Integration of Biosimilars in Oncology Care

Jorge J. García, PharmD, MS, MHA, MBA, FACHE
Assistant Vice President - System Oncology Pharmacy Service Line
Baptist Health South Florida

Why Have the Biosimilar Discussion?

- Biosimilars are here
- Payers, patients, providers, other stakeholders may request biosimilars
- Others turn to pharmacists as the experts on biosimilars
- Value proposition
- Implementation challenges

Learning Objectives

- Review biologic drug evolution and cost trends
- Define biosimilars and discuss manufacturing process
- Review biosimilar implementation barriers and best practices
- Discuss biosimilar reimbursement and role in value-based care

Background

Biologics have revolutionized treatment for serious conditions in past 20 years

- 1970 Biologic products mainly consisted of vaccines & blood products
  <10% pharmaceutical market

- 1980 Rise of cloning and gene expression technology
  Biosynthesis of genetically modified organisms
  Increasingly complex molecules
  1982 Genentech's recombinant human insulin
  1986 First FDA-approved monoclonal antibody (muromonab)
  1997 Entry of recombinant monoclonal antibodies for cancer treatment

1. Ledon, N., Lage, A. Biosimilars and the Real World. MEDICC, Vol 19, No 4. October 2017.
2. Kelley, T. *Biosimilars in Oncology: Reality Could Bite the Copycats, Dog Potential Major Savings.* Drug Management. MediMedia. March, 12, 2017

Background

- Cost of biologic pharmaceuticals have reached an all time high
- Cancer drug cost increasing at twice the rate of general healthcare cost
- Biologics net spending reached 125.5 billion in 2018
- Median monthly cost of new U.S. cancer drugs surpassed the median monthly household income in year 2000 and more than doubled by 2014

1. Medicine Use and Spending in the U.S. A Review of 2018 and Outlook to 2023. May 2019. IQVIA Institute for Human Data Science. https://www.iqvia.com/-/media/iqvia/pdfs/institute-reports/medicine-use-and-spending-in-the-us---a-review-of-2018-outlook-to-2023.pdf?_=1602972025818. Accessed October 17, 2020.

Definition

- A **biosimilar** is a biologic agent that is NOT chemically identical, but is highly similar, to an approved reference biologic agent, notwithstanding minor differences in clinically inactive components, and with no meaningful differences in efficacy, safety, and purity.

- A **reference product** is an approved drug that is compared with new generic or biosimilar version to show bioequivalence of biosimilarity respectively

1. Declerck, P., Bakalos, G., Zintzaras, E., Barton, B., Schreitmuller, T. *Monoclonal Antibody Biosimilars in Oncology: Critical Appraisal of Available Data on Switching*. Clinical Therapetuics. Vol. 40; Nov 5, 2018.
2. Lyman, G., Zon, R., Harvey, D., Schilsky R. *Rationale, Opportunities, and Reality of Biosimilar Medications.* The New England Journal of Medicine. 378;21 May 24, 2018.

Background

First biotech molecules to expire were relatively small

insulin	5,808	mass units
filgrastim	18,800	mass units
erythropoietin	30,400	mass units

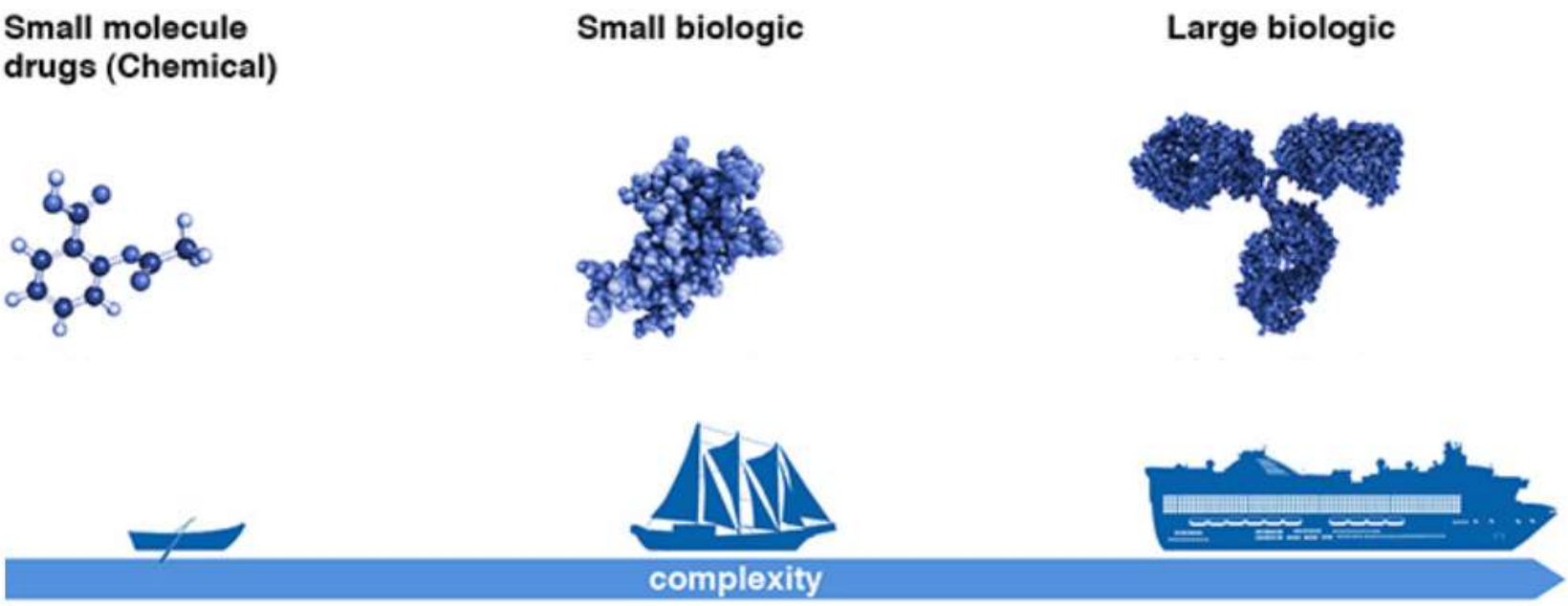
Monoclonal antibodies are larger molecules

Some	150,000	mass units

*Greater molecular heterogeneity

1. Ledon, N., Lage, A. Biosimilars and the Real World. MEDICC, Vol 19, No 4. October 2017.

Background



1. https://www.sandoz.com/stories/access-medicines/improving-access-biologic-medicines-through-biosimilars. Accessed 3/10/2019

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Biosimilar Manufacturing

Biosimilar Manufacturing

- Reverse-engineered
- Therapeutic proteins
  - Living cellular systems
  - Not stepwise chemical synthesis
- Essentially impossible to produce an identical copy of product
- Even batches of the same reference product that are produced with the use of the same cell line may be dissimilar.

1. Lyman, G., Zon, R., Harvey, D., Schilsky R. *Rationale, Opportunities, and Reality of Biosimilar Medications.* The New England Journal of Medicine. 378;21 May 24, 2018.

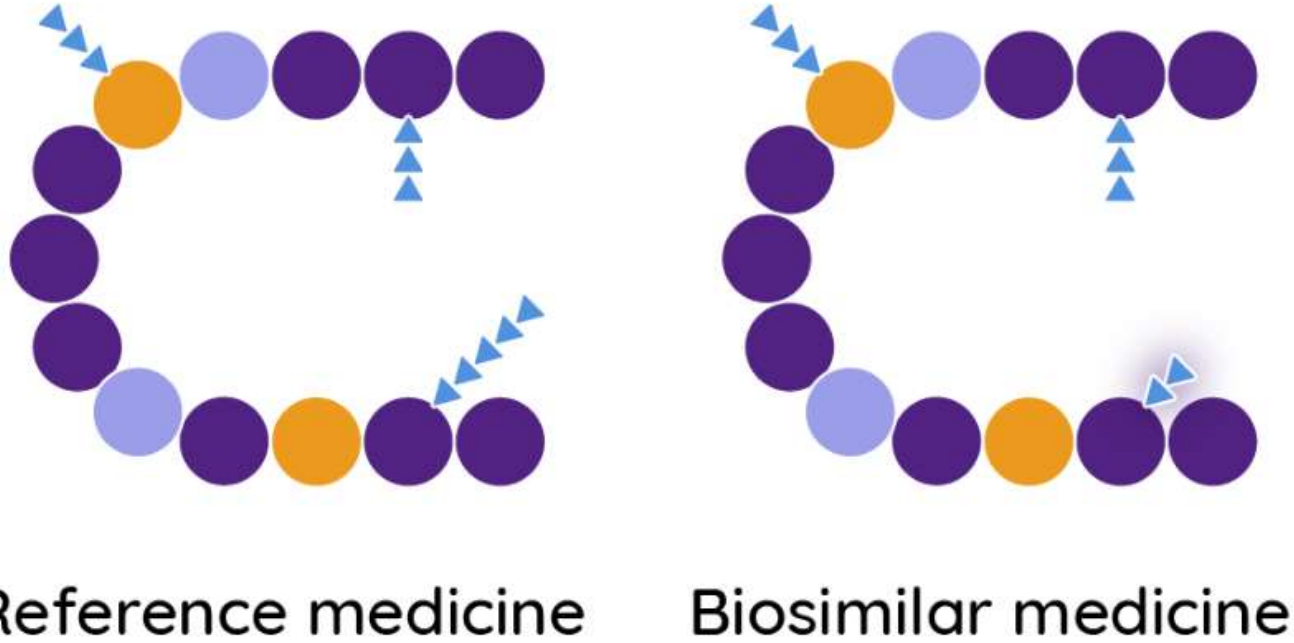
Biosimilar Manufacturing

Biosimilars MUST have amino acid sequences that are the same as those in reference drug but may have minor differences due to:

- Post-translational protein modifications (e.g. alterations to C or N terminals)
- Glycosylation (e.g. addition of sugar residues to amino acids bearing amino or hydroxyl groups)
- Formulation (e.g. due to different excipients)

1. Lyman, G., Zon, R., Harvey, D., Schilsky R. *Rationale, Opportunities, and Reality of Biosimilar Medications.* The New England Journal of Medicine. 378;21 May 24, 2018.

Biosimilar Manufacturing



1. https://www.epgonline.org/us/blogs/post/eular-2018-biosimilars.html. Accessed 3/10/2019

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Biosimilar Manufacturing

Molecular Variability "Drift"

- Differences at each step of manufacturing
- Not caused by production error
- Changes are inevitable based on current biologic production process
- Infliximab (37) etanercept (22) adalimumab (20) reported changes to regulator
- Accepted by regulatory entities without new clinical trials

1. Lyman, G., Zon, R., Harvey, D., Schilsky R. *Rationale, Opportunities, and Reality of Biosimilar Medications.* The New England Journal of Medicine. 378;21 May 24, 2018.
2. Ledon, N., Lage, A. Biosimilars and the Real World. MEDICC, Vol 19, No 4. October 2017.
3. Sullivan, P., DiGrazia, L. Analytical Characterization of Biosimilars. Am J Health-Syst Pharm Vo 74 No 8. April, 2017

Biosimilar Manufacturing

Molecular Variability "Drift"

- Manufacturer mandatory comparability plan
  - Product quality data compared before and after change
  - Routine continuous analyses on batches compared to historical data
- Biosimilar approval requires submission of *analytical comparability* and clinical studies that is much more extensive and in-depth compared to original producers after production process changes after regulatory approval

1. Lyman, G., Zon, R., Harvey, D., Schilsky R. *Rationale, Opportunities, and Reality of Biosimilar Medications.* The New England Journal of Medicine. 378;21 May 24, 2018.
2. Ledon, N., Lage, A. Biosimilars and the Real World. MEDICC, Vol 19, No 4. October 2017.
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Biosimilar Regulatory Approval

Regulatory Approval

Public Health Service Act

Biologic Price Competition and Innovation (BPCI) Act [351(k)]

2009

Amendment

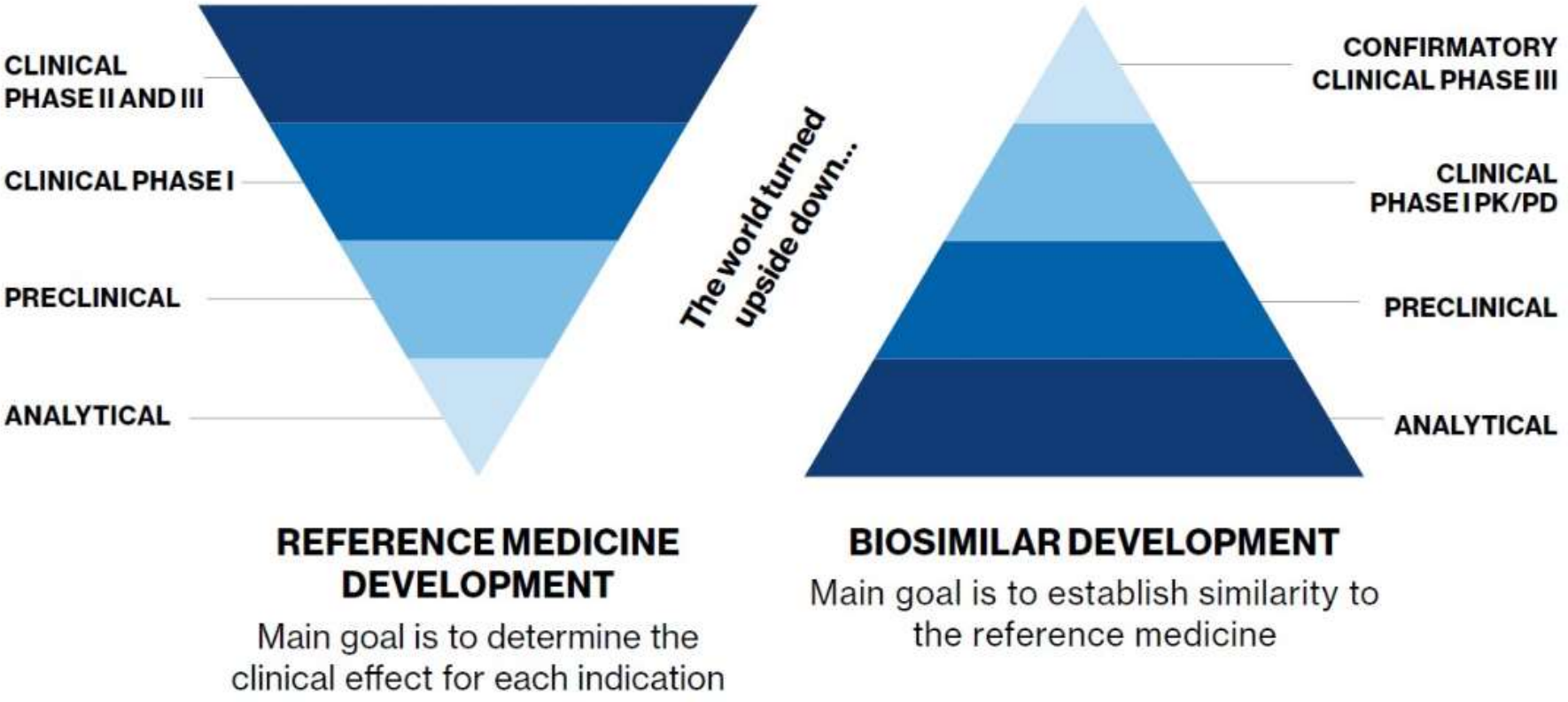
Abbreviated Licensure Pathways for biologics demonstrating “biosimilarity” or “Interchangeability” with FDA-licensed biologics

351(k) Not intended to re-establish proposed product “safety” & “efficacy”

351(k) Demonstrate proposed product is *highly similar* to reference biologic

1. Sullivan, P., DiGrazia, L. Analytical Characterization of Biosimilars. Am J Health-Syst Pharm Vo 74 No 8. April, 2017

Regulatory Approval



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

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Barriers to Entry

Operational Implementation

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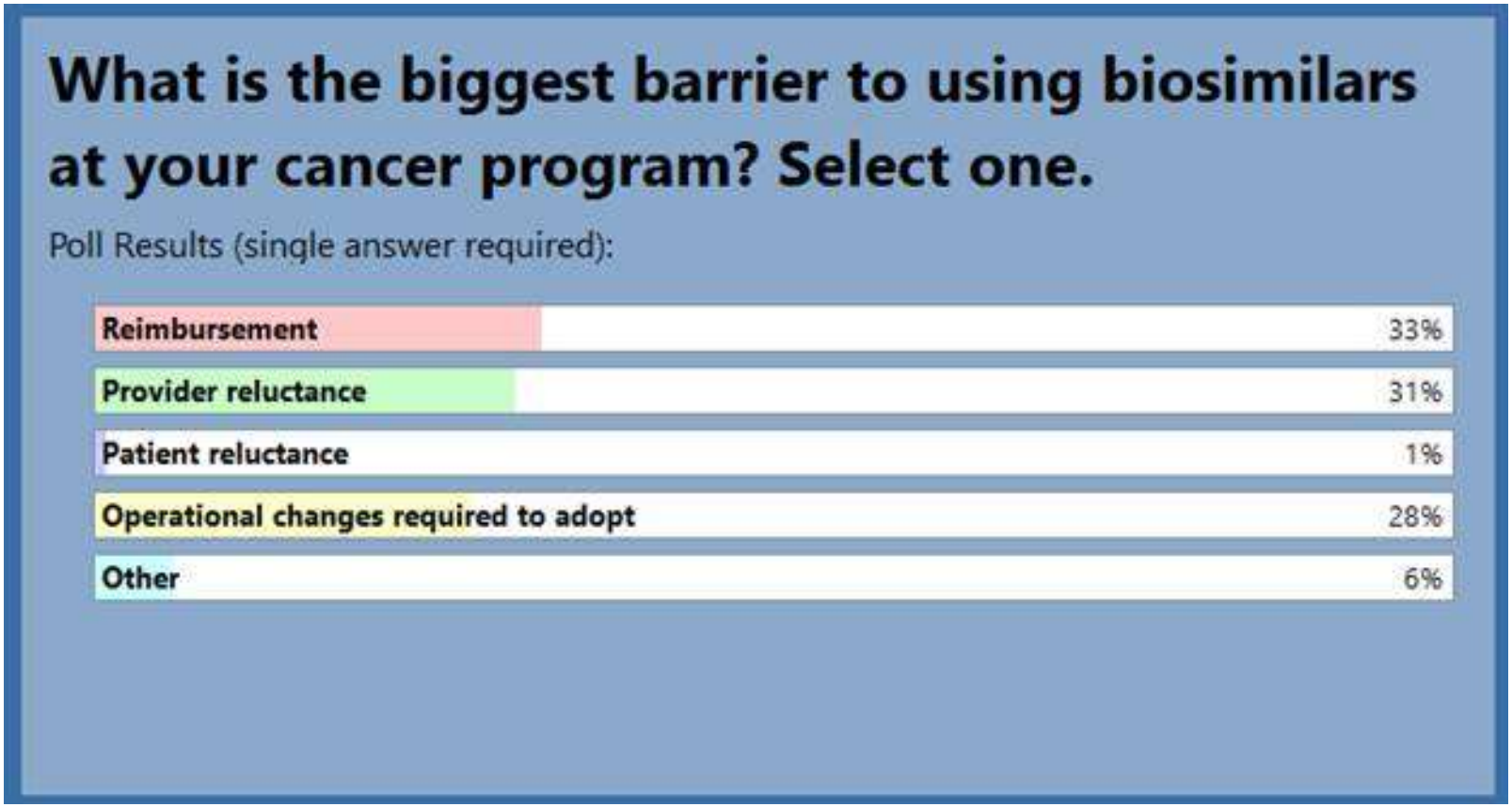
Barriers to Entry



1. "Managing Oncology Drug Cost" Live Poll. Advisory Board. 6/13/2019

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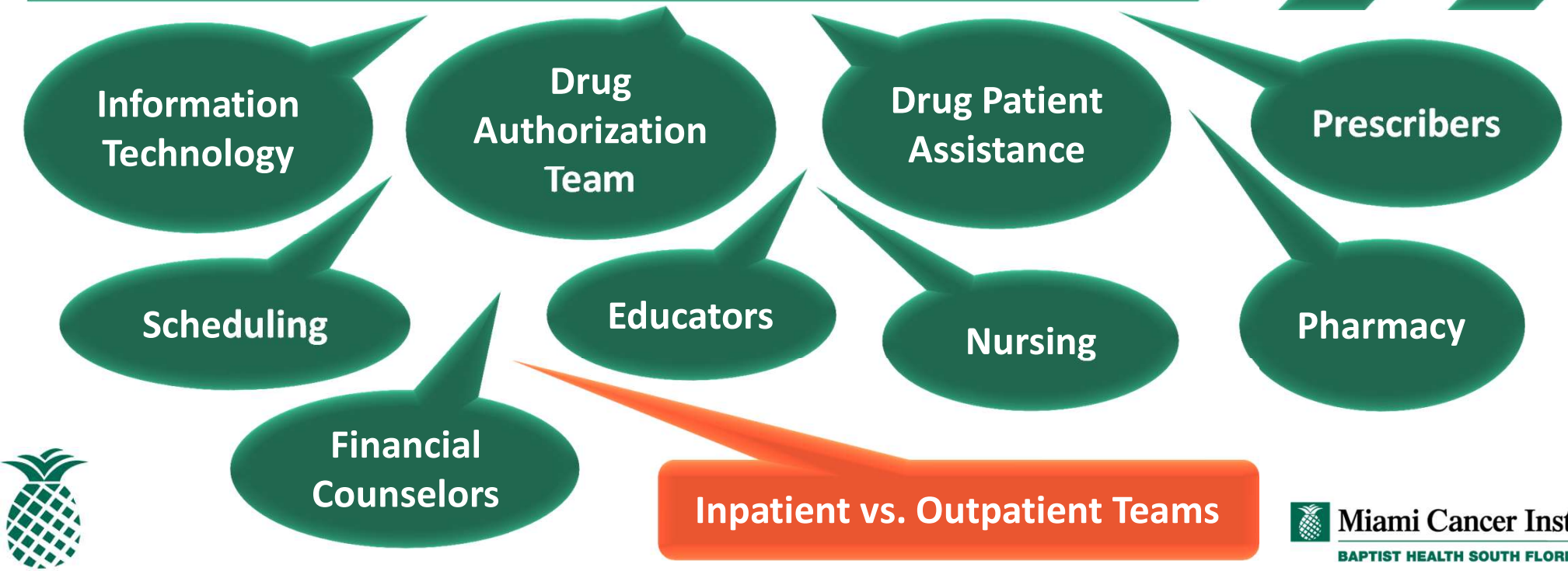
Operational Challenges

Mobilization of Resources and Teams



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Operational Challenges – Individualized Product Selection

Action	Previous	Current
Order	Specific Product e.g., OnPro	Generic order e.g., pegfilgrastim; not pointing to a particular product
Authorization Team Seeks Payer Certification	For specific product ordered by provider	As follow in order of preference: 1- Facility Preferred Product (previously determined by P&T) 2- If payer restrict to one product then tailor to payer coverage
Payer Certification Documentation	Only visible in Business Office (BO) system	Made available to pharmacy team via interface with pharmacy verification system
Product Selection	Back to prescribing provider if payer required a product different than originally order	Pharmacy selects product to be dispensed based on documentation payer certification

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Operational Challenges – Individualized Product Selection

- Transformational for efficiencies
- Satisfier to both Business Office and providers
- Pharmacy is in a lead role
  - Expecting provider to know which product to order relative to payer is unrealistic
- Positioned for success
  - Increasing number of biosimilar expected
  - Increasing number of formulations (e.g., SC)

Barriers to Entry

Reimbursement

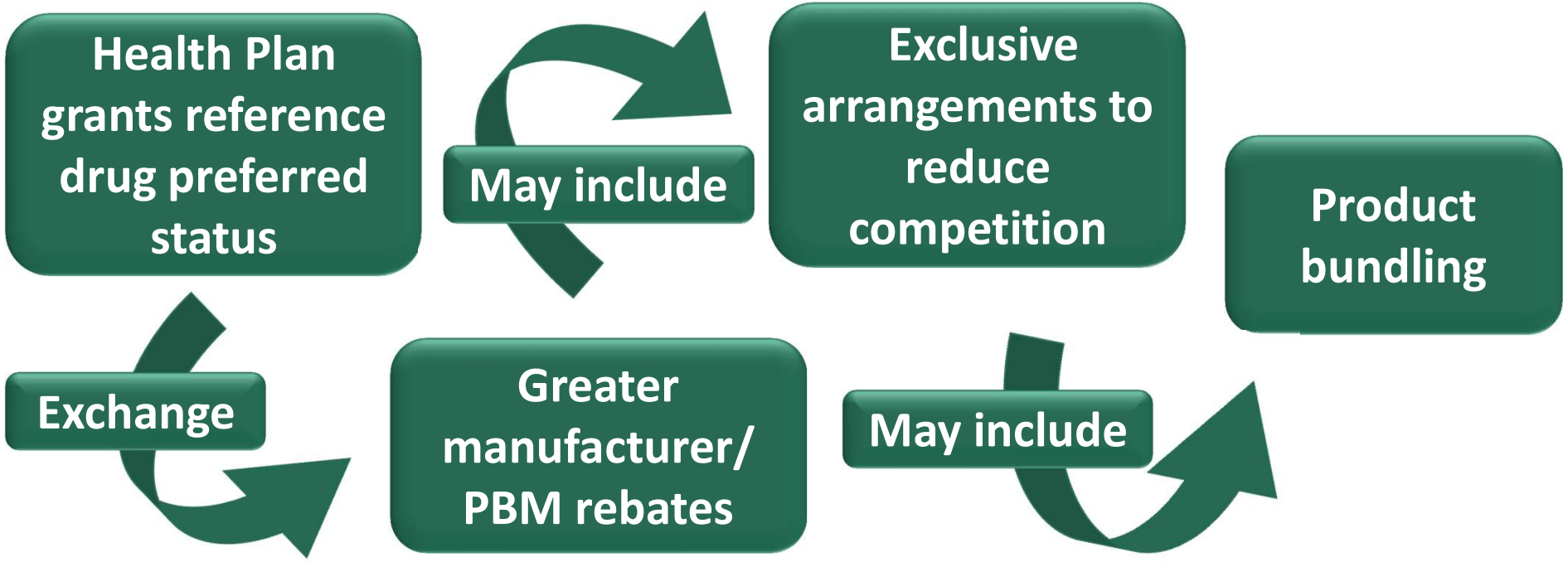
Barriers to Entry – Reimbursement

- Medicare, Medicaid and commercial payers have all approached biosimilar reimbursement differently

- Eroding revenue landscape
  1. new reimbursement models
  2. cuts from payer and government agencies
  3. marketplace ASP evolution
  4. margin declines

1. Wechsler, J. FDA Struggles to Advance Biosimilars. PharmExec.com Commercial Insights for the C-Suite. Volume 38, Issue 9. Sept,01,2018
2. Nabhan, C., Valley, A., Feinberg, B. *Barriers to Oncology Biosimilars Uptake in the United States*. The Oncologist. 2018;23:1261-1265
3. Lyman, G., Balaban, E., Diaz, M., Ferris, A., Tsao, A., Voest, E., Zon, R., Francisco, M., Green, S., Sherwood, S., Harvey, D., Schilsky, R. American Society of Clinical Oncology Statement: Biosimilars in Oncology. Journal of Clinical Oncology. Vol. 36 No. 12 April 2018.

Barriers to Entry – Rebate Arrangements "Rebate Trap"



- Highly controversial

Nabhan, C., Valley, A., Feinberg, B. *Barriers to Oncology Biosimilars Uptake in the United States*. The Oncologist. 2018;23:1261-1265
2. Editorial. Factors Influencing the Economics of Biosimilars in the US. Journal of Medical Economics. Vol 20, No 12, 1268-1271. 2017

Value-Based Oncology Care

Health Plan 1

[Rebate Model]

Drug A

Receives rebate from drug manufacturer

Requires practice to utilize higher cost reference product

Pays provider more based on higher charges

Health Plan 2

[No Rebate Model]

Drug A

DOES NOT receive rebate from drug manufacturer

Allows practice to use and realize cost savings from biosimilar

Benefits from lower charges from provider

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Barriers to Entry – Reimbursement

Medicare Reimbursement - Non 340b Entities

Reference	Average Selling Price (ASP) + 6%
Biosimilar WAC-Based	Biosimilar WAC* + 3%
Biosimilar ASP-Based	Biosimilar ASP + 6% of Reference ASP

ASP = Average Selling Price WAC = Wholesaler Acquisition Cost *Until ASP is established in 2-3 quarters

1. Part B Biosimilar Biological Product Payment and Required Modifiers. https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Part-B-Drugs/McrPartBDrugAvgSalesPrice/Part-B-Biosimilar-Biological-Product-Payment . Accessed October 19

Barriers to Entry – Reimbursement

Medicare Reimbursement - Non 340b Entities

Reference	Average Selling Price (ASP) – 22.5%
Biosimilar ASP-Based	Biosimilar ASP* + 6% of Reference ASP
Biosimilar ASP-Based	Biosimilar ASP – 22.5% of Biosimilar ASP

ASP = Average Selling Price WAC = Wholesaler Acquisition Cost *For at least 3 years after ASP is established

1. Part B Biosimilar Biological Product Payment and Required Modifiers. https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Part-B-Drugs/McrPartBDrugAvgSalesPrice/Part-B-Biosimilar-Biological-Product-Payment . Accessed October 19

Biosimilars in Value-Based Care

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Fee-For-Service Payment Model

Increased healthcare utilization and spending

Call for different types of contracts

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Value Driven Healthcare

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Oncology Care Model

Biosimilars Impact Goals

- Increase affordability
- Increase access to biologic treatments
- Improve outcomes
- Improve HRQoL
- Europe > U.S.

Biosimilars' Value Proposition

↓ cost

↔ quality

↑ access

↑ clinical outcomes

HRQoL = Health Related Quality of Life

1. Patel, K., Arantes, L., Tang, W., Fung, S. *The Role of Biosimilars in Value-Based Oncology Care*. Cancer management and Research 2018:10 4591-4602

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Value-Based – Patient Access

Biosimilars Impact on Patient Medication Access

Number Needed to Treat (NNT):

Number of patients needed to treat to:

1. prevent ONE additional bad outcome

2. achieve ONE additional good outcome

1. Sun, D., Andayani, T., Altyar, A., MacDonald, K., Abraham, I. *Potential Cost Savings From Chemotherapy-Induced Febrile Neutropenia With Biosimilar Filgrastim and Expanded Access to Targeted Antineoplastic Treatment Across the European Union G5 Countries: A Simulation Study.* Clinical Therapeutics. Vol 37 No. 4, 2015.

Value-Based – Patient Access

Potential Cost Savings From Chemotherapy-Induced Febrile Neutropenia With Biosimilar Filgrastim and Expanded Access to Targeted Antineoplastic Treatment Across the European Union G5 Countries: A Simulation Study

Diana Sun, MS[1,2]; Tri Murti Andayani, PhD[3]; Ahmed Altyar, PharmD[1,4]; Karen MacDonald, PhD[2]; and Ivo Abraham, PhD[1,2]

1. Sun, D., Andayani, T., Altyar, A., MacDonald, K., Abraham, I. *Potential Cost Savings From Chemotherapy-Induced Febrile Neutropenia With Biosimilar Filgrastim and Expanded Access to Targeted Antineoplastic Treatment Across the European Union G5 Countries: A Simulation Study.* Clinical Therapeutics. Vol 37 No. 4, 2015.

Value-Based – Patient Access

Number Needed to Convert (NNC)

Number of patients needed to convert, to treat ONE additional patient

Table III. Cost savings and expanded treatment access achieved under 100% conversion from originator filgrastim to biosimilar filgrastim (per a panel of 10,000 patients with cancer).

Variable	100% Conversion to Biosimilar Filgrastim
Day 14	
Cost savings from conversion, €	13,734,000
Expanded treatment access, No.	
Rituximab (NHL)	1213 (additional treatments, ie, 8% of annual incident patients)
Trastuzumab (BC)	461 (additional treatments, ie, 5% of annual incident patients)

BC = breast cancer; NHL = non-Hodgkin's lymphoma.

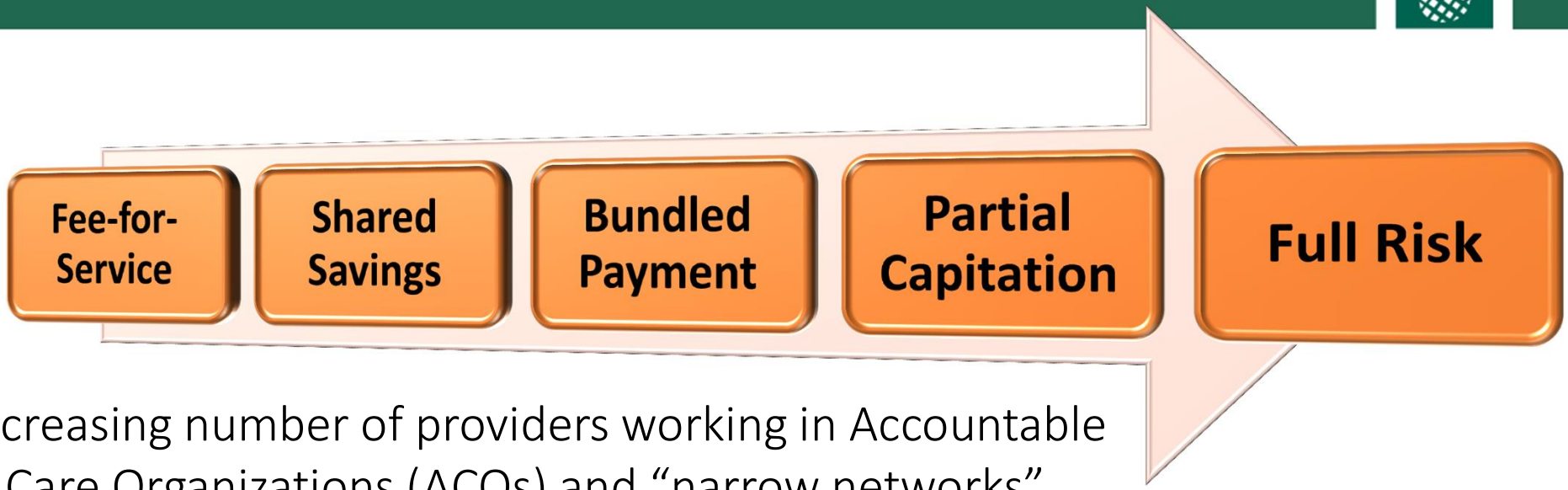
1. Sun, D., Andayani, T., Altyar, A., MacDonald, K., Abraham, I. *Potential Cost Savings From Chemotherapy-Induced Febrile Neutropenia With Biosimilar Filgrastim and Expanded Access to Targeted Antineoplastic Treatment Across the European Union G5 Countries: A Simulation Study.* Clinical Therapeutics. Vol 37 No. 4, 2015.

Value-Based – Patient Access

Reference bevacizumab	$790	*Access to ONE additional bevacizumab unit*
Biosimilar bevacizumab	$550	*per 2.3 purchases*
Reference trastuzumab	$1,540	*Access to ONE additional trastuzumab unit*
Biosimilar trastuzumab	$880	*per 1.3 purchases*

1. Sun, D., Andayani, T., Altyar, A., MacDonald, K., Abraham, I. *Potential Cost Savings From Chemotherapy-Induced Febrile Neutropenia With Biosimilar Filgrastim and Expanded Access to Targeted Antineoplastic Treatment Across the European Union G5 Countries: A Simulation Study.* Clinical Therapeutics. Vol 37 No. 4, 2015.

Payment Model Evolution



- Increasing number of providers working in Accountable Care Organizations (ACOs) and "narrow networks"
  - University of Pittsburgh Medical Center (UPMC) / Highmark - Allegheny Health System / Kaiser
    - Self-insured Employee Health Plans

Lawless, G. *Overcoming Challenges in the Emerging Biosimilar Landscape*. Journal of managed Care Medicine. Vol. 20 No. 4 July, 2017

Role of Employers in Value-Based Care

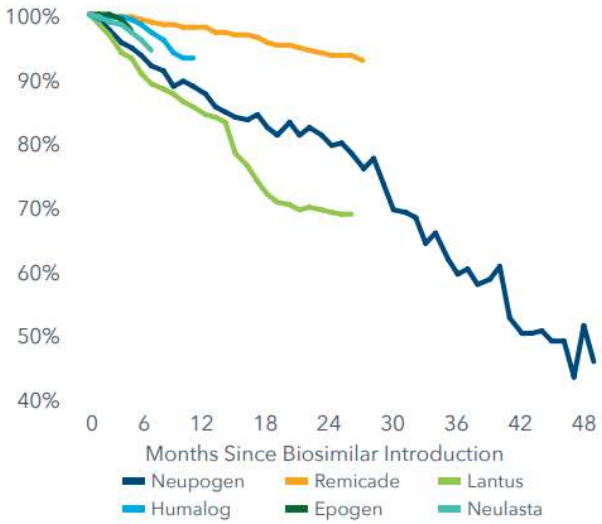
- Employers are the number one purchaser of health insurance
- Employers have a limited understanding of opportunities and risks
- Employers are in a position to influence benefit designs (e.g. biosimilar coverage) but need to understand obstacles
- Employers can align incentives at point of purchase
  - Getting system-owned specialty pharmacy in network
  - At parity biosimilar coverage

Current State of Affairs

Biologics growth continues and biosimilars now compete for market share among medicines with $15.9 billion in spending

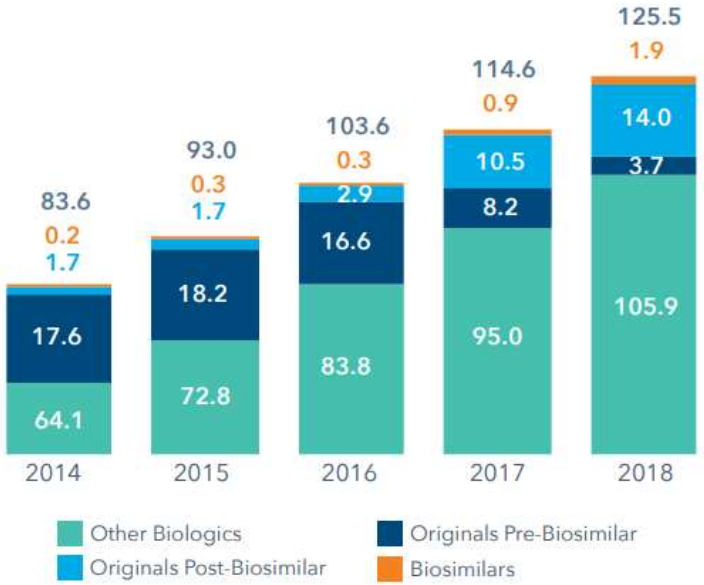
Exhibit 20: Impact of Biosimilars

Original Volume Share of Standard Units Since Biosimilar Introduction



Source: IQVIA National Sales Perspectives, IQVIA Institute, Jan 2019

Biologics Net Spending US$Bn



1. Medicine Use and Spending in the U.S. A Review of 2018 and Outlook to 2023. May 2019. IQVIA Institute for Human Data Science. https://www.iqvia.com/-/media/iqvia/pdfs/institute-reports/medicine-use-and-spending-in-the-us---a-review-of-2018-outlook-to-2023.pdf?_=1602972025818. Accessed October 17, 2020.

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Summary

- Biologics have revolutionized the treatment of serious health conditions over the last few decades
- Biologic innovation and marked utilization increases have led to a significant increase in healthcare spending
- Biosimilars offer high quality treatment alternatives at a fraction of the cost
    - Biosimilars provide a strong cost savings value proposition which helps practices achieve better performance in value-based payment models

Lawless, G. *Overcoming Challenges in the Emerging Biosimilar Landscape*. Journal of managed Care Medicine. Vol. 20 No. 4 July, 2017

Summary

- Many pre- and post-marketing implementation barriers exist leading to slow adoption of biosimilar utilization in the U.S.
- To reap the potential economic benefit biosimilars must be utilized
- Healthcare professionals uniquely positioned to promote the evaluation of the growing body of evidence and enable biosimilar utilization where there is evidence to support the use.

Integration of Biosimilars in Oncology Care

Jorge J. García, PharmD, MS, MHA, MBA, FACHE
Assistant Vice President - System Oncology Pharmacy Service Line
Baptist Health South Florida

Questions?

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