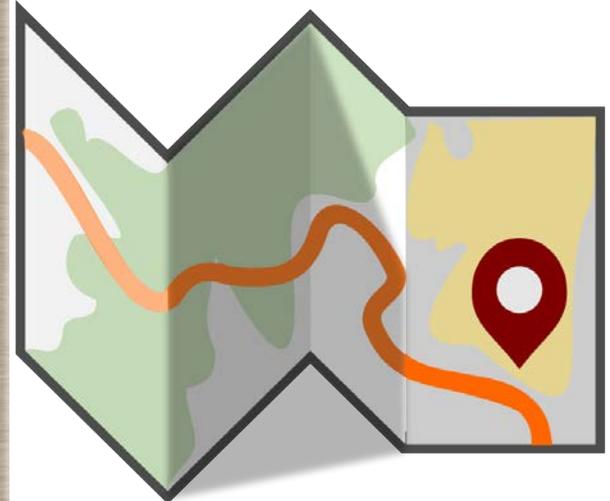


Biosimilars: Are we there yet?

Charles E. Daniels, BS Pharm, PhD
Clinical Professor & Pharmacist In Chief
UC San Diego Skaggs School of
Pharmacy and Pharmaceutical Sciences



Biosimilars on the Horizon



Why Look at Biosimilars?

“The biosimilars have the potential for significant cost savings and increasing patient access. This is in fact, *the only* apparent benefit of adoption of biosimilars.”

Ha CY, Kornbluth A. A critical review of biosimilars in IBD... *Inflamm Bowel Dis*. 2016; 22:2513-2526, October 2016.

Rx Drug Spending Increase Slows

- U.S. medication spending will grow between 6% and 9% through 2021
- *Increase* will decline from 12% to 6%-7% from 2015 to 2017
- Reflects the end of hepatitis C treatment-driven growth and ... the introduction of **biosimilars**

Outlook for Global Medicines Through 2021: Balancing Cost and Value, QuintilesIMS Institute

European Biosimilar Savings

- Mean price discounts of 15% to 40% have been seen for somatropin, epoetin, and filgrastim
- Germany
 - 30% to 40% reduction for epoetin and filgrastim
- Infliximab discounts
 - 25% in UK
 - 45% in France
 - 70% in Norway and Denmark

<http://www.quintiles.com/microsites/biosimilars-knowledge-connect/biosimilars-by-region/europe>, accessed September 27, 2016

Savings and Expanded Access

- Epoetins
 - European Union
 - Average increase of volume of treatment days = 16%
 - Change of price per treatment day = -27%
- G-CSFs
 - United Kingdom – from January 2009 (shortly after biosimilar launch) until January 2014
 - Volume of G-CSF use increased 104%
 - Volume of long acting G-CSF use decreased 18%

Delivering on the Potential of Biosimilar Medicines: The role of Functioning Competitive Markets, March 2016. IMS Institute for Healthcare Informatics



Perspective

Expert insights on a timely policy issue

The Cost Savings Potential of Biosimilar Drugs in the United States

Andrew W. Mulcahy, Zachary Predmore, and Soeren Mattke

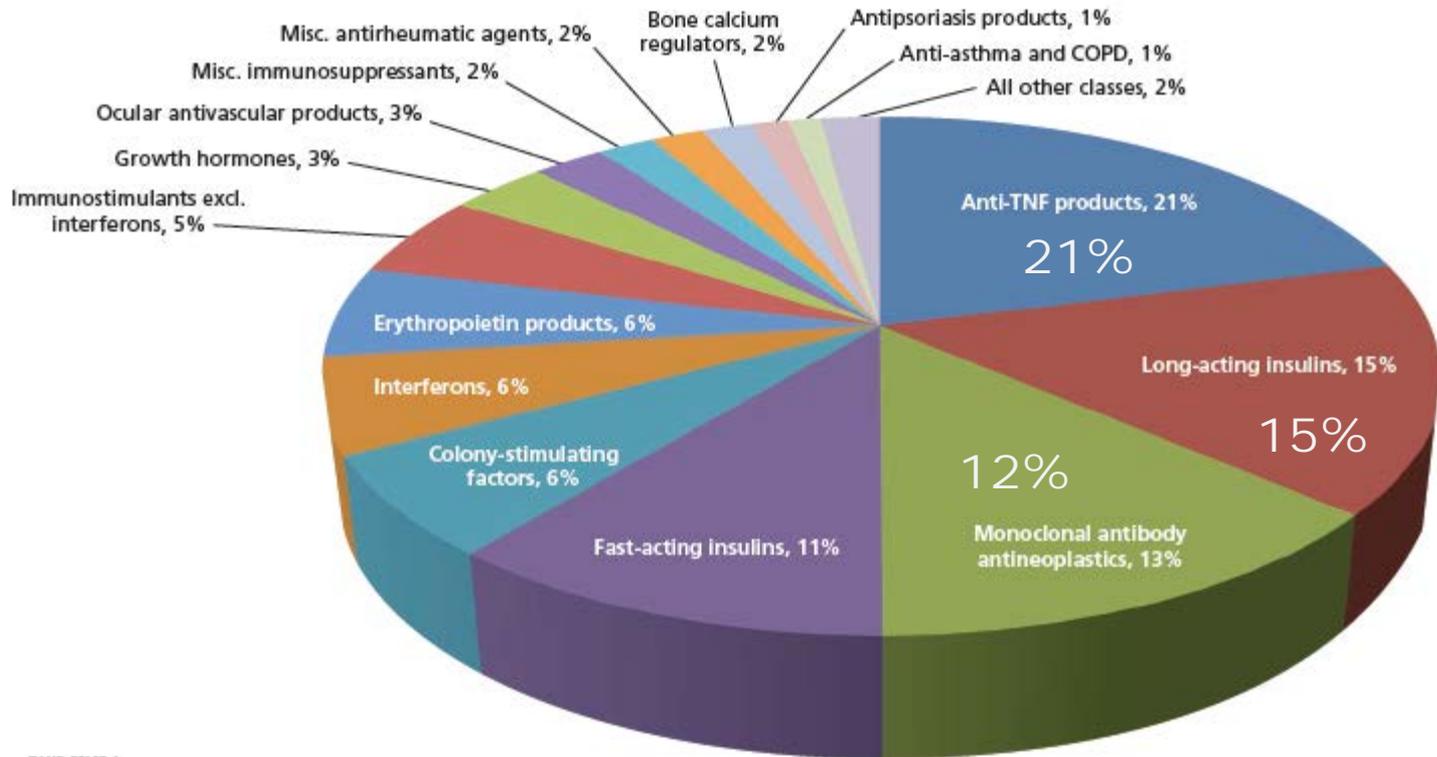
© Copyright 2014 RAND Corporation

RAND Corporation Estimate

- Analyzed top biologics purchases in 2013
 - included all biologics with sales over \$1 billion
 - Combined spend of \$66.3 billion
- Model developed a 10 year projection
 - 35% price discount and 60% biosimilar market penetration
- Direct potential cost savings of \$44.2 billion over 10 years
 - Reducing price discount to 10% = \$12.6 billion savings
 - Increasing penetration to 90% = \$66.2 billion savings

Potential Cost Savings Across Biologic Classes

Figure 1. Potential Cost Savings Across Biologic Classes

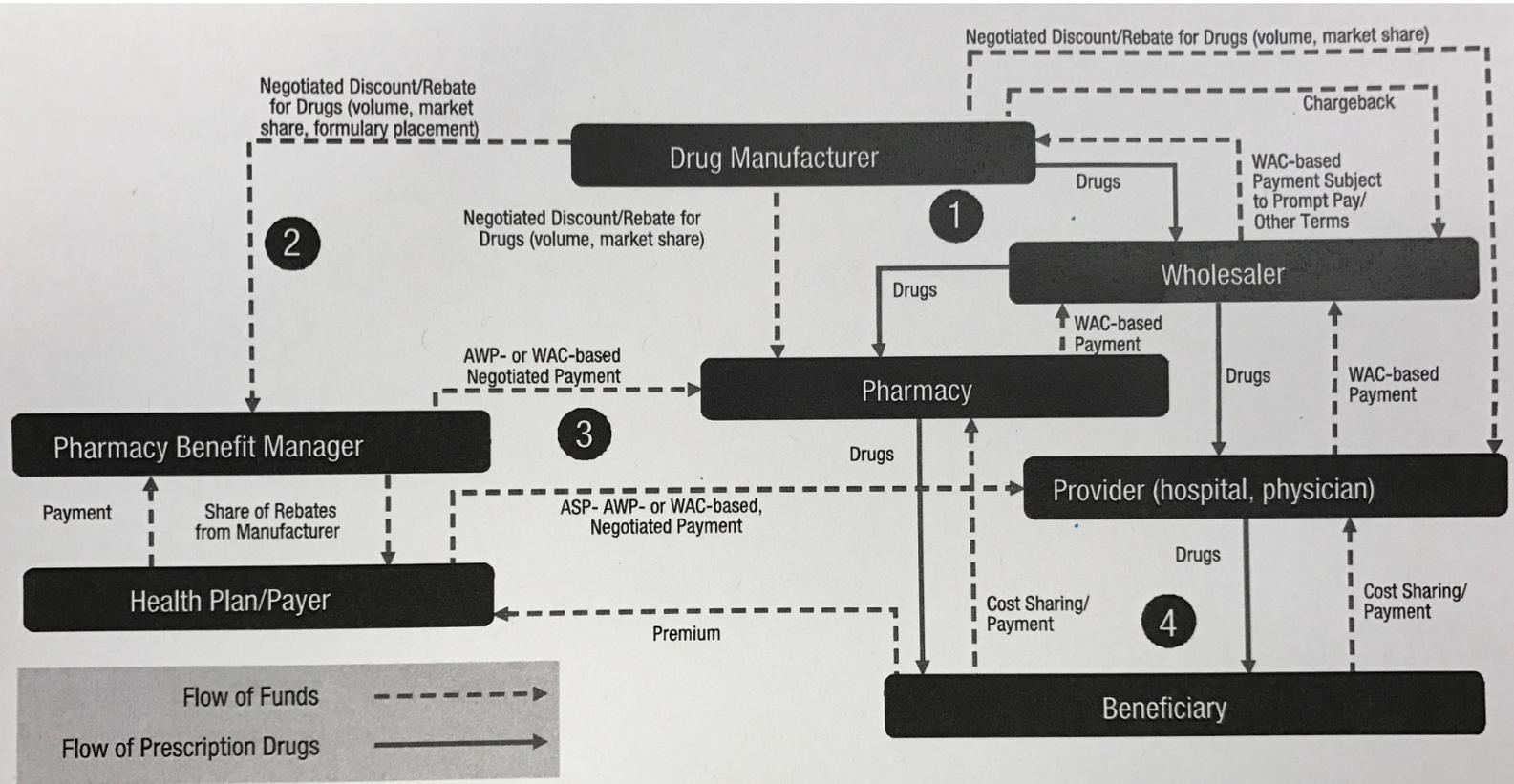


RAND PE127-1

Drivers of Biosimilar Cost Savings

- Currently approved biologic drugs
- FDA approval process
- Physician acceptance and prescribing patterns
- Price differential at entrance into the market and into the future
- Manufacturing costs
- Future trends in biologic utilization and cost per prescription
- Benefit coverage (pharmacy vs. medical)
- Safety and efficacy profile of biosimilar compared with reference biologic
- Employer benefit changes to incentivize use of biosimilars
- Therapeutic interchange
- Manufacturer rebates and discounts
- Approved indications for biosimilar

Pharmaceutical Payment Methods



Variation in Biosimilar Incentives

Medical Benefit

- Provider focused
- Focus on cost minimization
- Outpatient infused products
- Negotiated GPO prices

Pharmacy Benefit

- Payer focused
- Margin between cost and reimbursement
- Manufacturer rebates for formulary placement
- Influenced by PBM

Lucio S, Biosimilar Savings... ASHP Midyear. December 2016

Who Will Realize the Most from Biosimilar Cost Savings?

Setting	Self-administered from Retail or Mail-Order Pharmacy	Inpatient Facility Setting	Outpatient Facility Setting	Physician Office Setting
Insurers	++	+	++	++
Facilities	NA	+/-	+/-	NA
Physicians	NA	NA	+/-	+/-
Patients	++	+	+	+

++ = significant share of savings, + share of savings, +/- ambiguous, NA = not applicable

The Cost Savings Potential of Biosimilar Drugs in the United States. RAND Corporation, Perspective, 2014

Biosimilar Challenges

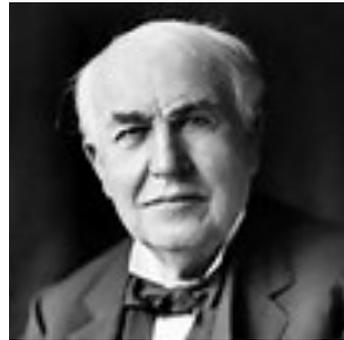
- Resolving provider confidence of biosimilar clinical issues
- Resolving provider knowledge of reimbursement process
- Creating shared payer and provider cost savings

JMCP Supplement Volume 22 Number 9a, September 2016

Recap

- Target: lower the price of biologic therapy
- Decreased prices and increased access have occurred within the EU market; too early to know about US
- Supply chain and reimbursement complexity make it challenging to evaluate the relative value of biosimilars and incentives to all stakeholders

“Opportunity is missed by most people because it is dressed in overalls and looks like work.”



Thomas A. Edison

Biosimilar Filgrastim USA

- Granix (Tbo-Filgrastim)
 - Not a “true” biosimilar
 - Not approved for all filgrastim indications
- Zarxio (Filgrastim-sndz)
 - True biosimilar (first FDA approved)
 - Same indications as Neupogen
- Tbo-filgrastim
 - 19% discount (WAC)
- Filgrastim-sndz
 - 15% initial discount (WAC)

<http://www.modernhealthcare.com/article/20160323/NEWS/160319919>, accessed September 27, 2016;
www.drugcodelookup.com, accessed September 27, 2016

Filgrastim Example

- Reviewed Granix at release
 - pharmacy department recommended to defer in anticipation of future biosimilar
- Reviewed idea for a full-swap of Zarxio for Neupogen with hematologists
- Waited for availability of Zarxio
- Waited for competitive price from Sandoz
- Got P&T approval to change for all new starts
- Implemented!

Zarxio conversion analysis 12/10/2015

Cost	Zarxio 300mcg syr	Neupogen 300mcg syr	Neupogen 300mcg vial	Zarxio 480mcg syr	Neupogen 480mcg syr	Neupogen 480mcg vial
340B subceiling	\$ 82.70	\$ 134.20	\$ 112.37	\$ 131.70	\$ 214.85	\$ 181.30
Inpatient DSH	\$ 192.96	\$ 212.50	\$ 200.19	\$ 307.30	\$ 338.34	\$ 318.77
Novation and 3% rebate	\$ 234.30			\$ 373.73		
Last 12 month purchases	Neupogen 300mcg vial	Neupogen 480mcg vial	Estimated annual expenses - Neupogen	Estimated annual expenses - Zarxio		
Inpatient	1680	1150				
Neupogen cost	\$ 336,319.20	\$ 366,585.50	\$ 702,904.70			
	Zarxio 300mcg syr	Zarxio 480mcg syr				
Zarxio cost	\$ 324,172.80	\$ 353,395.00		\$ 677,567.80		
Inpatient conversion saving	\$ 25,336.90					
Last 12 month purchases	Neupogen 300mcg syr	Neupogen 480mcg syr	Neupogen 300mcg vial	Neupogen 480mcg vial	Estimated annual expenses - Neupogen	Estimated annual expenses - Zarxio
Outpatient	1510	370	1710	750		
Neupogen cost	\$ 202,642.00	\$ 79,494.50	\$ 192,152.70	\$ 135,975.00	\$ 610,264.20	
Zarxio cost	\$ 124,877.00	\$ 48,729.00	\$ 141,417.00	\$ 98,775.00		\$ 413,798.00
Outpatient conversion saving	\$ 196,466.20					
Estimated IP+OP annual expenses (Neupogen)	\$ 1,313,168.90					
Estimated IP+OP annual expenses (Zarxio)	\$ 1,091,365.80					
Saving if full conversion	\$ 221,803.10					

\$220,000

Conversion Analysis

Inpatient Zarxio Ordering

The screenshot shows a software window titled "Preference List Search - Zziptwo,Liz". The search term "FILGRASTIM" is entered in the search bar. The window displays a table of search results with the following columns: Name, Type, Dose, Route, Frequency, Preference List, and Px Code. Two results are shown:

Name	Type	Dose	Route	Frequer	Pref List	Px Code
filgrastim (NEUPOGEN) injection			Subcuta	ONCE	UC IP HOSPI	
filgrastim-sndz (ZARXIO) injection			Subcuta	ONCE	UC IP HOSPI	

At the bottom of the window, it states "2 loaded. No more to load." and provides buttons for "Select & Stay", "Accept", and "Cancel".

Inpatient Zarxio Ordering

Alternative Selection

filgrastim (NEUPOGEN) injection: Subcutaneous, ONCE, 1 dose Today at 1045
Stored in the refrigerator.

The preferred G-CSF product at UC San Diego Health is filgrastim-sndz (Zarxio), which is the biosimilar equivalent of filgrastim (Neupogen).

Filgrastim-sndz is licensed for the same indications and dosing as the reference filgrastim with the exception of Hematopoietic Syndrome of Acute Radiation Syndrome, or H-ARS

Web Links
[UCSDH filgrastim-sndz \(ZARXIO\) Guideline](#)

Alternative	Details	Cost
filgrastim-sndz (ZARXIO) injection		
filgrastim-sndz (ZARXIO) IVPB		

Wholesaler Announcement

Good Morning,

Sandoz has announced their decision to add the full line pharmaceutical distribution channel of ZARXIO® effective January 3, 2017. Until this change, ZARXIO®, a biosimilar to Neupogen®, has been available only through the specialty channel. Please see attached for full details.

Thank you,

XXXXXXXXXXXXXXXXXXXX



FDA-approved!

Inflectra[®]
infliximab-dyyb

Pfizer Biosimilars

Dear Dr. Daniels,

INFLECTRA is approved by the FDA and is now available in the US

INFLECTRA for injection is the first biosimilar mAb* FDA-approved in the US.

INFLECTRA is biosimilar† to Remicade[®] (infliximab) and indicated for the treatment of the indications listed below. (Scroll down to read the full indications.)

Email on Pharmacist listserve, January 2017

Good morning,

We are in the process of reviewing Inflectra for formulary addition and are interested in how other institutions are addressing this biosimilar.

- Has your institution reviewed Inflectra?
- If so, has it been added to the formulary?
- What is your approach regarding interchangeability/switching from Remicade?

Kind regards,

XXXXX XXXXXXXX, PharmD, BCPS

Drug Information Specialist / Education Coordinator

XXXXXXXXXX University Hospital

Process or Fire Drill?

	Filgrastim	Infliximab
Confidence in Biosimilar manufacturer	Sandoz	Pfizer
Assessment of available data on likely clinical similarities	Bridging of Data	?
Patient level measure of effectiveness of biosimilar	Timely WBC Response	?
Prescriber homogeneity	Hematologists	?
Ease of product interchangeability	Straight Forward	?
Financial incentive to provider	Eventually	?
Reimbursement issues	Resolving	?

BIOSIMILARS



MEDICARE TO COVER PFIZER'S BIOSIMILAR INFLECTRA

January 9, 2017



The Centers for Medicare and Medicaid Services (CMS) has included Inflectra (infliximab-dyyb; Pfizer), a biosimilar to Remicade (infliximab; Janssen), in the 2017 Medicare Reimbursement schedule, according to a press release from Pfizer.

Inflectra will be available as a Medicare Part B-covered drug at a cost of 15% less than the wholesale acquisition price of the original formulation of Remicade. The current wholesale acquisition cost is not inclusive of discounts to payers, providers, distributors, and other purchasing organizations. The company announced that pricing for 340B hospitals is now also available, according to the press release.

In an effort to support patients and health care professionals, Pfizer also announced its enCompass program. The program is a comprehensive reimbursement service and patient support program that offers:

- coding and reimbursement support for providers;
- co-pay assistance to eligible patients who have commercial insurance that covers Inflectra; and,
- financial assistance for eligible uninsured and underinsured patients.

UnitedHealthcare to Change Lowest-cost Insulin Glargine on Commercial Plans

> Starting April 1, 2017, **BASAGLAR** will be the insulin glargine with the lowest co-pay for UnitedHealthcare commercial patients

basaglar®
insulin glargine injection
100 Units/mL

3 mL 100 units per mL
Basaglar®
KwikPen®
insulin glargine injection
For Single Patient Use Only
prefilled insulin delivery device

Not actual size.

JANUARY 6, 2017

Pfizer Announces Positive Results From the Comparative Study for Potential Biosimilar to Humira

By SPC News Staff

Pfizer Inc. announced that the comparative, confirmatory REFLECTIONS B538-02 study met its primary objective by demonstrating equivalent efficacy as measured by the American College of Rheumatology 20 (ACR20) response rate at week 12.

This trial is evaluating the efficacy, safety and immunogenicity of PF-06410293 compared with Humira (adalimumab, AbbVie), each taken with methotrexate, in patients with moderate to severe rheumatoid arthritis (RA). PF-06410293 is a monoclonal antibody being developed as a potential biosimilar to Humira.

U.S. SUPREME COURT DECLINES TO HEAR BIOLOGIC DRUG PATENT FIGHT

December 12, 2016



By Brendan Pierson

WASHINGTON (Reuters) - The U.S. Supreme Court on Monday declined to hear a case over whether companies that make copycat versions of biologic drugs must wait six months after winning federal approval before bringing them to the market.

The justices opted not to take up Apotex Inc's appeal of a July federal appeals court ruling that could delay the Canadian generic drug maker's launch of biosimilar versions of California-based Amgen Inc's Neulasta (pegfilgrastim), used to fight infection in cancer patients.

Approved by the U.S. Food and Drug Administration in 2002, Neulasta is one of Amgen's top-selling products, accounting for \$4.7 billion of its nearly \$21 billion in sales last year.

Biologic drugs like Neulasta are made using living cells. Unlike traditional drugs, biologic drugs cannot be copied exactly to make generic versions. A 2010 federal law, the Biologics Price Competition and Innovation Act, allows companies to seek approval to sell near-copies called biosimilars.

Novartis AG's Sandoz unit also has applied to make biosimilar versions of Neulasta and of Amgen's Neupogen (filgrastim), an older and less popular drug that works similarly but must be given more often. Neither application has yet been approved.



Are we there yet?

- Biosimilars have the potential to provide significant cost savings and improve patient access to key biologic medications
- Having a defined model for formulary decisions may help enable system-wide initiatives
- Release process, timing, pricing, reimbursement, and incentives are not predictable yet

Biosimilars on the Horizon

