Biosimilars: Market Disruption, Major Disappointment, or Still Too Early to Tell?

EMPAA 2018 Meeting

Steven Lucio, PharmD, BCPS

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Objectives

- **Describe the current regulatory, legal, and market landscape for biosimilars and the outlook for the next five years**
- **Identify the clinical and economic issues that have both enabled and hindered biosimilar uptake**
- **Discuss the patient care and financial impact of a less than robust biosimilar market and what can be done to avoid this outcome**

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What a Difference Four Years Can Make?

October 22, 2014

Regulatory actions

- No biosimilars approved
  - Tbo-filgrastim licensed (but not a biosimilar)
- 6 draft guidances published by the FDA
  - Interchangeability not covered

Legal challenges

- Impact of potential delays to the launch following biosimilar approvals
  - "Patent Dance"
  - 180 day notification

Economic issues

- Not clear given absence of biosimilars

Clinical concerns

- Lack of awareness of biosimilar concept

August 29, 2018

Regulation actions

- 12 biosimilars approved
  - 4 available (with 2 more pending launch)
- 10 biosimilar guidances
  - 6 finalized, 4 draft (including interchangeability), 1 withdrawn
  - Biosimilar Action Plan

Legal challenges

- June 2017 – U.S. Supreme Court ruled "Patent Dance" optional; 180 day notification can be given prior to approval

Economic issues

- Medicare Part B reimbursement change

Clinical concerns

- Somewhat abating; but still reflected in professional guidelines

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And Then There Were 12

	Product	Manufacturer	Date Approved	Date Marketed
1	Zarxio (filgrastim-sndz)	Sandoz	3/6/2015	9/3/2015
2	Inflectra (infliximab-dyyb)	Celltrion/Pfizer	4/5/2016	11/2016
3	Erelzi (etanercept-szzs)	Sandoz	8/30/2016	?
4	Amjevita (adalimumab-atto)	Amgen	9/23/2016	1/31/2023
5	Renflexis (infliximab-abda)	Samsung/Merck	4/21/2017	7/24/2017
6	Cyltezo (adalimumab-adbm)	Boehringer Ingelheim	8/5/2017	?
7	Mvasi (bevacizumab-awwb)	Amgen/Allergan	9/14/2017	?
8	Ogivri (trastuzumab-dkst)	Mylan	12/1/2017	?
9	Ixifi (infliximab-qbtx)	Pfizer	12/13/2017	?
10	Retacrit (epoetin alfa-epbx)	Pfizer	5/15/2018	Summer 2018?
11	Fulphila (pegfilgrastim-jmdb)	Mylan	6/4/2018	7/2018
12	Nivestym (filgrastim-aafi)	Pfizer	7/20/2018	Fall 2018?

The Pink Sheet, FDA Performance Tracker, Biosimilars, accessed 8/4/2018

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Known Biosimilar Pipeline for Remainder of 2018

INN	Manufacturer	Application Submitted	Estimated FDA Approval Date
Trastuzumab (CT-P6)	Teva and Celltrion	5/2017	3/2018#
Trastuzumab (ABP 980)	Amgen and Allergan	7/2017	5/2018#
Rituximab (GP2013)	Sandoz	7/2017	5/2018#
Trastuzumab (PF-05280014)	Pfizer	7/2017	5/2018#
Filgrastim	Adello Biologics	7/2017	5/2018?
Trastuzumab (SB3)	Samsung Bioepsis and Merck	10/2017	10/2018
Rituximab (CT-P10)	Teva and Celltrion	5/2018	11/2018
Adalimumab (GP2017)	Sandoz	11/2017	11/2018
Pegfilgrastim	Coherus	5/2018	11/3/2018

#Delayed due to receipt of complete response letter

The Pink Sheet, FDA Performance Tracker, Biosimilars, accessed 8/4/2018

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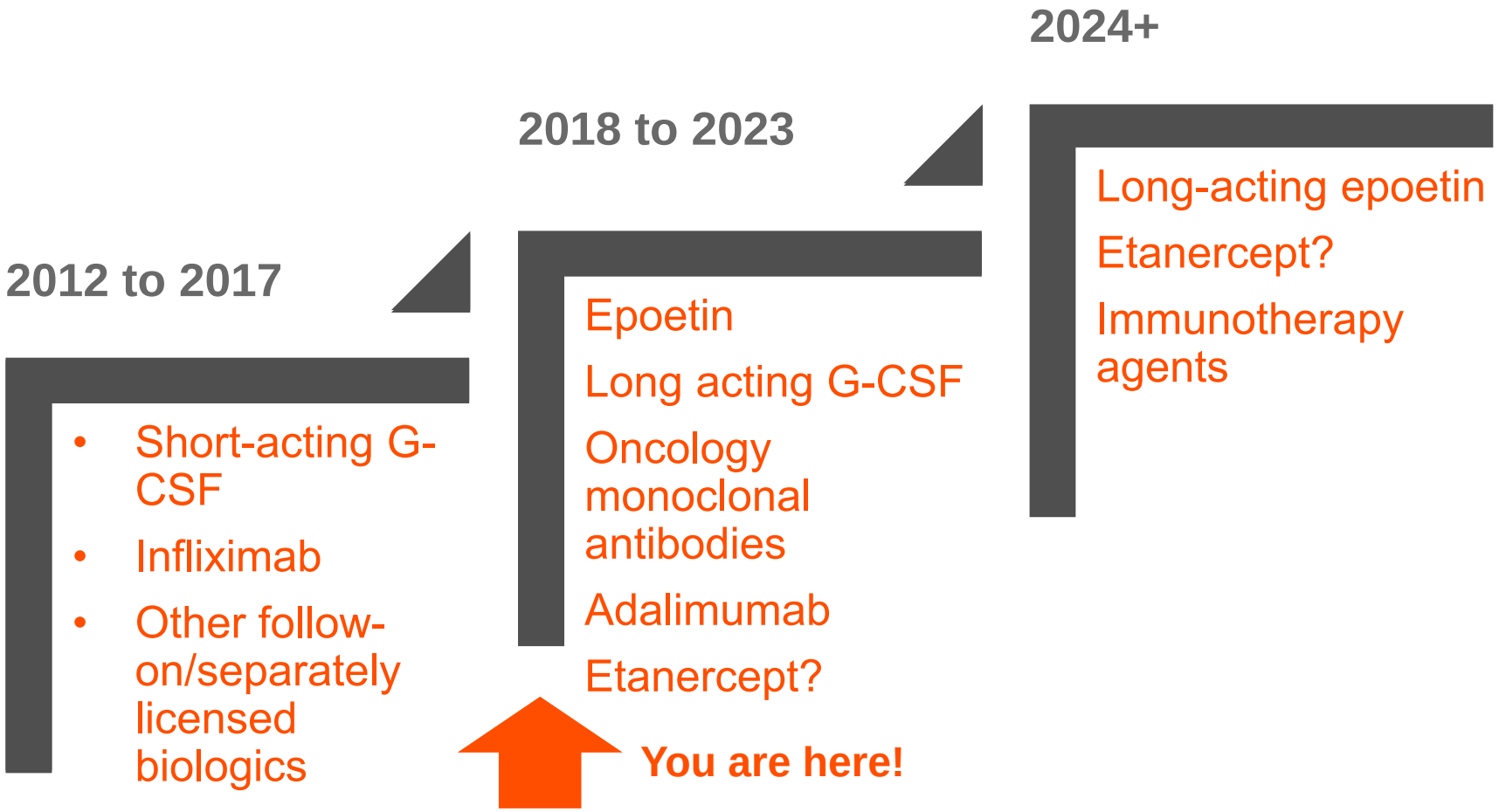
Phases of Biosimilar Market Development



G-CSF = granulocyte colony stimulating factor

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Biosimilar Legal and Regulatory Updates

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FDA Biosimilar Action Plan

11 actions identified by the Food and Drug Administration to:

- Improve the efficiency of biosimilar and interchangeable biologic development and approval
- Maximize scientific and regulatory clarify for the biosimilar development community
- Increase understanding of biosimilars among patients, clinicians, and payors
- Reduce gaming of FDA requirements or other attempts to unfairly delay competition

Open public hearing – September 4, 2018

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Biologic Competition on Granulocyte Colony Stimulating Factor Market

	2013	2014	2015	2016	2017	2018
Total Spend	$962 M	$927	$966M	$790 M	$682 M	$625 M*
Market share by product						
Filgrastim	100%	91%	84%	72%	57%	50%
Tbo-filgrastim		9%	15%	18%	19%	20%
Filgrastim-sndz			1%	9%	24%	30%

*annualized data

IQVIA SMART database, accessed August 4, 2018

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Biosimilar Competition in the Infliximab Market

	2016	2017	2018
Total Spend	$5.3B	$5.5B	$625 M*
Market share by product			
Infliximab	100%	99%	96.7%
Infliximab-dyyb		1%	3%
Infliximab-abda			0.3%

*annualized data

IQVIA SMART database, accessed August 4, 2018

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Why The Slow Uptake of Infliximab Biosimilars?

Scott Gottlieb's Comments Upon Release of Biosimilar Action Plan

"We've hear from multiple sources that some payors are requiring step-therapy or prior authorization on the reference biologic before patients can access a biosimilar. We see no clinical rationale for these practices, since a biosimilar must demonstrate, among other things, that is has no clinically meaningful differences from the reference product as a part of demonstrating biosimilarity."

https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm613881.htm, accessed August 4, 2018.

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Legal Updates

- **Pfizer lawsuit against J & J due to anticompetitive practices related to Remicade**
  - Kroger and Walgreen's filed a similar suit in June 2018
- **AbbVie and Amgen settlement**
  - AbbVie to grant non-exclusive patent licenses to Amgen
  - Amgen can launch biosimilar adalimumab in Europe Oct. 16, 2018 and in the U.S. Jan. 31, 2023
  - Amgen to pay AbbVie royalties
- **AbbVie and Samsung Bioepis agreement**
  - If approved, biosimilar can launch June 30, 2023
- **Many other legal issues remain throughout the court system**

The Pink Sheet, September 20, 26, and 28, 2017, January 3 and June 7,, 2018; https://www.reuters.com/article/us-abbvie-biogen/abbvie-samsung-bioepis-in-deal-humira-biosimilar-u-s-release-in-2023-idUSKCN1HC1SP, accessed April 6, 2018

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Are Coverage Levels Improving?

Example (filgrastim-sndz)

- **Cigna (Medical/Pharmacy) – 1 of 2 preferred**
- **CVS/Caremark (Medical/Pharmacy) – Exclusive**
- **ESI (Pharmacy) – 1 of 2 preferred**
- **Humana (Medical/Pharmacy) – 1 of 2 preferred**
- **Magellan (Medical) – Exclusive**
- **OptumRx (Pharmacy) – 1 of 3 preferred**
- **Prime Therapeutics (Pharmacy) 1 of 2 preferred**
- **United (Pharmacy) - Exclusive**

Source: Zarxio value proposition flashcard. Princeton, NJ: Sandoz, Inc: 2017.

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What Have We Learned from Biosimilars Approved to Date?

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The ABC's and E's of Biosimilars

Accept the Accuracy of Analytics

Build a Bridge between biosimilar and non-US licensed originator biologic

Curb the expectation of clinical trials in every indication

- Embrace extrapolation

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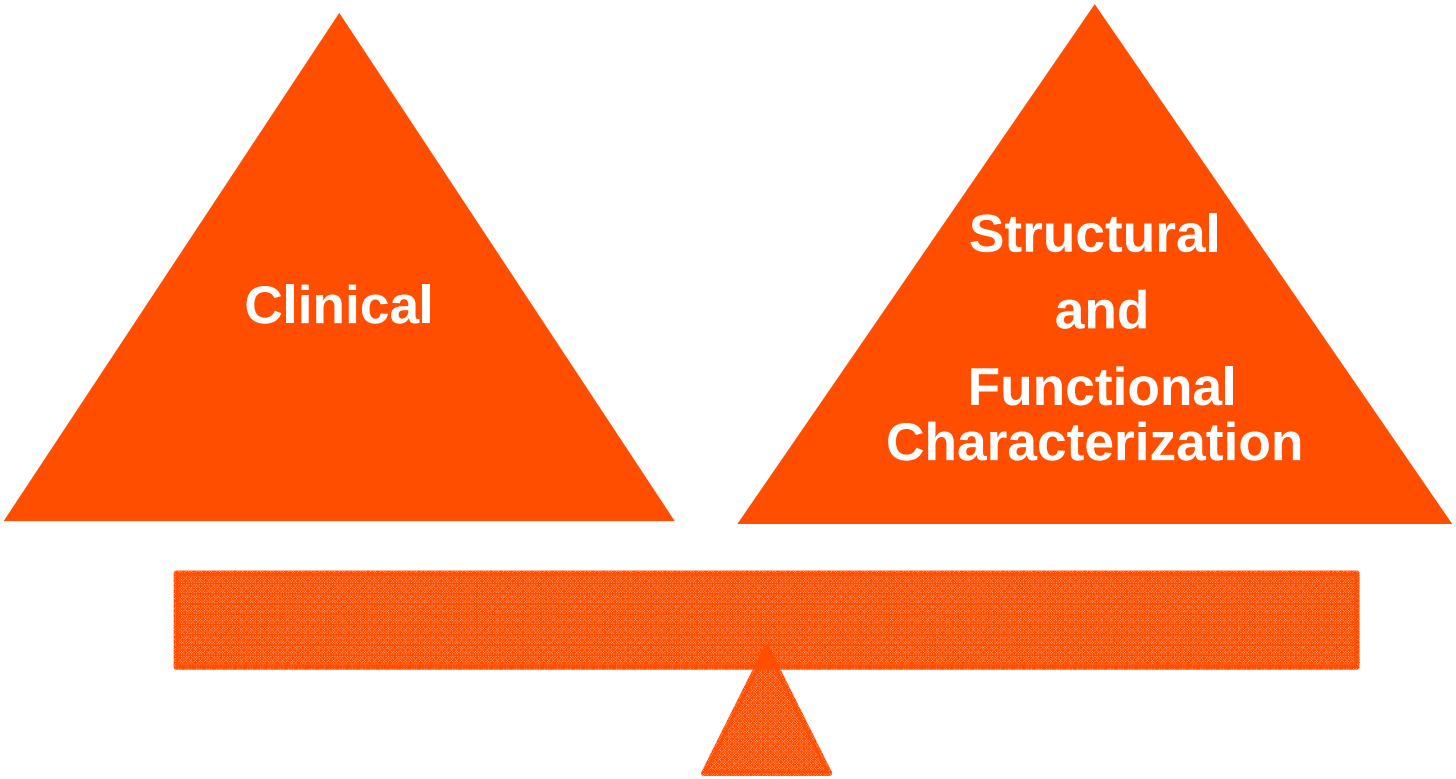
Biosimilars Balancing Act



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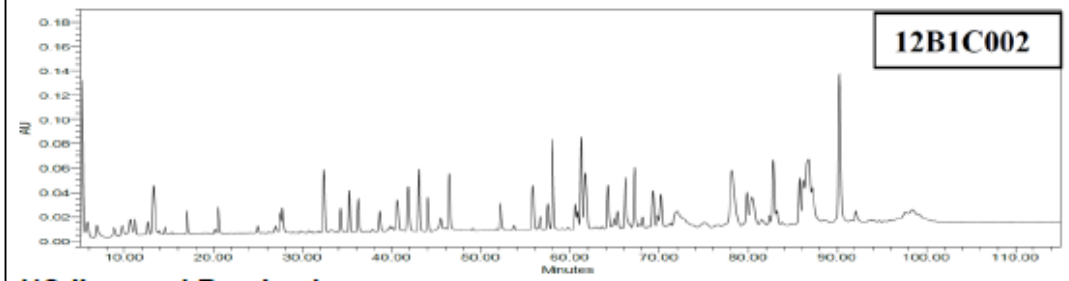
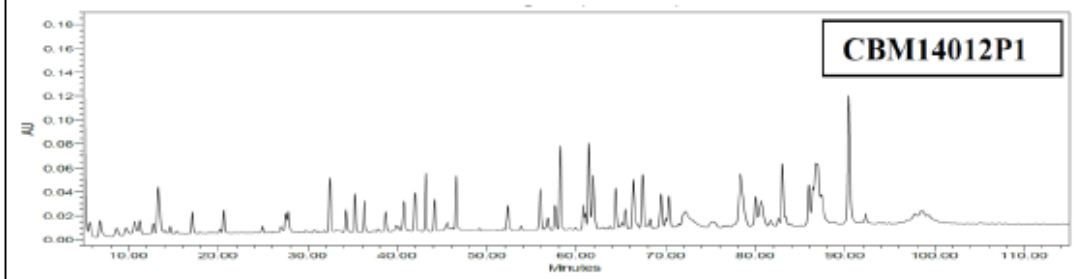
Infliximab-dyyb Analytical Characterization

Figure 2. RP-HPLC Chromatograms from the Tryptic Peptide Structural Characterization of CT-P13, US-licensed Remicade, and EU-approved Remicade

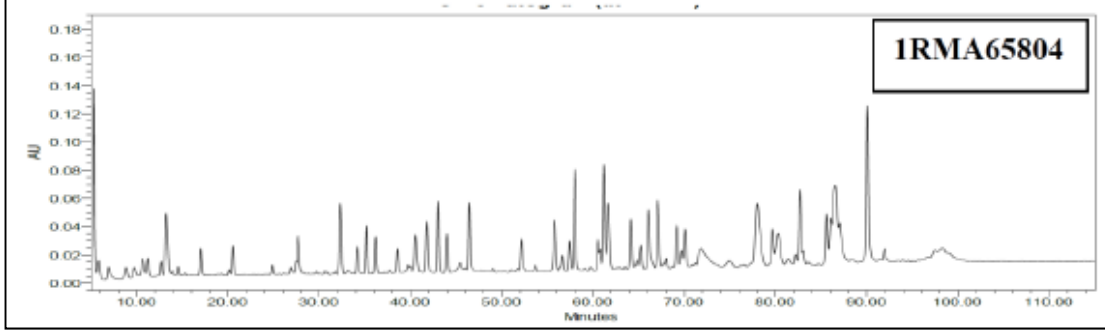
CT-P13



US-licensed Remicade



EU-approved Remicade



http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/ArthritisAdvisoryCommittee/UCM484859.pdf, accessed January 20, 2017

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The Efficiency of Bridging

Study (Dates)	Design (Objectives)	Patient Population (Total Number)	Treatment Arms	Number per arm
CT-P13 3.1 (Global, ex-US) 54 weeks (12/10 to 07/12)	R, DB, PG Comparative Clinical Study: Efficacy, Safety, PK, Immunogenicity	Moderate to Severe RA, MTX-IR N=606	CT-P13 3 mg/kg + MTX **EU-approved infliximab**	n = 302 n = 300
CT-P13 1.1 (Global, ex-US) 54 weeks (12/10 to 07/12)	R, DB, PG PK, Efficacy, Safety, Immunogenicity	Moderate to Severe AS N = 250	CT-P13 5 mg/kg **EU-approved infliximab**	n = 128 n = 122
CT-P13 1.4 Single Dose (10/13 to 02/14)	R, DB, PG, SD 3-way PK **bridging:** PK, Safety, Immunogenicity	Healthy volunteers N = 213	CT-P13 5 mg/kg EU-approved Remicade 5 mg/kg **US-licensed Remicade 5 mg/kg**	n = 71 n = 71 n = 71

http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/ArthritisAdvisoryCommittee/UCM484859.pdf, accessed January 20, 2017

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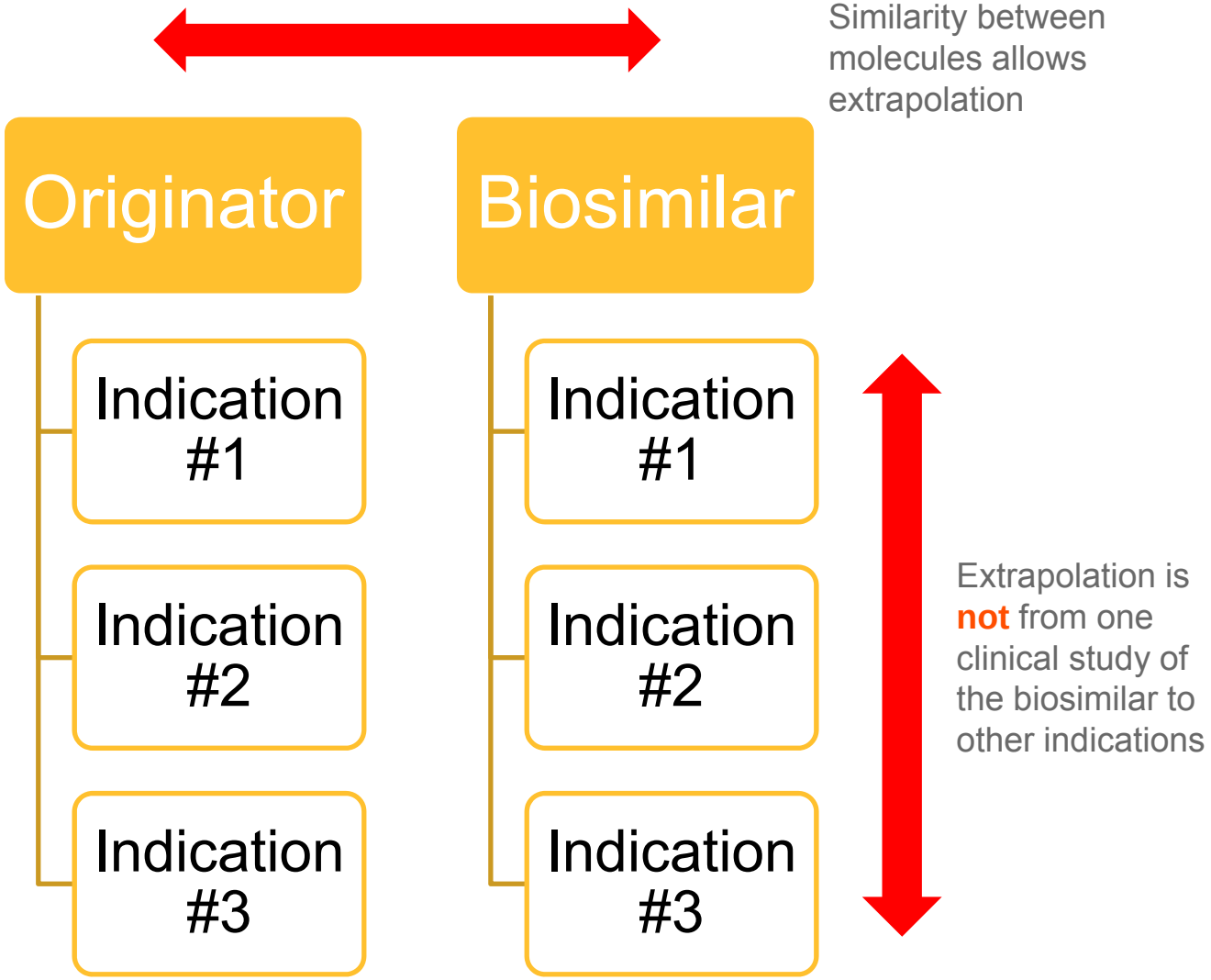
Understanding Extrapolation



Clin Pharmacol Ther 2015;97:215-7.

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Progression of Biosimilar Approvals

	Zarxio	Inflectra	Erelzi	Amjevita
Name	• Filgrastim-sndz (place holder) • Proposed name: filgrastim-bflm	• Infliximab-dyyb	• Etanercept-szzs	• Adalimumab-atto
Indications studied	• Myelosuppressive chemotherapy	• Rheumatoid arthritis • Ankylosing spondylitis	• Plaque psoriasis	• Rheumatoid arthritis • Plaque psoriasis
Indication coverage	• All non-orphan indications	• All non-orphan indications	• All indications* • However, no weight based dosing for children less than 63 kg (product only available in prefilled syringe)	• All non-orphan indications

*Since approval, Sandoz has requested removal of psoriatic arthritis and plaque psoriasis indication from label.

http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/OncologicDrugsAdvisoryCommittee/UCM428780.pdf;
http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/ArthritisAdvisoryCommittee/UCM484859.pdf;
http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/ArthritisAdvisoryCommittee/UCM510493.pdf;
http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/ArthritisAdvisoryCommittee/UCM510293.pdf;
https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2018/761042Orig1s001ltr.pdf, accessed April 6, 2018.

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What about Interchangeability?

Reference product

Biosimilar

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Fun with Biologic Naming

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What's in a Name?

Two names for biologics

Core name = (e.g. infliximab)

Proper name = core name plus four letter suffix (e.g. infliximab-dyyb)

- Suffix must be unique and devoid of meaning

Will ultimately apply to all biologics

Why?

Prevent inadvertent substitution

Improve pharmacovigilance

Encourage use of FDA-designated suffixes

Advance accurate perceptions about biologicals

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http://www.fda.gov/downloads/drugs/guidances/ucm459987.pdf, accessed May 23, 2018

Naming in Practice

Current	Proposed
Filgrastim	Filgrastim-jcwp
Filgrastim-sndz	Filgrastim-bflm
Tbo-filgrastim	Filgrastim-vkzt
Epoetin alfa	Epoetin alfa-cgkn
Infliximab	Infliximab-hjmt

- No timeline for implementation of proposed proper names for existing products
- However, have seen application to novel biologics (e.g. Helimbra – emicizumab-kxwh)

http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM459987.pdf; https://www.gene.com/download/pdf/hemlibra_prescribing.pdf, accessed May 23, 2018

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Changing Our Clinical Understanding

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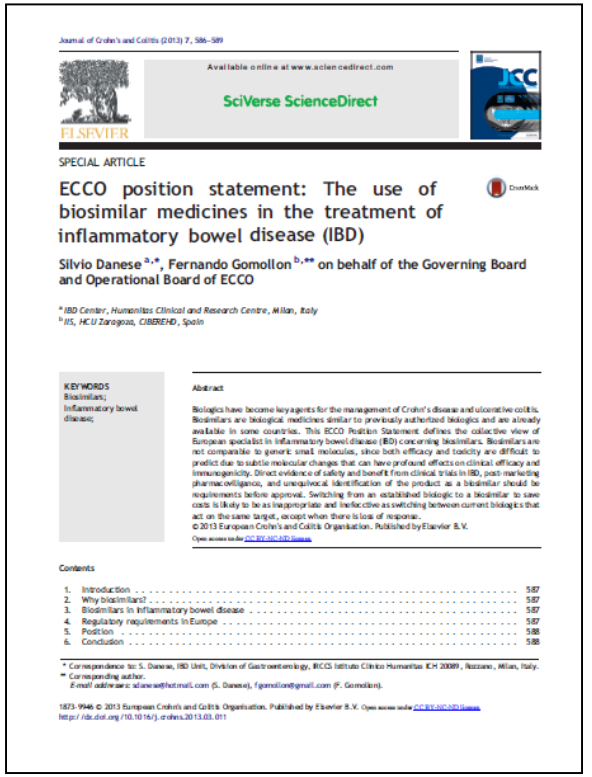
European Crohn's and Colitis Foundation Position Statement (2013)

- "Different biological and biosimilar medicines targeting the same molecule **are neither identical in efficacy nor toxicity**, even in the same clinical entity."
- "A biosimilar proven effective and safe for **one indication may not necessarily be effective and safe for a second indication** for which the reference biological has been shown to be safe and effective."
- "**Specific evidence obtained in patients with IBD should be required** to establish efficacy and safety for this specific indication, because experience with currently licensed biological medicines has already shown that clinical efficacy in IBD cannot be predicted by effectiveness in other indications, such as rheumatoid arthritis."



Journal of Crohn's and Colitis (2013) 7, 586–589

Available online at www.sciencedirect.com

SciVerse ScienceDirect

SPECIAL ARTICLE

ECCO position statement: The use of biosimilar medicines in the treatment of inflammatory bowel disease (IBD)

Silvio Danese [a,*], Fernando Gomollon [b,**] on behalf of the Governing Board and Operational Board of ECCO

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KEYWORDS
Biosimilars;
Inflammatory bowel disease;

Abstract

Biologics have become key agents for the management of Crohn's disease and ulcerative colitis. Biosimilars are biological medicines similar to previously authorized biologics and are already available in some countries. This ECCO Position Statement defines the collective view of European specialist in inflammatory bowel disease (IBD) concerning biosimilars. Biosimilars are not comparable to generic small molecules, since both efficacy and toxicity are difficult to predict due to subtle molecular changes that can have profound effects on clinical efficacy and immunogenicity. Direct evidence of safety and benefit from clinical trials in IBD, post-marketing pharmacovigilance, and unequivocal identification of the product as a biosimilar should be requirements before approval. Switching from an established biologic to a biosimilar to save costs is likely to be as inappropriate and ineffective as switching between current biologics that act on the same target, except when there is loss of response.

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Contents

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Journal of Crohn's and Colitis 2013;7:586-9.

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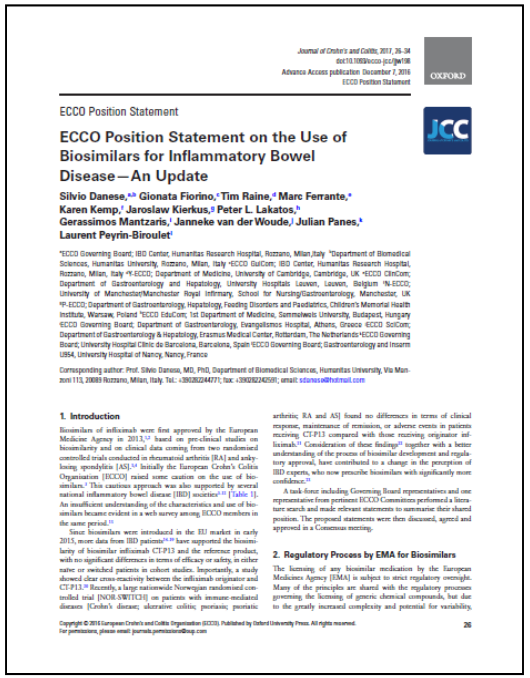
European Crohn's and Colitis Foundation Position Statement (2017)

- "Biosimilarity is **more sensitively** characterised by performing suitable in vitro assays than clinical studies."
- "Clinical studies of equivalence in the most sensitive indication can provide the basis for extrapolation. Therefore **data for the use of biosimilars in IBD can be extrapolated from another sensitive indication**."
- "When a biosimilar product is registered in the EU, it is considered to be **as efficacious as the reference product** when use in accordance with the information provided in the Summary of Product Characteristics."
- "**Switching from the originator to a biosimilar in patients with IBD is acceptable**. Studies of switching can provide valuable evidence for safety and efficacy. Scientific and clinical evidence is lacking regarding reverse switching, multiple switching, and cross-switching among biosimilars in IBD patients."



Journal of Crohn's and Colitis, 2017, 26–34
doi:10.1093/ecco-jcc/jjw186
Advance Access publication December 7, 2016
ECCO Position Statement

ECCO Position Statement

ECCO Position Statement on the Use of Biosimilars for Inflammatory Bowel Disease—An Update

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1. Introduction

Biosimilars of infliximab were first approved by the European Medicines Agency in 2013,[1,2] based on pre-clinical studies on biosimilarity and on clinical data coming from two randomised controlled trials conducted in rheumatoid arthritis [RA] and ankylosing spondylitis [AS].[3,4] Initially the European Crohn's Colitis Organisation [ECCO] raised some caution on the use of biosimilars.[5] This cautious approach was also supported by several national inflammatory bowel disease [IBD] societies[6–10] [Table 1]. An insufficient understanding of the characteristics and use of biosimilars became evident in a web survey among ECCO members in the same period.[11]

Since biosimilars were introduced in the EU market in early 2015, more data from IBD patients[12–14] have supported the biosimilarity of biosimilar infliximab CT-P13 and the reference product, with no significant differences in terms of efficacy or safety, in either naïve or switched patients in cohort studies. Importantly, a study showed clear cross-reactivity between the infliximab originator and CT-P13.[15] Recently, a large nationwide Norwegian randomised controlled trial [NOR-SWITCH] on patients with immune-mediated diseases [Crohn's disease; ulcerative colitis; psoriasis; psoriatic arthritis; RA and AS] found no differences in terms of clinical response, maintenance of remission, or adverse events in patients receiving CT-P13 compared with those receiving originator infliximab.[16] Consideration of these findings[17] together with a better understanding of the process of biosimilar development and regulatory approval, have contributed to a change in the perception of IBD experts, who now prescribe biosimilars with significantly more confidence.[18]

A task-force including Governing Board representatives and one representative from pertinent ECCO Committees performed a literature search and made relevant statements to summarise their shared position. The proposed statements were then discussed, agreed and approved in a Consensus meeting.

2. Regulatory Process by EMA for Biosimilars

The licensing of any biosimilar medication by the European Medicines Agency [EMA] is subject to strict regulatory oversight. Many of the principles are shared with the regulatory processes governing the licensing of generic chemical compounds, but due to the greatly increased complexity and potential for variability,

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Journal of Crohn's and Colitis 2017;11:26-34.

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Not All Mindsets Have Changed

- **“Generally, FDA approval of a biosimilar product is an indication that safety and efficacy are not meaningfully different from the reference product.”**
  - Not just a general assertion; it IS the definition of a biosimilar
- **“The FDA approval process for biosimilars makes it less likely that large, phase III trials will be undertaken for all approved indications of the reference product.”**
  - Not just less likely; it is guaranteed NOT to occur

JOURNAL OF CLINICAL ONCOLOGY | ASCO SPECIAL ARTICLE

American Society of Clinical Oncology Statement: Biosimilars in Oncology

Gary H. Lyman, Edward Balchen, Michael Dinc, Andrew Ferris, Anne Tsao, Emily Vont, Robin Zon, Michael Francisco, Sybil Green, Shimon Sherwood, R. Donald Harvey, and Richard L. Schilsky

ABSTRACT

As many biosimilars come to market in the next several years, their use in oncology will play an important role in the future care of patients with cancer. ASCO is committed to providing education and guidance to the oncology community on the use of biosimilars in the cancer setting; therefore, ASCO has developed this statement to offer guidance in the following areas: (1) naming, labeling, and other regulatory considerations, (2) safety and efficacy of biosimilars, (3) interchangeability, switching, and substitution, (4) value of biosimilars, and (5) prescriber and patient education.

J Clin Oncol 36. © 2018 by American Society of Clinical Oncology

INTRODUCTION

Despite considerable advances in cancer care, rising health care costs have prompted the need for cost-containment strategies.[1] This is especially true with regard to new oncology pharmaceuticals—eight of the 10 most expensive drugs on the market are cancer drugs. Since the enactment of the Biologics Price Competition and Innovation Act (BPCIA) in 2010, biosimilars have been developed and marketed as competitive, lower-cost alternatives to newer biologic treatments. In 2013, the Virginia General Assembly defined a biological product as a virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, protein other than a chemically synthesized polypeptide, or analogous product, or arsphenamine or any derivative of arsphenamine or any other trivalent organic arsenic compound, applicable to the prevention, treatment, or cure of a disease or condition of human beings. Biosimilar was defined as a biologic product that is highly similar to a specific reference biologic product, notwithstanding minor differences in clinically inactive components, such that there are no clinically meaningful differences between the reference biologic product and the biologic product that has been licensed as a biosimilar pursuant to 42 USC section 262(k) in terms of safety, purity, and potency of the product.

To date, the US Food and Drug Administration (FDA) has approved eight biosimilar products for use in the United States, including one product for use as a supportive care agent in the cancer setting (filgrastim-sndz, for use as an alternative to filgrastim) and two products for use in the treatment of cancer (bevacizumab-awwb, for use as an alternative to bevacizumab, and trastuzumab-dkst, for use as an alternative to trastuzumab). With the expiration of several biologic patents, a wave of biosimilars is expected in the United States, and cancer treatments are likely to consist of a significant proportion of the approved biosimilars. In fact, oncology biologic products with patents scheduled to expire by 2020 total global annual spending of more than $20 billion. The biosimilars for these products are expected to take over the majority of this market share.[2]

Whereas access to biosimilars could potentially reduce the cost of cancer therapies, inconsistent use and a lack of understanding of the terminology, evolving regulatory guidance, and questions about how biosimilars may be prescribed and dispensed, have contributed to an uncertain environment for all stakeholders. Moreover, there is growing concern that existing statutes regarding the regulation of generic drugs may be misapplied to biologic products, which has led several states to amend older state laws to address the complex molecular characteristics of biologics and biosimilars. ASCO, along with many other organizations, has commented on the evolving regulatory framework for biosimilars.[3,4] In addition, it has been noted in prior publications that physicians were initially concerned about the use of generic drugs and even the first monoclonal antibody therapies[5]; therefore, ASCO

Lyman GH, et al. J Clin Oncol. 2018 Feb 14:JCO2017774893. doi 10.1200/JCO.2017.77.4893 [epub ahead of print].

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Understanding of regulatory requirements is particularly critical

- "…multiple surveys of physicians reveal that even those who routinely use biologic products do not have a clear understanding of biosimilar products."
- "Physicians are therefore naturally hesitant to prescribe biosimilars — especially given that regulations create the impression that a biosimilar may not be all that similar to its originator."
- It's not the regulations, but the lack of understanding of the regulations!

Source: Frank RG. Friction in the path to use of biosimilar drugs. *N Engl J Med.* 2018;378(9):791-793.

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Understanding Biosimilar Value and Other Impossible Tasks

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New Medicare Part B approach to reimbursement

Biosimilar	Prior to April 1, 2018	On or after April 1, 2018
Infliximab-dyyb	Q5102 plus ZB modifier	Q5103
Infliximab-abda	Q5102 plus ZC modifier	Q5104

- Each biosimilar is now assigned a unique Healthcare Common Procedure Coding System (HCPCS) code. The originator retains its unique HCPCS code.
- Biosimilar reimbursement is 100% of average sales price (ASP) of the specific biosimilar + 6% of the ASP of the originator.
- All biosimilars are eligible for “pass-through” status.
  - Previously, only the first biosimilar of the reference product was eligible for this status.
  - Pass-through status lasts two to three years.
  - Payment is not ASP minus 22.5% for 340B disproportionate share hospitals during “pass-through” period
  - After pass through expires, payment is ASP of the biosimilar – 22.5% ASP of the reference product

Sources: Part B biosimilar biological product payment and required modifiers. Centers for Medicare & Medicaid Services website. https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Part-B-Drugs/McrPartBDrugAvgSalesPrice/Part-B-Biosimilar-Biological-Product-Payment.html. Updated February 2, 2018. Accessed, March 5, 2018.
Syrop J. CMS reverses its policy on biosimiar reimbursement, will issue unique J-codes. Center for Biosimilars website. http://www.centerforbiosimilars.com/news/cms-reverses-its-policy-on-biosimilars-reimbursement-will-issue-unique-jcodes. Published November 3, 2017. Accessed March 5, 5018.
Forys A. 340B changes: what biosimilar manufacturers need to know. Center for Biosimilars website. http://www.centerforbiosimilars.com/contributor/amanda-forys/340b-changes-what-biosimilar-manufacturers-need-to-know. February 19, 2018. Accessed March 6, 2018.

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Impact of 2018 Bipartisan Budget Act

Medicare Part D

- Previously, biosimilars were not eligible for the Coverage Gap Discount Program, which assists patients during the “doughnut hole” period.
- As a result, biosimilars could cost more than their originators under Part D.
- As a result of the Bipartisan Budget Act signed on Feb. 9, 2018, biosimilar manufacturers now can (and must) provide a discount.

Sources: Patient out-of-pocket costs for biosimilars in Medicare Part D. Avalere Health website. http://go.avalere.com/acton/attachment/12909/f-02c0/1/-/-/-/-/20160412_Patient%20OOP%20for%20Biosimilars%20in%20Part%20D.pdf. Published April 2016. Accessed March 9, 2018.
Kelly C. Fight brewing in Congress over Part D coverage gap discounts. *The Pink Sheet*. February 15, 2018. https://pink.pharmaintelligence.informa.com/PS122535/Fight-Brewing-In-Congress-Over-Part-D-Coverage-Gap-Discounts. Accessed March 16, 2018.
Burke SP, Rao A, Sadle SE. Bipartisan Budget Act of 2018: major impacts on health care. Lexicology website. https://www.lexology.com/library/detail.aspx?g=21fa076e-6461-47ad-9ad7-33392c3b415a. Published February 9, 218. Accessed March 9, 2018.

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Preparing for the Future

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Elements of a Formulary Review Document (Biosimilar perspective)

Brand and generic names and synonyms

FDA approval information

Pharmacology and mechanism of action

FDA approved indications

Potential non-FDA approved indications

Dosage form and storage

Recommended dosage regimens

Pharmacokinetic considerations

Use in special populations

Pregnancy category and use during breast-feeding

Comparisons of the drug's efficacy, safety, convenience, and costs with those of therapeutic alternatives

Clinical trial analysis and critique

Medication safety assessments and recommendations

- **Adverse drug reactions**
- **Drug-drug, drug-food interactions**
- **Sound-alike and look-alike issues**

Financial analysis

ASHP Guidelines on the Pharmacy and Therapeutics Committee and the Formulary System, Am J Health Syst Pharm 2008;65:1272-83.

Biobetters and Beyond

Existing agent	Modification
Neulasta (pegfilgrastim)	• Pegfilgrastim auto injector (Neulasta® OnPro®)
Rituxan (rituximab) intravenous injection	• Rituximab subcutaneous • Obinutuzumab
Herceptin (trastuzumab)	• Trastuzumab 150 mg • Pertuzumab • Ado-trastuzumab emtansine
Remicade (infliximab)	• Guselkumab (IL-23 inhibitor for plaque psoriasis)
Humira (adalimumab)	• ABT-122 (bispecific antibody for TNF and IL-17) • ABT-494 (Janus kinase-1 inhibitor) • ALX-0061 (anti-interleukin-6 receptor) mAb

Critical Steps

- **Remain vigilant for any and all news about biosimilars as the framework will continue to change**
  - Regulatory actions
    - Approval decisions
    - Complete response letters
  - Legal actions, patent settlements
  - Reimbursement changes
  - Practice perspectives
- **Educate, educate, educate!**
  - It's not the regulations, it's the lack of understanding of the regulations
- **Think both short and long term when assessing value**
- **Align with your business and financial colleagues**

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