Biosimilars: Where we've been and where we're headed

Sonia T. Oskouei, PharmD, BCMAS, DPLA

Vice President, Biosimilars
Cardinal Health

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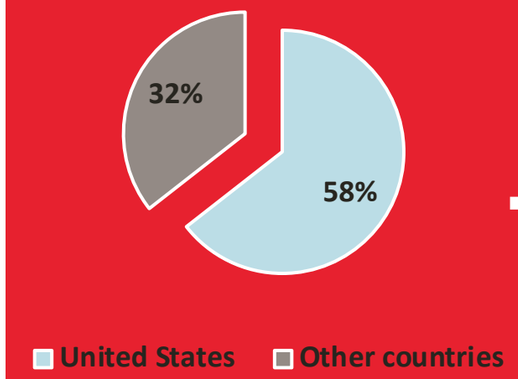
Objectives

- Discuss the current U.S. biosimilars landscape and market dynamics
- Review the U.S. biosimilars pipeline
- Understand recent policy activity that may influence biosimilar utilization
- Review various resources to support effective management of biosimilar products

Why biosimilars matter to the U.S. healthcare system

Biologics economic impact

Biologics are the most expensive drug category in the U.S. and world



Pharmaceutical prices in the U.S.

The U.S. has the highest pharmaceutical prices in the world. In 2018, the US accounted for 58% of global drug sales, but only 24% of volume.

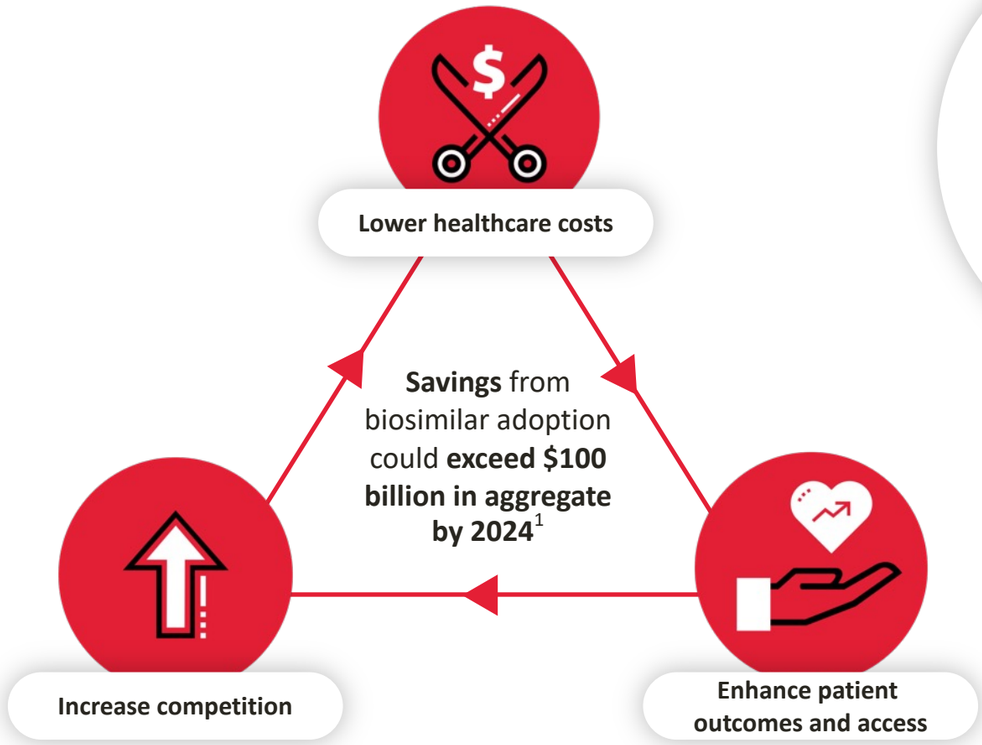
Economic burden associated with oncology care

Biologics used for treating many oncology related diseases may cost over $100,000 per year

Mulcahy W et al. International Prescription Drug Price Comparisons. RAND Corporation. www.rand.org/pubs/research_reports/RR2956.html. Accessed July 19, 2021.

2. AJMC. Utilizing Oncology Biosimilars to Minimize the Economic Burden Associated with Cancer Treatment. https://www.ajmc.com/view/utilizing-oncology-biosimilars-to-minimize-the-economic-burden-associated-with-cancer-treatment-managed-care-considerations. Accessed Oct. 3, 2022

Biosimilars target drugs with highest spending



There are more than 100 biosimilars in development across 22 molecules

Top Drugs by Overall Expenditure in 2021[2]

	Name	Category	2021 Expenditure
1	**Humira (adalimumab)**	Immunology	28,498M
2	**Eliquis (apixaban)**	Anticoagulant	15,795M
3	**Trulicity (dulaglutide)**	Diabetes	12,198M
4	**Ozempic (semaglutide)**	Diabetes	10,718M
5	**Stelara (ustekinumab)**	Immunology	10,682M
6	**Lantus (insulin glargine)**	Diabetes	10,027M
7	**Keytruda (pembrolizumab)**	Oncology	9,861M
8	**Biktarvy** (bictegravir/ emtricitabine/tenofovir/ alafenamide)	HIV	9,570M
9	**Enbrel (etanercept)**	Immunology	8,095M
10	**Jardiance (empagliflozin)**	Diabetes	8,022M
11	**Xarelto (rivaroxaban)**	Anticoagulant	7,135M
12	**Januvia (sitagliptin)**	Diabetes	6,407M
13	**Novolog (insulin aspart)**	Diabetes	6,043M
14	**Humalog (insulin lispro)**	Diabetes	5,701M
15	**Dupixent (dupilumab)**	Immunology	5,605M
16	**Immune globulin**	Blood	5,371M
17	**Cosentyx (secukinumab)**	Immunology	4,613M
18	**Victoza (liraglutide)**	Diabetes	4,546M
19	**Epinephrine**	Hormone	4,382M
20	**Opdivo (nivolumab)**	Oncology	4,223M

= has biosimilar approved or in pipeline

Reference: 1. Aitken M, Kleinrock M, Muñoz E. Biosimilars in the United States 2020-2024: competition, savings, and sustainability. IQVIA. September 29, 2020. https://www.iqvia.com/insights/the-iqvia-institute/reports/biosimilars-in-the-united-states-2020-2024 2. Tichy EM, Schumock GT, Hoffman JM, et al. National trends in prescription drug expenditures and projections for 2020. *Am J Health Syst Pharm*. 2020;77(15):1213-1230. https://pubmed.ncbi.nlm.nih.gov/32412055/

U.S. biosimilar market dynamics

Current U.S. biosimilars landscape

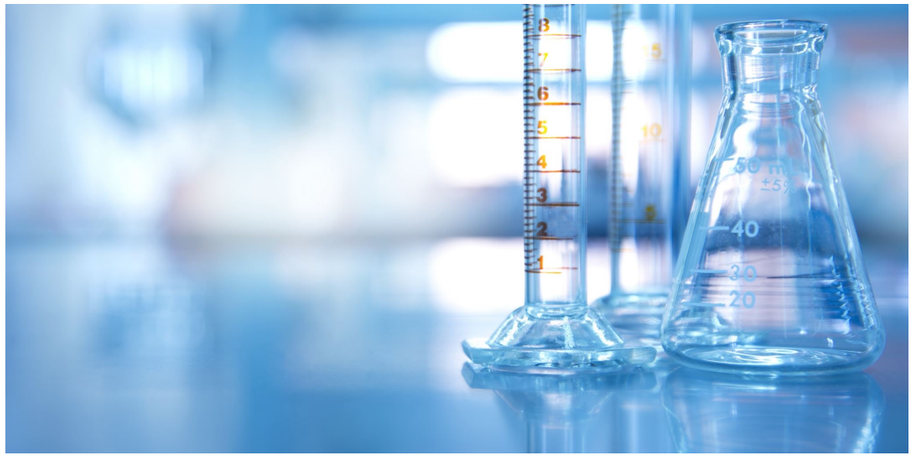
Significant growth in the past two years

U.S. market as of Oct 2022:

- 39 FDA-approved biosimilars; **23** commercially available

New biosimilar approvals during 2022

- Releuko – Amneal **filgrastim biosimilar**
- Alymsys – Amneal **bevacizumab biosimilar**
- Vegzelma – Celltrion **bevacizumab biosimilar**
- Fylnetra – Amneal **pegfilgrastim biosimilar**
- Stimufend – Fresenius Kabi **pegfilgrastim biosimilar**
- Cimerli – Coherus ranibizumab biosimilar



2022 Cardinal Health Biosimilars Report.
Available at: www.cardinalhealth.com/en/product-solutions/pharmaceutical-products/biosimilars/biosimilars-report.html.

Overall U.S. biosimilars market share

Product	Category	1st biosimilar launch	Current # biosimilar competitors	Biosimilar market share (July 2022)
Neupogen (filgrastim)	Supportive Care	2015	2[1]	**93%[1]**
Remicade (infliximab)	Immunology	2016	3	**42%**
Epogen/Procrit (epoetin alfa)	Supportive Care	2018	1	**43%**
Neulasta (pegfilgrastim)	Supportive Care	2018	4[2]	**42%**
Avastin (bevacizumab)	Oncology	2019	2[3]	**80%**
Herceptin (trastuzumab)	Oncology	2019	5	**64%**
Rituxan (rituximab)	Oncology	2019	3	**69%**
Lantus (insulin glargine)	Diabetes	2020*	1[4]	**9%**
Lucentis (ranibizumab)	Ophthalmology	2022	2	**0%**
9 Product Classes		**--**	**23**	**--**
Humira (adalimumab)	*Immunology*	*2023*	*7*	*Not Launched*
Enbrel (etanercept)	*Immunology*	*2029*	*2*	*Not Launched*

1Includes Teva's Granix, which is technically not a biosimilar since it was filed prior to the enactment of the Biosimilar Approval Pathway. Amneal's Releuko has not launched yet.
2Amneal's Fylnetra has not launched yet; Fresenius Kabo's stimufend has not launched yet
3Amneal's Alymsys has not launched yet; Celltrion Vegzelma has not launched yet
4Excludes Basaglar and yet to be launched Rezvoglar
*Neulasta Syr. Only biosimilars share is 77%
Note: italicized represents approved biosimilars that have not launched in the U.S. yet

IQVIA: Accessed via IQVIA National Sales Perspective (NSP) SMART Data. Sept 2022.

Considerations for biosimilar adoption in the U.S. cannot be generalized across products

Biosimilar considerations vary by:

- **Therapeutic area** (e.g., oncology vs rheumatology vs endocrinology)
- **Site of care** (e.g., inpatient vs outpatient, community practice vs health system)
- **Treatment type** (e.g., disease modifying vs supportive care)
- **Institution type** (e.g., 340B vs non-340B, value- based care participation)
- **Product type** (e.g., buy-and-bill vs retail)
- **Manufacturer commercialization strategy**

Financial

Clinical

Operational

Regulatory

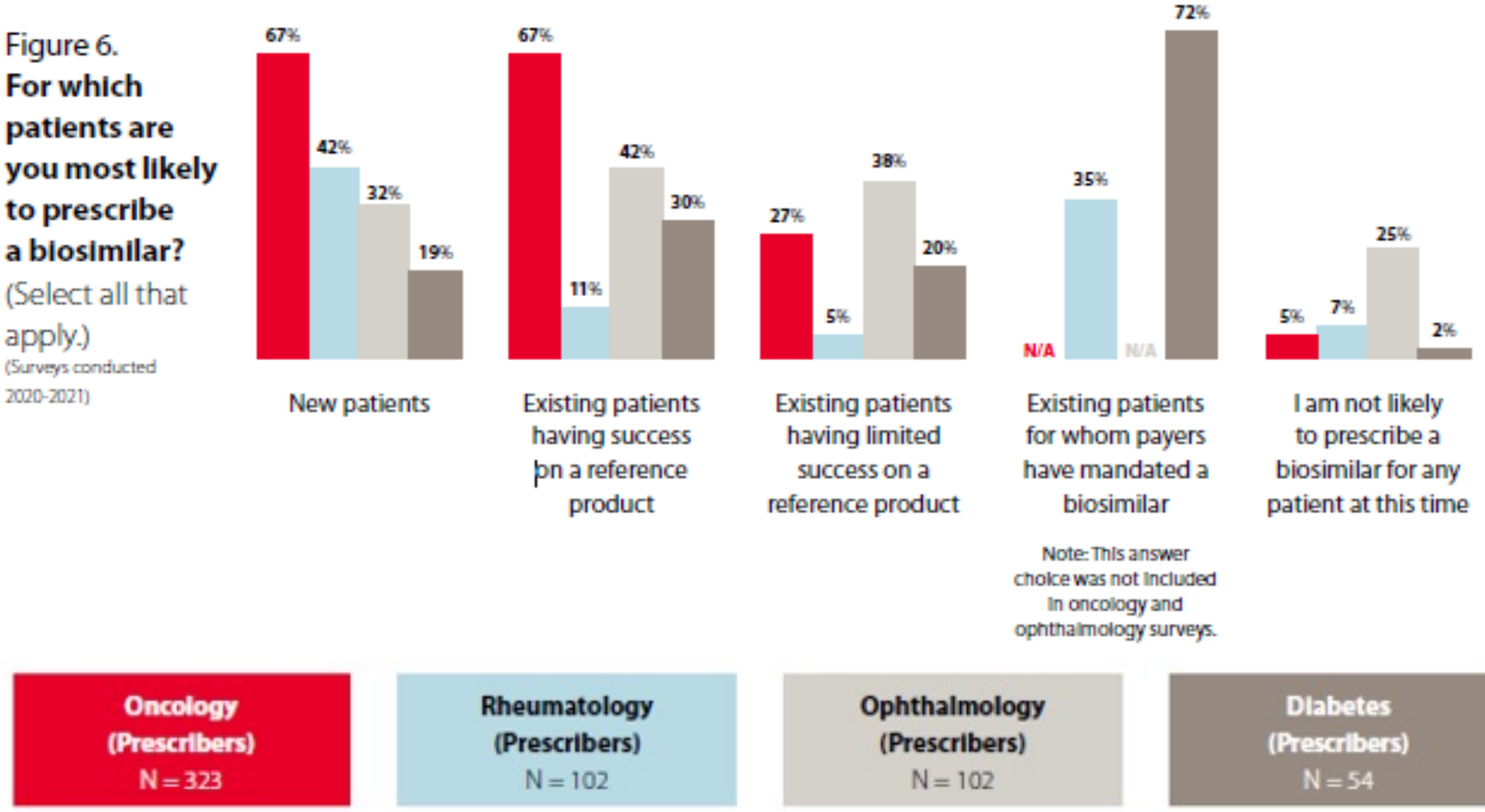
Perceptions on biosimilar prescribing continue to vary by specialty

Strong biosimilar acceptance and utilization in oncology

- >70% of surveyed oncologists feel comfortable switching between biosimilars
- Majority of surveyed oncologists feel comfortable switching patients to biosimilars for both curative and palliative intent

Greater hesitation with biosimilar utilization (generally or in switching scenarios) within rheumatology and ophthalmology

Figure 6.
For which patients are you most likely to prescribe a biosimilar?
(Select all that apply.)
(Surveys conducted 2020-2021)



Source: 2022 Cardinal Health Biosimilars Report: the U.S. journey and path ahead. Cardinal Health. Published Feb 2022. Available at: https://www.cardinalhealth.com/en/product-solutions/pharmaceutical-products/biosimilars/biosimilars-report.html

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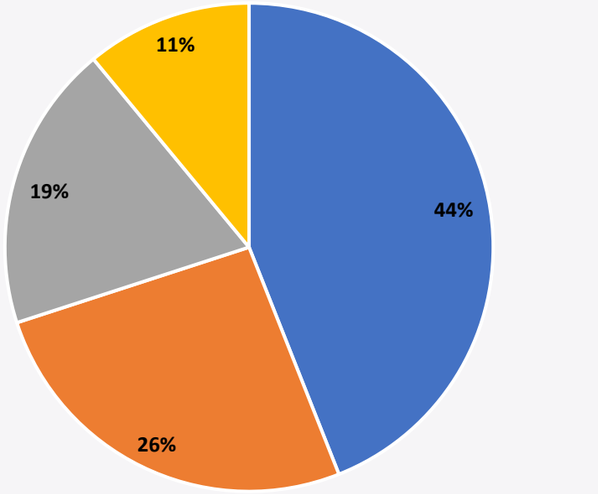
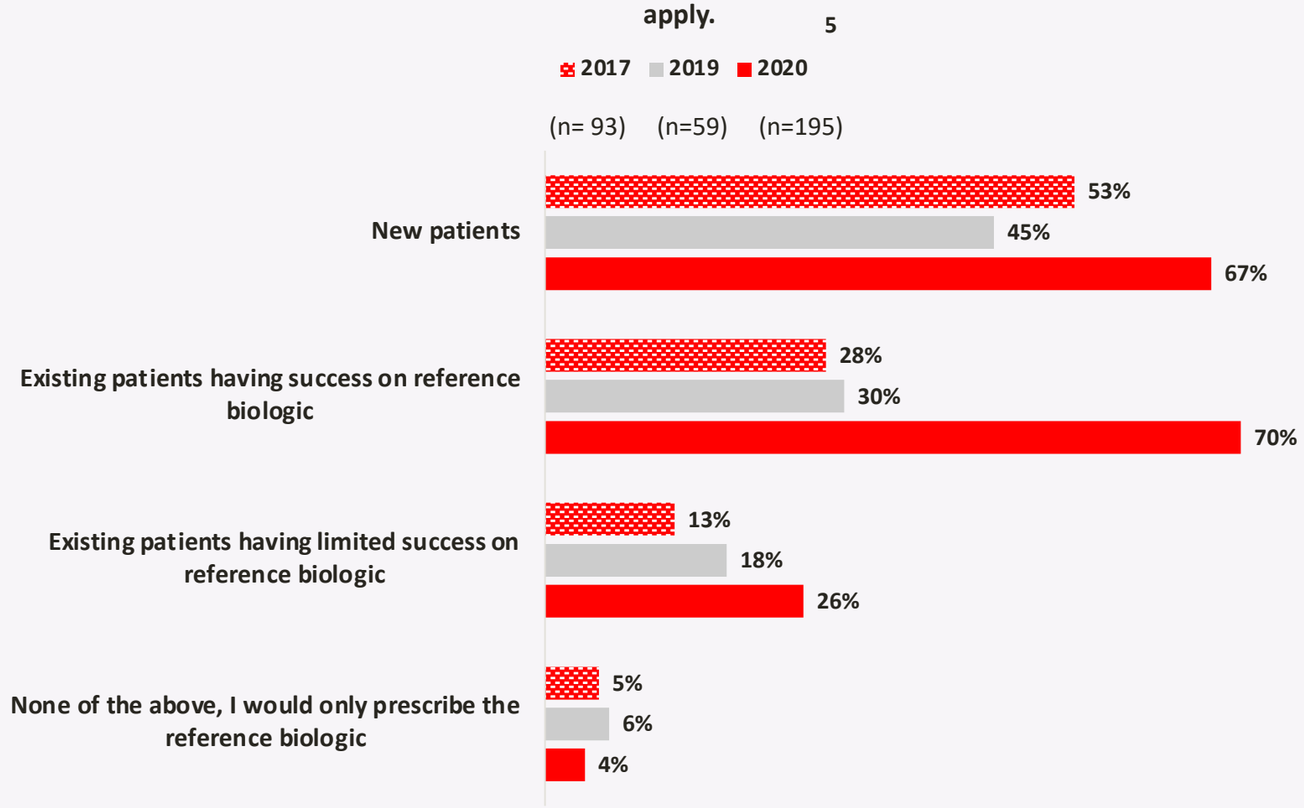
Provider Willingness to Prescribe Biosimilars for Existing Patients on Reference Biologics Has Significantly Increased

(2015-2017) **To which of these patient types are you prescribing or would you prescribe Zarxio? Please select all that apply. (n=280)**



For which patients would you likely prescribe biosimilars in cancer therapy? Select all that apply.



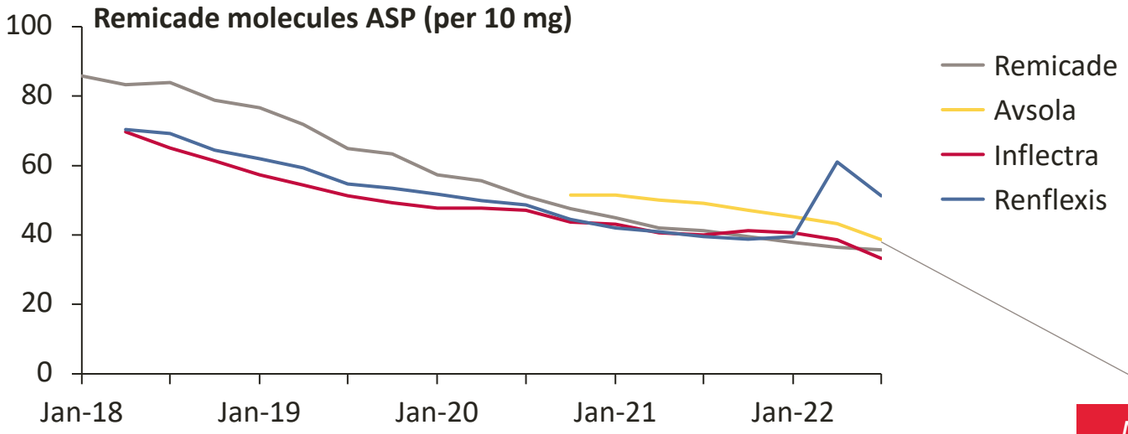
Biosimilar and brand manufacturer strategies vary

Biosimilar strategy examples

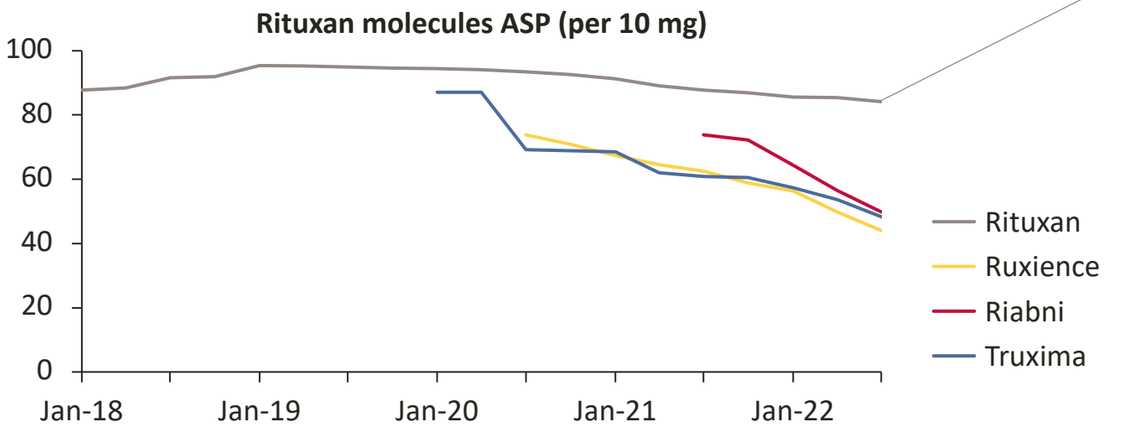
- *Brand-like* approach
- *Market similar* with *wrap-around services* (e.g., patient hub services)
- Multiple distribution channels
- Contracting/sourcing programs

Brand strategy examples

- Payer rebates for preferred status
- Portfolio/"basket" contracts
- Pricing strategies vary (see ASP chart)
- Innovative administration forms or combination products
- Patent protections



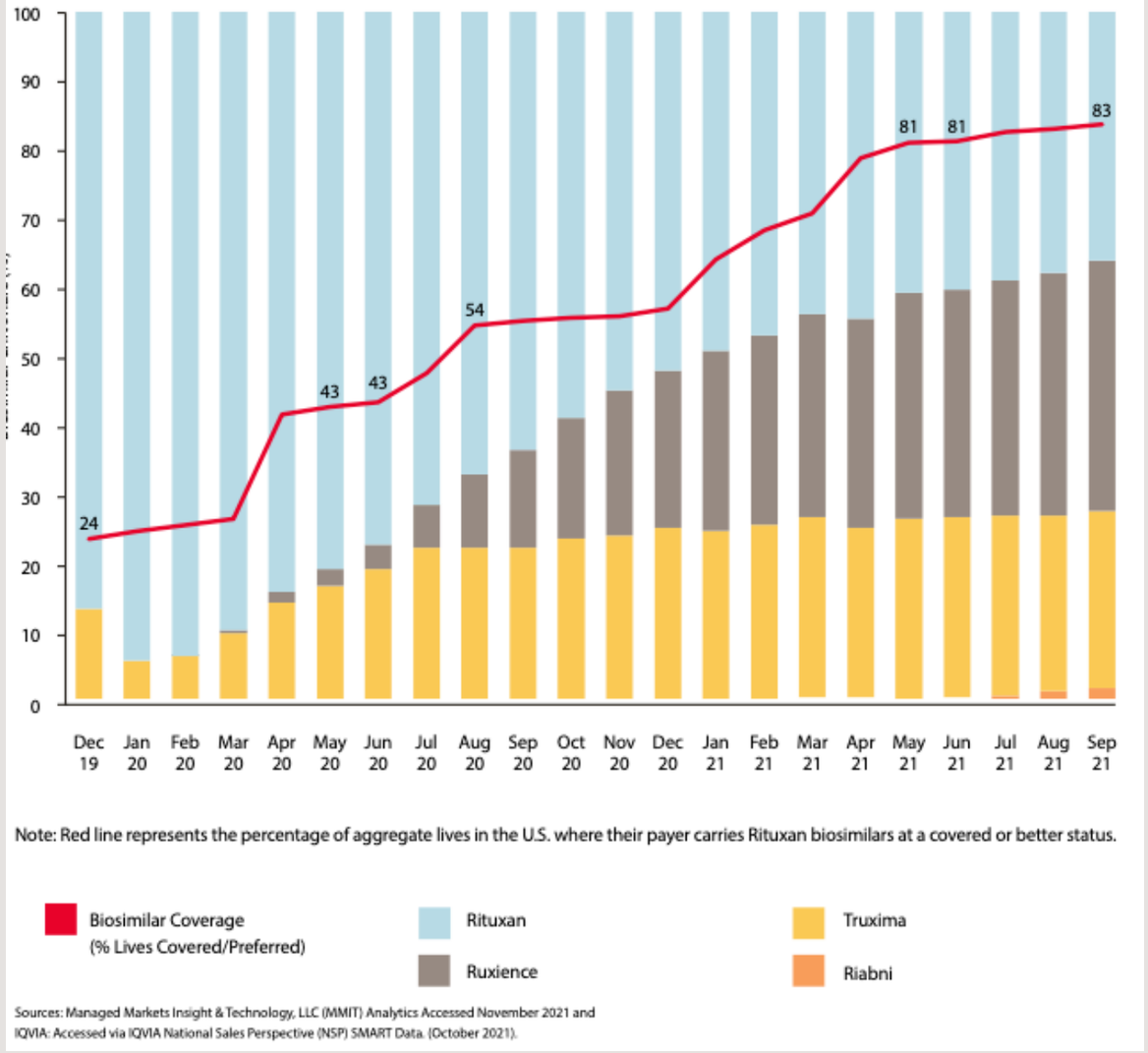
Note differences in brand reactions to biosimilar entry



Strong correlations between biosimilar adoption and payer coverage activity

- As an example, there is a 97% correlation between Rituxan biosimilars adoption and the percentage of plans covering Rituxan biosimilars at parity or in preferred positions.

Figure 42. **Rituxan Biosimilars Adoption vs. % of Covered or Better Status**



Note: Red line represents the percentage of aggregate lives in the U.S. where their payer carries Rituxan biosimilars at a covered or better status.

Sources: Managed Markets Insight & Technology, LLC (MMIT) Analytics Accessed November 2021 and IQVIA: Accessed via IQVIA National Sales Perspective (NSP) SMART Data. (October 2021).

Source: 2022 Cardinal Health Biosimilars Report: the U.S. journey and path ahead. Cardinal Health. Published Feb 2022. Available at: https://www.cardinalhealth.com/en/product-solutions/pharmaceutical-products/biosimilars/biosimilars-report.html

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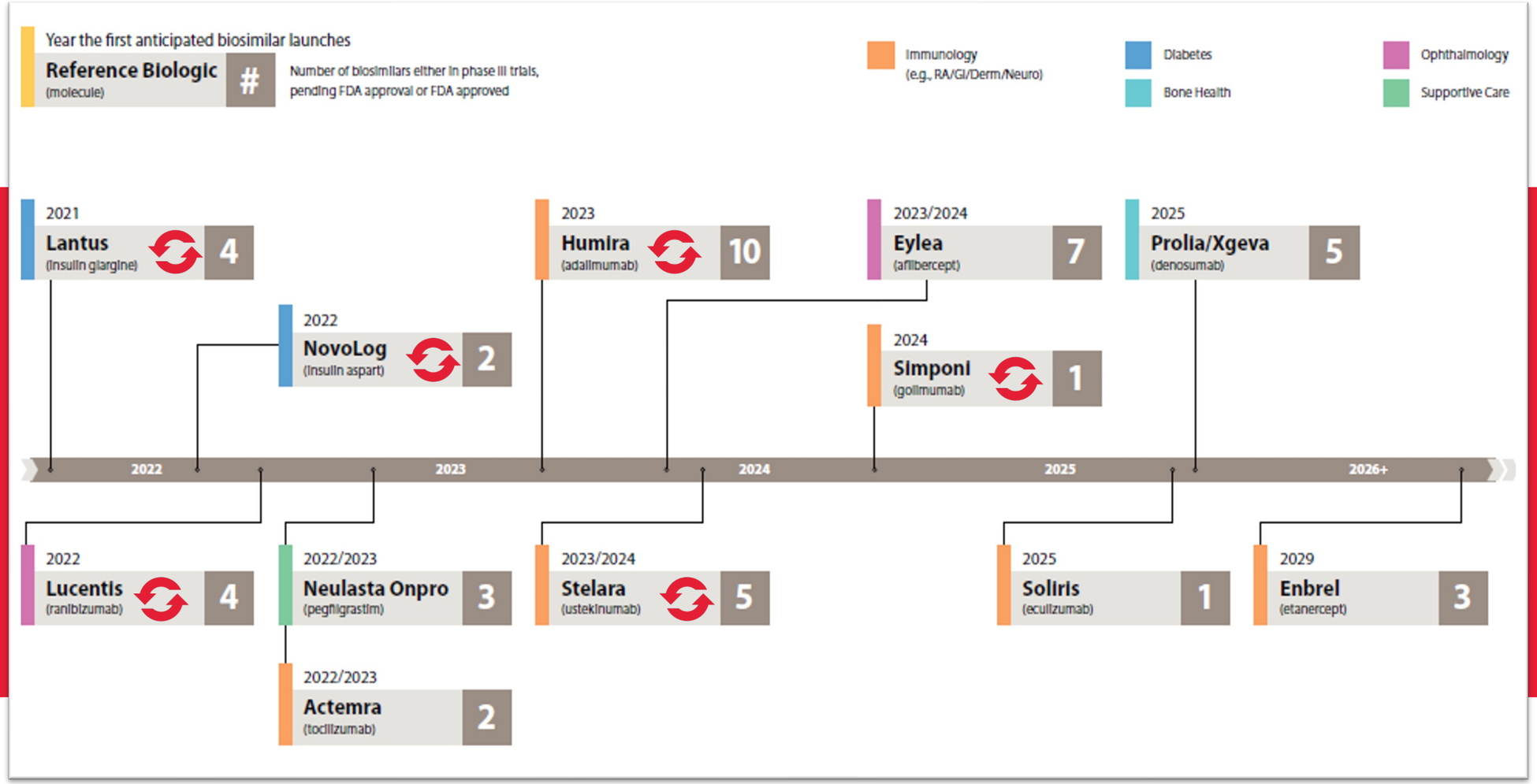
Biosimilars pipeline and opportunities in oncology

Biosimilars Pipeline

The number of biologics facing biosimilar competition will more than *double* by 2026



=has a biosimilar candidate that is seeking interchangeability designation

Source: IPD Analytics. Market & Financial Insights. December 2021. https://www.ipdanalytics.com.
Source: 2022 Cardinal Health Biosimilars Report: the U.S. journey and path ahead. Cardinal Health. Published Feb 2022. Available at: https://www.cardinalhealth.com/en/product-solutions/pharmaceutical-products/biosimilars/biosimilars-report.html

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Additional 2022 oncology biosimilar approvals

- **3rd filgrastim biosimilar**
  - Amneal's Releuko
- **3rd and 4th bevacizumab biosimilars**
  - Amneal's Alymsys
  - Celltrion's Vegzelma
- **5th pegfilgrastim biosimilar**
  - Fresenius Kabi's Stimufend

Snapshot of additional oncology biosimilars activity:

Launched reference product/current biosimilars	Pending biosimilars in 2022	Pending biosimilars – launch TBD
Avastin (bevacizumab)		
Biosimilars: Mvasi (Bevacizumab-awwb) Zirabev (Bevacizumab-bvzr)	BEVZ92 (Amneal) – Q2 2022 BAT1706 (Bio-Thera) – Q4 2022 FKB238 (Centus/AstraZeneca) – pending approval SB8 (Organon/Samsung) – pending approval Bmab-100 (Viatris/Biocon) – pending approval	TRS003 (TeRuisi)
Epogen/Procrit (epoetin alfa)		
Biosimilars: Retacrit (epoetin alfa-epbx)		APO-EPO (Apotex)
Herceptin (trastuzumab)		
Biosimilars: Herzuma (trastuzumab-pkrb) Kanjinti (trastuzumab-anns) Ogivri (trastuzumab-dkst) Ontruzant (trastuzumab-dttb) Trazimera (trastuzumab-qyyp)		EG12014 (Sandoz) HD201 (Prestige) TX05 (Tanvex)

Launched reference product/current biosimilars	Pending biosimilars in 2022	Pending biosimilars – launch TBD
Neulasta syringe (pegfilgrastim)		
Biosimilars: Udenyca (pegfilgrastim-cbqv) Fulphila (pegfilgrastim-jmdb) Ziextenzo (pegfilgrastim-bmez) Nyvepria (pegfilgrastim-apgf)	Lupifil-P (Lupin) – Q2 2022 MSB11455 (Fresenius Kabi) – pending approval TPI-120 (Adello) – pending approval	Lapelga Neupeg (Apotex/Accord)
Neupogen (filgrastim)		
Biosimilars: Granix† Zarxio (Filgrastim-sndz) Nivestym (Filgrastim-aafi)	TX-01 (Tanvex) – Q2-Q3 2022 Filgrastim Kashiv (Adello/Kashiv) – pending approval	
Rituxan (rituximab)		
Biosimilars: Riabni (rituximab-arrx) Ruxience (rituximab-pvvr) Truxima (rituximab-abbs)		SAIT101 (Archigen/AZ) MabionCD20 DRL RI (Dr. Reddy's)

† Not a biosimilar

Source: IPD Analytics. Market & Financial Insights. Aug 2022. https://www.ipdanalytics.com.

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The biosimilar pipeline will continually replenish as biologics continue to lose exclusivity

Next 10 Years

$273 Billion Global Sales

57 blockbuster product LOEs

The number of blockbuster drugs losing exclusivity is set to rise over the next 10 years

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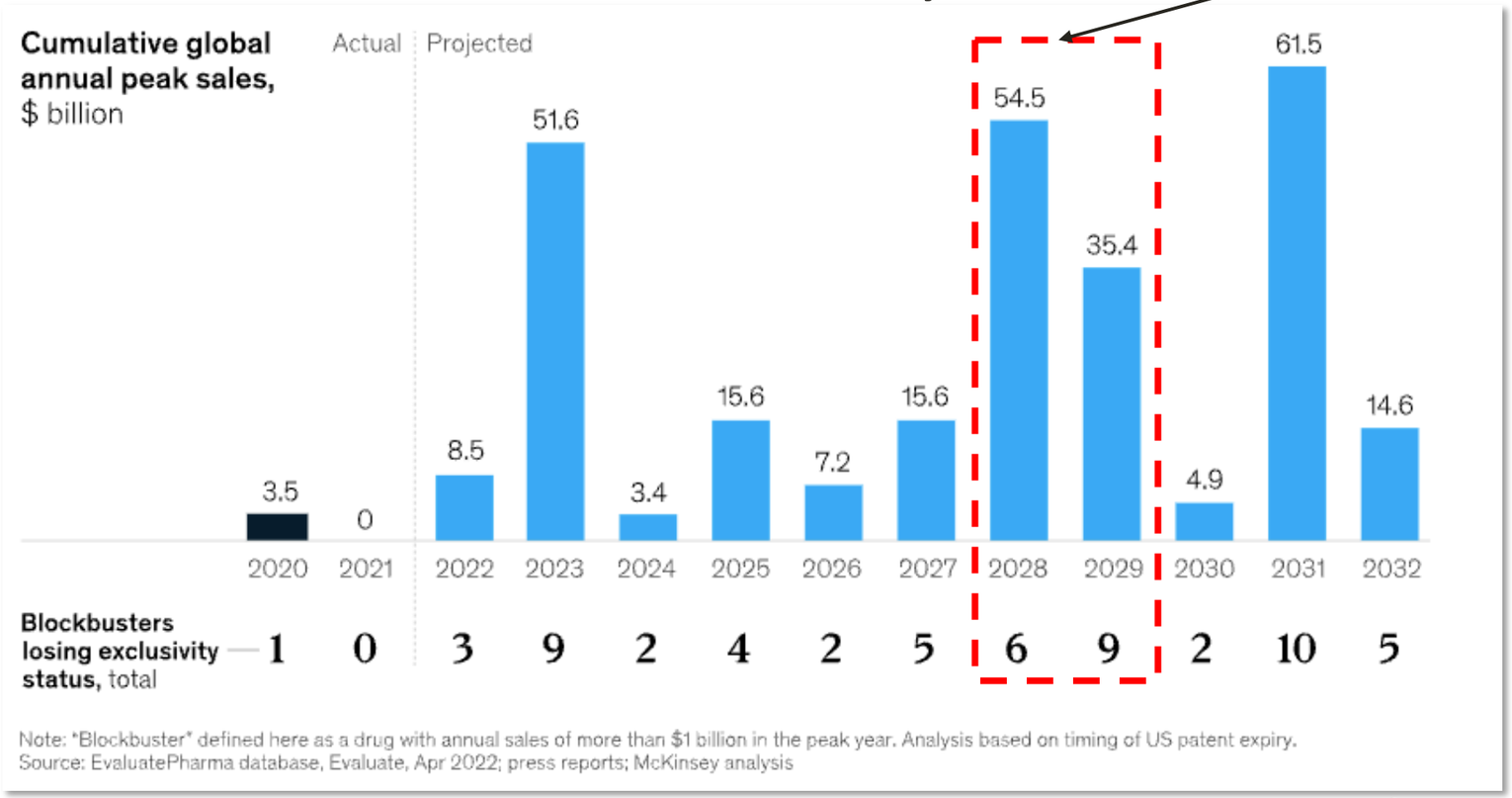

https://www.mckinsey.com/industries/life-sciences/our-insights/three-imperatives-for-r-and-d-in-biosimilars

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Policy Activity

Inflation Reduction Act signed into law August 16, 2022

Prescription drug proposals include:

- Require the federal government to negotiate prices for some drugs covered under Medicare Part B and Part D with the highest total spending, beginning in 2026
- Require drug companies to pay rebates to Medicare if prices rise faster than inflation for drugs used by Medicare beneficiaries, beginning in 2023
- Cap out-of-pocket spending for Medicare Part D enrollees and make other Part D benefit design changes, beginning in 2024
- Limit monthly cost sharing for insulin to $35 for people with Medicare, beginning in 2023
- Eliminate cost sharing for adult vaccines covered under Medicare Part D and improve access to adult vaccines in Medicaid and CHIP, beginning in 2023
- Expand eligibility for full benefits under the Medicare Part D Low-Income Subsidy Program, beginning in 2024
- Further delay implementation of the Trump Administration's drug rebate rule, beginning in 2027

https://www.kff.org/medicare/issue-brief/explaining-the-prescription-drug-provisions-in-the-inflation-reduction-act/
https://www.congress.gov/bill/117th-congress/house-bill/5376

Temporary Increase in Medicare Part B Payment for Certain Biosimilar Products

Inflation Reduction Act signed into law August 16, 2022

- **Under section 11403 of the Inflation Reduction Act, Medicare payment for certain biosimilar biological products is required to be the average sales price (ASP) plus 8 percent (rather than 6 percent) of the ASP of the reference biological for a 5 year period defined in the statute.**
- A qualifying biosimilar biological product is defined as a biosimilar with an ASP that is not more than the ASP of the reference biological.
- In accordance with these provisions, the ASP Drug Pricing File reflects the temporary increased amount for qualifying biosimilar biological products for a period of 5 years beginning with the October 2022 file.
  - October 1, 2022 through December 31, 2027.

https://www.congress.gov/bill/117th-congress/house-bill/5376

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Leveraging U.S. biosimilars experiences thus far to prepare for future biosimilar launches

- Policy activities to ensure a conducive environment for high quality, lower cost treatment options (e.g., cost-savings emphasis and alignment of incentives)

A successful biosimilars market will enable the investment necessary to bring the next generation of innovative treatments to patients

Strategies & resources for effective biosimilars management

Essential considerations for effective biosimilars management

Clinical considerations

- Provider confidence and clinical comfort
- Patient/Caretaker confidence in safety and efficacy
- Patient counseling and education

Financial Considerations

- Product purchase costs
- Reimbursement rates
- Patient out-of-pocket costs
- Patient assistant or copay programs

Operational Considerations

- Procurement and inventory management
- Product storage and refrigeration
- Prior authorization and workflow efficiencies
- EHR and order set maintenance

Ability to adopt/utilize outpatient infused biosimilars are ultimately dictated by payer landscape

Commercial insurers often utilize formulary management tools to control costs and utilization of products

Payer policies can vary by region, patient, and product depending on the time of year

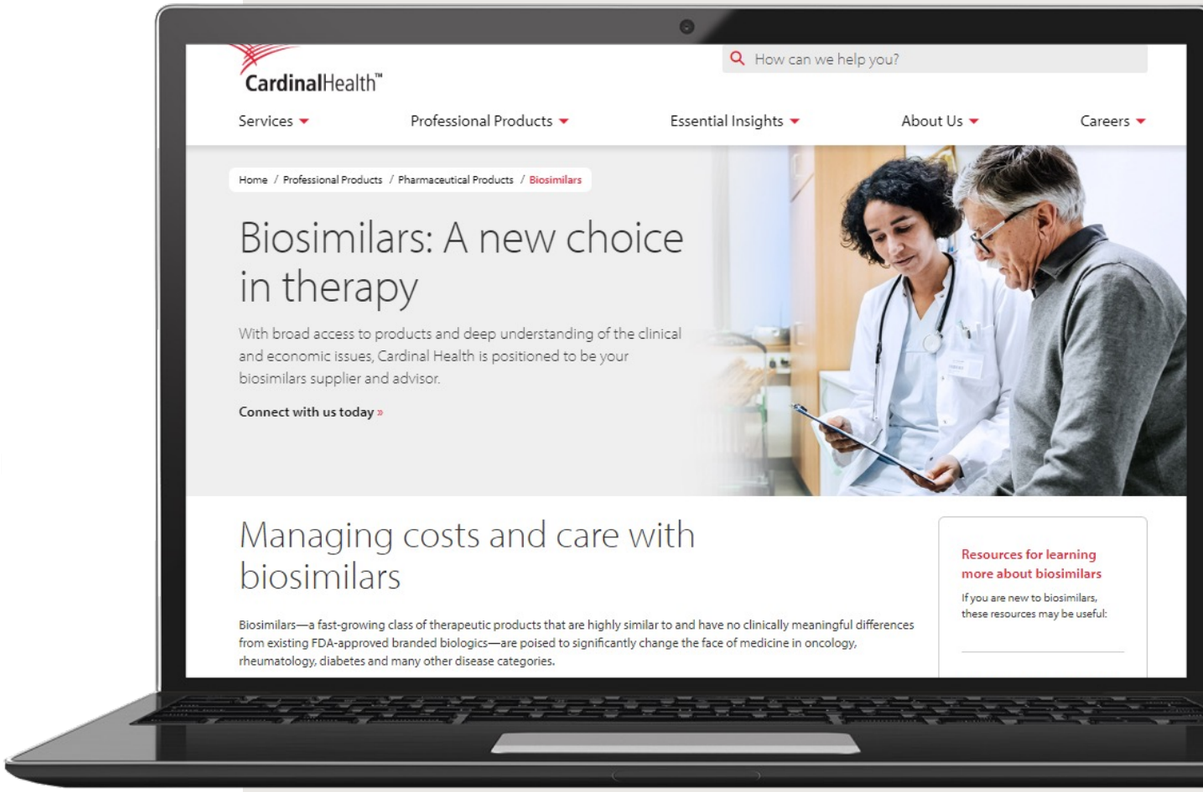
Cardinal Health is dedicated to managing costs and enhancing care with biosimilars

With a broad access to biosimilars and a deep understanding of the considerations for biosimilar utilization, Cardinal Health is positioned to be your trusted healthcare advisor and partner

- Access to biosimilars through multiple distribution channels
- Clinical resources and tools to support evaluation and adoption of biosimilars
- Education and market insights
- Dedicated biosimilars resources and access to subject matter experts

Biosimilars are on track to reduce U.S. drug expenditure by **$133 billion** by 2025[1]

View resources at
cardinalhealth.com/biosimilars



1. Association for Accessible Medicines. (2021, October). *2021 U.S. Generic and Biosimilar Medicines Savings Report*. Retrieved from Association for Accessible Medicines: Generics & Biosimilars: https://accessiblemeds.org/sites/default/files/2021-10/AAM-2021-US-Generic-Biosimilar-Medicines-Savings-Report-web.pdf

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Navigating the biosimilars payer landscape

Cardinal Health has invested in Payer Intelligence tools to help enhance visibility to commercial payer policies

Understand and compare commercial payer policies for both reference products and biosimilars

Understand detailed payer requirements such as step therapy and prior authorization requirements

View product coverage information for specific payers and plans, including number of lives covered

Payer coverage – New Jersey region

Payer	Covered Lives	% of Market	Largest Channel
Horizon BCBS Commercial	2,106k	25.4%	Commercial
Horizon NJ Health Managed Medicaid	1,036k	12.5%	Managed Medicaid
UnitedHealthcare Commercial	941k	11.3%	Commercial
Aetna Commercial	780k	9.4%	Commercial
MAC Jurisdiction L	624k	7.5%	Medicare
Cigna Commercial	493k	5.9%	Commercial
UnitedHealthcare Community Plan Managed Medicaid NJ	365k	4.4%	Managed Medicaid
Amerigroup Managed Medicaid New Jersey	234k	2.8%	Managed Medicaid
UnitedHealthcare Medicare	187k	2.3%	Medicare
Horizon BCBS Health Exchange	168k	2.0%	Health Exchange
Top 10 Totals	**6.9M**	**83.5%**	**Various**

**This information is derived from third party sources and is provided 'as is.'*
Cardinal Health makes no representations or warranties regarding the accuracy or completeness of such third-party information

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Coverage Insights

Top ten health plans in the New Jersey have various access requirements for rituximab molecule usage

Plan	Channel	Lives	% of Market	Biosimilar Step Requirements
Horizon BCBS Commercial	Commercial	2,105,974	25.4%	1 of Ruxience or Truxima
Horizon NJ Managed Medicaid	Managed Medicaid	1,035,710	12.5%	No step requirements, parity coverage
UnitedHealthcare Commercial	Commercial	940,983	11.3%	1 of Ruxience or Truxima
Aetna Commercial	Commercial	780,103	9.4%	Truxima
MAC Jurisdiction L	Medicare	624,462	7.5%	Parity coverage, PA only required for Riabni
Cigna Commercial	Commercial	492,550	5.9%	Riabni, Ruxience, and Truxima all preferred
UnitedHealthcare Community Plan Managed Medicaid NJ	Managed Medicaid	365,304	4.4%	1 of Ruxience or Truxima
Amerigroup Managed Medicaid	Managed Medicaid	233,619	2.8%	Riabni
UnitedHealthcare Medicare	Medicare	187,382	2.3%	1 of Ruxience or Truxima
Horizon BCBS Health Exchange	Health Exchange	167,768	2.0%	1 of Ruxience or Truxima
Top Ten Payers	**Various**	**6,933,855**	**83.5%**	**Various**

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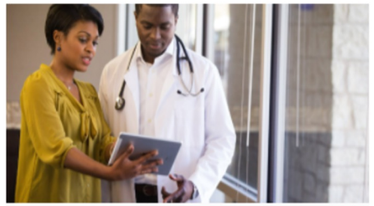
Cardinal Health Biosimilar Resources

CardinalHealth.com/biosimilars

Biosimilars pipeline report

The importance of healthcare provider education in biosimilar uptake

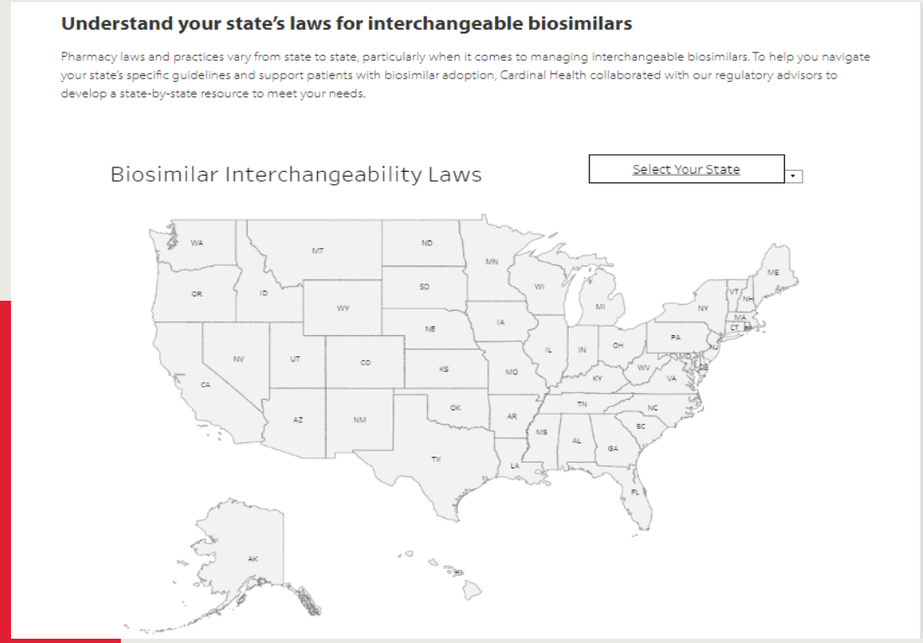


Biosimilars: What we can learn from early adopters

Humira® biosimilar landscape overview

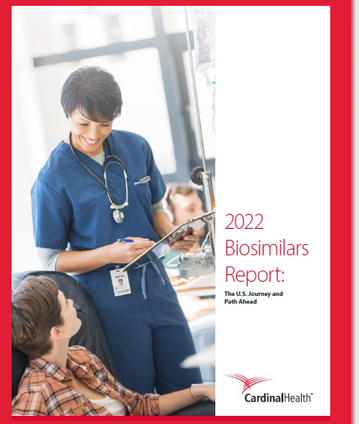
Cardinal Health Interchangeability Map

www.cardinalhealth.com/biosimilars/statelaws



2022 Cardinal Health Biosimilars report

Cardinal Health 2022 Biosimilars Report



FDA Resources and Regulatory Activities

27-page HHS report, *Comprehensive Plan for Addressing High Drug Prices* mentions biosimilars >90 times

FDA educational resources for both providers and patients: **FDA biosimilars website**

New:* *Curriculum Materials for Health Care Degree Programs | Biosimilars

Congress passed two bills in 2021:

Advancing Education on Biosimilars Act

- Calls for a website "to provide educational materials for health care providers, patients, and caregivers, regarding the meaning of the terms, and the standards for review and licensing of, biological products, including biosimilar biological products and interchangeable biosimilar biological products."

Ensuring Innovation Act

- "Provide clarity for drug exclusivity to prevent awarding market exclusivity to products that do not represent true innovation and unduly delay cheaper generics from entering the market."

Thank you!