2023 Biosimilars Report

Tracking market expansion and sustainability amidst a shifting industry
Welcome to our 2023 Biosimilars Report

Cardinal Health works with stakeholders across the healthcare continuum providing support as they navigate the evolving biosimilars landscape to support care for patients. From working with manufacturers to gain regulatory approval to distributing biosimilars to providers and pharmacies, we have the unique opportunity to gather insights about the interaction with and adoption of this new class of therapies.

Since we released our last report, the biosimilars market has continued to expand both in scope and utilization. Our analysts predicted that 2022 would be a turning point for biosimilars in the U.S., and we witnessed first-hand the expansion of biosimilars into a new therapeutic area (ophthalmology), the push for competition as more manufacturers submitted their biosimilars for interchangeability designations, and a handful of new approvals and commercial launches.

As we look toward what’s next, we begin to see how this momentum in the biosimilars space will actualize the promise of patient accessibility and affordability for some of the costliest and critical treatments on the market. In fact, 2023 marks the end of exclusivity for the world’s top-selling drug, Humira™ (adalimumab), and we expect new competition from at least eight biosimilars.

In this report, we analyze the perspectives of more than 350 providers in the therapeutic areas with the most potential for disruption in the year ahead: rheumatology, gastroenterology, dermatology and ophthalmology. Combined with perspectives from leading experts, we give a view of the industry and the imminent market shift that will come from competition with Humira™ and biosimilar utilization. We also analyze the latest industry data on utilization, government pricing reform, and payer coverage.

With more than 50 blockbuster biologics set to lose exclusivity in the next decade, the adoption of biosimilars can greatly affect the trajectory of healthcare costs and, ultimately, patient access. Cardinal Health remains committed to helping our customers improve patient health outcomes by supporting biosimilar development and adoption.

Sincerely,

Debbie Weitzman
CEO, Pharmaceutical Segment
Cardinal Health
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Reviewing the 2022 biosimilars landscape
Introduction

In the first month of 2023, the top healthcare story was the launch of the first of at least 8 expected Humira™ biosimilars. These biosimilars will compete with the number one drug in worldwide sales for nearly a decade, after six years of regulatory delay. As big as this story is, the backstory may be bigger. This year’s annual report continues that backstory as we review highlights and insights from the biosimilar marketplace in 2022.

The U.S. market now has 40 FDA-approved biosimilar products with 25 commercially available, including four products with an interchangeable designation. Biosimilar adoption has continued to grow year-over-year in almost all product classes facing competition, with several classes experiencing high single-digit, or even, double-digit adoption growth. But perhaps most importantly, according to the most recent 2022 U.S. Generic and Biosimilar Medicines Savings Report from the Association for Accessible Medicines (AAM), biosimilars were responsible for driving savings of $7 billion in biologic spending in 2021 alone. According to the report, cumulative savings since 2015 have now climbed to $13 billion. Within the provider networks of Cardinal Health, we’ve seen purchase cost savings exceed $3 billion over our last four fiscal years from the transition to biosimilar products. From slower beginnings, biosimilars have developed into an integral class of products driving substantial cost-savings for some of the most expensive biologic treatments available.

With seven new approvals, and several new commercial launches, 2022 brought much excitement. The following represent what we feel to be some of the most noteworthy milestones.

Bruce Feinberg, DO
VP and Chief Medical Officer
Milestone 1: The first biosimilar(s) launch in ophthalmology

After receiving initial FDA approval in 2021, the first biosimilar referencing an ophthalmology product was officially launched in July 2022. Byooviz™ (ranibizumab-nuna), the first ophthalmology biosimilar product commercialized in the U.S. market by Biogen (in partnership with Samsung Bioepis), launched with a significant 40% discount to its reference product, Lucentis™ (ranibizumab) by Genentech.

Quickly following the launch of the first ophthalmology biosimilar in the U.S., a second ranibizumab biosimilar, Cimerli™ (ranibizumab-eqrn), launched in October 2022 by Coherus Biosciences. In an interesting turn of events, this second ranibizumab biosimilar was also awarded an interchangeability designation making it the first and only predominantly medical benefit biosimilar to achieve the designation thus far. Although the regulatory implications of interchangeability (e.g., pharmacist-level substitution) are not as operationally relevant for provider-administered products predominantly billed to a patient’s medical benefit, the pursuit of interchangeability can also be viewed as further supporting of a manufacturer’s commercial strategy.

While it is still too early to tell as of this writing how the early launches have fared from an adoption standpoint, we expect share shifts in the ophthalmology market to evolve more slowly as our market research data reveals significant provider hesitation with biosimilars remains.

An interchangeability designation allows for the biosimilar to be automatically substituted for its reference product, per state laws, and is generally most relevant for products primarily dispensed in the pharmacy benefit.

Milestone 2: Growth in products pursuing and achieving interchangeability

An important milestone achieved in 2021 was the award of the first interchangeability designation in the U.S. for insulin. Fast forward to a year later and we now have four interchangeable biosimilars: two long-acting insulin biosimilars, one adalimumab biosimilar, and one ranibizumab biosimilar. As a reminder, interchangeability is a regulatory designation, unique to the U.S. market, that allows for a biosimilar to be automatically substituted for its reference product by a pharmacist (pharmacist-level substitution), per state laws. Interchangeability does not denote any clinical superiority over a non-interchangeable biosimilar.

While adoption of Semglee™ (insulin glargine-yfgn) has increased over the last year and now hovers around 10% market share, we believe the transition to this first biosimilar insulin will be viewed by many as slower than expected considering the significant cost challenges facing insulin-dependent patients with diabetes. In an updated report, it was still cited that nearly 20% of Americans resort to insulin rationing.1 As this dynamic continues to play out, it highlights the significant complexities within U.S. pharmaceutical channels and brings to light the additional adoption challenges biosimilars may face in the retail class of trade.

As the biosimilars market continues to grow and shift more squarely into the pharmacy benefit, we will expect to see commensurate growth in the number of products pursuing, and ultimately, achieving an interchangeability designation. We anticipate many manufacturers of biosimilar assets will view interchangeability in the pharmacy benefit as a competitive advantage and choose to conduct the additional research generally required. Looking to 2023, at least four additional adalimumab biosimilar manufacturers are pursuing interchangeability. Beyond adalimumab, several manufacturers have signaled they plan to pursue interchangeability for biosimilar candidates referencing ustekinumab, insulin aspart and golimumab.
## 2022 BIOSIMILARS LANDSCAPE

### Figure 1. FDA-Approved Biosimilars

<table>
<thead>
<tr>
<th>Product</th>
<th>Category</th>
<th>1st biosimilar launch</th>
<th>Current # of biosimilar competitors</th>
<th>Biosimilar market share (Nov. 2022)</th>
<th>Biosimilar share change (since Nov. 2021)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neupogen™ (filgrastim)</td>
<td>Supportive care</td>
<td>2015</td>
<td>3</td>
<td>93%</td>
<td>+2%</td>
</tr>
<tr>
<td>Remicade™ (infliximab)</td>
<td>Immunology</td>
<td>2016</td>
<td>3</td>
<td>44%</td>
<td>+12%</td>
</tr>
<tr>
<td>EpoGen™/Procrit™ (epoetin alfa)</td>
<td>Supportive care</td>
<td>2018</td>
<td>1</td>
<td>42%</td>
<td>-10%</td>
</tr>
<tr>
<td>Neulasta™ (pegfilgrastim)</td>
<td>Supportive care</td>
<td>2018</td>
<td>4²</td>
<td>43%</td>
<td>+4%</td>
</tr>
<tr>
<td>Avastin™ (bevacizumab)</td>
<td>Oncology</td>
<td>2019</td>
<td>3³</td>
<td>82%</td>
<td>+7%</td>
</tr>
<tr>
<td>Herceptin™ (trastuzumab)</td>
<td>Oncology</td>
<td>2019</td>
<td>5</td>
<td>67%</td>
<td>+11%</td>
</tr>
<tr>
<td>Rituxan™ (rituximab)</td>
<td>Oncology</td>
<td>2019</td>
<td>3</td>
<td>72%</td>
<td>+7%</td>
</tr>
<tr>
<td>Lantus™ (insulin glargine)</td>
<td>Diabetes</td>
<td>2020*</td>
<td>1⁴</td>
<td>10%</td>
<td>+7%</td>
</tr>
<tr>
<td>Lucentis™ (ranibizumab)</td>
<td>Ophthalmology</td>
<td>2022</td>
<td>2</td>
<td>3%</td>
<td>+3%</td>
</tr>
<tr>
<td>Humira™ (adalimumab)</td>
<td>Immunology</td>
<td>2023</td>
<td>9⁵</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td><strong>10 Product classes</strong></td>
<td></td>
<td></td>
<td></td>
<td><strong>25</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Enbrel™ (etanercept)</strong></td>
<td>Immunology</td>
<td>2029</td>
<td>2</td>
<td>Not launched</td>
<td></td>
</tr>
</tbody>
</table>


1. Includes Teva’s Granix™, which is technically not a biosimilar since it was filed prior to the enactment of the Biosimilar Approval Pathway.
2. Amneal’s Fylnetra™ has not launched yet; Fresenius Kabi’s Stimufend™ has not launched yet.
3. Celltrion Vegzelma™ has not launched yet.
4. Excludes Basaglar™ and yet to be launched Rezvoglar™.
5. As of date of this publication, only 1 adalimumab biosimilar has launched.

*Nelasta Syr. Only biosimilars share is 77%.*

Note: italicized represents approved biosimilars that have not launched in the U.S. yet.
Milestone 3: Unveiling Enhancing Oncology Model (EOM) and reauthorization of BsUFA III

With the former Oncology Care Model (OCM) sunsetting on June 30, 2022, the Centers for Medicare and Medicaid Innovation (CMMI) unveiled a replacement program named the Enhancing Oncology Model (EOM) in June 2022. Unfortunately, given delays in releasing the new program, there will be a roughly 1-year gap between the expiration of OCM and the launch of EOM. EOM is now set to launch July 1, 2023. EOM (like OCM) is a 5-year, voluntary model that will require participating oncology practices to take on both financial risk and performance accountability for treating patients with common cancer types. With a continued focus on value-based patient care, EOM aims to add an additional focus on health equity along with added enhancements gleaned from feedback on OCM from providers, patients, and advocacy groups.

OCM proved to be a powerful model that contributed, in part, to the dramatic growth and adoption of biosimilars in the oncology market. With a focus on providing high-quality cancer care, at the lowest cost, biosimilars proved to be powerful tools in this value-based care environment. As the market prepares for the launch of EOM, we are hopeful biosimilars will continue to be viewed as integral in providing high-quality, low-cost, cancer care in the U.S. market.

Separately, on September 30, 2022, President Biden signed into law the FDA User Fee Reauthorization Act of 2022, which includes the Biosimilar User Fee Act (BsUFA III). BsUFA III authorizes FDA to assess and collect fees for biosimilar products over the 5-year period from October 2022 through September 2027. These biosimilar user fees are dedicated to helping expedite the time needed to review biosimilar applications for approval and facilitate timely access to safe and effective biosimilar treatment options for patients. Additionally, the BsUFA III commitment letter also outlined the creation of a new biosimilar Regulatory Research Pilot Program. The Regulatory Research Pilot Program has two key focuses:

1. Improving the efficiency of biosimilar product development
2. Advancing the development of interchangeable products

In October 2022, five research grants were awarded and funded by FDA as part of the pilot.

With the reauthorization behind us, we can be further ensured of the regulatory commitment to timely review of biosimilar assets in the pipeline and advancement of biosimilar development policies in the U.S. market.
Figure 2. **Biosimilar market share (as of Sept. 2022)**

Market share data source: IQVIA: Accessed via IQVIA National Sales Perspective (NSP) SMART Data. Sept 2022
Figure 3. Adoption speed (as of Sept. 2022)

Market share data source: IQVIA: Accessed via IQVIA National Sales Perspective (NSP) SMART Data. Sept 2022
Milestone 4: Inflation Reduction Act
Signed into law in August 2022, the Inflation Reduction Act (IRA) has several direct, and indirect, connections to the biosimilars market. Given the potentially significant impact of this new legislation, we have chosen to dedicate an entire section of our report to review and focus on the biosimilar-specific implications of the IRA. Suffice it to say, there are too many noteworthy implications for biosimilars in the IRA to do it justice in our introduction alone. From changes to reimbursement add-on rates in Medicare Part B, to indirect impacts on determining which products are eligible for Medicare negotiation, biosimilars are a key topic in the IRA. Our more detailed review on the IRA can be found on page 57.

Milestone 5: Early indications of formulary coverage for adalimumab biosimilars
One of the biggest previously unanswered questions regarding the adalimumab biosimilar “event” was whether these products would be able to gain coverage on payer/pharmacy benefit management (PBM) formularies quickly. January 2023 represents a watershed moment for the biosimilars market as the first adalimumab biosimilar is finally expected to launch commercially in the U.S. after originally receiving FDA approval in September 2016. Several additional biosimilars are expected to launch mid-year, including at least one biosimilar carrying an interchangeability designation. As of our writing, two major PBMs (OptumRx and Express Scripts) have issued public statements indicating that they plan to cover both reference adalimumab and several adalimumab biosimilars once available.

The clarity that potentially several adalimumab biosimilars will become preferred products on major PBM formularies in 2023 is cause for celebration. However, with current indications that reference adalimumab will also be retained as a preferred product along with the biosimilars (known as parity coverage), it will be difficult to gauge how much utilization will transition to the biosimilars in 2023. Assessing the pros and cons of a potential patient transition will become increasingly important for patients and providers. Patient out-of-pocket costs between the reference product and biosimilars, comparing product differences (e.g., citrate-free, concentration differences, device differences), presence of an interchangeability designation and the level of manufacturer wrap around patient support programs will all add to this complexity.

We expect this year will be filled with much analysis and discussion regarding adalimumab’s official loss of exclusivity and anticipate the entire healthcare industry will be watching for early signs of adoption, potential cost-savings and increased access for patients in one of the costliest disease states globally.

"Biosimilars continue to hold significant promise to positively impact patient care for millions in the U.S. and globally."

Conclusion
While much has changed, the continued need for multi-stakeholder education, awareness and dedicated research remains even more important as we expand into newer therapeutic areas and classes of trade. To that end, the Accreditation Council for Medical Affairs (ACMA) has created the Board Certified Biologics and Biosimilars Specialists Program (BCBBS) an on-line, self-paced, 9-module, 40 hour curriculum to establish expertise among healthcare professionals. Biosimilars will continue to hold significant promise to positively impact patient care for millions in the U.S. and globally. In this, our 2023 Biosimilars Report, we are proud to bring you new perspectives and insights from a new slate of key opinion leaders across four therapeutic areas. As an organization, we remain committed to playing a key role in creating awareness of biosimilar products and increasing education across our industry.
As the U.S. biosimilars market continues to grow and expand into additional therapeutic areas, understanding the provider experience across various specialties has become even more important.

With the largest loss of exclusivity event, perhaps ever in the U.S., set to take place for Humira™ (adalimumab) in 2023, providers that treat immune-mediated inflammatory diseases will be presented with more treatment options for their patients than ever before. While overall biosimilar adoption has increased over the past year, certain therapeutic areas that are less experienced with these products—like dermatology and ophthalmology— continue to face additional barriers to adoption. This poses an interesting dynamic for these providers and raises the importance of how they view biosimilars as an available option. To capture this dynamic, we expanded our provider surveys to include gastroenterologists and dermatologists, accompanying the rheumatology and ophthalmology research we’ve begun collecting over the last few years.

This research provides unique insights and views of each provider group, and better showcases their familiarity with biosimilars, concerns with prescribing and expected utilization as new biosimilars come to market. Insights are taken from our most recent healthcare provider surveys conducted between July – October 2022, with commentary and analysis provided by leading physicians in each therapeutic area.
Most participating physicians cited familiarity with biosimilars and the interchangeability designation.

Figure 4.
How would you describe your familiarity with biosimilars?

Figure 5.
How would you describe your familiarity with the interchangeability designation for biosimilars?
Provider views on the discount needed to motivate a switch to a biosimilar varied by specialty.

Figure 6.
If you assume all clinical factors to be equal, how much of the discount from the reference product would be necessary for you to prescribe a biosimilar versus the reference product?

- Greater than 40%
  - Ophthalmology: 36%
  - Rheumatology: 25%
  - Dermatology: 21%
  - Gastroenterology: 22%

- 31-40%
  - Ophthalmology: 14%
  - Rheumatology: 21%
  - Dermatology: 17%
  - Gastroenterology: 13%

- 21-30%
  - Ophthalmology: 9%
  - Rheumatology: 11%
  - Dermatology: 11%
  - Gastroenterology: 13%

- 11-20%
  - Ophthalmology: 4%
  - Rheumatology: 11%
  - Dermatology: 8%
  - Gastroenterology: 3%

- 5-10%
  - Ophthalmology: 9%
  - Rheumatology: 10%
  - Dermatology: 3%
  - Gastroenterology: 0%

- Less than 5%
  - None: Ophthalmology: 16%
  - Rheumatology: 20%
  - Dermatology: 21
  - Gastroenterology: 10%

- Ophthalmology: N = 64
- Rheumatology: N = 103
- Dermatology: N = 126
- Gastroenterology: N = 72
Biosimilars in rheumatology: The forthcoming season of change in 2023

Jeffrey R. Curtis, MD, MS, MPH
Professor of Medicine, Division of Clinical Immunology & Rheumatology, UAB

This upcoming year will yield important transitions in the treatment landscape for inflammatory conditions once self-administered biosimilars enter the rheumatology market. Beginning first with Amjevita™ (adalimumab-atto) in the first quarter of 2023, followed by at least seven more in the months to follow, the impact on rheumatology patients, their providers, and office staff likely will be profound. A survey of 103 rheumatologists conducted by Cardinal Health in July and August of 2022 provides helpful insights into what rheumatologists believe, and subsequently may do, as it relates to biosimilars.

Based on the survey results, while most rheumatologists (76%) stated that they are ‘very familiar’ with biosimilars and 62% said that they would be ‘very comfortable’ with prescribing, the motivations and concerns of rheumatologists elicited important learnings. First, there was some ambivalence among rheumatologists about the opportunities with biosimilars. Only about half (54%) agreed or strongly agreed that biosimilars would positively impact care. About the same proportion were not excited about the growing number of biosimilars anticipated to come to market. Secondly, given the anticipated cost-savings and hoped-for improvement in access to care, the median discount that rheumatologists expected to see with biosimilars to consider transitioning a patient was 21-30%. Importantly, more than half of rheumatologists felt that the economic benefits observed to date from having biosimilars were not favorable enough to motivate switching. Both biosimilar efficacy, and the lack of economic benefit (to patients and/or to providers), were rheumatologists’ top concerns related to increasing uptake. Not surprisingly, the group of patients where there was the greatest comfort to use a biosimilar was for patients initiating therapy, rather than those who were already established on a reference biologic treatment.

Several therapy-specific features were found to be important to rheumatologists and their patients. For example, the product attributes of biosimilar adalimumab that rheumatologists rated as ‘very important’ were a citrate-free formulation (62%) and an interchangeability designation (60%). Beyond those, one of the biggest potential threats to realizing the potential for biosimilars to save cost and improve access is the need for patient education. Of survey respondents, 85% agreed or strongly agreed that patient education would be important. Patient education needs regarding self-administered biosimilars will be a unique feature in 2023 compared to past years when only intravenous formulations were available. Given that all rheumatology biosimilars available in the U.S. to date (e.g., infliximab, rituximab) have been provider-administered, the need for patient education has been less pronounced. Indeed, many rheumatology patients receiving an intravenously administered biologic like infliximab may have had little to no awareness as to whether they were receiving one of the several biosimilars or the reference product. In contrast, for a forthcoming self-administered injectable therapy like biosimilar adalimumab, the need to educate patients will become more pressing and will put additional burden on rheumatologists and their office staff. Of note, 47% of rheumatologists did not indicate that they were ‘very comfortable’ with discussing the option with patients, suggesting an important need to train rheumatology providers and their staff on how to effectively educate their patients regarding biosimilar use.

Ultimately, biosimilars need to deliver on their oft-promised savings and deliver value to all stakeholders. For rheumatology patients with adequate commercial insurance coverage, biosimilars may offer little upside, and may be met with skepticism as to their benefit. Ensuring that all stakeholders’ needs are met to affect a smooth transition to biosimilars remains an important challenge in the year to come.
Most rheumatologists surveyed said they are very comfortable prescribing biosimilars, particularly for new patients and existing patients for whom payers have mandated a biosimilar.

Figure 7. How comfortable do you feel prescribing biosimilars to your patients?

N = 103

- Very comfortable: 62%
- Somewhat comfortable: 32%
- Not very comfortable: 6%

Figure 8. For which patients are you most likely to prescribe a biosimilar?

N = 103

- Existing patients for whom payers have mandated a biosimilar: 41%
- New patients: 40%
- Existing patients having success on a reference product: 9%
- Existing patients having limited success on a reference product: 4%
- I am not likely to prescribe a biosimilar for any patient at this time: 6%

85% of participating rheumatologists said educating patients about biosimilars is important.
RHEUMATOLOGY TRENDS

About half of the surveyed rheumatologists are excited about the growing number of biosimilars coming to market.

Figure 9. To what extent do you agree with the following statement? I am excited about the growing number of rheumatology biosimilars anticipated to come to market. N = 103

- Strongly agree: 13%
- Agree: 34%
- Neither agree nor disagree: 33%
- Disagree: 15%
- Strongly disagree: 5%

Strongly agree 
Agree 
Neither agree nor disagree 
Disagree 
Strongly disagree
Participating rheumatologists cited citrate-free formulation and interchangeability as the most important product attributes for prescribing an adalimumab biosimilar.

Figure 10. How important are the following product attributes when it comes to utilizing an adalimumab biosimilar? N = 103

- Concentration: 43% Very important, 50% Somewhat important, 7% Not important at all
- Citrate-free: 62% Very important, 33% Somewhat important, 5% Not important at all
- Latex-free: 47% Very important, 46% Somewhat important, 7% Not important at all
- Device: 54% Very important, 43% Somewhat important, 3% Not important at all
- Interchangeability: 60% Very important, 36% Somewhat important, 4% Not important at all

Figure 11. To what extent do you agree with the following statement? I believe that biosimilars will positively impact rheumatology care. N = 103

- Strongly agree: 15%
- Agree: 38%
- Neither agree nor disagree: 32%
- Disagree: 13%
- Strongly disagree: 2%

More than 50% of rheumatologists surveyed believe biosimilars will positively impact care for their patients.
Concerns about efficacy and lack of economic benefit are viewed as the primary barriers to adoption for participating rheumatologists.

Figure 12. Which of the following is your top concern about prescribing biosimilars?

<table>
<thead>
<tr>
<th>Concern</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Concerns about efficacy of biosimilars</td>
<td>36%</td>
</tr>
<tr>
<td>Concerns about lack of economic benefit</td>
<td>24%</td>
</tr>
<tr>
<td>Evaluating when to prescribe a biosimilar versus a reference product</td>
<td>17%</td>
</tr>
<tr>
<td>Lack of payer adoption</td>
<td>10%</td>
</tr>
<tr>
<td>Concerns about manufacturing</td>
<td>7%</td>
</tr>
<tr>
<td>Providing patient education</td>
<td>6%</td>
</tr>
</tbody>
</table>

Figure 13. To what extent do you agree with the following statement? Today, the economics of biosimilars are not favorable enough to motivate me to switch from the reference products.

Less than one in five rheumatologists (18%) surveyed believe that today’s biosimilar economics are favorable enough to motivate them to switch.

53% of participating rheumatologists cited feeling very comfortable discussing biosimilar options with patients.
More than two-thirds of participating rheumatologists said they are at least somewhat comfortable switching from one biosimilar to another.

Figure 14. How comfortable do you feel switching from one biosimilar to another? 

N = 103

- Very comfortable: 18%
- Somewhat comfortable: 52%
- Somewhat uncomfortable: 20%
- Very uncomfortable: 10%
The advent of biologic therapy (TNF inhibitors) has transformed the management of patients with IBD (inflammatory bowel disease) over the last two decades. The introduction of biosimilars in this realm presents an opportunity to provide comparable products to patients at a lower cost. In a recent survey of 72 gastroenterologists conducted by Cardinal Health, 80% responded that they are very familiar with biosimilars. All physicians reported being very comfortable (or somewhat comfortable) prescribing these agents. In fact, over 95% of those who responded to the survey had prescribed an infliximab biosimilar in the prior 12-month period.

While gastroenterology has lagged behind other specialties (e.g., oncology) in the biosimilar space, the availability and utilization of and the competition of these agents with their reference products, is expected to significantly increase in 2023 with the release of at least seven adalimumab biosimilars. Nearly all (93%) of the physicians surveyed indicated they are at least somewhat comfortable prescribing an adalimumab biosimilar once it becomes available. This survey indicated that biosimilars are prescribed most commonly for new patients or patients for whom a payer requires a biosimilar, although this paradigm may change with the addition of more biosimilar options, along with payer and gastroenterologist stakeholder adoption in the future.

When considering the option of prescribing an adalimumab biosimilar, clinical and/or real-world evidence studies were cited as playing a key role in medical decision-making, along with consideration for patient out-of-pocket cost and payer coverage. Based on this survey, the top concerns for adalimumab biosimilars include transitioning patients from Humira™ to a biosimilar (44%) and the interchangeability of biosimilars (38%). Patient education regarding biosimilar safety, efficacy and interchangeability appears paramount to the acceptance of these products, particularly for patients who are switched from a reference product.

Despite general acceptance of biosimilars, there remains some uncertainty regarding their place in the current gastroenterology landscape. This is likely because only half of the survey respondents believed that biosimilars will positively impact gastroenterology care, further highlighting the ongoing need for real-world data and incorporation of biosimilar use and interchangeability into clinical guidelines. Additionally, there continues to be concern over payer coverage and patient out-of-pocket costs which may impact their utilization. Despite these challenges, we anticipate that the rapid growth of biosimilars will play a greater role in clinical practice and reimbursement models of the future.
All surveyed gastroenterologists said they are at least somewhat comfortable prescribing biosimilars for patients, primarily to new patients and those for whom payers have mandated a biosimilar.

Figure 15. How comfortable do you feel prescribing biosimilars to your patients? N = 72

- Very comfortable: 86%
- Somewhat comfortable: 14%
- Not very comfortable: 0%

Figure 16. For which patients are you most likely to prescribe a biosimilar? N = 72

- Existing patients for whom payers have mandated a biosimilar: 49%
- New patients: 36%
- Existing patients having limited success on a reference product: 7%
- Existing patients having success on a reference product: 5%
- I am not likely to prescribe a biosimilar for any patient at this time: 3%
More than 60% of gastroenterologists surveyed believe biosimilars will positively impact care in gastroenterology.

Figure 17. To what extent do you agree with the following statement? I believe that biosimilars will positively impact gastroenterology care. N = 72

<table>
<thead>
<tr>
<th>Strongly agree</th>
<th>Agree</th>
<th>Neither agree nor disagree</th>
<th>Disagree</th>
<th>Strongly disagree</th>
</tr>
</thead>
<tbody>
<tr>
<td>28%</td>
<td>33%</td>
<td>31%</td>
<td>5%</td>
<td>3%</td>
</tr>
</tbody>
</table>

Half of gastroenterologists are excited and a third are indifferent on how they feel about the growing number of biosimilars anticipated in gastroenterology with the top response being neutral.

Figure 18. To what extent do you agree with the following statement? I am excited about the growing number of gastroenterology biosimilars anticipated to come to market. N = 72

<table>
<thead>
<tr>
<th>Strongly agree</th>
<th>Agree</th>
<th>Neither agree nor disagree</th>
<th>Disagree</th>
<th>Strongly disagree</th>
</tr>
</thead>
<tbody>
<tr>
<td>22%</td>
<td>28%</td>
<td>35%</td>
<td>11%</td>
<td>4%</td>
</tr>
</tbody>
</table>
Participating gastroenterologists cite concerns about biosimilar efficacy, providing patient education, and lack of economic benefit as primary barriers to adoption.

Figure 19. Which of the following is your top concern about prescribing biosimilars?

- Concerns about efficacy of biosimilars: 31%
- Providing patient education: 18%
- Concerns about lack of economic benefit: 17%
- Lack of payer adoption: 14%
- Evaluating when to prescribe a biosimilar versus a reference product: 12%
- Concerns about manufacturing: 8%

Figure 20. To what extent do you agree with the following statement? Educating patients about biosimilars as safe and effective treatment options is important.

- Strongly agree: 35%
- Agree: 49%
- Neither agree nor disagree: 14%
- Disagree: 1%
- Strongly disagree: 1%

Nearly 100% of gastroenterologists surveyed feel at least somewhat comfortable discussing biosimilar options with patients.
Participating gastroenterologists are divided on the issue of whether the economics of biosimilars are favorable enough to motivate a switch from reference products.

Figure 21. To what extent do you agree with the following statement? Today, the economics of biosimilars are not favorable enough to motivate me to switch from the reference products.

N = 72

- Strongly agree: 14%
- Agree: 22%
- Neither agree nor disagree: 29%
- Disagree: 29%
- Strongly disagree: 6%

36% of gastroenterologists surveyed believe the economics of biosimilars are favorable enough to motivate a switch.
Nearly 80% of gastroenterologists surveyed said they are at least somewhat comfortable switching from one biosimilar to another.

Figure 22. How comfortable do you feel switching from one biosimilar to another?

N = 72

33% Very comfortable
46% Somewhat comfortable
17% Somewhat uncomfortable
4% Very uncomfortable
Participating gastroenterologists cited device ease-of-use, citrate-free formulation, and interchangeability as the most important attributes for prescribing an adalimumab biosimilar.

Figure 23. How important are the following product attributes when it comes to utilizing an adalimumab biosimilar?

More than 95% of surveyed gastroenterologists said that the device and interchangeability were at least somewhat important when determining to utilize an adalimumab biosimilar.
Will safety concerns impact dermatologist adoption of biosimilars?

Alex S. Gross, MD
Medical Director, Northside Hospital Forsyth

Dermatologists believe biosimilars will positively impact care, but safety/efficacy concerns may impact adoption. The imminent launch of at least seven adalimumab biosimilars in 2023 is expected to greatly impact competition and the availability of biologic treatment options in the dermatology space. With the approaching growth of biosimilar options in dermatology, Cardinal Health surveyed 126 dermatologists in September of 2022 to better understand how they plan to adopt these biosimilars into their prescribing patterns and uncover any potential roadblocks.

Compared to other therapeutic areas which have, historically, not been receptive to new products like biosimilars at the onset, an overwhelming 80% of respondents reported being at least somewhat comfortable prescribing a biosimilar. Of those respondents, 75% specifically noted being comfortable prescribing an adalimumab biosimilar once it becomes available. As part of the survey, they also indicated that the ease of use of the device (72%) and presence of an interchangeability designation (69%) would be the most important product attributes when deciding to prescribe an adalimumab biosimilar.

Despite the relatively high level of prescribing comfort dermatologists displayed in their responses, less than 20% of respondents have prescribed a biosimilar within the last 12 months, indicating limited use of infliximab biosimilars — the only biosimilars currently approved for dermatologic indications. This may indicate that future product adoption could be slower than one would expect despite the relative familiarity and comfort prescribed cited in this survey. When it comes to how providers review new products, the three most important considerations in the review hierarchy are safety, efficacy and accessibility. I see this clearly reflected in the responses from the survey with safety/efficacy concerns representing the highest ranked results when asked about the top concern of prescribing biosimilars (47%) and top concerns when considering future adalimumab biosimilars (70%).

Similar to other therapeutic areas, adoption of biosimilars can be influenced by more than just physician prescribing patterns. Patient out-of-pocket costs and managed care strategies will play key roles in the utilization of these products in the future. In fact, we see from the results that over 50% of respondents noted that they are most likely to prescribe a biosimilar for existing patients for whom payers have mandated a biosimilar. Further, 65% of dermatologists stated that patient out-of-pocket costs would be a key-decision criteria for prescribing an adalimumab biosimilar once available.

Despite these challenges, dermatologists appear optimistic about the potential for biosimilars to positively impact dermatology care once available to them and their patients. Real-world evidence, both international or domestic, was most cited as an important factor to support clinical confidence in using adalimumab biosimilars in the future. With robust utilization of adalimumab biosimilars internationally for several years, I believe this type of data will serve as a strong tool to address existing concerns around the safety and efficacy of biosimilar products.
80% of dermatologists surveyed are at least somewhat comfortable prescribing biosimilars, primarily to existing patients for whom payers have mandated a biosimilar.

Figure 24. How comfortable do you feel prescribing biosimilars to your patients?

N = 126

- Very comfortable: 35%
- Somewhat comfortable: 45%
- Not very uncomfortable: 20%

Figure 25. For which patients are you most likely to prescribe a biosimilar?

N = 126

- Existing patients for whom payers have mandated a biosimilar: 51%
- New patients: 18%
- Existing patients having limited success on a reference product: 13%
- Existing patients having success on a reference product: 9%
- I am not likely to prescribe a biosimilar for any patient at this time: 9%
53% of the surveyed dermatologists believe biosimilars will positively impact care.

Figure 26. **To what extent do you agree with the following statement?** I believe that biosimilars will positively impact dermatology care.  

N = 126

- **Strongly agree**: 13%
- **Agree**: 40%
- **Neither agree nor disagree**: 32%
- **Disagree**: 13%
- **Strongly disagree**: 2%

Only 15% of dermatologists surveyed disagree or strongly disagree that biosimilars will positively impact care.

41% of participating dermatologists say they are excited about the growing number of dermatology biosimilars anticipated to come to market while another 40% are neutral.
Efficacy of biosimilars is cited as the top concern for participating dermatologists.

Figure 27. Which of the following is your top concern about prescribing biosimilars?

- Concerns about efficacy of biosimilars: 48%
- Evaluating when to prescribe a biosimilar versus a reference product: 14%
- Lack of payer adoption: 13%
- Concerns about lack of economic benefit: 10%
- Concerns about manufacturing: 9%
- Providing patient education: 6%

Figure 28. To what extent do you agree with the following statement? Today, the economics of biosimilars are not favorable enough to motivate me to switch from the reference products.

- Strongly agree: 16%
- Agree: 31%
- Neither agree nor disagree: 41%
- Disagree: 10%
- Strongly disagree: 2%

Nearly 50% of dermatologists surveyed agreed or strongly agreed that the economics of biosimilars are not favorable enough to motivate a switch from reference products.
Nearly three out of four dermatologists surveyed are at least somewhat comfortable discussing biosimilar options with patients.

82% of participating dermatologists strongly agree or agree that educating patients on the safety and effectiveness of biosimilars is a key priority.
About 60% of dermatologists surveyed said they are at least somewhat comfortable switching from one biosimilar to another.

Figure 30. How comfortable do you feel switching from one biosimilar to another?

<table>
<thead>
<tr>
<th>Comfort Level</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very comfortable</td>
<td>12%</td>
</tr>
<tr>
<td>Somewhat comfortable</td>
<td>47%</td>
</tr>
<tr>
<td>Somewhat uncomfortable</td>
<td>32%</td>
</tr>
<tr>
<td>Very uncomfortable</td>
<td>9%</td>
</tr>
</tbody>
</table>

Participating dermatologists cited device ease-of-use and interchangeability as the most important attributes when deciding to utilize an adalimumab biosimilar.

Figure 31. How important are the following product attributes when it comes to utilizing an adalimumab biosimilar?

- **Concentration**
  - Very important: 48%
  - Somewhat important: 43%
  - Not important at all: 9%

- **Citrate-free**
  - Very important: 41%
  - Somewhat important: 46%
  - Not important at all: 13%

- **Latex-free**
  - Very important: 46%
  - Somewhat important: 45%
  - Not important at all: 9%

- **Device**
  - Very important: 72%
  - Somewhat important: 25%
  - Not important at all: 3%

- **Interchangeability**
  - Very important: 70%
  - Somewhat important: 25%
  - Not important at all: 5%
The 2023 Biosimilars Report would not be complete without a dedicated review of the adalimumab biosimilar event scheduled to transpire over the course of 2023. Arguably the single largest pharmaceutical loss of exclusivity (LOE) event of all time, the LOE of Humira™ (adalimumab) is poised to change the biosimilar landscape as we know it. To better understand the implications of this biosimilar event, we surveyed providers across rheumatology, gastroenterology/GI and dermatology (key therapeutic areas that make up the vast majority of indications approved for adalimumab) to capture their insights and perspectives.

Overall, providers appear to be generally comfortable prescribing an adalimumab biosimilar once available with at least 75% of providers surveyed across rheumatology, gastroenterology and dermatology stating that they were at least somewhat comfortable with this practice. Gastroenterologists appear to be the most comfortable provider type with 50% of specialists in this area indicating they would be very comfortable prescribing an adalimumab biosimilar once available. This is an interesting result given previous market research revealed gastroenterology specialists have historically been some of the most hesitant providers to accept biosimilars. With eight already FDA-approved biosimilar versions scheduled to launch throughout 2023, to say the biosimilar bench is deep is an understatement. Since first launching in 2003, adalimumab as a product has evolved in many ways including new concentrations, citrate-free versions, latex-free delivery devices and smaller needle gauges. Given the numerous product attributes that have been introduced over the last 18 years, understanding what to anticipate from a product differentiation standpoint will be a challenging task for providers and patients. When asked what product attributes would be most important when deciding to utilize an adalimumab biosimilar; the device’s
ease of use, interchangeability and citrate-free formulations rose to the top of the list. Product concentration and the presence of latex in the device were viewed as less important attributes when compared against the full slate. An interesting point to note is that despite all provider types citing that interchangeability would be a key product attribute when deciding to use a biosimilar adalimumab, less than 50% of providers across all therapeutic areas described their familiarity with the interchangeability designation as “very familiar.” Further, an average of 64% of providers surveyed agreed or strongly agreed with the statement that they “will only feel comfortable prescribing an adalimumab biosimilar if it has an interchangeability designation.” These results suggest that further efforts are needed to strengthen education on interchangeability in the provider community.

When discussing their top concerns regarding adalimumab biosimilars, safety and efficacy, interchangeability and having substitutions at the pharmacy level and transitioning a patient from adalimumab to an adalimumab biosimilar rose to the top as of most concern. These were followed closely by no cost savings to patients and payer coverage decisions. Surveyed providers’ top concerns correlated strongly with their key decision criteria for deciding when to utilize an adalimumab biosimilar. Clinical and/or real-world evidence (RWE) studies, patient out-of-pocket costs and payer coverage each occupied top spots in this category followed by price/cost discounts to the practice, and manufacturer’s supply reliability.

When asked what would best support their clinical confidence in utilizing adalimumab biosimilars with new and existing patients, the top response with at least 40% of providers across all therapeutic areas was RWE, both international and domestic, followed distantly by acceptance into clinical guidelines for practice management. These findings further highlight the continued need for education to strengthen clinical confidence in these agents and help overcome key barriers to a more robust biosimilars market in the U.S.
ADALIMUMAB BIOSIMILARS
93% of gastroenterologists said they are at least somewhat comfortable prescribing adalimumab biosimilars compared to 86% for rheumatologists and 75% of dermatologists.

Gastroenterologists reported the highest comfort levels with adalimumab biosimilars compared to dermatologists and rheumatologists.

Figure 32.
How comfortable are you prescribing an adalimumab biosimilar to your patients, once available?

- Dermatology  N = 126
- Rheumatology  N = 103
- Gastroenterology  N = 72

Very comfortable
31% 37% 50%
Somewhat comfortable
44% 49% 43%
Somewhat uncomfortable
19% 12% 4%
Very uncomfortable
6% 3% 3%
Attitudes about which product attributes are most important when deciding to utilize an adalimumab biosimilar were generally similar across specialties.

How important are the following product attributes when it comes to utilizing an adalimumab biosimilar?
Figure 38. To what extent do you agree with the following statement? I will only feel comfortable prescribing an adalimumab biosimilar if it has the interchangeability designation.

Over 60% of providers across all therapeutic areas will only feel comfortable prescribing an adalimumab biosimilar if it has an interchangeability designation.

<table>
<thead>
<tr>
<th>Dermatology</th>
<th>N = 126</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strongly agree</td>
<td>25%</td>
</tr>
<tr>
<td>Agree</td>
<td>25%</td>
</tr>
<tr>
<td>Neither agree nor disagree</td>
<td>41%</td>
</tr>
<tr>
<td>Disagree</td>
<td>4%</td>
</tr>
<tr>
<td>Strongly disagree</td>
<td>18%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Rheumatology</th>
<th>N = 103</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strongly agree</td>
<td>28%</td>
</tr>
<tr>
<td>Agree</td>
<td>28%</td>
</tr>
<tr>
<td>Neither agree nor disagree</td>
<td>22%</td>
</tr>
<tr>
<td>Disagree</td>
<td>3%</td>
</tr>
<tr>
<td>Strongly disagree</td>
<td>3%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Gastroenterology</th>
<th>N = 72</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strongly agree</td>
<td>25%</td>
</tr>
<tr>
<td>Agree</td>
<td>25%</td>
</tr>
<tr>
<td>Neither agree nor disagree</td>
<td>44%</td>
</tr>
<tr>
<td>Disagree</td>
<td>6%</td>
</tr>
<tr>
<td>Strongly disagree</td>
<td>9%</td>
</tr>
</tbody>
</table>

Product attributes most commonly cited as “very important”

<table>
<thead>
<tr>
<th>Dermatologists</th>
<th>Rheumatologists</th>
<th>Gastroenterologists</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Device/Ease of use (72%)</td>
<td>• Citrate-free (62%)</td>
<td>• Device/Ease of use (69%)</td>
</tr>
<tr>
<td>• Interchangeability (70%)</td>
<td>• Interchangeability (60%)</td>
<td>• Citrate-free (67%)</td>
</tr>
</tbody>
</table>
Safety and efficacy of adalimumab biosimilars were the top concerns for participating dermatologists and rheumatologists, while gastroenterologists were most concerned about transitioning patients from adalimumab to an adalimumab biosimilar.

Figure 39.
What are your top concerns regarding adalimumab biosimilars? Please select up to 3.

- **Dermatology** N = 126
- **Rheumatology** N = 103
- **Gastroenterology** N = 72

- Safety and efficacy
- Interchangeability and having substitutions at the pharmacist level
- No cost savings to patients

- Transitioning a patient from adalimumab to an adalimumab biosimilar
- Switching between adalimumab biosimilars
- Payer or Pharmacy Benefit Manager (PBM) coverage decisions
- Lack of patient support programs (e.g., patient assistance programs)
- Other, please specify

- I have no hesitations about prescribing adalimumab biosimilars to my patients
Across disciplines, participating specialists identified clinical and real-world evidence and patient out-of-pocket costs as key decision criteria when prescribing adalimumab biosimilars.

Figure 40. What would be key decision criteria for utilizing an adalimumab biosimilar? Please select up to 3.

Cost/price discount to the practice
Clinical and/or real-world evidence studies
PBM/Payer coverage
Manufacturer’s supply reliability
Patient out-of-pocket cost

Figure 41. Which of the following would best support your clinical confidence in utilizing adalimumab biosimilars in both new and existing adalimumab-eligible patients?

Real-world evidence, international or domestic
Real-world evidence, domestic only
Uptake among my peers/colleagues
Greater information on FDA regulatory approval process
Acceptance into clinical guidelines for patient management

- Dermatology N = 126
- Rheumatology N = 103
- Gastroenterology N = 72
Biosimilars in ophthalmology: hesitancy remains, but providers showing positive acceptance

Arghavan Almony, MD
Partner and Vice President, Carolina Eye Associates

Although biosimilars have been utilized in oncology and rheumatology for years, ophthalmologists in the U.S. have had no experience with these products until 2022. In September 2021, the first ranibizumab biosimilar (ranibizumab-nuna) was approved by the FDA and launched in July 2022. A second (ranibizumab-eqrn) was approved in August 2022 with a launch in October 2022. Recently, Cardinal Health surveyed 64 retina specialists to gauge their understanding of, and patterns in, adopting biosimilars in ophthalmology.

While concerns over payer coverage and administrative burdens are at the top of the list, clinical questions of efficacy and safety appear to be one of the greatest barriers to adoption of biosimilars among retina specialists. In the survey, physicians were asked about clinical trial designs for biosimilar development and in 2021 and 2022, the majority of respondents (61% and 57% respectively) felt that they either had very limited knowledge of clinical trial design or that the clinical trials are not adequate to investigate biosimilar efficacy and safety.

Previous negative or unexpected experiences with newer retina products in the past decade have left many in the profession leery of change. We see this hesitance in the survey data which shows that although 67% of physicians felt that the FDA approval process for biosimilars is sufficient to evaluate efficacy and safety, only 48% stated that they would prescribe biosimilars themselves. Additionally, half of the respondents also stated they would not prescribe a biosimilar without clinical data to demonstrate safety and efficacy for a specific indication, highlighting the need for further data.

Despite these concerns, there does appear to be overall positive acceptance of biosimilars in the retina space. In this survey, 73% of retina specialists reported that they would be likely to prescribe a biosimilar in neovascular age-related macular degeneration (nAMD), while 64% of retina specialists would be likely to switch to a ranibizumab biosimilar for a stable patient. Further, 71% would be likely to switch to an aflibercept biosimilar when it becomes available. Reasons for this include the benefits of expanded drug options and potential to lower healthcare costs. Going forward, robust clinical trials, real-world data, concerted efforts at educating retina specialists, reduced administrative burdens and payer coverage will all prove to be critical for wider adoption and acceptance of biosimilars in ophthalmology. Biosimilars will also have to compete with new classes of medications, such as faricimab, new platforms, such as Susvimo™ and its port-delivery device and off-label bevacizumab, which is both cheaper and carries 15 years of data and experience with retina specialists.
Participating ophthalmologists stated that the primary role of biosimilars is to keep drug costs down, and that discounts play a key role in decisions about switching to biosimilars.

Figure 42. How do you perceive the role of biosimilars in ophthalmology? Please select all that apply. N = 64

- 84% Keep drug costs down
- 31% Expand drug options
- 6% Not needed as they are redundant to their biologic reference product
- 6% Not needed as they are becoming obsolete
Top concerns among participating ophthalmologists include payer coverage, lack of comfort from a clinical standpoint, and administrative barriers (such as prior authorization processes).

Figure 43. What are your primary concerns with prescribing biosimilars? Please select all that apply. N = 64

<table>
<thead>
<tr>
<th>Concern</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Payer coverage concerns</td>
<td>52%</td>
</tr>
<tr>
<td>Uncomfortable from a clinical standpoint</td>
<td>48%</td>
</tr>
<tr>
<td>Administrative barriers (e.g., prior authorization process)</td>
<td>45%</td>
</tr>
<tr>
<td>Not enough financial incentive</td>
<td>31%</td>
</tr>
<tr>
<td>Other</td>
<td>11%</td>
</tr>
<tr>
<td>No concerns</td>
<td>13%</td>
</tr>
</tbody>
</table>

About half of ophthalmologists surveyed believe the FDA approval process for biosimilars is sufficient to evaluate their efficacy and safety despite lack of clinical comfort being cited as a top concern.

Figure 44. Do you think the FDA approval process of biosimilars is sufficient to evaluate their efficacy and safety? N = 64

<table>
<thead>
<tr>
<th>Response</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes, and I do/will prescribe biosimilars</td>
<td>48%</td>
</tr>
<tr>
<td>Yes, but I do/will not prescribe biosimilars</td>
<td>19%</td>
</tr>
<tr>
<td>No, and I will not prescribe biosimilars</td>
<td>6%</td>
</tr>
<tr>
<td>I am not familiar enough with biosimilars to assess</td>
<td>27%</td>
</tr>
</tbody>
</table>
Nearly 25% of surveyed ophthalmologists are either not familiar with the FDA approval process for biologics or believe there are no differences between the approval process for chemical and biologic drugs. This shows the need for additional education on the biologic and biosimilar approval pathways.

Figure 45. Which statement best reflects your knowledge of the FDA approval pathways for chemical and biologic drugs?

- 6% The FDA approval pathways are the same for chemical and biologic drugs.
- 41% The FDA approval pathways are slightly different for chemical and biologic drugs.
- 36% The FDA approval pathways are completely different for chemical and biologic drugs.
- 17% I have little knowledge on the FDA approval pathway for biologics.
Today, more of the surveyed ophthalmologists reported they feel more knowledgeable about the clinical trials design for biosimilars compared to the 2021 cohort.

Figure 46.
Which of these statements best reflects your understanding on clinical trial design for biosimilar development?

- Clinical trials conducted on biosimilars are adequate given the totality of evidence required for regulatory approval.
- Clinical trials conducted on biosimilars are not large enough in size in order to adequately investigate efficacy and safety.
- I have very limited knowledge of clinical trial design for biosimilars.

Less than 20% of ophthalmologists surveyed said they have “very limited knowledge of clinical trial design” compared to 34% in 2021.

Nearly 60% of participating ophthalmologists are aware of extrapolation of biosimilars but still have concerns about it, while one in four are fully supportive.

50% of ophthalmologists surveyed would not prescribe biosimilars that have been granted approval based on extrapolation.
OPHTHALMOLOGY TRENDS

Participating ophthalmologists are equally open to prescribing a ranibizumab or aflibercept biosimilar once commercially available.

Figure 47. What is the likelihood that you would use a ranibizumab biosimilar in your clinical practice? What is the likelihood that you would use an aflibercept biosimilar in your clinical practice once it is commercially available?

Figure 48. What is the likelihood you would switch a current stable patient on Eylea™ to its biosimilar once it is commercially available?

Figure 49. What is the likelihood you would switch a current stable patient on Lucentis™ to its biosimilar?
Figure 50. To what extent do you agree with this statement? The availability of Lucentis™ or Eylea™ biosimilars will shift utilization away from off-label Avastin™ if price discounts are significant enough.

![Graph showing survey responses]

- **2022**: N = 64
  - Strongly agree: 24%
  - Agree: 53%
  - Disagree: 20%
  - Strongly disagree: 3%

- **2021**: N = 65
  - Strongly agree: 29%
  - Agree: 51%
  - Disagree: 17%
  - Strongly disagree: 3%

Similar to our 2021 report findings, close to 80% of ophthalmologists said they believed availability of retina biosimilars would shift utilization away from off-label Avastin™ if discounts are significant enough.

Figure 51. Byooviz™ (ranibizumab-nuna), a biosimilar to Lucentis™, was approved by the FDA in 2021 and was launched at a 40% discount on 7/1/22. How does the 40% price difference impact your likelihood to prescribe Byooviz™ over Lucentis™?

- **More likely to prescribe Byooviz™ over Lucentis™**: 58%
- **Less likely to prescribe Byooviz™ over Lucentis™**: 11%
- **No impact**: 31%

Nearly 60% of ophthalmologists said they are more likely to prescribe Byooviz™ following its announced 40% discount compared to Lucentis™.
Compared to a 2021 survey, ophthalmologists were more likely to prescribe biosimilars for new patients and existing patients having success on a reference biologic for treatment of neovascular age-related macular degeneration.

Figure 52.
For which patients would you likely prescribe biosimilars for the treatment of neovascular age-related macular degeneration?
Please select all that apply.

New patients
- 39% 2022
- 32% 2021

Existing patients having success on reference biologic
- 53% 2022
- 42% 2021

Existing patients having limited success on reference biologic
- 23% 2022
- 38% 2021

None of the above, I would only prescribe the reference biologic
- 27% 2022
- 25% 2021

92% of ophthalmologists surveyed stated they would inform patients when prescribing a biosimilar.
56% of ophthalmologists only feel comfortable prescribing a biosimilar if it has an interchangeability designation.

Figure 53.
To what extent do you agree with the following statement? I will only feel comfortable prescribing an ophthalmology biosimilar if it has the interchangeability designation.

N = 64

- 8% Strongly agree
- 48% Agree
- 36% Neither agree nor disagree
- 6% Disagree
- 2% Strongly disagree
Government relations analysis
President Biden signed the Inflation Reduction Act (IRA) into law on August 16, 2022.13 With a robust set of funding, this act incorporates several of President Biden’s domestic policy priorities and sweeping reforms to environmental, healthcare, tax and infrastructure policy. Perhaps the most well-known healthcare reform in the IRA is the federal government’s ability to negotiate pharmaceutical prices for Medicare. The negotiation methodology has many complexities and limitations. More specifically, biologics that have been on the market for at least 13 years will be subject to negotiation starting in 2026 for Medicare Part D drugs and 2028 for Part B drugs. However, certain branded reference products may petition to be excluded from negotiation if a biosimilar is anticipated to come to market within two years. Figure 54, shows a more detailed timeline of the implementation of the IRA.

Beyond negotiation, the most direct and immediate impact on the biosimilars market is an update to the payment structure for biologics reimbursed under Part B. This is designed to incentivize providers to prescribe biosimilars by paying them an additional 2-percentage point increase or Average Sales Price (ASP) + 8% effective October 1, 2022, for qualifying biosimilars. The increase, from ASP + 6% to ASP + 8%, lasts for five years, and is intended to help providers increase access to and utilization of biosimilars while also promoting competition in the marketplace. For beneficiaries, there may be a slight variation in cost-sharing obligations every quarter due to the fluctuating ASP. For the initial implementation period, there are 15 biosimilars that qualify for the add-on payment. Note a biosimilar’s ASP must be lower than its reference product’s ASP to qualify for ASP + 8%.

In addition to the changes to reimbursement methodology, the IRA, as its name implies, also imposes requirements for drug manufacturers to pay the federal government if prices for single-source drugs and biologics covered under Medicare Part B and nearly all covered drugs under Part D increase faster than the rate of inflation. If price increases are higher than inflation, manufacturers will be required to pay Medicare the difference in the form of a rebate. From 2019 to 2020, 50% of drugs reimbursed by Medicare had price increases that exceeded the rate of inflation.14

Another change stemming from the IRA is the Medicare Part D benefit redesign. Part of this provision will restructure and eliminate the Medicare Part D “donut hole.” In 2024, the redesign will effectively cap out-of-pocket (OOP) spending at roughly $3,250 per year by eliminating the 5% beneficiary coinsurance requirement when above the catastrophic coverage threshold. By 2025, there will be a hard

cap on OOP at $2,000 per year eliminating the coverage gap or “donut hole.” Prior to IRA, there was not an OOP cap. This restructuring will impose more financial responsibility on drug manufacturers, potentially having an indirect impact on the biosimilar market.15 Finally, the IRA capped out-of-pocket spending for Medicare beneficiaries to $35 per month for insulin.

We will continue to see the federal government pay close attention to biosimilars in the coming year, through new or continued action. The universal question that weighs on the biosimilar world’s mind is: will the IRA succeed as it intended and protect and foster the biosimilar market? Perhaps to stakeholder dismay, only time will tell. The legislation created a long runway for CMS to implement these crucial provisions, most of which are unprecedented in American federal government.

GOVERNMENT RELATIONS ANALYSIS

Abby Barnes
Senior Manager, Federal Government Relations, Cardinal Health
Figure 54.
Implementation timeline of the prescription drug provisions in the Inflation Reduction Act

<table>
<thead>
<tr>
<th>2023</th>
<th>2024</th>
<th>2025</th>
</tr>
</thead>
<tbody>
<tr>
<td>Requires drug companies to pay rebates if drug prices rise faster than inflation</td>
<td>Eliminates 5% coinsurance for Medicare catastrophic coverage</td>
<td>Adds $2,000 out-of-pocket cap in Medicare Part D and other drug benefit changes</td>
</tr>
<tr>
<td>Limits insulin copays to $35/month in Medicare Part D</td>
<td>Expands eligibility for Medicare Part D Low-Income Subsidy full benefits up to 150% FPL</td>
<td></td>
</tr>
<tr>
<td>Reduces costs and expands coverage for adult vaccines in Medicare Part D, Medicaid &amp; CHIP</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Further delays in implementation of the Trump Administration’s drug rebate rule to 2032

Implements negotiated prices for certain high-cost drugs

- **2026**: 10 Medicare Part D drugs
- **2027**: 15 Medicare Part D drugs
- **2028**: 15 Medicare Part B and Part D drugs
- **2029**: 20 Medicare Part B and Part D drugs

2024 – 2030: Limits Medicare Part D premium growth to no more than 6% per year
Figure 55.
Changes to Medicare Part D for brand name drug costs

Share of brand-name drug costs paid by:
- **Enrollees**
- **Part D Plans**
- **Drug manufacturers**
- **Medicare**

**Current law: 2023 / 5% enrollee**

<table>
<thead>
<tr>
<th>Coverage</th>
<th>Initial coverage</th>
<th>Deductible</th>
</tr>
</thead>
<tbody>
<tr>
<td>85%</td>
<td>25%</td>
<td>15%</td>
</tr>
<tr>
<td>25%</td>
<td>70%</td>
<td>5%</td>
</tr>
<tr>
<td>25%</td>
<td>75%</td>
<td>100%</td>
</tr>
</tbody>
</table>

OOP spending threshold

~$3,100

**Inflation Reduction Act**

<table>
<thead>
<tr>
<th>Coverage</th>
<th>Initial coverage</th>
<th>Deductible</th>
</tr>
</thead>
<tbody>
<tr>
<td>80%</td>
<td>25%</td>
<td>20%</td>
</tr>
<tr>
<td>25%</td>
<td>70%</td>
<td>5%</td>
</tr>
<tr>
<td>25%</td>
<td>75%</td>
<td>100%</td>
</tr>
</tbody>
</table>

OOP spending threshold

~$3,250

OOP spending cap

$2,000
NOTE: OOP is out-of-pocket. The out-of-pocket spending threshold will be $7,400 in 2023 and is projected to be $7,750 in 2024 and $8,100 in 2025, including what beneficiaries pay directly out of pocket and the value of the manufacturer discount on brand-name drugs in the coverage gap phase. These amounts translate to out-of-pocket spending of approximately $3,100, $3,250, and $3,400 (based on brand-name drug use only).
What is the most critical action needed to ensure a sustainable U.S. biosimilars market?

We asked leaders across the healthcare continuum one question: what is the most critical action needed to ensure a sustainable U.S. biosimilars market. Here’s what they said:

“The Biosimilars Forum supports a competitive market environment that enables safe, effective, and lower-cost biosimilars and innovation to thrive long-term. To ensure sustainability, we must support patients and providers by enabling fair and equitable access to all lower-cost biosimilars.”

— Julie Reed, Executive Director, The Biosimilars Forum

“Policymakers, plans and providers alike must further embrace the value provided by biosimilars. Biosimilars have made great progress but face continued challenges from misinformation and distorted payment and coverage policies. By addressing these, I am optimistic that we can align incentives and support a more sustainable biosimilar market.”

— Craig Burton, Executive Director, Biosimilars Council

“Physicians and patient education are key to boost confidence and improve biosimilar adoption. As the pipeline of biosimilars grows, education in non-cancer therapeutic classes such as autoimmune, ophthalmology, diabetes, growth hormone and bone health will be crucial. Staff education is an integral part of successful biosimilar Utilization Management (UM) programs.”

— Sophia Humphreys, Director of System Pharmacy Formulary Management & Clinical Programs, Sutter Health
“One of the most critical actions needed to ensure a sustainable biosimilars market in the U.S. is to build patient confidence in taking biosimilars, which happens through proactive education and communications that respect where patients are in their disease journey and meaningfully addresses their questions and concerns.”

— Anna Hyde, Vice President of Advocacy and Access, Arthritis Foundation
New and upcoming biosimilars launches

Year the first anticipated biosimilar launches

<table>
<thead>
<tr>
<th>Reference biologic (molecule)</th>
<th>#</th>
</tr>
</thead>
<tbody>
<tr>
<td>Humira™ (adalimumab)</td>
<td>10</td>
</tr>
<tr>
<td>NovoLog™ (insulin aspart)</td>
<td>3</td>
</tr>
<tr>
<td>Actemra™ (tocilizumab)</td>
<td>3</td>
</tr>
<tr>
<td>rHI (recombinant Human Insulin)</td>
<td>1</td>
</tr>
<tr>
<td>Neulasta™ Onpro™ (pegfilgrastim)</td>
<td>3</td>
</tr>
<tr>
<td>Eylea™ (aflibercept)</td>
<td>8</td>
</tr>
<tr>
<td>Tysabri™ (natalizumab)</td>
<td>1</td>
</tr>
<tr>
<td>Stelara™ (ustekinumab)</td>
<td>8</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Year</th>
<th>Product</th>
<th>Category</th>
</tr>
</thead>
<tbody>
<tr>
<td>2025</td>
<td>Perjeta™ (pertuzumab)</td>
<td>Immunology</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(e.g., RA/GI/Derm/Neuro)</td>
</tr>
<tr>
<td>2025</td>
<td>Xolair™ (omalizumab)</td>
<td>Supportive care</td>
</tr>
<tr>
<td>2024/2025</td>
<td>Simponi™ (golimumab)</td>
<td>Bone health</td>
</tr>
<tr>
<td>2029</td>
<td>Cosentyx™ (Secukinumab)</td>
<td>Ophthalmology</td>
</tr>
<tr>
<td></td>
<td>Enbrel™ (etanercept)</td>
<td>Diabetes</td>
</tr>
<tr>
<td></td>
<td>Prolia™/Xgeva™ (denosumab)</td>
<td>Bone health</td>
</tr>
<tr>
<td></td>
<td>Soliris™ (eculizumab)</td>
<td>Oncology</td>
</tr>
</tbody>
</table>

*2025 is the earliest a pertuzumab biosimilar could launch given ongoing patent litigation.

Last updated: 01.18.2023

For the most updated new and upcoming biosimilar launches, please visit cardinalhealth.com/biosimilars.
Humira™ (adalimumab) biosimilars pipeline

- **Amjevita™** (Amgen) - 1.31.2023
- **Cyltezo™** (Boehringer Ingelheim) - 7.1.2023
- **Hadlima™** (Organon/Samsung Bioepis) - 7.1.2023
- **Yusimry™** (Coherus) - 7.1.2023
- **Hyrimoz™** (Sandoz) - 7.1.2023
- **Abrilada™** (Pfizer) - 7.1.2023
- **Idacio™** (Fresenius Kabi) - 7.1.2023

*pending approval
7.31.2023
**Hulio™**
(Viatris/Biocon)

7.1.2023*
**AVT02**
(Teva/Alvotech)
*pending approval

7.1.2023*
**CT-P17**
(Celltrion)
*pending approval

7.31.2023
**Hulio™**
(Viatris/Biocon)
Expert contributors

Debbie Weitzman is the Chief Executive Officer, Pharmaceutical Segment at Cardinal Health. Throughout her 17-year career at Cardinal Health, Weitzman has served in varying leadership roles across sales and distribution operations, most recently as president, Pharmaceutical Distribution and The Medicine Shoppe International, Inc., leading the company’s distribution efforts to thousands of pharmacies across the care continuum. Weitzman serves on the Board of Directors for the Healthcare Distribution Alliance. She also serves as an independent director for Filtration Group. She leads the Women’s Impact Network at Cardinal Health.

Abby Barnes is the Senior Manager, Federal Government Relations at Cardinal Health. Prior to joining Cardinal Health, Abby served as a Health Legislative Assistant for then-Congressman Pat Tiberi under his leadership as the Chairman of the House Ways and Means Health Subcommittee. In this role Abby led the Chairman’s healthcare initiatives and worked with House leadership to pass legislation. Abby has also held government relations roles at major institutions. She holds a Bachelor’s from the American University in Washington, D.C.

Jeffrey R. Curtis, MD, MPH, MS, is a Professor of Medicine in the Division of Clinical Immunology and Rheumatology at the University of Alabama at Birmingham (UAB). Dr. Curtis received a Doctor of Medicine (MD) and a Master of Public Health (MPH) degree from Oregon Health & Sciences University in Portland, OR. He subsequently completed a residency in internal medicine at Oregon Health & Science University and a fellowship in rheumatology at UAB. He completed a graduate program in Clinical Informatics at Stanford University and received his Master of Science (MS) degree in epidemiology at the Harvard School of Public Health. He is board certified in both rheumatology and clinical informatics.

Bruce Feinberg, DO, is Vice President and Chief Medical Officer at Cardinal Health. He is nationally recognized for his expertise in specialty oncology and the business of specialty healthcare. Dr. Feinberg has been instrumental in the development of clinical pathways that aim to control costs, improve quality and increase predictability, all of which are key factors in developing a sustainable approach for caring for patients with high-cost diseases. A highly sought-after researcher and speaker on healthcare policy, value-based care and real-world evidence research, Dr. Feinberg has over 200 publications in peer-review; and he is also the author of the bestselling Breast Cancer Answers and its follow-up book, Colon Cancer Answers.
Alex Gross, MD, grew up in Plantation, Florida and moved to Georgia to attend Emory University in 1977. After receiving his Bachelors Degree in Biology, he returned to Florida and earned his MD degree at the University of South Florida College of Medicine in Tampa. He completed residencies in Internal Medicine at Emory and Dermatology at Vanderbilt and is Board Certified in both specialties. He lives in Dunwoody with his wife, Joanne, and has been practicing dermatology in the greater Atlanta area since 1991. In 1995, he established the Georgia Dermatology Center in Cumming where he currently serves as Medical Director and a staff member at Northside Hospital Forsyth.

Arghavan Almony, MD, received her medical degree from the Keck School of Medicine and completed her residency training at Washington University in St. Louis. She received her fellowship in vitreoretinal surgery from Barnes Retina Institute and Washington University in St. Louis. Dr. Almony is certified by the American Board of Ophthalmology and a member of the Retina Society. She is a fellow of both the American Academy of Ophthalmology and the American Society of Retina Specialists. Dr. Almony has received numerous honors including the Heed Fellowship, the Retina Fellows Forum Research Award, the American Society of Retina Specialists Honor Award, and the American Academy of Ophthalmology Achievement Award. Dr. Almony is a partner and vice-president at Carolina Eye Associates in North Carolina. She has published over 30 peer-reviewed ophthalmology articles and her research has been presented at over 70 national and international conferences. Dr. Almony also serves as an Adjunct Assistant Professor at the Campbell University School of Medicine.

Vivek Kaul, MD, FACP, FASGE, AGAF, NYSGEF is the Segal-Watson Professor of Medicine (and former Division Chief) in the Gastroenterology & Hepatology Division at the University of Rochester Medical Center. His clinical, research and medical education efforts are focused in Therapeutic Endoscopy. He is a PI and/or co-investigator on several national and international trials in endoscopy, pancreatic and esophageal disease. Dr Kaul serves on several national committees with the ASGE and the ACG and is a past Governor of the ACG for Northern NY. He is chair of the ACG Innovation & Technology Committee and also immediate past Chair of the EUS special interest group (SIG) for the ASGE. He is also Chair of the World Gastroenterology Organization’s Endoscopy Committee and serves on the WGO Governing council. Dr Kaul also serves as the alternate ASGE RUC advisor to the AMA and serves on several national and international task forces such as the ACG GI-On Demand task force and the WGO Global Climate Change & Green Endoscopy Working Group. Dr Kaul is a reviewer for several journals, is a sought-after speaker and has published extensively in the field of interventional endoscopy and gastroenterology. He regularly lectures and shares his endoscopy expertise at centers in the USA and around the world.
References


3 Cardinal Health, 2021, Sales Data

4 IQVIA SMART Data Analytics Platform. Accessed September 2022. Subscription required to access data


10 See reference 8


Methodology

The healthcare provider research was conducted by Cardinal Health using web-based surveys in 2022 from a mix of community- and hospital-based practices.

The rheumatology surveys were fielded from July to August and included more than 100 rheumatologists.

The dermatology surveys were fielded in September and included more than 125 dermatologists.

The gastroenterology surveys were fielded from September to October and included more than 70 gastroenterologists.

The ophthalmology surveys were fielded from September to October and included more than 60 retina specialists.

About Cardinal Health and biosimilars

With 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.

For hospitals, health systems, pharmacies and specialty physician practices, we not only distribute products — we also deliver the insights, tools and expert support providers need to evaluate biosimilars for adoption, enabling them to make clinically sound and cost-effective treatment decisions.

For biopharma companies bringing new biosimilars to market, our capabilities support the product lifecycle from pre-clinical to post-commercial launch. Our team of seasoned experts works to accelerate and simplify the process to achieve commercial success with guidance on regulatory approval pathways, real-world evidence generation, educational programs and market insights, logistics planning and implementation and patient hub services to support patients through their treatment journeys.

Cardinal Health works with all healthcare stakeholders, including providers, payers, pharmacists, biopharma companies, policymakers and patients, to provide education and build a broader understanding of the role that biosimilars can play in facilitating high-quality, lower cost care. Learn more about our solutions and resources at www.cardinalhealth.com/biosimilars.