Baptist Health

What are the challenges with Biosimilars?

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Objectives

1. Define the concept of biosimilars and discuss their relevance in oncology treatment.
2. Identify and analyze the key challenges associated with the adoption and utilization of biosimilars in oncology practice.
3. Discuss strategies to overcome these challenges and facilitate the effective integration of biosimilars into oncology treatment protocols.

Abbreviations

ASCO- American Society of Clinical Oncology
BPCIA- Biologics Price Competition and Innovation Act
CBERS- Centers for Biologics Evaluation and Research
EMA- European Medicines Agency
FDA- Food and Drug Administration
FFDCA- Federal Food Drugs and Cosmetic Act
FAERS- FDA Adverse Event Reporting Systems

Biosimilar Experience

143 Patients and 33 Medical Oncologists completed an Internet Survey on experience with trastuzumab biosimilar

Results

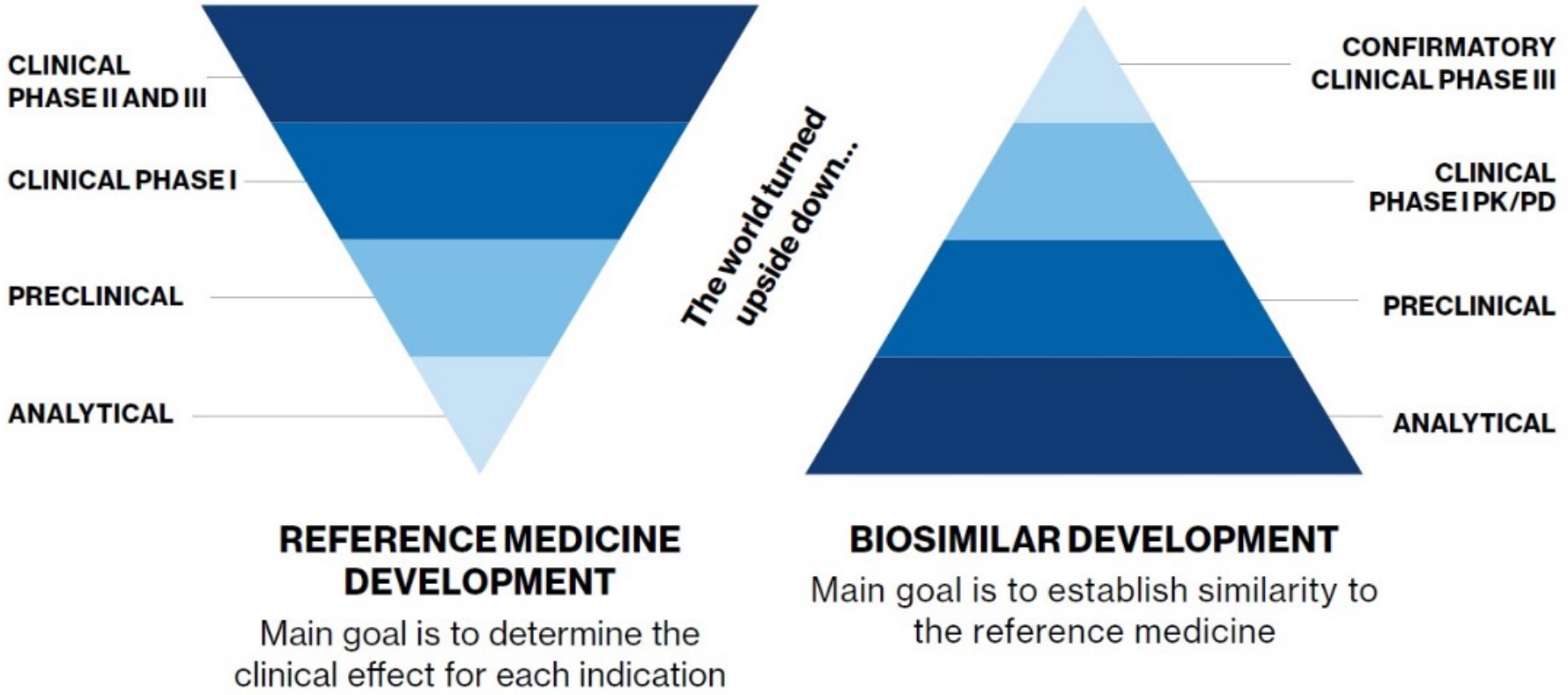
- 55.2% of patients who responded were presented with an option to switch
- 63.9% patients reported having switched to a trastuzumab biosimilar
- 40.8% of patients reported receiving no prior notification about switching
- 26.4% reported the physician first discussed biosimilars with them
- others reported that information came from an advanced practice provider (5.7%), chemotherapy nurse (15.5%), pharmacist (2.9%) or insurer (4.0%)
- Oncologists reported that the decision to switch a patient from biosimilar trastuzumab was not initiated by them (0.0%)
- insurer (45.2%), pharmacy (29.0%), or hospital/center administration (19.4%)

Papautsky EL, Carlson M, Johnson SM, Montague H, Attai DJ, Lustberg MB. Characterizing experiences of non-medical switching to trastuzumab biosimilars using data from internet-based surveys with US-based oncologists and breast cancer patients. Breast Cancer Res Treat. 2022 Jul;194(1):25-33. doi: 10.1007/s10549-022-06615-2. Epub 2022 May 14. PMID: 35568748; PMCID: PMC9107314.

Biosimilars

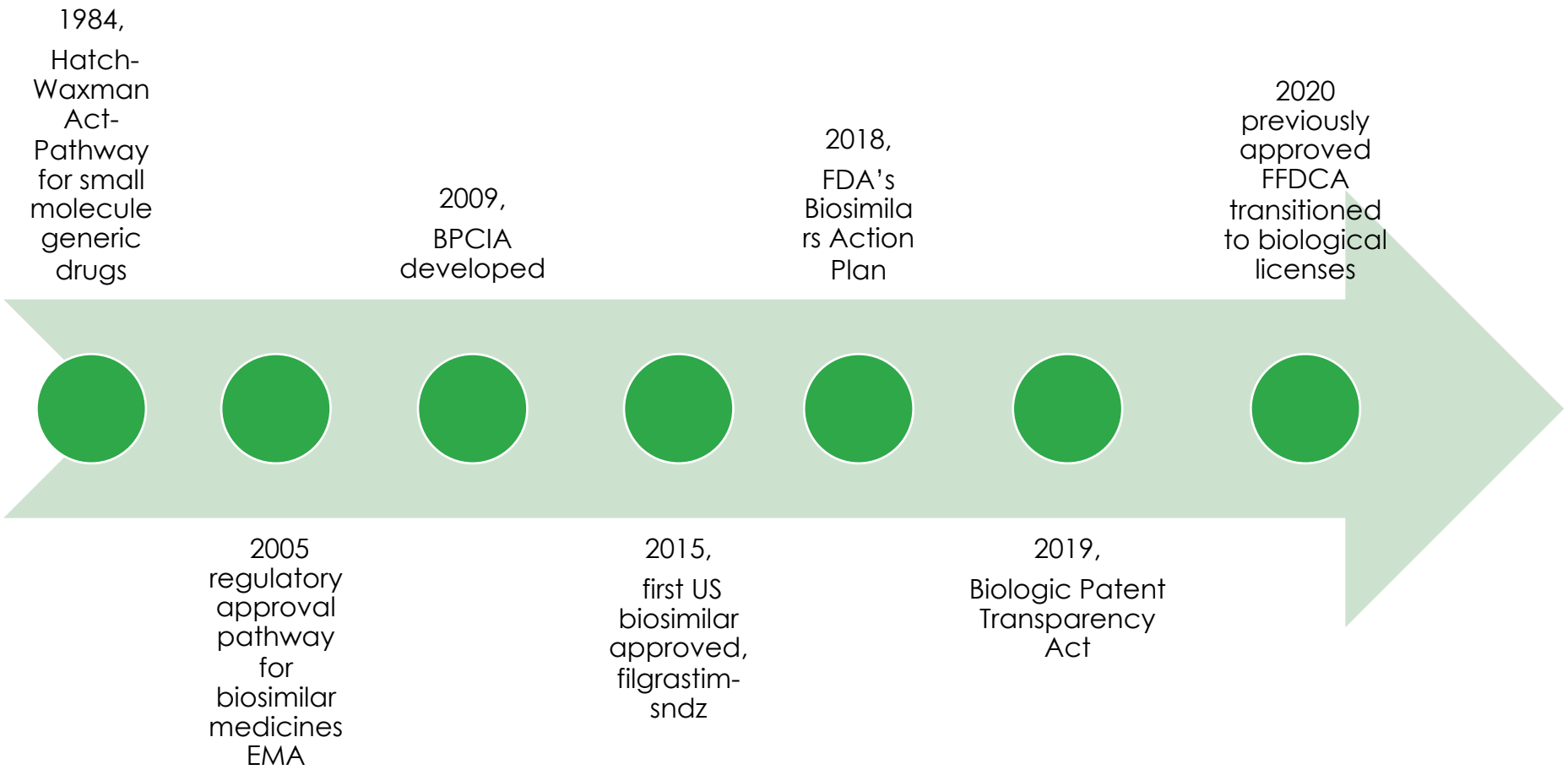
- Biological therapeutic agents—or biologics—substances that are manufactured by cells or living organisms via various biological processes, such as controlled gene expression, antibody technologies, or recombinant DNA technologies.
- Biosimilars are biopharmaceutical products that highly resemble already existing reference products in terms of safety, potency, and purity
- **not exact copies of the reference products**
- **mechanism of action, dosage form, route of administration, therapeutic indication, and strength must be identical to those of the reference product**

Regulatory Approval



1. https://www.sandoz.com/our-work/biopharmaceuticals/development-biosimilars.
2. Accessed 3/10/2019

Regulatory Approval Timeline



Gherghescu I, Delgado-Charro MB. The Biosimilar Landscape: An Overview of Regulatory Approvals by the EMA and FDA. Pharmaceutics. 2020 Dec 31;13(1):48. d

Comparative Regulatory Guidelines

EMA	WHO	FDA
Biological Medicinal Products, Good Pharmacovigilance practices	Guidelines on Evaluations of Similar Biotherapeutics products	BPCIA, CBER, FAERS
10 Y + patent expiration	License based on complete registration dossier	12 Y + Patent expiration
Toxicology. Non-clinical pharmacology, PK, PD, manufacturing	Quality, non-clinical parameters, clinical parameters	Pre-clinical and clinical, functional and physio assays, etc. PK, PD in humans,
Surveillance required	Pharmcovigilence	Safety efficacy, and immunogenicity in humans, FDA-EMA collaboration, Post marketing surveillance
Identical route, form and strength	Comparable in terms of dosage and route	Identical MOA, dosage form, route, strength, and indication

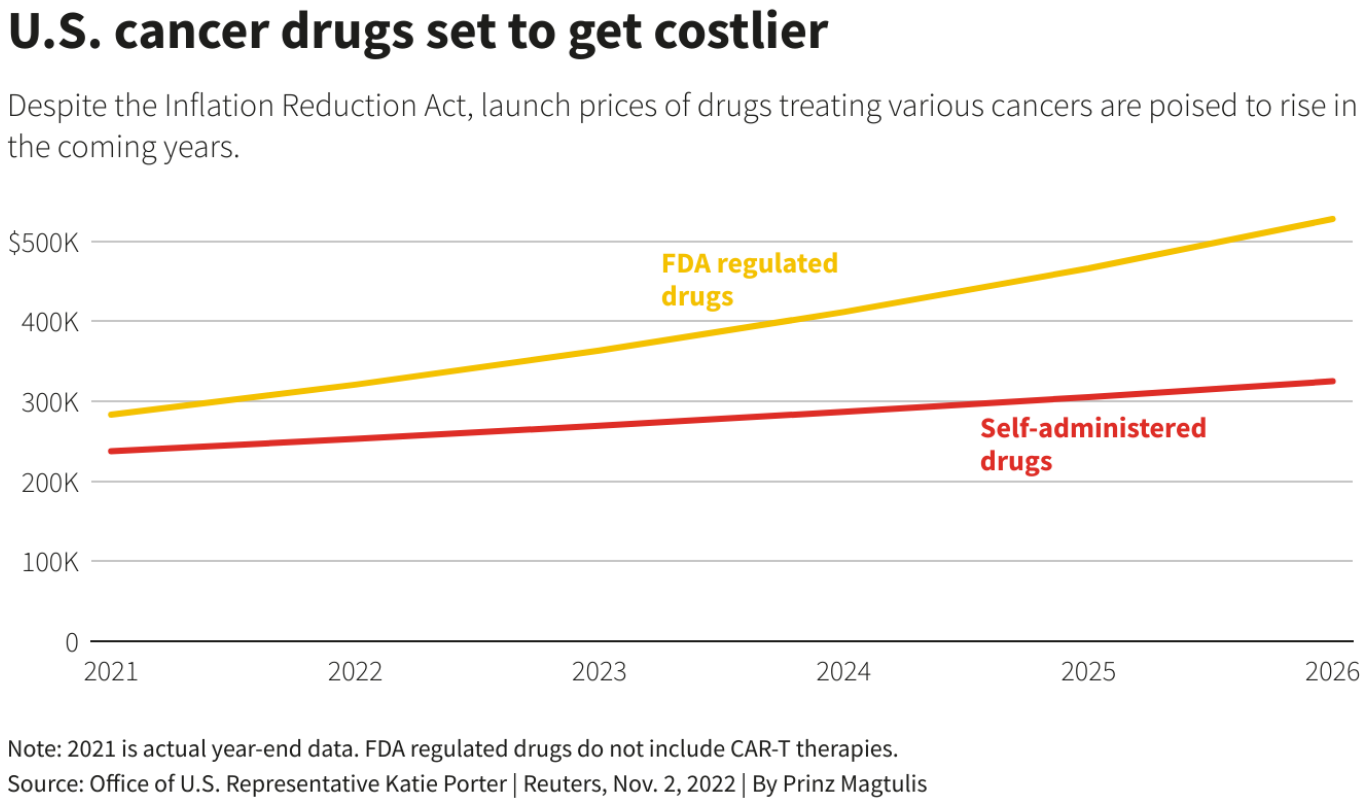
Current Challenges

- Awareness and adoption by providers
- High cost
- Biosimilar competition
- Interchangeability and/or pharmacy substitution
- Formulary management
- Patient education and awareness

Cost of Cancer Medications

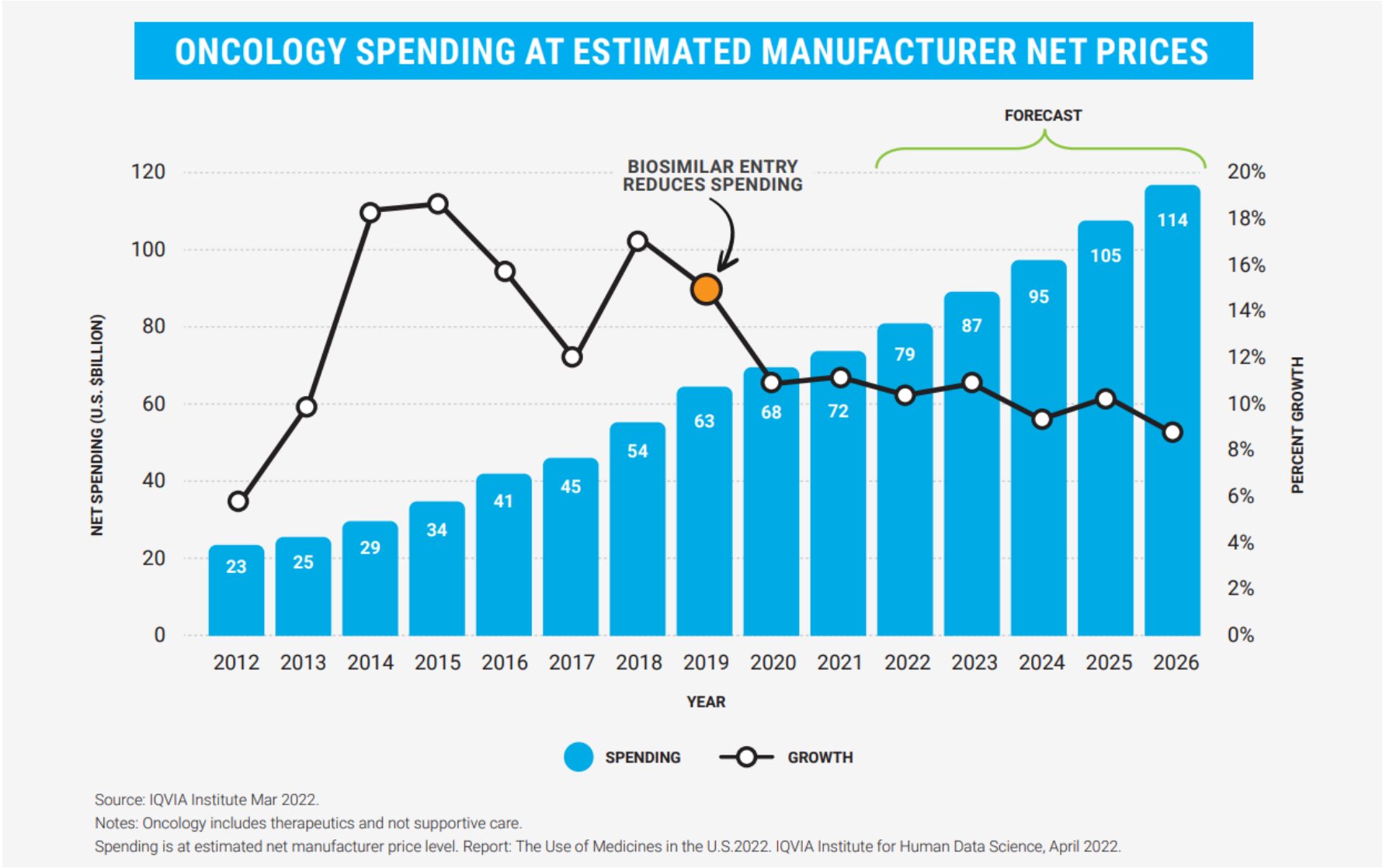
The National Cancer Institute estimates the direct medical costs related to cancer treatment in the United States were $183 billion in 2015 and are expected to increase to $246 billion by 2030, a 34% raise.[1]

Biosimilars for the treatment of cancer have captured less of the market share than generic drugs would typically achieve in the first two years of approval, typically around 75%-90% market share[2]



1. Ofman JJ, Fendrick AM, Raza A. Novel multicancer early detection technology-potential value to employers and the workforce. *Am J Manag Care*. 2020;26: (10 Spec No.):SP363. 2. Bloomfield D, D'Andrea E, Nagar S, et al: Characteristics of clinical trials evaluating biosimilars in the treatment of cancer: A systematic review and meta-analysis. *JAMA Oncol* 8:537-545, 2022

Financial Impact of Biosimilars



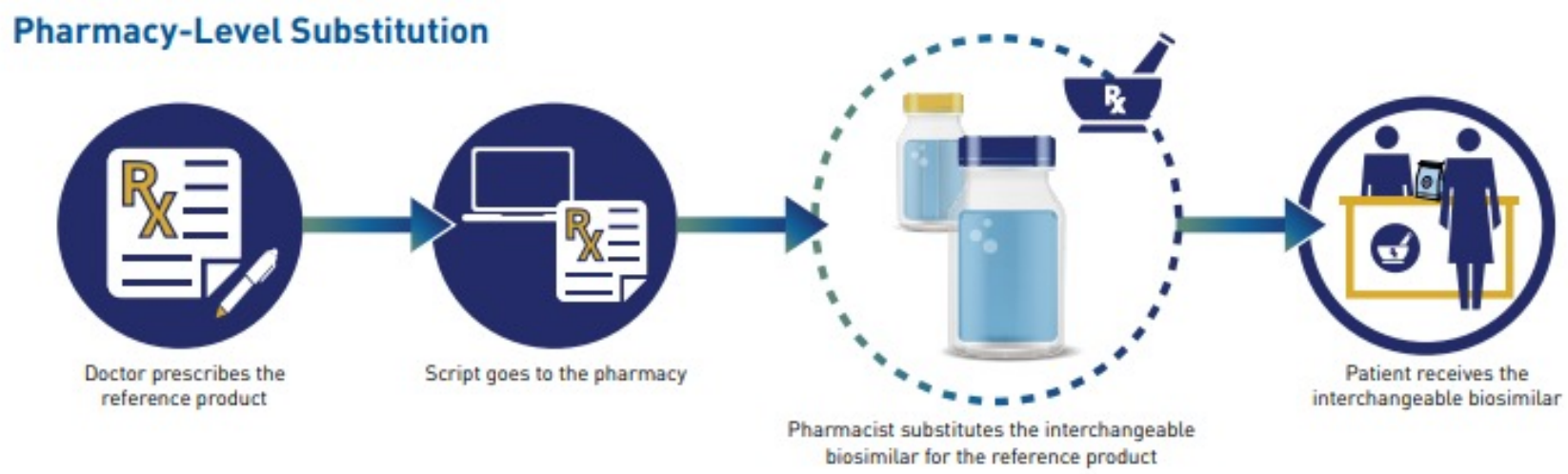
Source: IQVIA Institute Mar 2022.
Notes: Oncology includes therapeutics and not supportive care.
Spending is at estimated net manufacturer price level. Report: The Use of Medicines in the U.S.2022. IQVIA Institute for Human Data Science, April 2022.

US Biosimilar Market (Oncology/ Supportive care)

Class	Supportive Care			Oncology			TNF Blokers
Molecule	**filgrastim**	**pegfilgrastim**	**epoetin alfa**	**rituximab**	**trastuzumab**	**bevacizumab**	**infliximab**
Innovator/ Reference	**filgrastim**	**pegfilgrastim**	**epoetin alfa**	**rituximab**	**trastuzumab**	**bevacizumab**	**infliximab**
Biosimilar (Launched)	filgrastim-sndz 03/2015	pegfilgrastim-jmdb 06/2018	epoetin alfa-epbx 05/2018	rituximab-abbs 11/2018	trastuzumab-dkst 12/2017	bevacizumab-awwb 09/2017	infliximab-dyyb 04/2016
	filgrastim-aafi 07/2018	pegfilgrastim-cbqv 11/2018		rituximab-pvvr 07/2019	Trastuzumab-pkrb 12/2018	bevacizumab-bvzr 06/2019	infliximab-abda 05/2017
	filgrastim-ayow 02/2022	pegfilgrastim-bmez 11/2019		rituximab-arrx 12/2020	trastuzumab-dttb 01/2019	bevacizumab-maly 04/2022	infliximab-qbtx 12/2017
		pegfilgrastim-apgf 06/2020			trastuzumab-qyyp 03/2019	bevacizumab-adcd 09/2022	infliximab-axxq 12/2019
		pegfilgrastim-pbbk 05/2022			trastuzumab-anns 06/2019		
		(pegfilgrastim-fpgk) 09/2022 N					

Interchangeable Biological Products

- Biosimilar that meets additional requirements and may be substituted for the reference product
- Companies must apply with adequate information to support an interchangeability determination for their product to be approved as an interchangeable biosimilar
- **Does not mean that an interchangeable biosimilar is safer or more effective than other biosimilars**



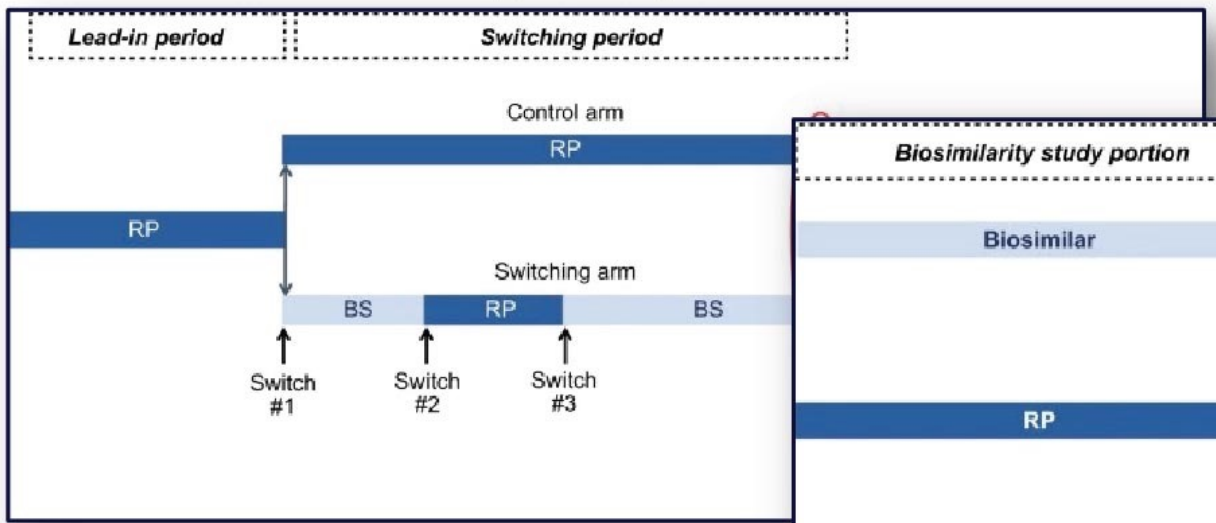
US FDA Administration. Interchangeable Biological Products. https://www.fda.gov/media/151094/download Accessed 2/15/2024

Demonstration of Interchangeability

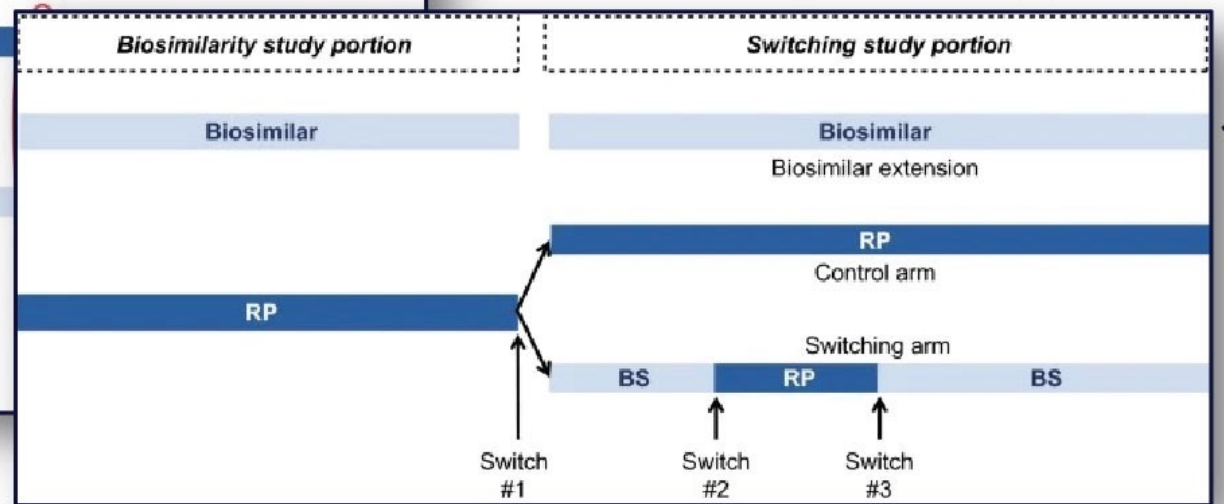
The FDA outlined guidelines for a switching study that sponsors may use to demonstrate interchangeability

A switching study is expected to demonstrate interchangeability. The exact details of the study design need to be negotiated with the FDA on a product- and regimen-specific basis.[1] While switching studies are required for biosimilars that are administered to patients more than once, the FDA does not require them for once-only administered biosimilars.

Dedicated Switching Study



Integrated Approach



Used to demonstrate both biosimilarity AND interchangeability

Study Endpoints: PK and PD

[1]https://www.fda.gov/media/124907/download, *BioDrugs* volume 34, pp. 723–732 (2020)

Interchangeability Considerations

FDA interchangeability designation is a legal distinction

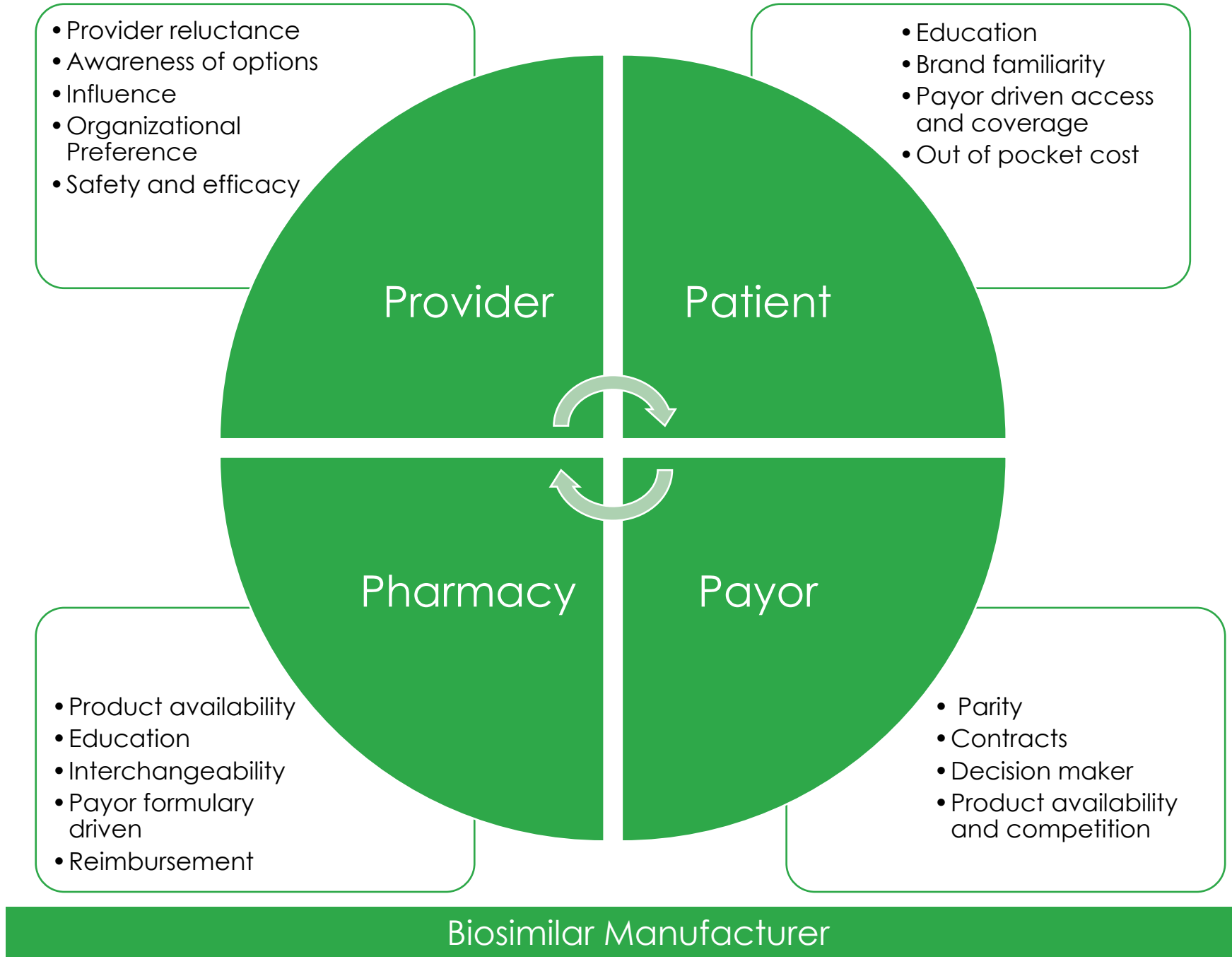
Real world experience

Health plans consider them interchangeable

Pharmacy & Therapeutic Committee approved protocols

Scientific and clinical matter, all biosimilars are considered “interchangeable” with their reference product

Stakeholders



Our Centers Process

Education on Biosimilar approval process to P&T Committee

Developed an Internal Policy on review, approval and implementation process

Established a Biosimilar Steering Committee (Meets quarterly)

Review new product to market

Payor formulary and preferences

Reimbursement within organization

P&T abbreviated review

Education to clinical team (Nurses, Providers, Educators, etc.)

Pharmacy auto-substitution for provider efficiency

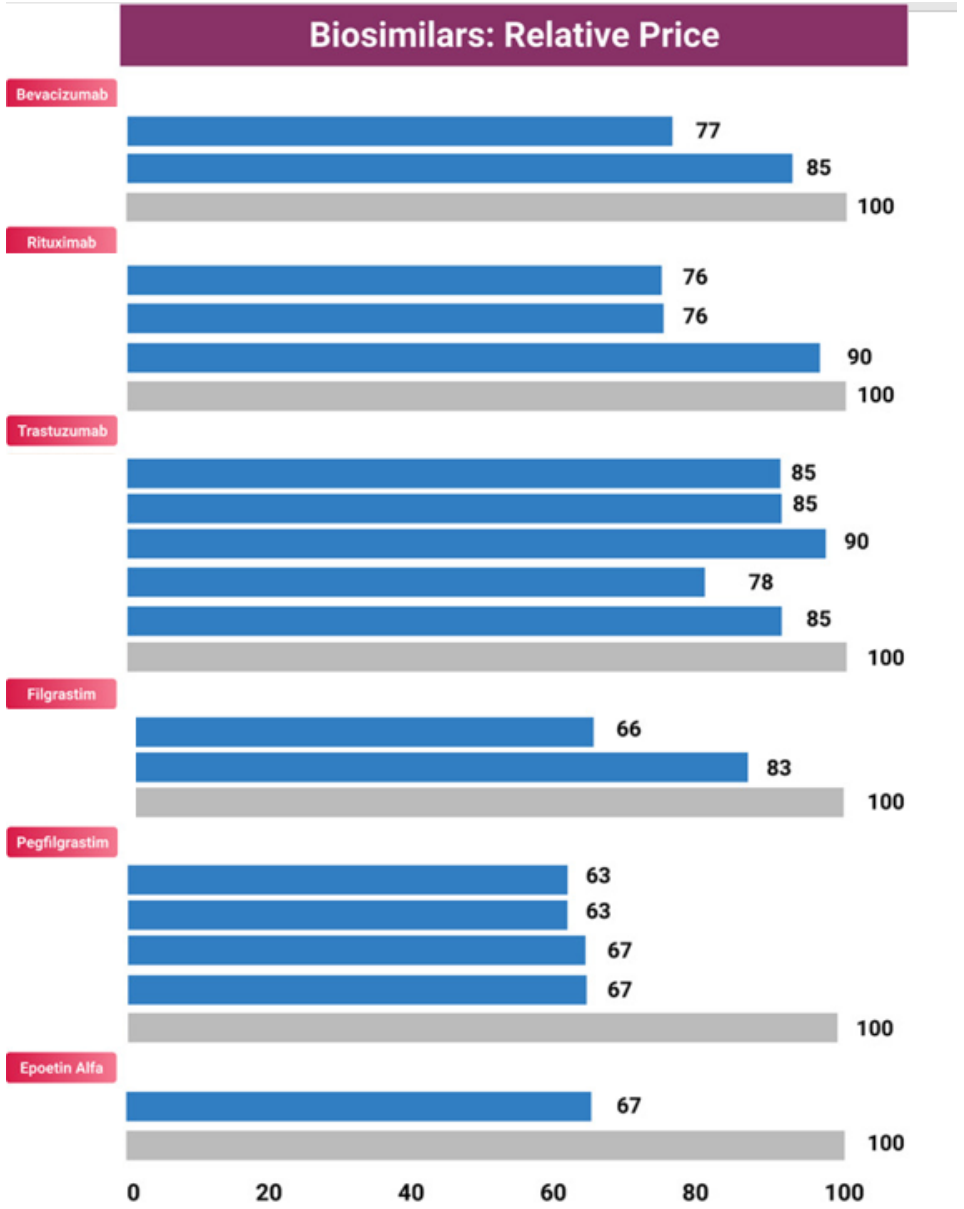
Monitor utilization through Pharmacy Business affairs dashboard

Monitor for safety through established Adverse drug reporting process

Patient education by systemic therapy educators and providers

Our Centers process

- Organization Acquisition cost
- Payor Mix
- ASP projections
- Reimbursement
  - ASP+6%
  - ASP +6% of RP ASP
- Impact of the Inflation Reduction act
  - ASP + 8% RP ASP
  - Oct 202 to Dec 31. 2027



Operational Challenges and Considerations

- Plan for switching patient orders
  - **New vs. existing patients**
  - **Single order vs. treatment plan**
  - **Drug authorization switch**
  - **Route for co-signature**

- Product inventory
  - **Lack of payer & facility formulary alignment**
  - **Storage capacity**
  - **Automatic Dispensing Cabinets (ADC)**

ASCO Policy Statement on Biosimilar and Interchangeable Products in Oncology

2018, ASCO released its Statement on Biosimilars in Oncology which was subsequently published in the Journal of Clinical Oncology to serve as an educational tool

2023, ASCO Published the ASCO Policy Statement on Biosimilar and Interchangeable Products in Oncology

- Summary of the Current state of Biosimilars in the US and Europe
- Describes the biologics evaluation and approval process
- Provides and update on the experiences with biosimilars over the last 15 years

[1] Gladys Rodriguez et al. , ASCO Policy Statement on Biosimilar and Interchangeable Products in Oncology. *JCO Oncol Pract* **19**, 411-419(2023).

ASCO Policy Statement on Biosimilar and Interchangeable Products in Oncology

TABLE 1. ASCO Recommendations on Biosimilar and Interchangeable Products in Oncology

Patients and clinicians
Stakeholders should ensure equitable access to high-quality care, including financial counseling to access patient assistance programs that provide financial assistance to low-income individuals for biosimilars
In its commitment to expand education on biosimilar products, ASCO and other organizations should develop and maintain up-to-date, audience-appropriate educational materials that are readily available for patients to ensure confidence in the safety and efficacy of biosimilar products
Physicians should discuss with their patients any proposed switching and whether this is the best treatment option according to evidence."
Payers
Payers should ensure that changes to prescribed therapies for patients are made only in the context of prior consultation between the patient and physician. At a minimum, payers should continually update and ensure transparency by clearly describing their formulary design and preferred choice of biologic products
Individual payers should develop plans to help clinicians mitigate or avoid complications with stocking and maintaining multiple biosimilars of the same class
Pharmacy
Both federal and state entities should ensure that pharmacists are educated and aware of allowable biosimilar substitutions to their reference product
If a patient is already on an established therapy, the final decision to switch to a biosimilar product should be made by the patient and physician. In all cases of substitution, patients and physicians should be notified immediately
Government
The BPCIA distinction between interchangeability designation and biosimilars is unnecessary, burdensome, and creates barriers to high value care. Therefore, the US Congress should enact legislation amending the BPCIA to remove the term, designation, and additional requirements for interchangeability
To protect patients, federal and state governments should ensure the appropriate regulation of biosimilars in accordance with its FDA designation
The federal government should enact legislation limiting the ability of biologic and biosimilar manufacturers to delay market entry of biosimilars
The federal government should enact legislation to reduce data exclusivity on biologic products
The federal government should enact legislation that authorizes the Federal Trade Commission to initiate enforcement proceedings against manufacturers on any patent infringement claim in connection with the sale of biologic products
Research
Robust clinical data are necessary to ensure continued safety and efficacy of biosimilars. FDA and industry should continue to ensure rigorous pharmacovigilance monitoring, including evaluating any product quality concerns. Such data should provide the necessary level of confidence for their use by patients and clinicians
ASCO and the stakeholder community should encourage research on cost-effectiveness of biosimilars, including adequate inclusion of indirect costs of cancer, particularly between biosimilars and subcutaneous formulations

Abbreviations: BPCIA, Biologics Price Competition and Innovation Act; FDA, US Food and Drug Administration.

Gladys Rodriguez et al.

Conclusion

- Clinicians must take time to understand the regulatory approval processes and criteria for approval for biosimilars
- All biological products, including reference products, are heterogeneous mixes of molecular variants and will exhibit variability among lots
  - variability is controlled and carefully monitored
- Post approval surveillance and reporting of adverse effects
- Educate patients who may be uncomfortable with changing treatment from a more familiar agent
- Consider the operational implications of biosimilar adoption in the ordering workflow, pharmacy storage implications and authorization workflow of the practice
- Biosimilar through reducing the cost of care for patients will increase access and expand treatment options for patients