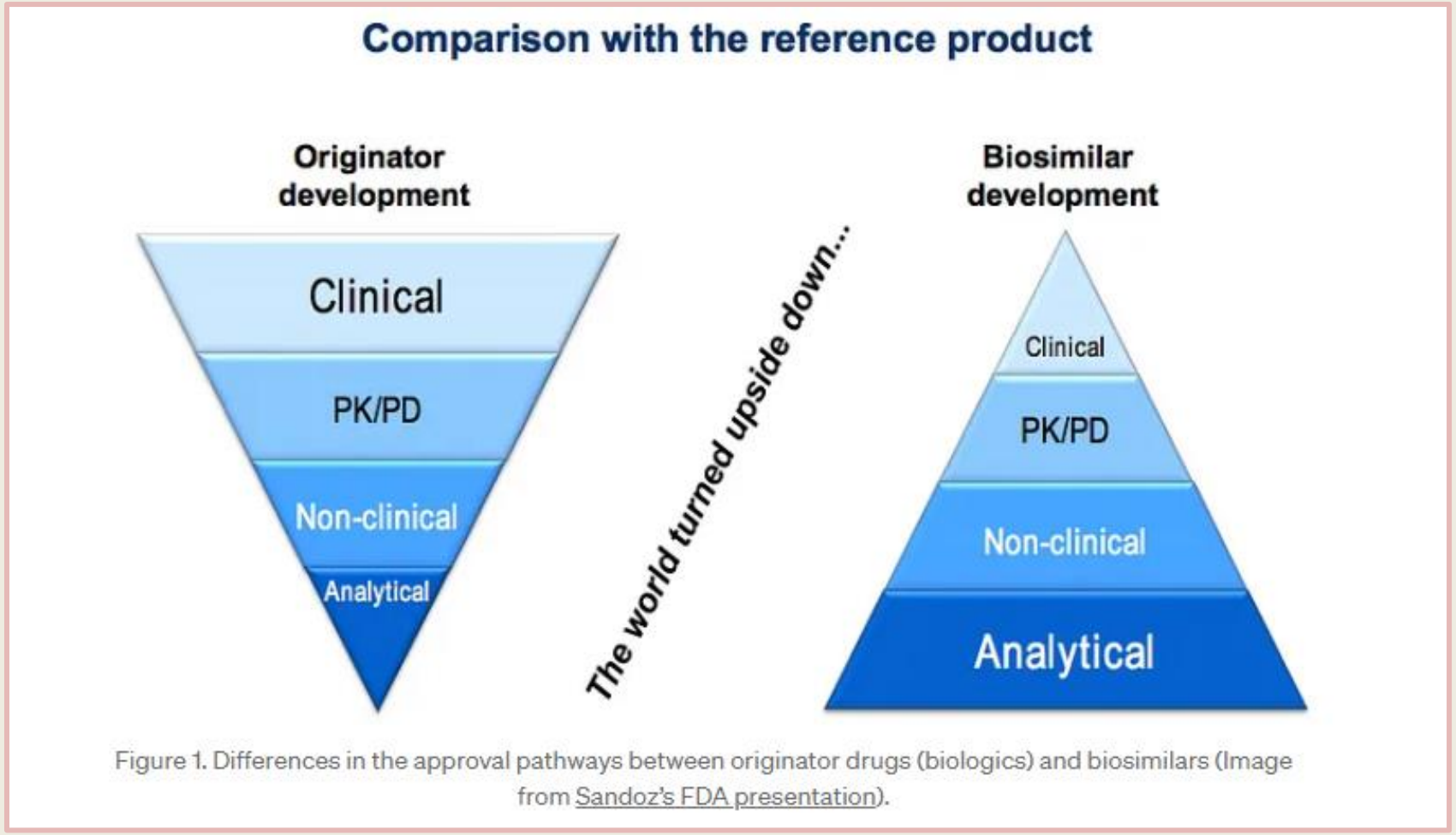


Figure 1. Differences in the approval pathways between originator drugs (biologics) and biosimilars (Image from Sandoz's FDA presentation).

Biologic vs. Biosimilar

Select Biosimilars, Indications, and Nomenclature

Insulins: Diabetes

PROPER NAME	PROPRIETARY NAME		INTERCHANGEABLE?
Insulin glargine	Lantus©	Reference Product	YES
Insulin glargine	Basaglar©	Reference Product	NO
Insulin glargine	Semglee©	Reference Product	NO
Insulin glargine	Toujeo©	Reference Product	NO
Insulin glargine-yfgn	Semglee©		YES
Insulin glargine-aglr	Rezvoglar©		YES

Products are interchangeable if indicated by 351 (k) notation.
*Screenshot from Purple Book.

Biosimilar(s)

No biosimilar data at this time.

Interchangeable(s)

Proprietary Name
Rezvoglar

Proper Name
insulin glargine-aglr

PRODUCT LABEL

Proprietary Name
Semglee

Proper Name
insulin glargine-yfgn

PRODUCT LABEL

Reference Product(s)

Proprietary Name
Basaglar

Proper Name
insulin glargine

PRODUCT LABEL

Proprietary Name
Lantus

Proper Name
insulin glargine

PRODUCT LABEL

Proprietary Name
Semglee

Proper Name
insulin glargine

PRODUCT LABEL

Proprietary Name
Toujeo

Proper Name
insulin glargine

PRODUCT LABEL

Adalimumab: Tumor Necrosis Factor (TNF)-alpha Inhibitor

- Many biosimilars
  - Not all interchangeable
  - Not all indicated for same diagnoses
- Many indications
  - Rheumatoid Arthritis
  - Juvenile idiopathic arthritis
  - Psoriatic arthritis
  - Ankylosing Spondylitis
  - Crohn's disease
  - Plaque psoriasis
- Several product sizes
  - Syringes
  - Pens
  - Vials

Interchangeable(s)

Proprietary Name
Abrilada

Proper Name
adalimumab-afzb

PRODUCT LABEL

Proprietary Name
Cyltezo

Proper Name
adalimumab-adbm

PRODUCT LABEL

Proprietary Name
Simlandi

Proper Name
adalimumab-ryvk

PRODUCT LABEL

Reference Product(s)

Proprietary Name
Humira

Proper Name
adalimumab

PRODUCT LABEL

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PRODUCT LABEL

Proprietary Name
Hyrimoz

Proper Name
adalimumab-adaz

PRODUCT LABEL

Proprietary Name
Idacio

Proper Name
adalimumab-aacf

PRODUCT LABEL

Proprietary Name
Yuflyma

Proper Name
adalimumab-aaty

PRODUCT LABEL

Proprietary Name
Yusimry

Proper Name
adalimumab-aqvh

PRODUCT LABEL

Table 2. Biosimilar Indications Compared to Humira

Indication	Crohn's disease	Ulcerative colitis	Hidradenitis suppurativa	Juvenile idiopathic arthritis	Plaque psoriasis	Rheumatoid arthritis	Spondylo-arthritis	Uveitis
Humira	X	X[a]	X[b]	X	X	X	X	X[c]
Adalimumab-afzb (Abrilada, Pfizer)	X	X	X	X	X	X	X	X
Adalimumab-atto (Amjevita, Amgen)	X	X	X	X	X	X	X	X
Adalimumab-adbm (Cyltezo, Boehringer Ingelheim)	X	X	X	X	X	X	X	X
Adalimumab-bwwd (Hadlima, Organon/ Samsung Bioepis)	X	X	X	X	X	X	X	X
Adalimumab-fkjp (Hulio, Mylan/Viatris/ Fujifilm Kyowa Kirin/ Biocon)	X	X	X	X	X	X	X	X
Adalimumab-adaz (Hyrimoz, Sandoz/ Novartis)	X	X	X	X	X	X	X	X
Adalimumab-aacf (Idacio, Fresenius Kabi)	X	X		X	X	X	X	
Adalimumab-aaty (Yuflyma, Celltrion)	X	X	X	X	X	X	X	
Adalimumab-aqvh (Yusimry, Coherus BioSciences)	X	X	X	X	X	X	X	X

[a] Humira only (no biosimilars) for ulcerative colitis in pediatric patients aged ≥5 y.

[b] Humira only (no biosimilars) for hidradenitis suppurativa in pediatric patients aged ≥12 y.

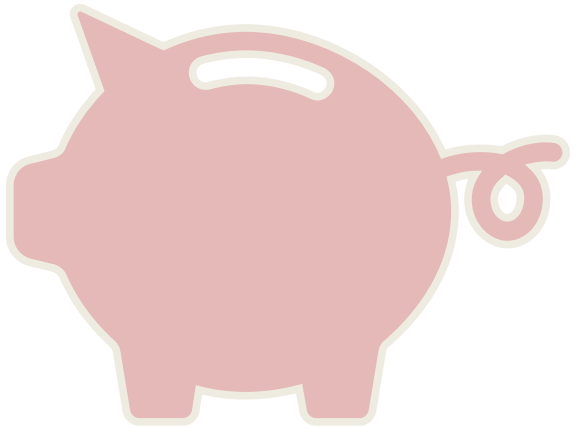
[c] Humira only (no biosimilars) for uveitis in pediatric patients aged ≥2 y.

Based on references 1 and 4-12.

Others

Reference Product	Biosimilars	Indication
Epogen©	Epoetin alfa-epbx	• Anemia
Neulasta©	Pegfilgrastim-fpgk Pegfilgrastim-pbbk Pegfilgrastim-apgf Pegfilgrastim-bmez Pegfilgrastim-cbqv Pegfilgrastim-jmdb	• Neutropenia
Neupogen©	Filgrastim-aafi Filgrastim-ayow Filgrastim-sndz	• Neutropenia
Remicade©	Infliximab-axxq Infliximab-abda Infliximab-dyyb	• COVID • Rheumatology • UC, Crohn's
Rituxan©	Rituximab-arrx Rituximab-pvvr Rituximab-abbs	• Certain lymphomas, leukemias • MS, RA, many others!

Patient Assistance and Copay Card Options



Definitions

- Copay card
  - Commercial primary insurance that is paying for the medication
- Patient assistance
  - Government funded insurance (most often Medicare)
  - No prescription insurance coverage
  - No coverage for the medication through insurance

Insulins

Lantus©

- Copay card: Copay Card & Savings Programs | Lantus® (insulin glargine injection) 100 Units/mL
- PAP: SPC_Application.pdf (sanofipatientconnection.com)

Rezvoglar©

- Copay card: REZVOGLAR™ (insulin glargine-aglr) injection | Long-Acting Insulin Analog
- No PAP

Basaglar©

- Copay card: Savings & Resources | BASAGLAR® (insulin glargine) injection
- PAP: Lilly Cares Application | Lilly Cares

Semglee©

- Copay card: Savings Program for SEMGLEE® (insulin glargine-yfgn)
- PAP: https://bioconbiologicsus.com/pap

Adalimumab

Humira©

- Copay card
  - Will cover commercial patients down to a $5 copay
  - Will not help if patients insurance is part of a maximizer program
- PAP
  - Through Abbvie
  - Will not help if patients have a plan that excludes all specialty medications- where I have seen other biosimilars come into play

Adalimumab

Amjevita©

- PAP through Amgen- will help even if the insurance excludes all specialty medications

Cyltezo©

- Interchangeable with Humira
- Least experience with their PAP program

Hadlima©

- Copay card and PAP available

Adalimumab

Abrilada©

- Interchangeable with Humira
- Pfizer- copay card and PAP

Hyrimoz©

- Sandoz/ Novartis- "Patient Transition program with a one-time reimbursement of $200 on a healthcare debt card"

Adalimumab

Idacio©

- IDACIO® (adalimumab-aacf) - KabiCare

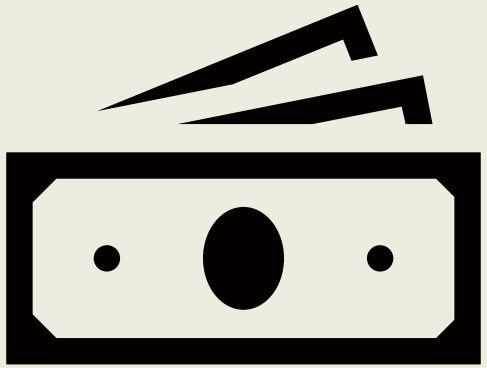
Yuflyma©

Hulio©

- Biocon Biologics- copay card and PAP

Others

- Avastin©
- Epogen©
- Herceptin©
- Lucentis©
- Neulasta©
- Neupogen©
- Remicade©
- Rituxan©



Other Considerations

- Insurance- must approve the medication first before a copay card can be used
- PAP- most won't help unless the patient has no coverage for the medication
- Insurance maximizer programs- require patients to sign up for copay cards as a requirement of their insurance which can make copay card funds run out and shift cost savings to the insurance rather than the patient

Managed Care Implications of Biosimilars

Specialty Drug Spend

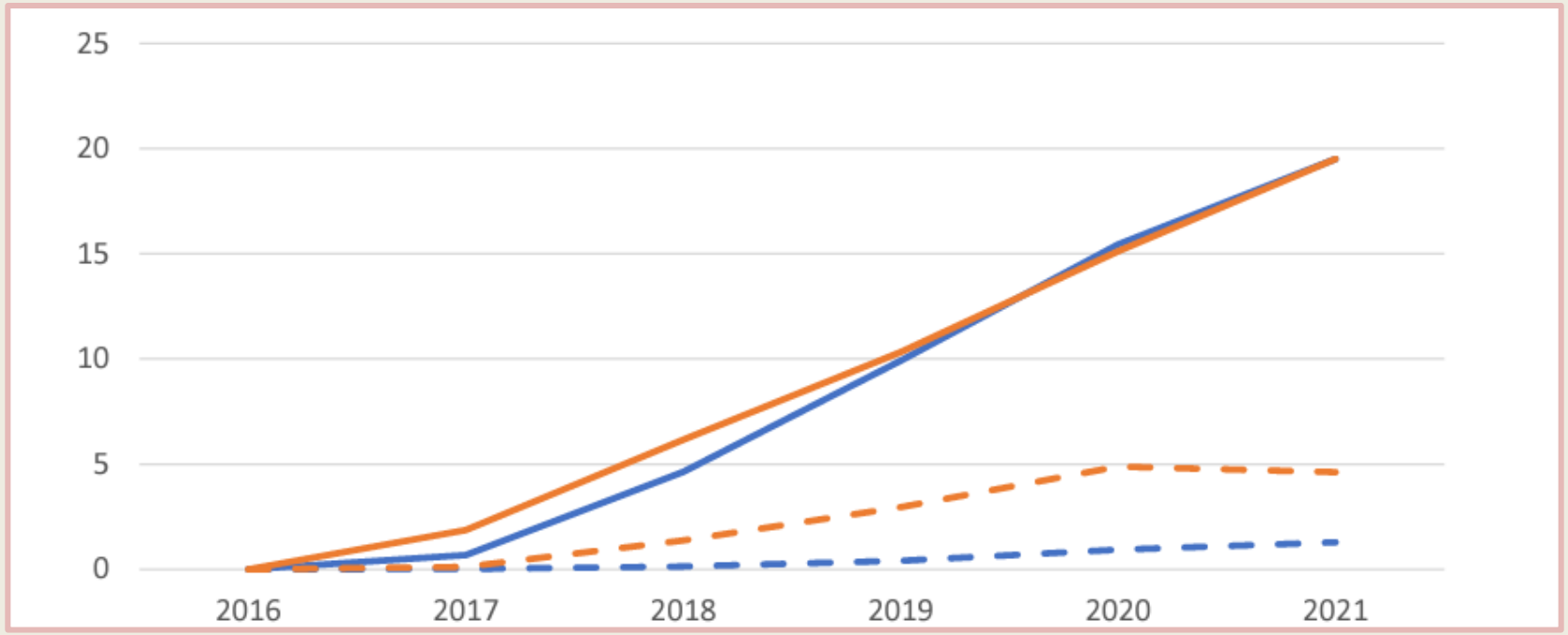
- By the year 2021 , specialty drugs were more than 40% of retail drug spend and nearly 70% of non-retail drug spend
- Spending growth largely due to higher prices per prescription, not increases in utilization

Specialty Drug Expenditures (in Inflation Adjusted Dollars), 2016-2021

	Total Specialty Spending Billions, $	Number of Specialty Prescriptions Millions	Retail Spending		Non-Retail Spending	
			% Retail Spending on Specialty	% Retail Prescriptions on Specialty	% Non-Retail Spending on Specialty	% Non-Retail Prescriptions on Specialty
2016	211	1,107	34.3	18.9	57.2	6.4
2017	225	1,160	36.5	19.3	60.0	6.8
2018	245	1,443	37.6	21.3	63.6	11.0
2019	268	1,413	39.7	20.4	65.8	9.8
2020	287	1,161	41.3	16.9	67.8	9.1
2021	301	1,113	41.8	15.4	68.8	8.9
% Change 2016-2021	42.5%	0.5%	21.9%	-18.3%	20.3%	40.0%

Source: ASPE analysis of IQVIA data. All dollar amounts include an adjustment for inflation so they represent a “real dollar” as of quarter 1 of 2022.

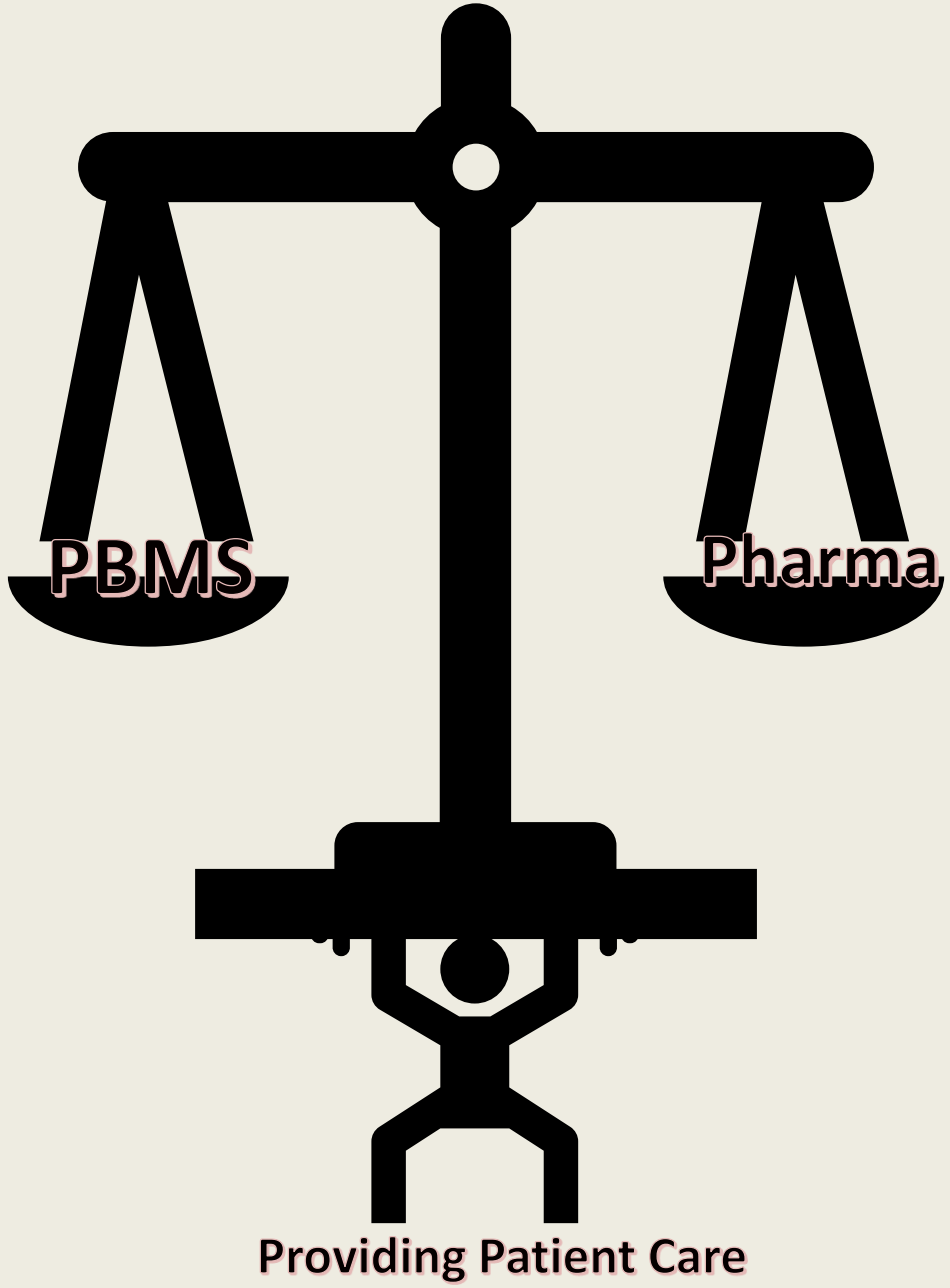
Share of New Drugs (Introduced Since 2016) as a Share of Specialty Drug Spending, 2016-2021



Specialty Pharmacy Continues to Grow

- Larger share of drug approvals are for specialty medications
- Nearly 80% of drugs the FDA was slated to approve in 2023 were for specialty medications[1]
- In the retail setting, 1% of prescriptions for new specialty drugs accounted for 20% of spending ($25billion) in the US

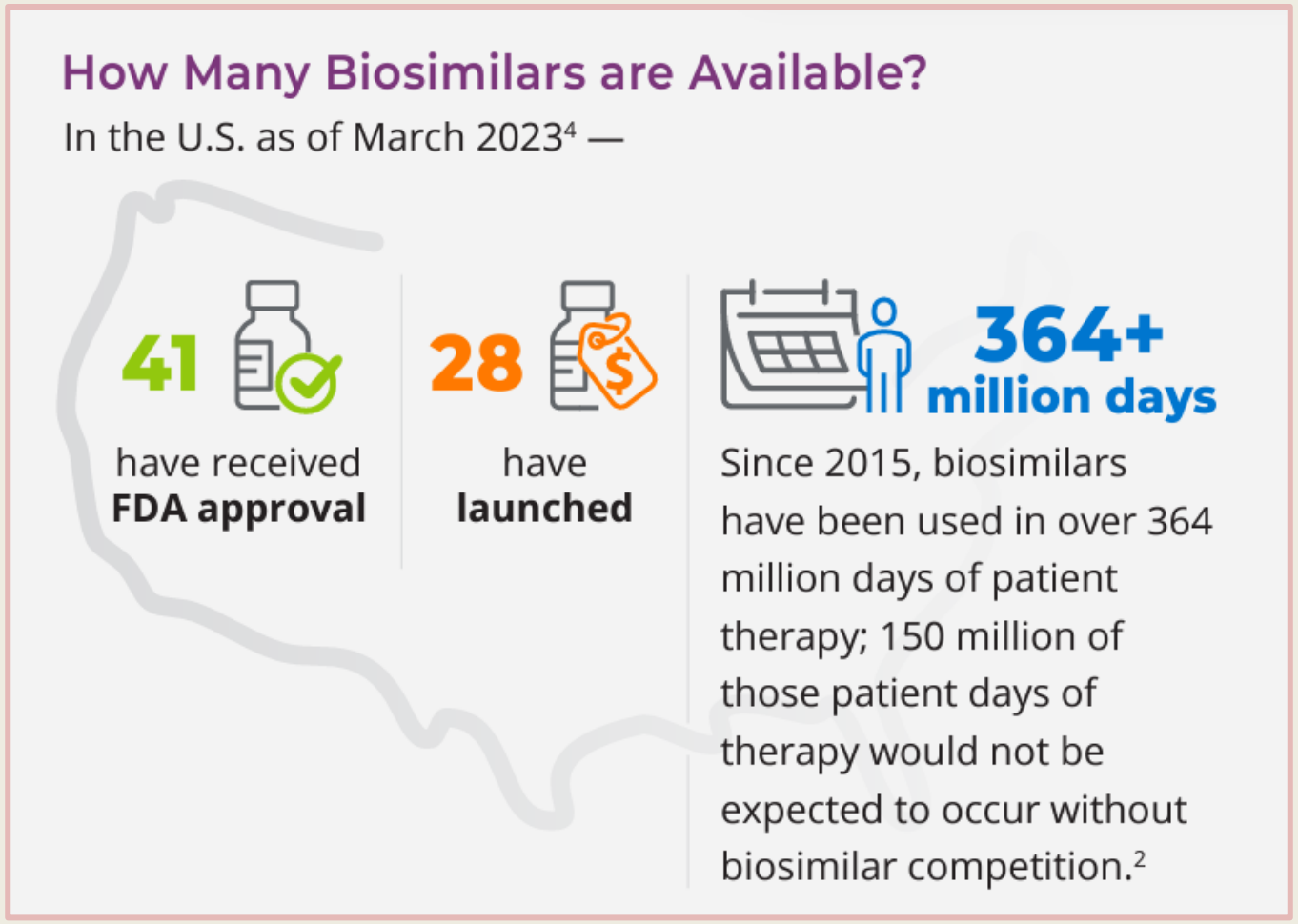
The Balancing Act



Enter: Biosimilars

- Lots of promises!
  - Overall cost savings!
  - Improved affordability for patients!
  - Better access to medications!
- Legalities with patents made some products slow to come to market
- Let's do a pulse check...

AMCP Infographic



Formulary Placement

We know there are many factors that go into formulary placement of products

Rebates play a large role with many commercial plans

From a practical standpoint, it makes the most sense to pursue products that are preferred first

- Coverage changes make patient care challenging with the added layer of purple book substitutions

AWP Comparisons: Insulin Glargine

Product	**AWP (March 2024)**
LANTUS SOLOSTAR PEN© (15ML) *insulin glargine*	$115.66
BASAGLAR KWIKPEN© (15ML) *insulin glargine*	$391.63
INSULIN GLARGINE PEN© (15ML)	$204.14
INSULIN GLARGINE-YFGN PEN© (15ML)	$110.40
SEMGLEE-YFGN PEN© (15ML)	$484.85
REZVOGLAR© (15ML) *insulin glargine-aglr*	$110.40

AWP Comparisons: adalimumab

Product: AWP Listed for typical 28DS	AWP (March 2024)
HUMIRA PENS© adalimumab	$8307.14
ABRILADA© adalimumab-afzb	$7891.79
AMJEVITA© adalimumab-atto	$1662.26
CYLTEZO © adalimumab-adbm	$7891.79
HADLIMA© adalimumab-bwwd	$1245.60
HULIO © adalimumab-fkjp	$7891.79
Adalimumab-fkjp	$1194.00
HYRIMOZ © adalimumab-adaz	$7891.79
Adalimumab-adaz	$1578.36
Idacio © adalimumab-aacf	$7891.79
Yuflyma © adalimumab-aaty	$1194.00

What are the Two Pricing Strategies Happening in Biosimilars?

In the pharmacy benefit space, the same product is sometimes offered at two different price points. One includes a small discount off the reference-product's list price with the assumption that it will be supplemented by rebates, and the second option provides a larger discount off the reference product's list price, with the assumption that there would be no rebates. If the lower-cost product is covered, patients will likely have lower out-of-pocket costs and the net costs to health plans and employers will be similar. Of note, the lower cost product would likely decrease rebate revenue.

What is an Example of the Two Pricing Strategies?

AMJEVITA™ (adalimumab-atto), a biosimilar to HUMIRA® (adalimumab), has NDCs (packages) offered at two price points. The high list price option is 5% less than HUMIRA's list price while the low is 55% less.[5] The high list price option would likely provide rebates to the payer and offer plan design flexibility, but it may not provide incentives for patients to switch to a biosimilar and lower their cost share.

How Important are Out-of-Pocket Costs to Patient Adherence?

Very important. Studies have shown that high patient out-of-pocket costs can negatively impact patient adherence, persistence, and/or discontinuation of therapy. This can lead to higher overall health care costs in the future.[6] In addition, increased medication adherence lowers indirect costs (like workdays missed) compared to non-adherent patients.[7]

PBM Response: What We've Seen with insulins

In previous years, no major PBM formulary has preferred the lower priced versions of branded insulin products (potentially rebate-driven decisions) however, Eli Lilly, Novo Nordisk and Sanofi have all reduced their WAC pricing by 65-75%

- Price reduction has limited PBM ability to block the lower-priced products from their formularies.

All of the formularies for the different PBMs vary quite a bit—it's difficult to encompass on one page! This information is so fluid and is always subject to change

- OptumRx: most recently has all products on first tier, which does help with lowering patient out of pocket cost
- Express Scripts: tends to have preference of the higher priced products, but includes Semglee©, the high-priced glargine biosimilar (low-priced version and Rezvoglar© excluded)
- CVS includes Lantus©, excludes biosimilar Basaglar© and the formulary doesn't mention Semglee©, unbranded Semglee©, or Rezvoglar

PBM Response: What We've Seen with adalimumab

CVS Caremark, Express Scripts, and OptumRx have all placed Sandoz biosimilars on their formularies

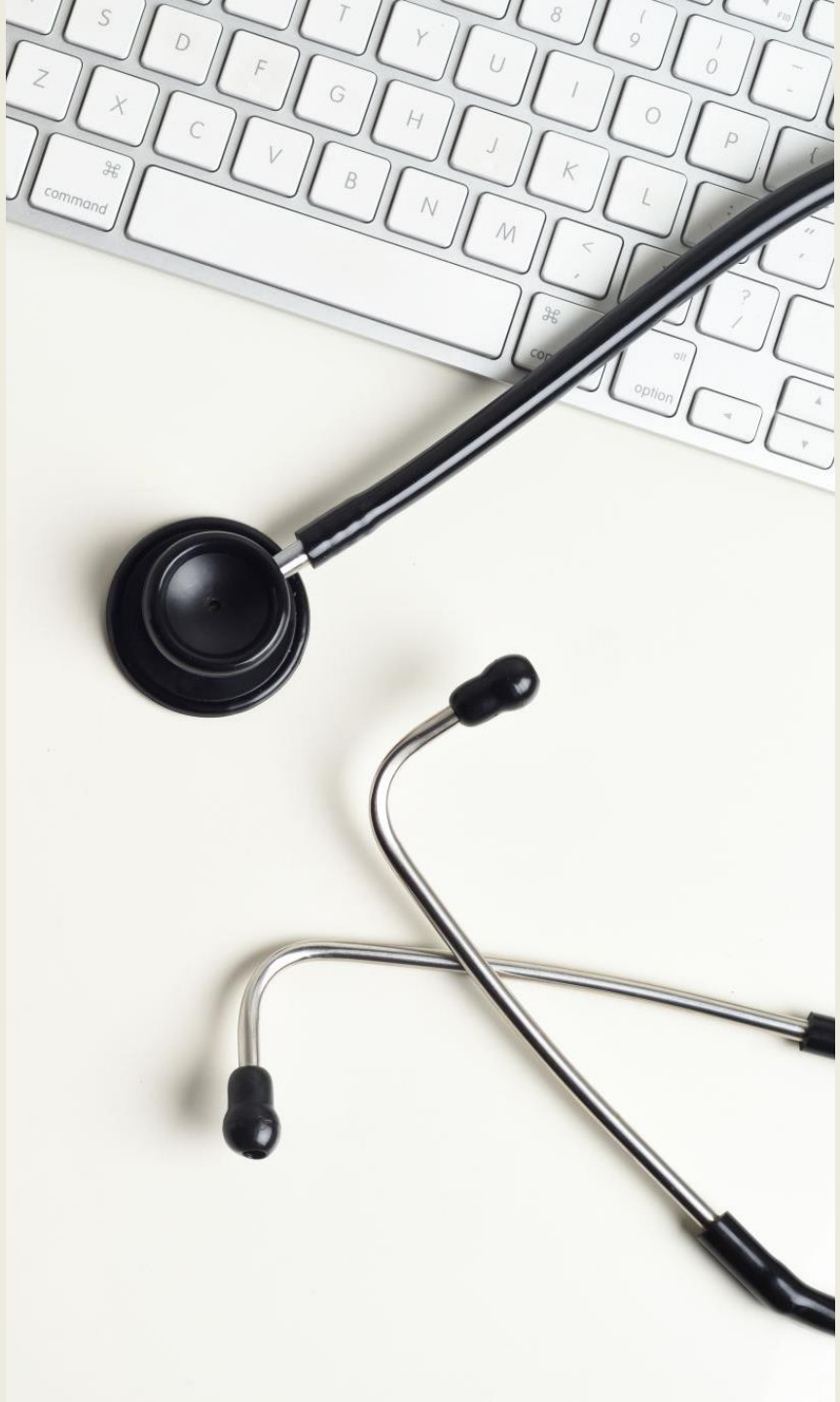
- Express Scripts and OptumRx also have interchangeable products from Boehringer Ingelheim
- Optum has also maintained formulary placement for Amgen's product
- These decisions mean that the manufacturers of the non-selected products will struggle to gain traction in the marketplace

Many of the PBMs have both the high and low list price products from the same manufacturers—this means that the health plans themselves are still utilizing rebate programs

- Plans that adopt the higher priced products will have larger rebates but patient responsibility (coinsurance and deductibles) will likely end up being more

Most rebates (not all) are passed through PBMs back to the plan sponsors

- Employers use these dollars to offset non-drug healthcare costs and reduce premiums for all beneficiaries, not just those receiving Humira



Reminder

- Patient access to treatment and out of pocket costs are determined by both PBM formulary decisions and their benefit structures
  - Exclusion lists also exist and play a role in something we call “non-medical” switching
  - Exclusions sometimes include lower-priced products which also impacts a patient’s out of pocket cost


HELLO I'M
trying my best

Learning Objectives

At the completion of this activity, the participant will be able to:

Define	Describe	Explain	Identify	Summarize	Describe
Define what a biologic product is	Describe the difference between a generic and a biosimilar drug product	Explain the different regulatory approval pathways for reference products and biosimilars	Identify selected biosimilars, their associated nomenclatures, and the disease states for which they are indicated	Summarize patient assistance and copay card options for biosimilars	Describe managed care implications of biosimilar availability and the potential impact of such availability on patient care

Need More Information?

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Outpatient Clinical Pharmacists: Specialty Pharmacy

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Specialty drugs are defined by IQVIA as products used to treat chronic, rare or complex diseases and that meet 4 or more of the following criteria[3]:

- Initiated and maintained by a specialist
- Generally injectable and/or not self-administered
- Products that require an additional level of care in their chain of custody (i.e., refrigerated, frozen, chemo, biohazard, etc.)
- Expensive (USD $6K annual cost of therapy)
- Unique distribution (e.g., specialty MO, REMS)
- Requires extensive or in-depth monitoring/patient counseling
- Requires reimbursement assistance
- Products that clearly meet the above criteria are defined as Specialty. Products that are borderline (e.g. meet three, rather than four criteria) will be brought before the Specialty Governance Board for review and final decision.

Appendix 1: IVQA Analysis Definition of Specialty

Formulary Coverage for Humira and Its Biosimilars, by PBM, 2024

Product name	Manufacturer	WAC (2023)	WAC vs. Humira	Express Scripts	CVS Caremark	OptumRx
Humira	AbbVie	$6,922	n.a.	✓	✓[4]	✓
Humira[4]	AbbVie/Cordavis	TBD	-0%	-	-[4]	-
Amjevita (High WAC)	Amgen	$6,576	-5%	-	-	✓
Amjevita (Low WAC)	Amgen	$3,115	-55%	-	-	✓
Hulio	Biocon Biologics	$6,576	-5%	-	-[3]	-
adalimumab-fkjp	Biocon Biologics	$995	-86%	-	-[3]	-
Cyltezo[1]	Boehringer Ingelheim	$6,576	-5%	✓	-[3]	✓
adalimumab-adbm[1]	Boehringer Ingelheim	$1,315	-81%	✓	-[3]	✓
Yuflyma[2]	Celltrion	$6,576	-5%	-	-[3]	-
Yusimry	Coherus	$995	-86%	-	-[3]	-
Idacio	Fresenius Kabi	$6,576	-5%	-	-[3]	-
Abrilada[1]	Pfizer	$6,576	-5%	-	-[3]	-[3]
Hadlima[2]	Samsung Bioepis/Organon	$1,038	-85%	-	-[3]	-
Hyrimoz[2]	Sandoz	$6,576	-5%	✓	✓	✓
Hyrimoz[2]	Sandoz/Cordavis	$1,315	-81%	-	✓	-
adalimumab-adaz[2]	Sandoz	$1,315	-81%	✓	✓	✓

WAC = wholesale acquisition cost
1. Indicates product is interchangeable with Humira reference product.
2. Indicates product is available in high concentration formulation.
3. Indicates that product's status was not identified in published formulary lists.
4. In April 2024, CVS Caremark will remove both Humira and the co-branded Cordavis Humira from its major commercial formularies. Both products will remain on CVS Caremark's Choice and Standard Opt Out commercial formularies., which account for a small share of its customers and covered lives.
Source: Drug Channels Institute research. Table shows products approved as of January 1, 2024.
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APPENDIX 2 FORMULARY COVERAGE