RhAPP

RHEUMATOLOGY ADVANCED PRACTICE PROVIDERS

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Biosimilars

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Learning Objectives

- Define Biosimilar
- Review the History of Biosimilar market
- Understand how FDA approves Biosimilar agents
- Appreciate the need for Biosimilars
- Apply Biosimilar understanding to your practice

Biotherapeutics or Biologicals

- Drug therapy products where the active substance is extracted or produced from a biological source
- Recombinant proteins and hormones, monoclonal antibodies (mAbs), cytokines, growth factors, gene therapy products, vaccines, cell-based products, gene-silencing/editing therapies, tissue-engineered products, and stem cell therapies

FDA Definition of a Biosimilar

An FDA-approved biosimilar is a biological product that is highly similar to and has no clinically meaningful differences in terms of safety, purity and potency (safety and effectiveness) from an already FDA-approved product, called the reference product.

Biological products are highly complex, and often used to treat patients with serious and life-threatening conditions. The law allowing FDA to approve biosimilars was designed to create competition, increase patient access, and potentially reduce cost of important therapies.

Biosimilar Definition

- US FDA [53]: “A biosimilar is a biological product that is highly similar to and has no clinically meaningful differences from an existing FDA-approved reference product.”
- EU EMA [5]: “A biosimilar is a biological medicine highly similar to another already approved biological medicine.”
- WHO [31]: “Similar biotherapeutic product (SBP). A biotherapeutic product that is similar in terms of quality, safety and efficacy to an already licensed reference biotherapeutic product.”

Approval History

- Small molecules -regulated under the federal Food, Drug, and Cosmetic Act (FDCA).
  - New Drug Application (NDA) to the FDA.
- Biologics - regulated under the Public Health Service Act (PHSA)
  - Biologics Licensing Application (BLA) for approval.
- Line between small-molecule and biologic is not always clear
  - Older biologics were approved under the FDCA. –
  - Examples are insulin, glucagon, and human growth hormone.
- The Affordable Care Act - pathway for abbreviated biosimilar approval in 2009 (via the Biologics Price Competition and Innovation Act - BPCIA).
  - Abbreviated pathway under section 351(k) of the PHSA by proving comparability to a previously approved reference biologic.

The First Biologics

- 1980s: The first biological medicinal products produced by DNA recombinant techniques were approved
- 1986: First monoclonal antibody receives FDA approval
- 1998: First biologic for rheumatoid arthritis is introduced: Omnitrope

2010-2014

- 2010: The Biologics Price Competition and Innovation Act (BPCIA), enacted in 2010, provided a framework for biosimilars approval, adoption and access in the U.S.

- 2014: FDA's first guidance issued on Development and Approval of Biosimilar Products in the U.S., creating clear regulatory expectations for biosimilar products. This guidance provides information on developing biosimilarity, safety and efficacy.

2015

- 2015: FDA Final Guidance issued on demonstrating biosimilarity with a reference product

- March 2015: First US biosimilar approved: ZARZIO (filgrastim-sndz) for patients with cancer receiving chemotherapy and radiation to support white blood cell creation

2016-2019

- 2016: FDA Final Guidance issued on naming and labeling for biosimilar products
- 2017: Centers for Medicare & Medicaid Services issues policy on biosimilars reimbursement, giving each biosimilar its own average sales price.
- 2018: FDA Revised Guidance on biosimilar extrapolation of indications and biosimilar interchangeability
- 2019: Bipartisan members of Congress introduced multiple pieces of legislation to incentivize biosimilar use and adoption

Extrapolation

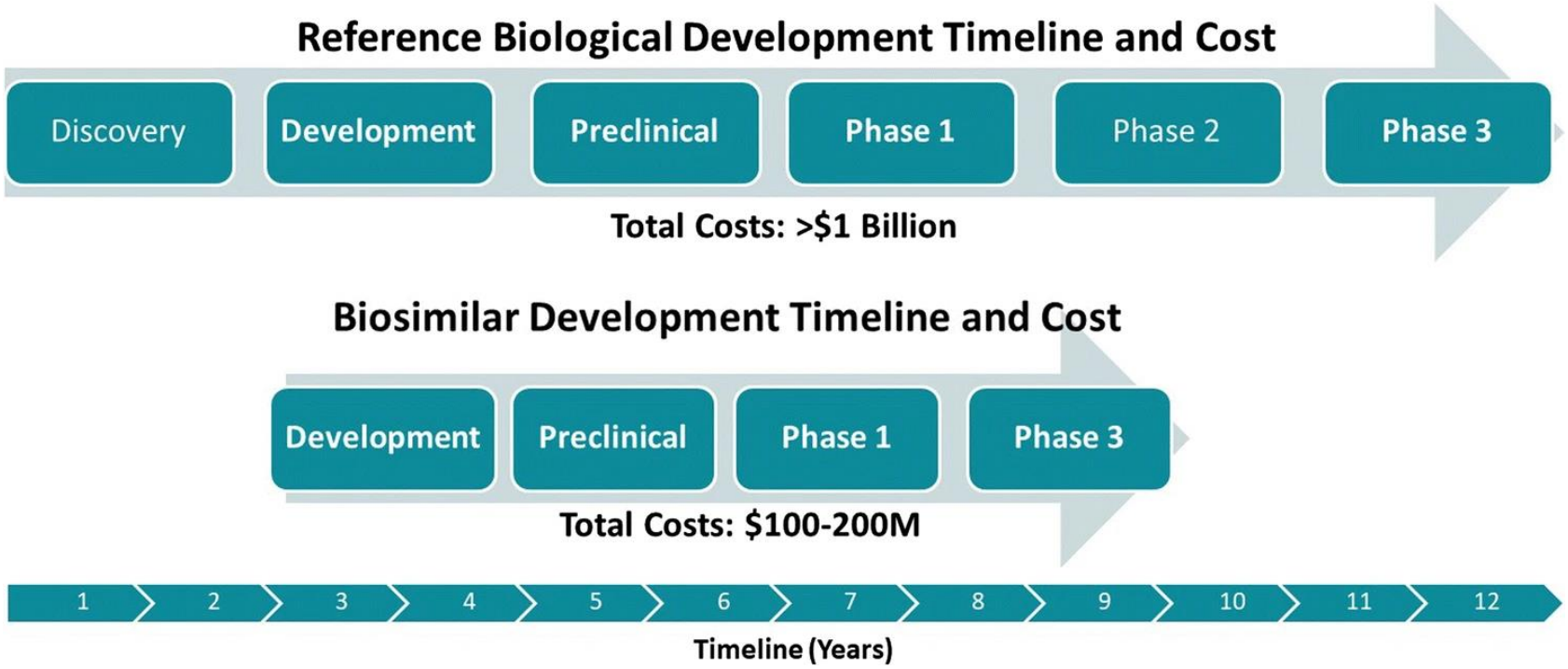
- Approval for same multiple indications the reference product was originally approved
  - Done without explicit clinical study of the biosimilar in each indications
  - Must provide adequate evidence that approach is justified
  - Data may only be extrapolated to indications approved for the reference product
- Biosimilar approval includes:
  - ALL indications of the innovator
  - Exception! May not Include indications protected by exclusive license (e.g. orphan or pediatric designations)
    - Ruxience (Rituxan Biosimilar) not indicated for RA until license runs out

Why Extrapolation?

- Biosimilar already known to be highly similar to the innovator chemically.
  - Clinical trial is simply a check that no surprises occur clinically, and a step BEYOND what generic drugs are required to show
  - If a biosimilar is clinically similar to the innovator in one indication, we can safely extrapolate to all other indications

- Financial benefits
  - Reduces the costs of biosimilar development and production
  - Reduces the number of indications that must be tested in clinical trials

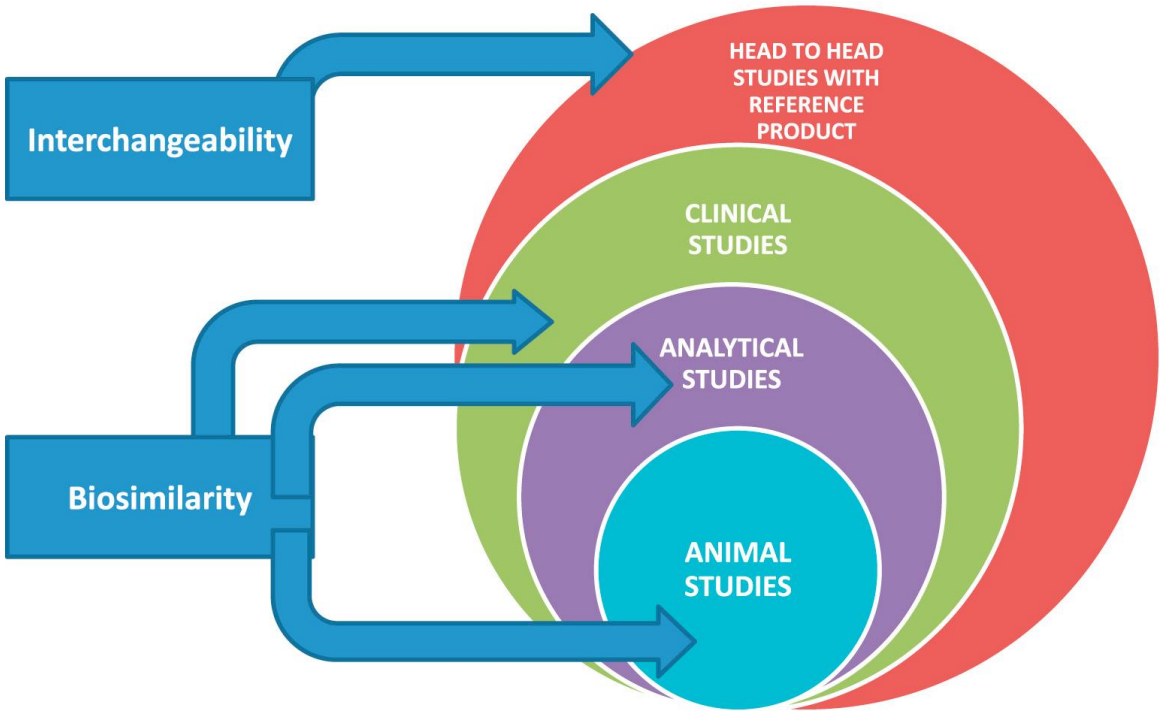
Biosimilar Approval Process



Interchangeability

- Interchangeability requires “the proposed interchangeable product can be expected to produce the same clinical result as the reference product in any given patient.”
- Designation also requires “for a biological product that is administered more than once to an individual, the risk in terms of safety or diminished efficacy of alternating or switching between use of the biological product and the reference product is not greater than the risk of using the reference product without such an alternation or switch.”
- The safety of switching is a commonly cited concern in regard to biosimilars, and many studies have recently been conducted to address this. Implementation of the Biologics Price Competition and Innovation Act of 2009 | FDA

Interchangeability



www.npjournal.orgBiosimilars: Opportunities and Challenges for Nurse Practitioners - The Journal for Nurse ... | 1541 x 949 · 196 kB · jpeg

Interchangeability Economic Incentives

- BPCIA awards one year of exclusivity to the first sponsor of an interchangeable product over subsequent interchangeable products for the same biologic

- Pharmacists able to automatically substitute the interchangeable product
  - Could speed biosimilar adoption
  - Pharmacist interchangeable ability defined under state vs federal law

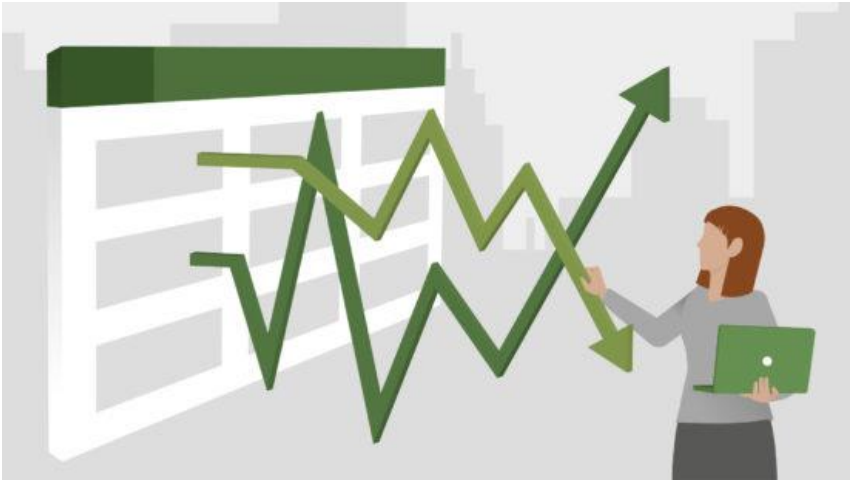
Social and Economic Challenges

- Population is aging → rising prevalence of Chronic Conditions
- Global spending on pharmaceutical products continues to increase (~81 billion in 2018)
- Biologics are an important but expensive portion of new drugs (40% of US pharmaceutical spending)

Generic Drug Landscape

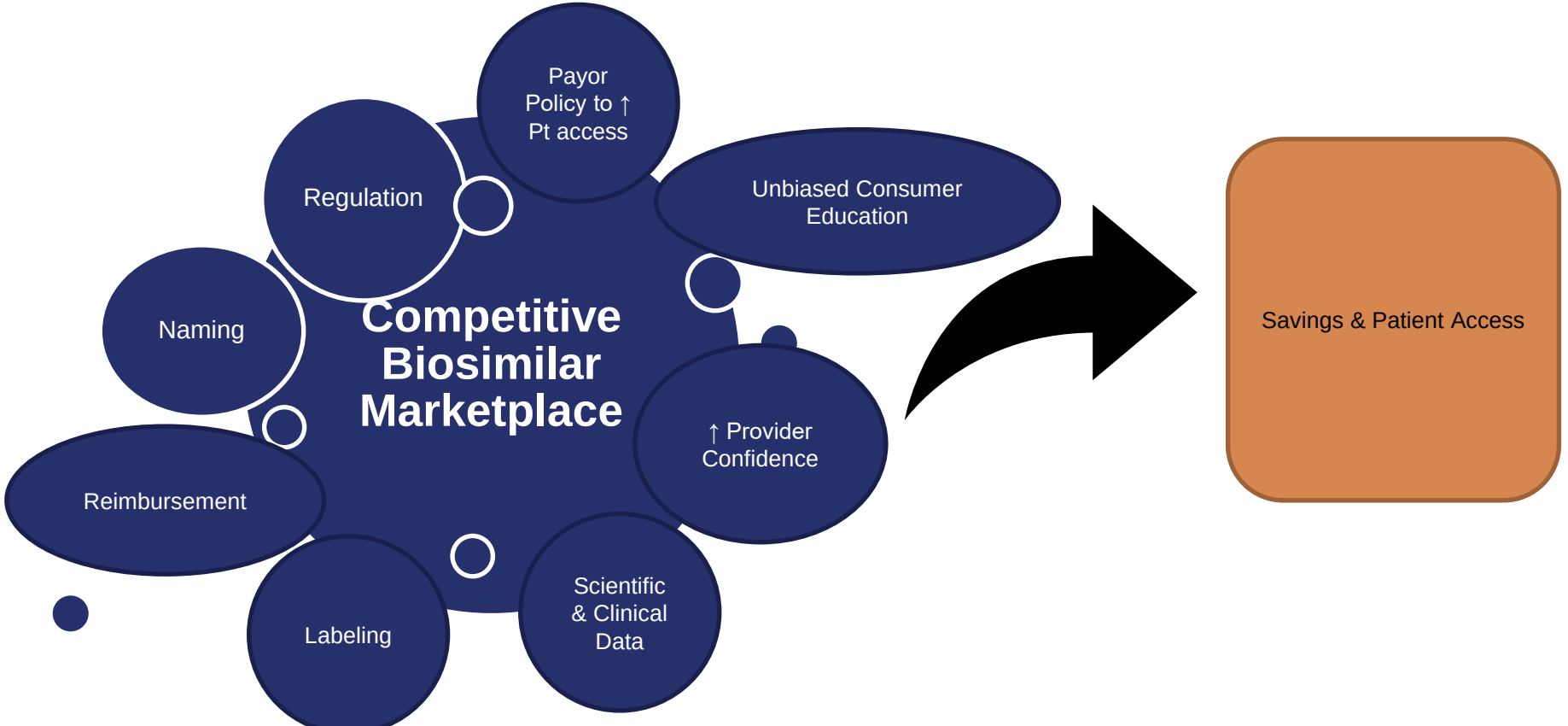
- 1984- Hatch-Waxman Drug Price Competition and Patent Term Restoration Act
  - Generic Share is nearly 90% today
  - ~293 BILLION Saved in 2018 alone

RAND reports Cost Savings



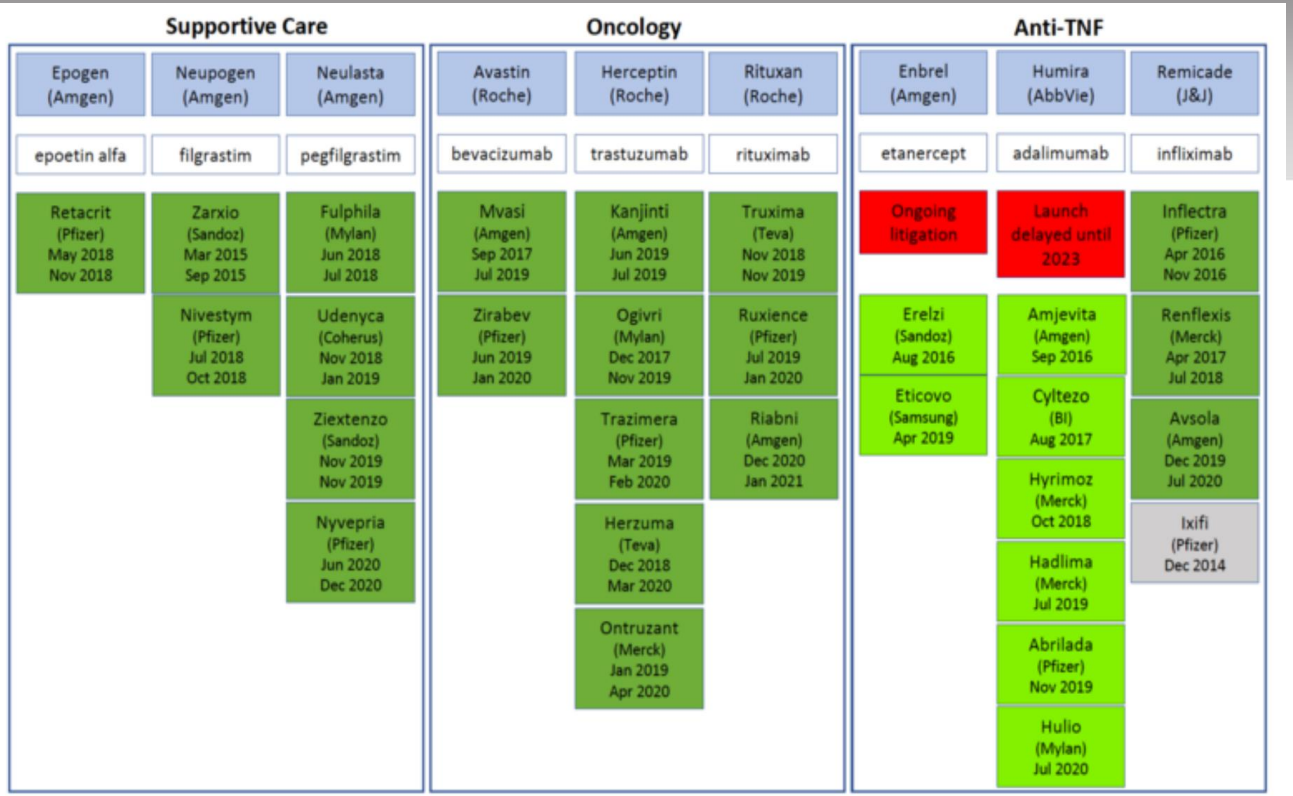
- Cost savings potential of biosimilars to be $54 billion over ten years
- Lower- to upper-bound range of $25 billion to $150 billion.

Several Aspects Required for Successful Biosimilar Market Formation



Reality for Biosimilars

- Patent Abuse Blocking access due to delayed launch of biosimilars
  - Cost US health system greater than $7.6 billion in lost savings since 2015
- Adoption Barriers- brand-name biologic company anti-competitive tactics
  - Additional $2.2 billion in lost savings



Approval and launch dates for US biosimilars – 2021 (gabionline.net)

Reactions

- Commercial payors dictating what biosimilar will be approved
  - In some cases they do not let you know the biosimilar must be prescribed.
- The infusion center of choice may have specific formularies
- Some medical benefits differ from drug benefit coverage (office vs home infusion)

Reactions

Treatment guidelines are discussing biosimilars

- 2021 ACR states under Guiding Principles: Biosimilars are considered equivalent to FDA-approved originator bDMARDs

Large push for both provider and consumer education around biosimilars

- Drug companies
- Association participation offering Continued Education Credit

Change Continues with YOU

Biosimilar Market Has Increased in US by 10-15% in the last 2 years

- Keeping up to date with the Biosimilar Market
  - Ask your Pharmacist!
  - Find out what biosimilars are approved per payor
- Attitudes when talking with patients when making therapy choices
  - Explain what biosimilars
  - Discuss biosimilar availability and payor requirements
- Using generic names vs brand
  - Infliximab vs Remicade
  - Create order templates that include biosimilar names to ease ordering

Keep up to Date

- Biosimilarscouncil.org
- FDA website:
  - https://www.fda.gov/drugs/therapeutic-biologics-applications-bla/biosimilars
- FDA Purple Book: Database of Licensed Biological Products
  - https://purplebooksearch.fda.gov/

Summary

- Biosimilar agents go through extensive testing to ensure they are similar in nature to the reference biologic and prove no clinically meaningful difference.
- Biosimilar uptake has been slow in the united states market
- Several factors affect successful uptake of biosimilar market
- Biosimilar agents for use in rheumatology are currently available in the US for infliximab & rituximab

Questions?