FÓRUM BIOSSIMILARES 2014

Important Considerations on Biosimilar Interchangeability and Automatic Substitution:

Physician (and Patient) Perspectives

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5th Brasilian Forum on Biosimilars
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DISCLOSURES

- I am a speaker for Abbvie
- I have performed consulting for Amgen & Novartis

- BUT … I am a pediatrician in private practice who cares for kids with chronic illnesses and disabilities

- How much can there be for me to disclose?

Who Cares?
What's the Big Deal?
Aren't these all the same?

If that were the case, we wouldn't be here

Unfortunately, this is a prevailing opinion about biosimilars, if there is any thought about it at all

But the reality is ….

One of These Things is Not Like The Other…

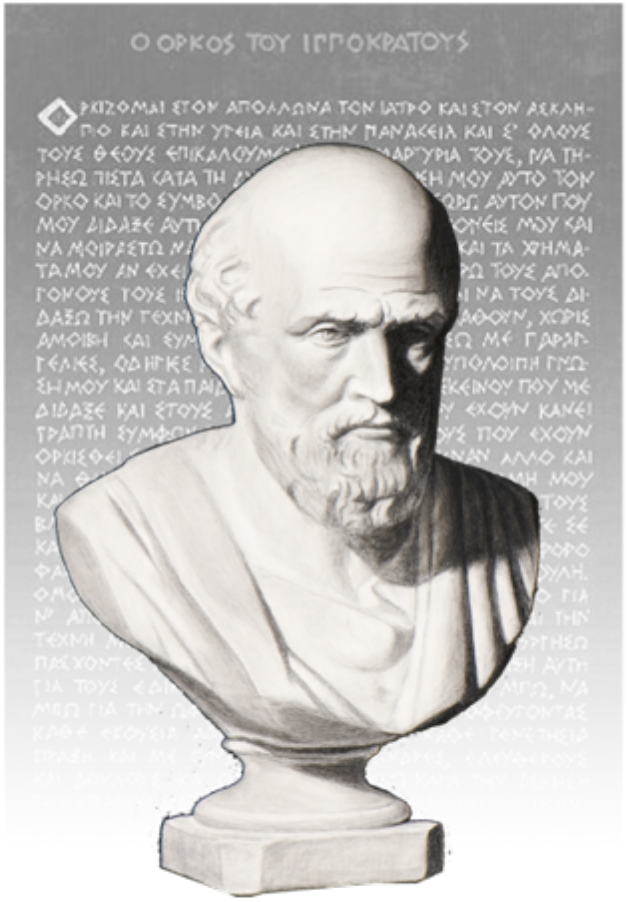
Building Physician and Patient Confidence is Key To The Successful Introduction, Adoption and Use of Biosimilars

Areas of physician and patient concern with biosimilars (or other medications):

- **What medicine is the patient actually receiving?**
- **If there is a substitution:** When? By whom?
- **Are the medicines really the same:** If not, should biosimilars have unique nonproprietary names?
- **What are the oversight rules:** Will there be regulatory consistency? How well will they protect patients?

A Physician's Guiding Principles

- Patient safety is paramount.
- Information, Communication and Collaboration is critical: the more we know, the more we work together, the better we can serve our patients.
- Data , short and long term, is essential to ensure confidence in these medications and improve their appropriate use.



Hippocratic oath: "first, do no harm"

Review: What Makes Biologics Special?

Biologic vs. Chemical Medicines

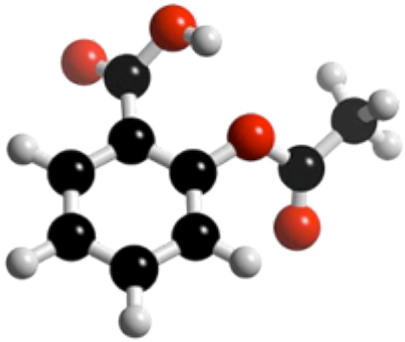
SIZE: significantly larger

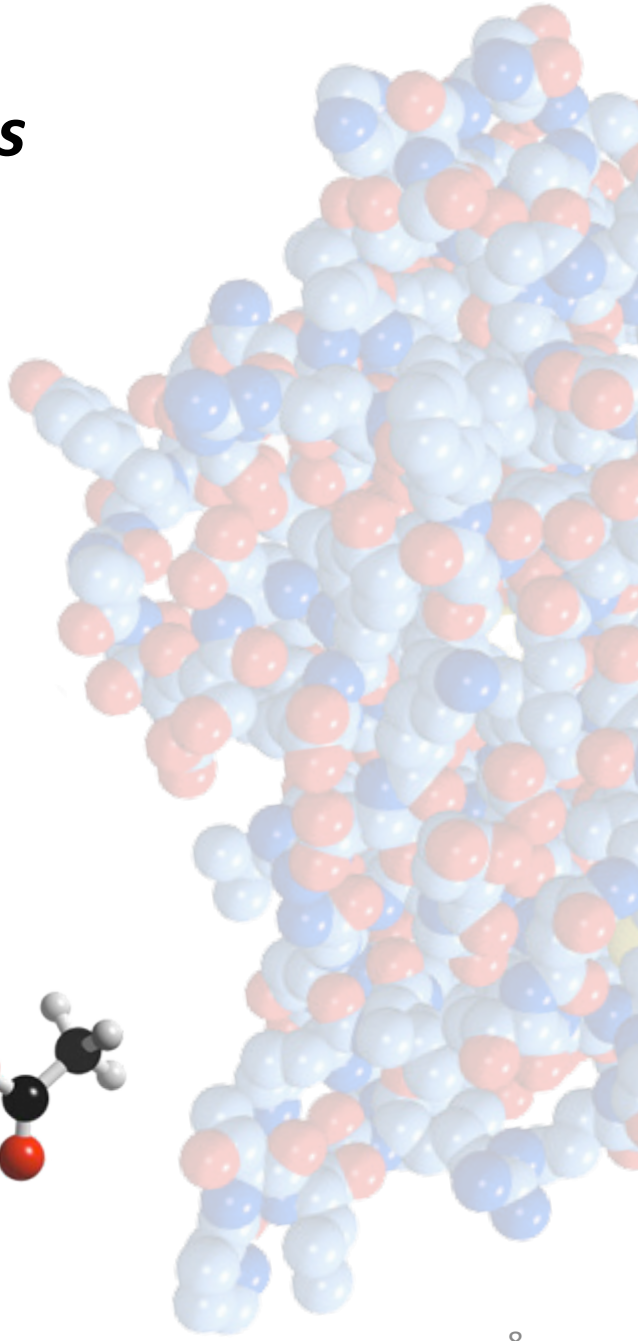
STRUCTURE: more complex

STABILITY: susceptible to light, heat, denaturing / degradation

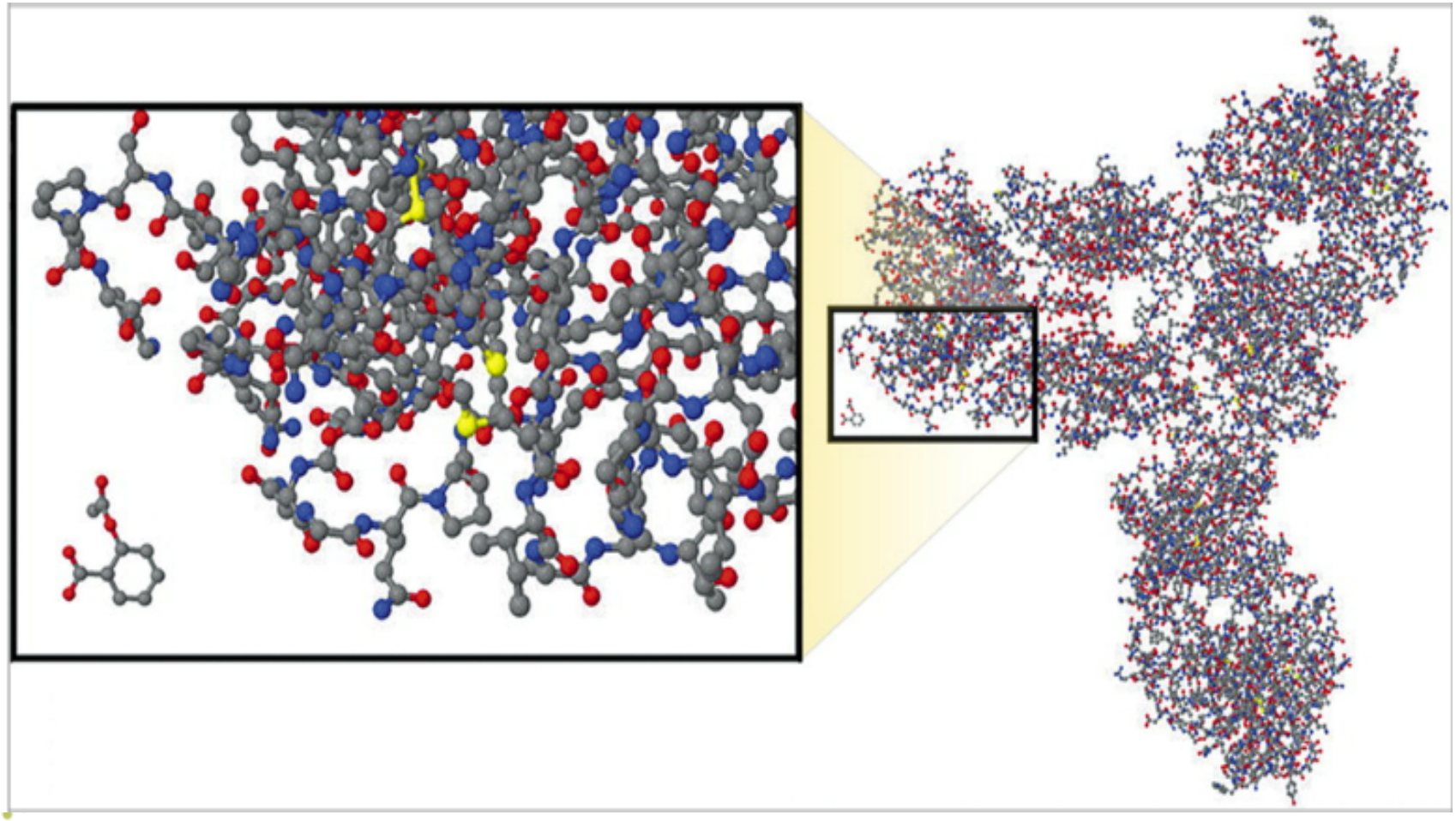
SENSITIVITY: even small manufacturing changes can cause changes in efficacy and/or adverse effects

DRIFT: can change with time





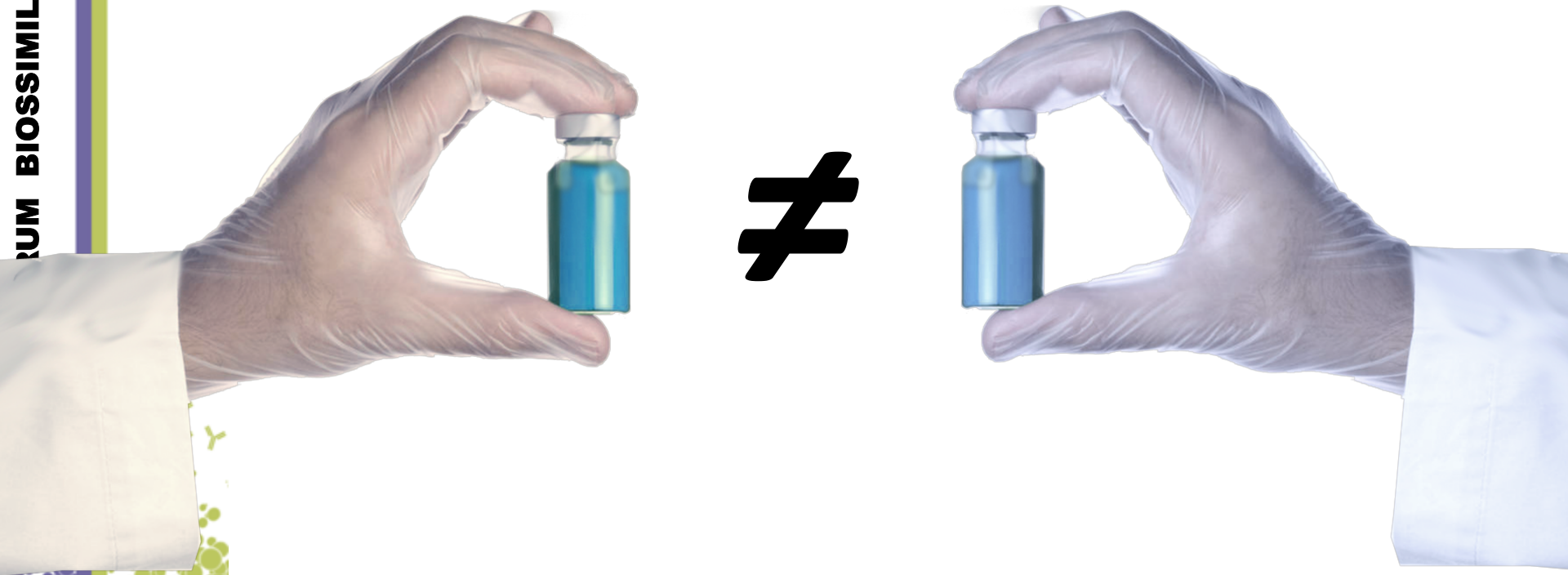
Molecular Comparison: Aspirin vs. Monoclonal Antibody



Source: New England Journal of Medicines, "Developing the Nation's Biosimilars Program," August 4, 2011

The Complexity of Biologics Means <u>They Cannot Be Exactly Copied.</u>

Thus, Biosimilars are <u>NOT Identical to their reference product</u>……They can only be "SIMILAR"



Critical Question

If the medications are similar but not identical, how much difference is acceptable if we are going to allow them to be used interchangeably?

What Do The Physicians Who Use Them Think About Biologics and Biosimilars?

About The Alliance for Safe Biologic Medicines (ASBM)

- 2010: ASBM was formed to provide STAKEHOLDER GUIDANCE to FDA in development of US Biosimilar Pathway
- STEERING COMMITTEE: Composed of physician and patient groups; runs day-to-day operations.
- ADVISORY BOARD: Composed of Physicians, Researchers, Pharmacists, and Patients from around the world. Serves as resource on the science and clinical use of biosimilars, guides our policy recommendations.

SafeBiologics

STEERING COMMITTEE

AfPA Alliance for Patient Access

American Autoimmune Related Diseases Association, Inc.

AAD American Academy of Dermatology

ACRO Association of Clinical Research Organizations

Colon Cancer Alliance

Global Colon Cancer Association

ican international cancer advocacy network

Global Healthy Living Foundation

Kidney Cancer Association www.KidneyCancer.org

HealthHIV

ZERO The End of Prostate Cancer

ASBM Physician Surveys

ASBM has conducted two surveys that examine the perspectives of the physicians who prescribe biologics:

- *U.S. Prescriber Survey (conducted September 2012)*
- *E.U. Prescriber Survey (conducted November 2013)*
- *Canadian Prescriber Survey (tentative Autumn 2014)*

Use of ASBM Physician Survey Data in Development of International Naming Standards

ASBM has twice presented its survey findings to the WHO to aid in the development of international naming standards for biosimilars:

- U.S. Prescriber Survey results presented at the 57th Consultation on International Nonproprietary Names (INN), October 22, 2013

- European Prescriber Survey results presented at 58th INN Consultation, April 8, 2014.

World Health Organization

Substitution of Biosimilars (Automatic or Otherwise)

What is "Automatic Substitution"?

1) Physician writes a prescription

2) Pharmacist is allowed, or required, to provide a different medicine to the patient without consulting prescribing doctor

Substitution Policy in the U.S.

CONGRESS

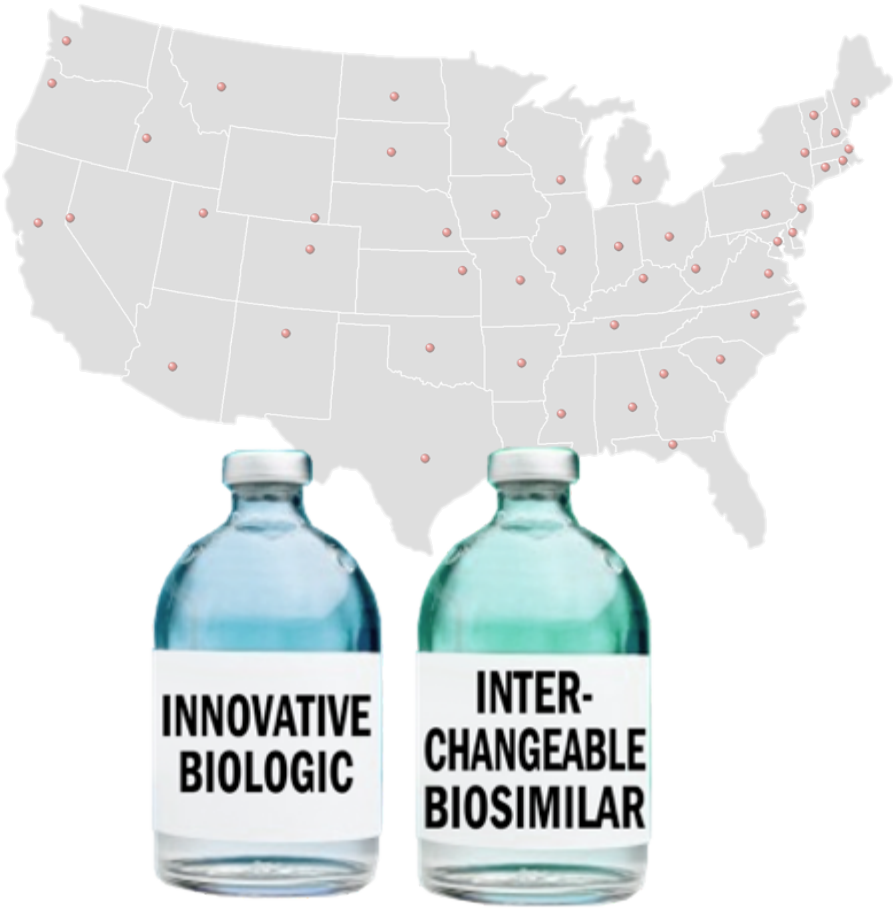
- Sets Legal definition
- Interchangeable: substitution without physician intervention

FDA

- Makes Scientific decisions
- Sets Interchangeability criteria

STATES

- Decides what pharmacists are allowed to do



How do the EU and Canada Address the Role of Physicians in Substitution of Biosimilars?

- The EMA advises that: **"<u>the physician should be in charge of the decision to switch</u>** between the reference and Biosimilar, or vice versa."[1]

- "Health Canada **<u>does not support</u> automatic substitution** of a Subsequent Entry Biologic for its reference biologic drug and recommends that physicians make only well informed decisions regarding therapeutic interchange".[2]

1 European Medicines Agency. Questions and Answers on Biosimilar Medicines (Similar Biological Medicinal Products). London: European Medicines Agency; 2012. Available from: http://www.ema.europa.eu/docs/en_GB/document_library/Medicine_QA/2009/12/WC500020062.pdf. Accessed November 6, 2012.

2 http://www.hc-sc.gc.ca/dhp-mps/brgtherap/applic-demande/guides/seb-pbu/01-2010-seb-pbu-qa-qr-eng.php

U.S. Prescriber Survey: Physician Attitudes on Substitution

More than 80% felt the authority to write "DISPENSE AS WRITTEN" was "very important" or "critical".

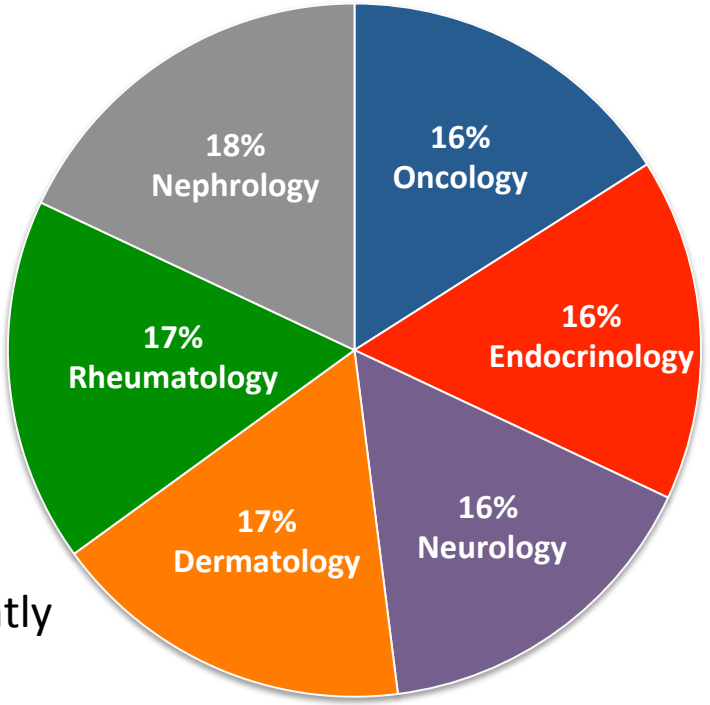
62% felt A PHARMACIST'S DETERMINATION of this was "not acceptable"

86% would prefer to be NOTIFIED **"**BEFORE THE PATIENT RECEIVES THE MEDICINE."

European Prescriber Survey

- First large-scale survey on biosimilars in Europe.
- Examined physician knowledge and prescribing practices.

- 15-Minute Web-based Survey
- 470 Prescribers distributed equally between 5 countries in Western Europe:
  - France
  - Germany
  - Italy
  - Spain
  - United Kingdom
- Roughly equal distribution between six specialties in which biologics are frequently prescribed.



Conducted by Industry Standard Research, October-November 2013

GaBI Published White Paper on ASBM EU Survey June 2014

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Biosimilars naming, label transparency and authority of choice

Tyrosine kinase inhibitors becoming generic drugs – risks and chances from a regulatory perspective

Interchangeability. An insurmountable fifth hurdle?

Generics and Biosimilars Initiative J

Editorial

Complex molecules –

Commentary

Defining and character complex drugs (NBCDs) The case for liposomal ('liposomal nanosimilars

Original Researc

Biosimilars naming, labe authority of choice – surv European physicians

Perceptions of physicians medical centres in Malay medicine usage: a qualit

Review Article

Clinical development, imm interchangeability of follow

Tyrosine kinase inhibitors b drugs – risks and chances f perspective

Interchangeability. An insu hurdle?

Perspective

Role of hospital clinical pharm transplantation, and generic immunosuppressive therapies

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ORIGINAL RESEARCH

Biosimilars for Healthcare Professionals

Biosimilars naming, label transparency and authority of choice – survey findings among European physicians

Richard O Dolinar, MD; Michael S Reilly

Introduction: A survey of the views of European physicians on familiarity of biosimilar medicines has demonstrated the need for distinguishable non-proprietary names to be given to all biologicals.

Methods: The Alliance for Safe Biologic Medicines recruited 470 prescribers with clinical experience of biologicals in France, Germany, Italy, Spain and the UK to answer questions relating to their experience with these medicines in a 15-minute web-based survey which was carried out in the last quarter of 2013.

Results: Of the physicians surveyed, 53% mistakenly felt that an identical non-proprietary name implies identical structure; 61% said that identical non-proprietary names imply that the medicines are approved for the same indications, which they may not be, and 24% said they recorded only the non-proprietary name of the biological product in the patient record.

Conclusions: The responses of the European physicians demonstrate the need for distinguishable non-proprietary names to be given for all biologicals. Biosimilars, in contrast to generic drugs, have different structures, may have a different therapeutic profile, and may not be approved for all the indications for which the reference product has been approved.

Keywords: Biological, biosimilar, Europe, INN, pharmacy substitution, prescriber

Introduction

With the growing number of biosimilar medicines on the European market [1], the Alliance for Safe Biologic Medicines (ASBM) has completed a survey of European physicians to:

- examine attitudes of European physicians on biosimilar naming and substitution
- assess physician knowledge, sources of information and need for further education on biosimilars and
- provide data to put policy developments at EU and national level into perspective and inform policy recommendations.

Responses from 470 prescribers located in France, Germany, Italy, Spain and the UK were collected and analysed. Respondents were all specialists who prescribe biologicals, including dermatologists, neurologists,

Participants were selected from a large global market research panel of prescribers; 1,002 responded, giving a total response rate of 23.1%. 62 of the 1,002 screened out. 470 prescribers (20% from each of the five European countries) completed the survey. Oncologists were paid the US equivalent of $32.00 to complete the survey. All other participants were paid the US equivalent of US$25.00. All surveys were presented in the local language (English, French, German, Italian and Spanish). Prescribers answered questions in a 15-minute web-based survey.

Prescribers included nephrologists (18%), rheumatologists (17%), dermatologists (17%), neurologists (16%), endocrinologists (16%) and oncologists (16%). They were based in hospitals (58%); academic medical centres (24%); private, family practices (8%); community settings (8%); multi-specialty clinics (2%); or other settings (1%).

European Prescriber Survey: Physician Attitudes on Substitution

74% felt the authority to write "DISPENSE AS WRITTEN" was "very important" or "critical".

72% felt the HAVING SOLE AUTHORITY to decide which biologic is used is "very important" or "critical".

80% felt NOTIFICATION OF SUBSTITUTION was "very important" or "critical".

What's In a Name?

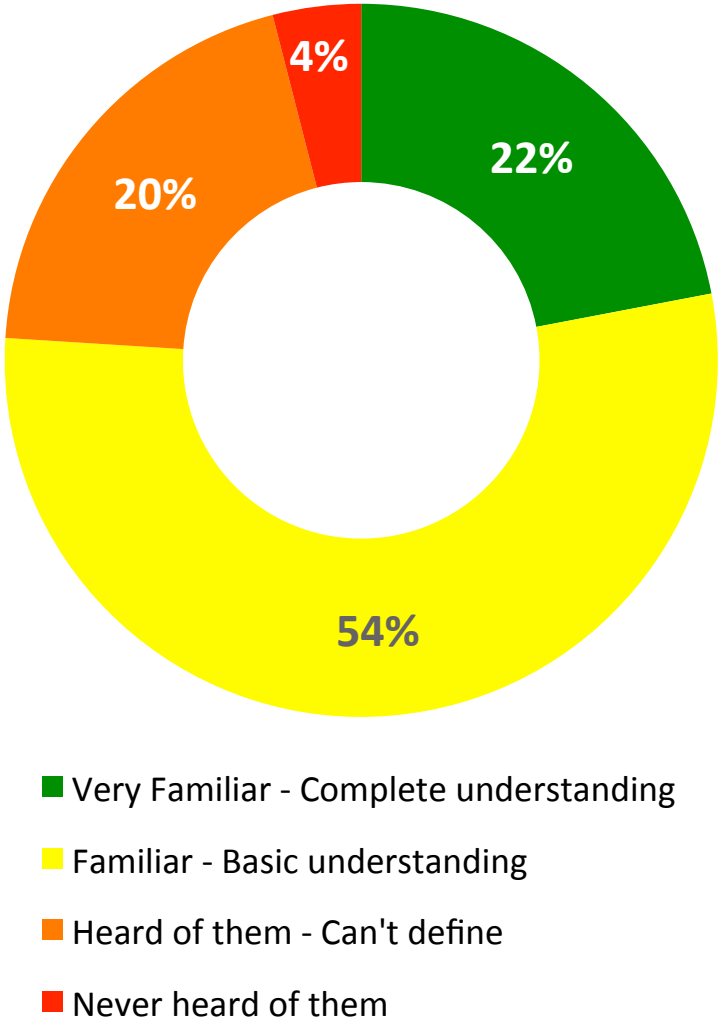
Surveys Identified A Need for Education… and for Clear Naming of Biologic Medicines.

Physicians' misconceptions about biosimilars, prescribing and AE reporting practices in Europe underscore a need for a clear naming system with distinguishable nonproprietary names for all biologics, including biosimilars, to facilitate intended prescribing and traceability.

EVEN where biosimilars have been available longest AND a system for tracking exists, providers still strongly support distinguishable names for ALL biologics.

E.U. Prescriber Survey: Familiarity Level with Biosimilars

- 54% possess only a “basic understanding” of biosimilars
- Only 22% consider themselves “very familiar” with biosimilars
- 20% have heard of them but cannot define
- 4% have never heard of them



E.U. Prescriber Survey: Physician Attitudes on Biosimilar Naming

- **53%** of respondents mistakenly believe a biosimilar with an identical non-proprietary name as its reference biologic is STRUCTURALLY IDENTICAL. *(Compared to 76% of U.S. respondents which believed this)*
- **61%** of respondents believe biosimilar with an identical non-proprietary name as its reference biologic is APPROVED FOR THE SAME INDICATIONS (*This may or may not be true)*

E.U. Prescriber Survey: Physician Attitudes on Biosimilar Naming

WHEN IDENTFYING IN PATIENT RECORD:

- **Only 32% of respondents** use brand name and non-proprietary name (INN) to identify the exact biologic being prescribed
- **24% use INN only**, which could result in patients receiving a different medicine than the physician intended or thought was prescribed.

WHEN REPORTING ADVERSE EVENTS:

- **27%** of prescribers NEVER include the batch number
- **33%** only SOMETIMES include the batch number
- **40%** ALWAYS include the batch number

The Role of Names in Pharmacovigilance and Safety

IDENTIFICATION

- Patients, physicians and pharmacists should be able to **accurately identify the product, ensure it is the intended prescription, and avoid inadvertent substitution.**

- A biosimilar should be **distinguishable both from its reference product and from other approved biosimilars which reference the same biologic.**

The Role of Names in Pharmacovigilance and Safety

PHARMACOVIGILANCE

- Distinguishable naming helps differentiate **products for observing and reporting adverse events.**
- **Tracking and tracing of biologics** is more challenging than with chemical drugs. An adverse impact from a biologic may take months to be recognized.
- **Multiple means of product identification** avoid a single point of information failure.

MANUFACTURER RESPONSIBILITY

- Patient response, good or not-so-good, should be traceable to the correct manufacturer's product.
- This helps everyone better understand the effects of each medicine and make improvements as needed.

Summary: Key Findings of ASBM Surveys

- There is a need for further education about biosimilars among physicians in the U.S., Europe and, therefore, worldwide.
- It is important to physicians they retain the authority to use "do not substitute" to ensure the patient receives their chosen medicine
- It is important to physicians they be informed in a timely fashion the medicine(s) the patient receives and if it is different than what they prescribed
- Distinguishable INNs are important to the practicing physicians in the U.S. and Europe

So … What's the Point?

Given the complexity of these medications , their potential adverse effects and the long-term potential outcomes of inadequate treatment it is ESSENTIAL that EVERYONE involved in the care of patients receiving biologics adequately and appropriately communicate and collaborate in the manufacturing, distribution and use of these agents.

It's All About the Patient

Therefore:

- Patients
- Pharmacists
- Payers
- Physicians
- Manufacturers
- Regulators

Must be on the same page regarding the identification and use of these medications

It's All About The Patient

Patients and Physicians must know what medication the patient is actually receiving in a timely fashion to appropriately assess its efficacy, determine potential AE's and make appropriate therapeutic decisions

We cannot provide quality care for our patients without knowing the specific medication the patient is actually taking.

One of These Things is Not Like The Other…

Thank You for Your Attention