Bringing Patient Perspectives to the Global Biosimilars Discussion

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Steering Committee Member, Alliance for Safe Biologic Medicines

6th Latin American Forum on Biosimilars (2016)/7th Brazilian Forum on Biosimilars

Brasilia, Brasil

June 29, 2016

SafeBiologics
ALLIANCE for SAFE BIOLOGIC MEDICINES

Introduction

Andrew Spiegel, Esq.

- Patient Advocate since 1998
- Co-Founded the Colon Cancer Alliance
- Executive Director of the Global Colon Cancer Association (GCCA)
- Chair, Digestive Disease National Coalition
- Board Member, International Association of Patient Organizations (IAPO)
- Co-Founder and Steering Committee Member of the **Alliance for Safe Biologic Medicines**

Patient Advocacy

- Over 1.2 Million diagnosed with CRC EACH YEAR worldwide, over 600K deaths.
- Global Colon Cancer Association, advocates for a global community of over 6 million colorectal cancer patients.
- Global experience has raised awareness of the importance of physician/ patient-led, not government or payer-led decision-making in treatment.
- Biologics have had huge impact in CRC (5 of 10 approved drugs)
- In late 2010, Co-founded ASBM to bring the PATIENT PERSPECTIVE to discussion about biologics/biosimilar policy.

About The Alliance for Safe Biologic Medicines (ASBM)

Harry L. Gewanter, MD, FAAP, FACR: Chairman, pediatric rheumatologist

Philip Schneider: Dean, University of Arizona College of Pharmacy- Advisory Board Chair

Michael Reilly, Executive Director
michael@safebiologics.org

- Steering Committee composed of patient and physician groups.
- Advisory Board of physicians, researchers, pharmacists, and patients.

Gathering the Perspectives of Providers Around the World

Canadian Physician Survey
(December 2014): 427 physicians

U.S. Physician Surveys
(September 2012): 376 physicians
(February 2015): 400 physicians (Labeling)
(November 2015): 400 physicians

E.U. (France, Italy, Spain, UK) Physician Survey
(November 2013): 470 physicians

U.S. Pharmacist Survey
(September 2015) 401 pharmacists

Latin America (Argentina, Brazil, Colombia, Mexico) Physician Survey
(May 2015): 399 physicians

All surveys available at www.SafeBiologics.org

Connecting the Global Patient Community

- International Alliance of Patients' Organizations (IAPO) Biosimilars Workshop,
  May 2, 2013, Geneva
- IAPO Latin American Multi-Stakeholder Seminar
  September 23, 2013, Mexico City
- IAPO Meeting *"Increasing the Patient Voice in Drug Regulatory Authorities"* in Rio de Janeiro,
  August 22, 2014
- Biosimilars LATAM Conference
  November 2015, Sao Paulo
- All Together Against Cancer
  September 27, 2016, Sao Paulo

Patients and Biologics

- About 350 million people around the world are benefiting from a biologic medicine.
- Biologics are unique medicines used to treat serious, long lasting conditions.
- Many patients take years to find a medicine that works for them to help control disease:
  - biologic medicines may be the most or even the only effective treatment.
  - For patients that are on a biologic that is working for them, decisions related to switching therapy should be carefully considered.
  - Changes in therapy could lead to an immune response and/or a loss of response to the new and old therapy, exposing patients to a scenario with no or fewer, or more serious treatment options.

Example: Improved Treatments For Colorectal Cancer Patients

- Access to new medicines have given our patients TIME and HOPE.
- We've gone from one drug to nearly ten in a decade, half biologics.
- The life expectancy of late stage patients has almost TRIPLED, from 11 months to almost THREE YEARS. From "months" to "years".
- This means more time with their families- meeting their grandchildren, attending weddings of their children.

The Promise of Biosimilars

- Biosimilars offer benefits to patients:
  - Increased access to biologic therapies
    - Lower-cost alternatives
  - New therapeutic choices

- Available in E.U. and Canada for several years, now in U.S. and Latin America
- U.S. currently developing biosimilar policy at the Federal and State level.
- <u>We want to make sure these policies work for patients.</u>

What Are Our Overall Objectives?

To be unbiased representatives of the patient community, advocating on critical issues important to patients.

- **Increased access** to biosimilars.
- **Patient-centered standards** for naming, safety approval and tracking of all biologic medicines, including biosimilars.
- **Informed patient/physician** in the case of substitution of a biosimilar in place of prescribed biologic.

Biosimilar Uptake: Patient/Physician Confidence Is Key

Naming, Labeling, Pharmacovigilance and Substitution are all fundamentally issues of TRANSPARENCY and DATA.

ASBM's approach has been to EDUCATE stakeholders, and to work with regulators to promote policies which BUILD PHYSICIAN/PATIENT CONFIDENCE IN BIOSIMILARS by requiring TRANSPARENCY and DATA.

Biosimilar Substitution: Patient Perspective

Non-Medical Switching

Switching a patient's medicine, often by a third party for reasons other than that patient's health and safety.

Issues Surrounding Non-Medical Switching

- Changing a patient's treatment may change the control a patient and/or doctor has over their condition.
- Patient and doctor should have the final say about treatment choices- which biologic to use, and if and when switching is appropriate.
- If your medicine is working for you, most doctors don't think it is a good idea to switch from one biologic to another for cost reasons only.

Forcing Patients to Switch Medicines

- Health insurers or Government payers may encourage a change from a biologic to a biosimilar, for the sole reason of reducing costs.

- Often no patient protections exist to prevent payers from forcing a patient to switch therapies. Possible results:
  - Higher out of pocket costs (coinsurance, copay, etc.) for current therapy
  - Formulary design changes mid-plan year and plan-year to plan-year
  - Disadvantage products by changing tiers
  - Blocking the use of co-pay cards

Some data suggests that Non-Medical Switching actually increases costs for the individual and the health care system because of an increase in hospitalizations, doctor visits and other health care services.

Some Stakeholders Are Frustrated

- Governments
- Payers
- Pharmacy Benefit Managers
- Insurers

- *COST PRESSURES for these groups are immense.*
- *After 10 years, why still only very limited data on biosimilars?*
- *They are incentivized to FIND WAYS AROUND BUILDING PHYSICIAN/ PATIENT CONFIDENCE which can be seen as an obstacle.*

Latest Attempts to Circumvent Physicians

1) PRICING/TENDERING

- Change risk/reward equation.
- SAVINGS so high for payers it outweighs risks; even if these are unsustainable.

GaBi

Huge discount on biosimilar infliximab in Norway

13/03/2015

Norway's price regulator has been offered a discount of 72% for biosimilar infliximab in the country's latest tender for drugs.

Latest Attempts to Circumvent Physicians

2) OVERGENERALIZING VERY LIMITED DATA SETS

- Give ammunition to payers to justify switching
- Data could satisfy casual observer or one with vested interest, but not regulator
- NOR-SWITCH Study: n= 498

NEWS MEDICAL
LIFE SCIENCES & MEDICINE

New data shows safety and efficacy of biosimilar infliximab treatment in IBD patients

Clinical experience of biosimilar infliximab in **78 inflammatory bowel disease (IBD) patients** presented at Digestive Diseases Week (DDW) 2015 in Washington D.C. showed that the treatment is comparable to the reference medicinal product (RMP) in terms of efficacy and safety.

February 9, 2016
FDA Arthritis Advisory Committee Hearing

- On February 9th, 2016 the FDA's Arthritis Advisory Committee (AAC) held a day-long meeting to discuss CT-P13, a proposed biosimilar to infliximab, which treats Rheumatoid Arthritis, Ankylosing Spondylitis, Psoriasis, Crohn's Disease and Ulcerative Colitis.
- Marketed internationally as Remsima or Inflectra.
- FDA required more data to extrapolate to all indications; AAC voted 21-3 to recommend FDA approval for all indications of its reference product.
- The 3 Advisory Committee Members who voted NOT to approve expressed concern about EXTRAPOLATION to the IBD Indications (Crohn's Disease, Ulcerative Colitis).

February 9, 2016
FDA Arthritis Advisory Committee Hearing

Globally, Regulators have Disagreed About Extrapolation with Remsima/Inflectra:

- In 2013, the EMA approved Remsima for ALL indications of its reference product.

- In 2014, Canada approved for RA and AS indications based on data, allowed extrapolation for Psoriasis due to a similar mechanism of action, but found insufficient data to approve for IBD indications. Changed June, 2016.

- But, FDA AAC Members were only given the choice to recommend approval for ALL INDICATIONS or NONE AT ALL.

- This Omnibus “All or Nothing” approach does not support patient safety.
- What would the vote have been had they been allowed to vote on each indication?

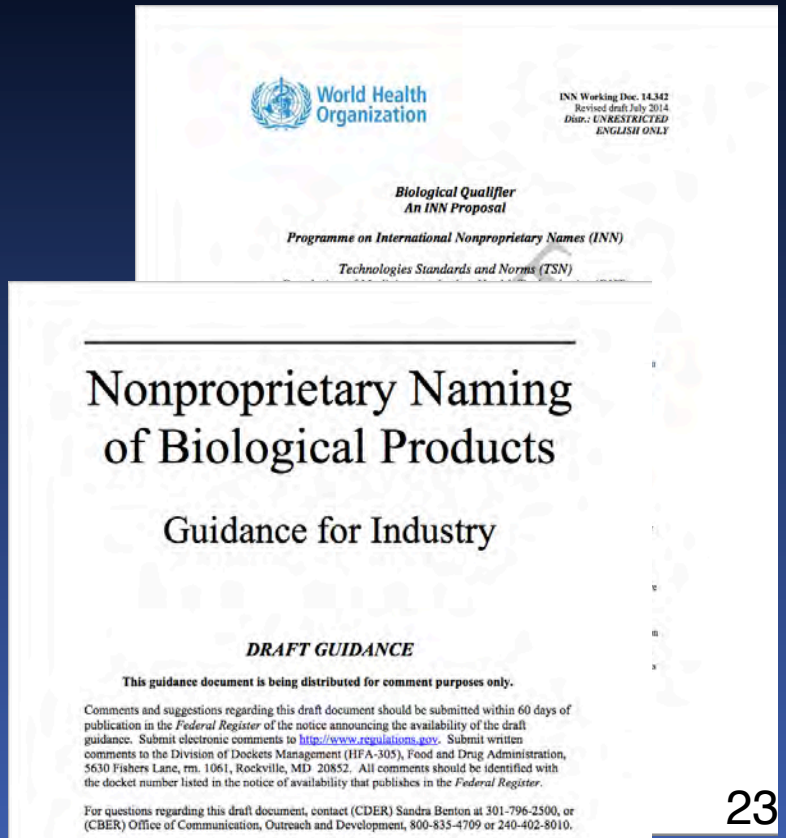
Conclusions on Substitution

- Non medical switching is not in the best interests of patients
- Patients and Physicians should decide which drug is best
- Patients and Physicians must be informed if switch occurs
- Pharmacovigilance must exist after approval to track patients reactions to medication changes
- Approval must be science based and approval based upon extrapolation must not be an all or nothing approach
- Data and transparency


Biologic & Biosimilar Naming:
Patient Perspective

WHO and FDA: Distinguishable Naming Proposals

- Both regulators are updating their naming systems for biosimilars.
- Distinguishability aids in clear communication throughout treatment, improves tracking of safety and efficacy, and promotes manufacturer accountability.
- Both call for similar biologics (including biosimilars) to have a shared root name (International Nonproprietary Name/ INN) followed by a four-letter suffix.
- The WHO calls this a “Biological Qualifier”


World Health Organization

INN Working Doc. 14.342
Revised draft July 2014
Distr.: UNRESTRICTED
ENGLISH ONLY

Biological Qualifier
An INN Proposal

Programme on International Nonproprietary Names (INN)

Technologies Standards and Norms (TSN)

Nonproprietary Naming of Biological Products

Guidance for Industry

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to http://www.regulations.gov. Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document, contact (CDER) Sandra Benton at 301-796-2500, or (CBER) Office of Communication, Outreach and Development, 800-835-4709 or 240-402-8010.

Benefits of Distinguishable Biologic Names

ASBM is a strong supporter of the FDA and WHO proposals.

- This helps ensure the patient receives the intended medicine.
- It allows the patient, physician, and pharmacist to always know which medicine the patient receives, to make informed treatment decisions.
- It allows accurate tracking of long-term safety including adverse events.
- It promotes manufacturer accountability for their products.

Global Surveys Demonstrate Broad Physician Support for Distinguishable Naming

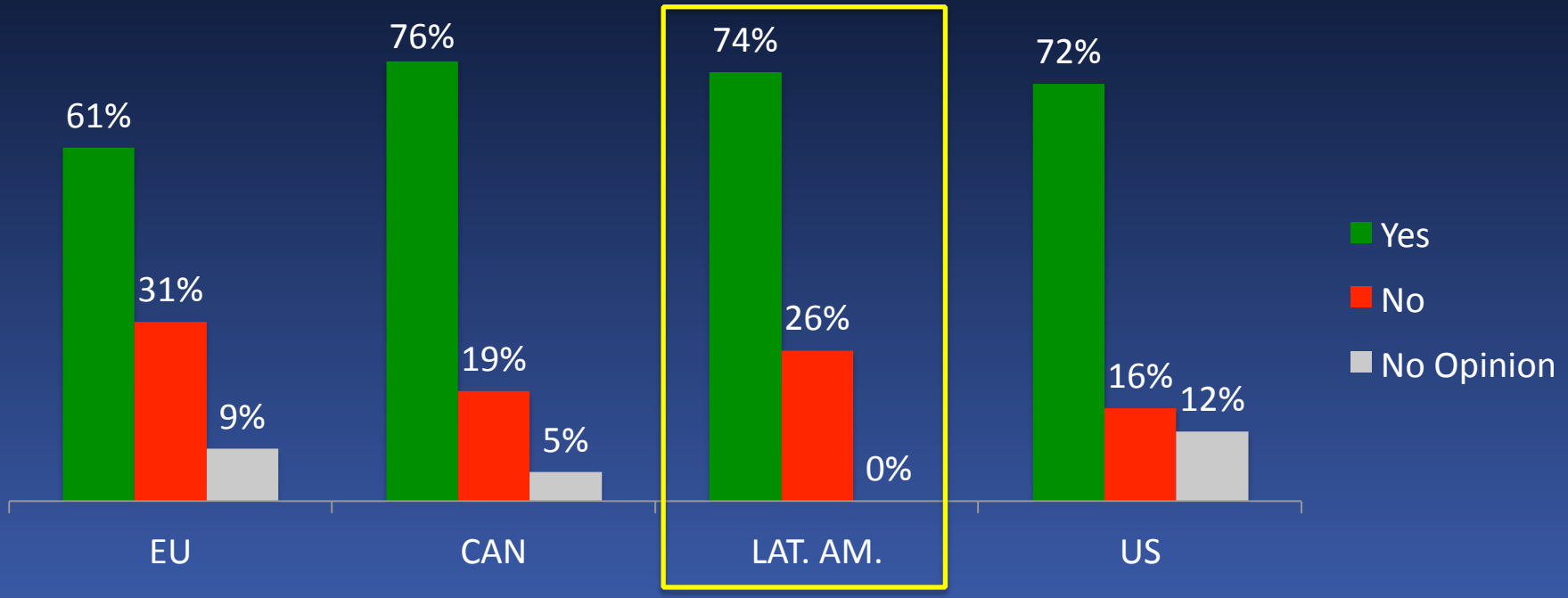
79% of Canadian physicians support Health Canada issuing distinct names. (2015)

94% of Latin American Physicians consider WHO's BQ Proposal to be "useful" in helping patients receive the correct medicine. (2015)

66% of US physicians support FDA issuing distinct names. (2015)

Percentage of Physicians Saying A Biosimilar Sharing an INN with its Reference Product Implies Approval for the Same Indications:

(This may or may not be the case…)

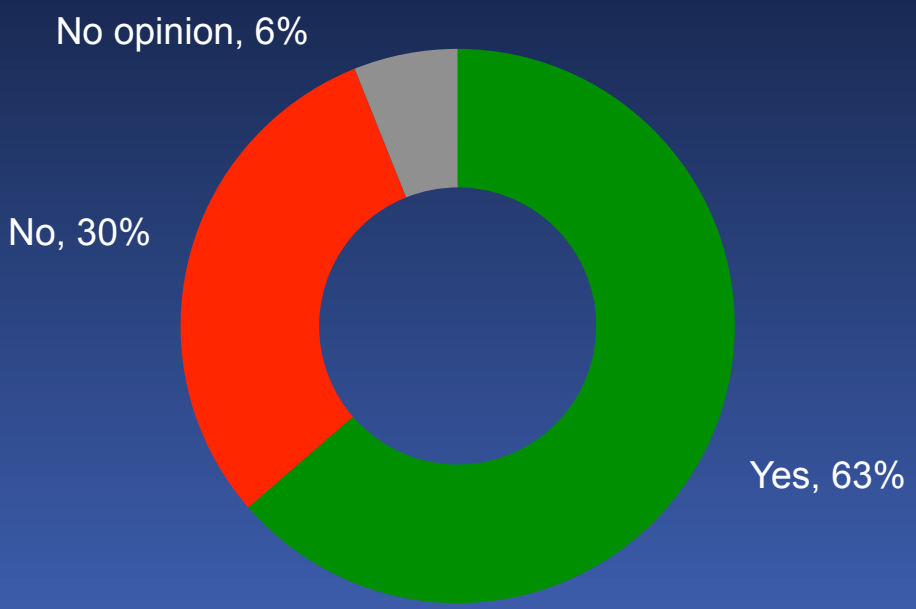


U.S. Pharmacist Survey:

Does a Shared INN Imply…

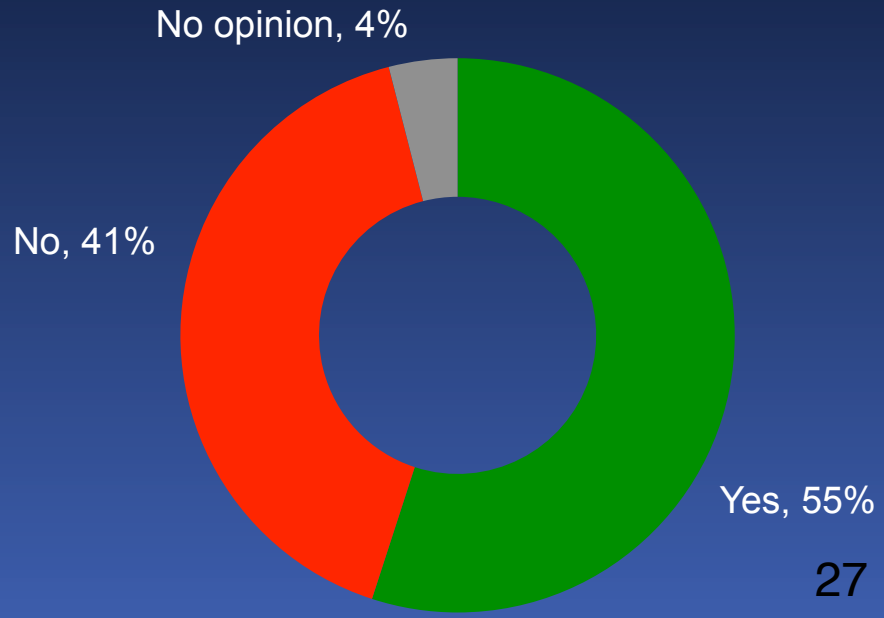
…Structural Identicality?

(this is not possible)



…Approval for the Same Indications?

(this may or may not be the case)

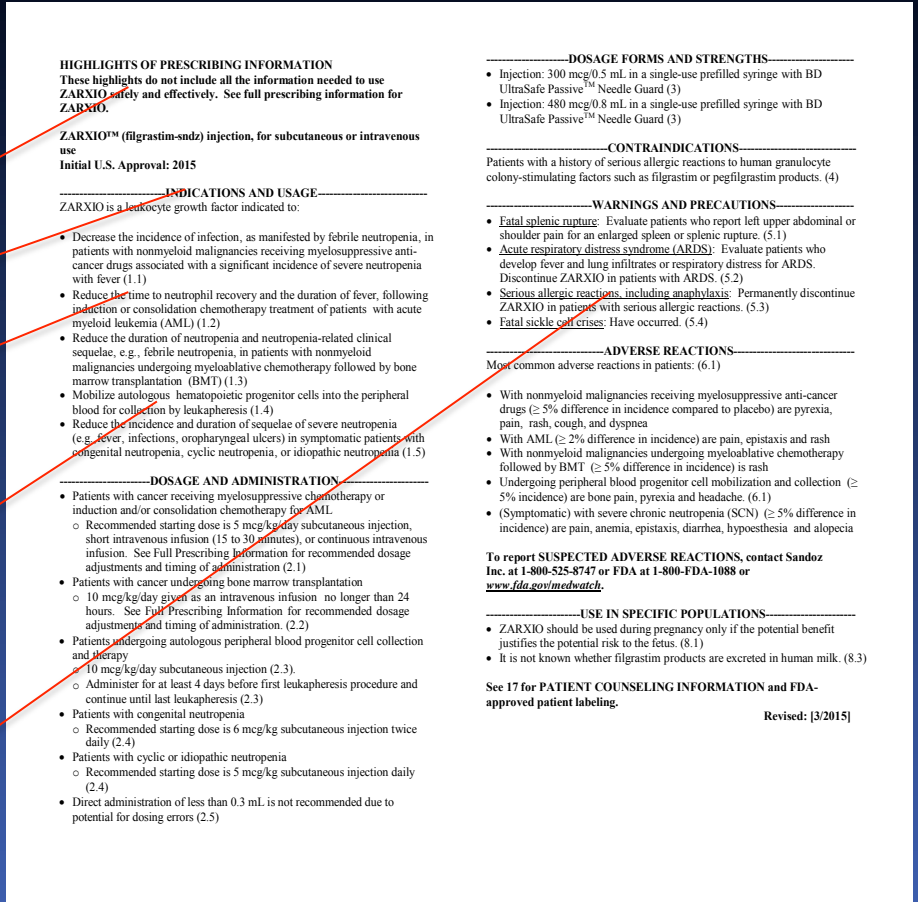


Biosimilar Labeling

Concerns Surrounding Biosimilar Labeling

Some concerns surrounding insufficient transparency in Zarxio's labeling:

- It is not identified as a biosimilar.
- No data used to demonstrate biosimilarity is included.
- Not specified for which indications approval was based on trial data, or extrapolation.
- Data from innovator product is not identified as such.



HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use ZARXIO safely and effectively. See full prescribing information for ZARXIO.

ZARXIO™ (filgrastim-sndz) injection, for subcutaneous or intravenous use
Initial U.S. Approval: 2015

----------INDICATIONS AND USAGE----------
ZARXIO is a leukocyte growth factor indicated to:

- Decrease the incidence of infection, as manifested by febrile neutropenia, in patients with nonmyeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a significant incidence of severe neutropenia with fever (1.1)
- Reduce the time to neutrophil recovery and the duration of fever, following induction or consolidation chemotherapy treatment of patients with acute myeloid leukemia (AML) (1.2)
- Reduce the duration of neutropenia and neutropenia-related clinical sequelae, e.g., febrile neutropenia, in patients with nonmyeloid malignancies undergoing myeloablative chemotherapy followed by bone marrow transplantation (BMT) (1.3)
- Mobilize autologous hematopoietic progenitor cells into the peripheral blood for collection by leukapheresis (1.4)
- Reduce the incidence and duration of sequelae of severe neutropenia (e.g., fever, infections, oropharyngeal ulcers) in symptomatic patients with congenital neutropenia, cyclic neutropenia, or idiopathic neutropenia (1.5)

----------DOSAGE AND ADMINISTRATION----------

- Patients with cancer receiving myelosuppressive chemotherapy or induction and/or consolidation chemotherapy for AML
  - Recommended starting dose is 5 mcg/kg/day subcutaneous injection, short intravenous infusion (15 to 30 minutes), or continuous intravenous infusion. See Full Prescribing Information for recommended dosage adjustments and timing of administration (2.1)
- Patients with cancer undergoing bone marrow transplantation
  - 10 mcg/kg/day given as an intravenous infusion no longer than 24 hours. See Full Prescribing Information for recommended dosage adjustments and timing of administration. (2.2)
- Patients undergoing autologous peripheral blood progenitor cell collection and therapy
  - 10 mcg/kg/day subcutaneous injection (2.3).
  - Administer for at least 4 days before first leukapheresis procedure and continue until last leukapheresis (2.3)
- Patients with congenital neutropenia
  - Recommended starting dose is 6 mcg/kg subcutaneous injection twice daily (2.4)
- Patients with cyclic or idiopathic neutropenia
  - Recommended starting dose is 5 mcg/kg subcutaneous injection daily (2.4)
- Direct administration of less than 0.3 mL is not recommended due to potential for dosing errors (2.5)

----------DOSAGE FORMS AND STRENGTHS----------

- Injection: 300 mcg/0.5 mL in a single-use prefilled syringe with BD UltraSafe Passive™ Needle Guard (3)
- Injection: 480 mcg/0.8 mL in a single-use prefilled syringe with BD UltraSafe Passive™ Needle Guard (3)

----------CONTRAINDICATIONS----------
Patients with a history of serious allergic reactions to human granulocyte colony-stimulating factors such as filgrastim or pegfilgrastim products. (4)

----------WARNINGS AND PRECAUTIONS----------

- Fatal splenic rupture: Evaluate patients who report left upper abdominal or shoulder pain for an enlarged spleen or splenic rupture. (5.1)
- Acute respiratory distress syndrome (ARDS): Evaluate patients who develop fever and lung infiltrates or respiratory distress for ARDS. Discontinue ZARXIO in patients with ARDS. (5.2)
- Serious allergic reactions, including anaphylaxis: Permanently discontinue ZARXIO in patients with serious allergic reactions. (5.3)
- Fatal sickle cell crises: Have occurred. (5.4)

----------ADVERSE REACTIONS----------
Most common adverse reactions in patients: (6.1)

- With nonmyeloid malignancies receiving myelosuppressive anti-cancer drugs (≥ 5% difference in incidence compared to placebo) are pyrexia, pain, rash, cough, and dyspnea
- With AML (≥ 2% difference in incidence) are pain, epistaxis and rash
- With nonmyeloid malignancies undergoing myeloablative chemotherapy followed by BMT (≥ 5% difference in incidence) is rash
- Undergoing peripheral blood progenitor cell mobilization and collection (≥ 5% incidence) are bone pain, pyrexia and headache. (6.1)
- (Symptomatic) with severe chronic neutropenia (SCN) (≥ 5% difference in incidence) are pain, anemia, epistaxis, diarrhea, hypoesthesia and alopecia

To report SUSPECTED ADVERSE REACTIONS, contact Sandoz Inc. at 1-800-525-8747 or FDA at 1-800-FDA-1088 or *www.fda.gov/medwatch*.

----------USE IN SPECIFIC POPULATIONS----------

- ZARXIO should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. (8.1)
- It is not known whether filgrastim products are excreted in human milk. (8.3)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: [3/2015]

ASBM Surveys: What Do Providers Want In Biosimilar Labeling?

	Physicians (Feb 2015) (n= 400)	**Pharmacists** (Sept. 2015) (n =401)	**Included in Zarxio labeling?**	**Included in FDA draft labeling guidance?**
	Rated as *important* or *very important*			
ID product as a biosimilar	90%	81%	X	✓
Name of biosimilar's reference product	77%	71%	X	✓
Analytical data used to demonstrate biosimilarity	82%	71%	X	X
Clinical data used to demonstrate biosimilarity	83%	71%	X	X
Indications for which originator is approved, but biosimilar is not	79%	76%	X	✓
Approved indications studied or extrapolated?	80%	76%	X	X
Interchangeable with originator product?	79%	88%	X	✓
Identify source of data: Originator or Biosimilar	79%	69%	X	X

1 Feb. 2015 Survey of 400 U.S. physicians *2 Sept. 2015 survey of 401 U.S. pharmacists*

Example of Informative, Transparent Labeling: Canada

- On December 7th 2015, Health Canada released updated SEB (biosimilar) guidance, which calls for more transparency than is required by the FDA:

✔ Identify as SEB

✔ Show data from SEB

✔ Extrapolation information


Health Canada Santé Canada

Draft - Revised Guidance Document

Information and Submission Requirements for Subsequent Entry Biologics (SEBs)

This guidance document is being distributed for comment purposes only.

Published by authority
of the Minister of Health

What We, As Patients, Expect:

- We have the right to expect that **the life of the patient** remains the primary guiding principle of biosimilar policy discussions- not potential cost savings.
- We have the right to expect access to biosimilars and assurance that they are held to a similar standard of **safety, purity, and efficacy as their reference medicine.**
- We have the right, with our physicians, to determine the course of our treatment. This includes choosing which biologic medicine to use initially, and choosing if and when to switch.
- We have a right to expect that regulators will provide us with **accurate, transparent information** about medicines so we make informed decisions.


SafeBiologics
ALLIANCE for SAFE BIOLOGIC MEDICINES
Thank You For Your Attention