Emerging Biosimilars in Therapeutics

PAST, PRESENT AND FUTURE

Agenda

Biosimilar and Interchangeable Biological Product

Regulatory Framework

Biosimilar Now: Existing Biosimilar Market

Biosimilar Future: Emerging Biosimilar Opportunity

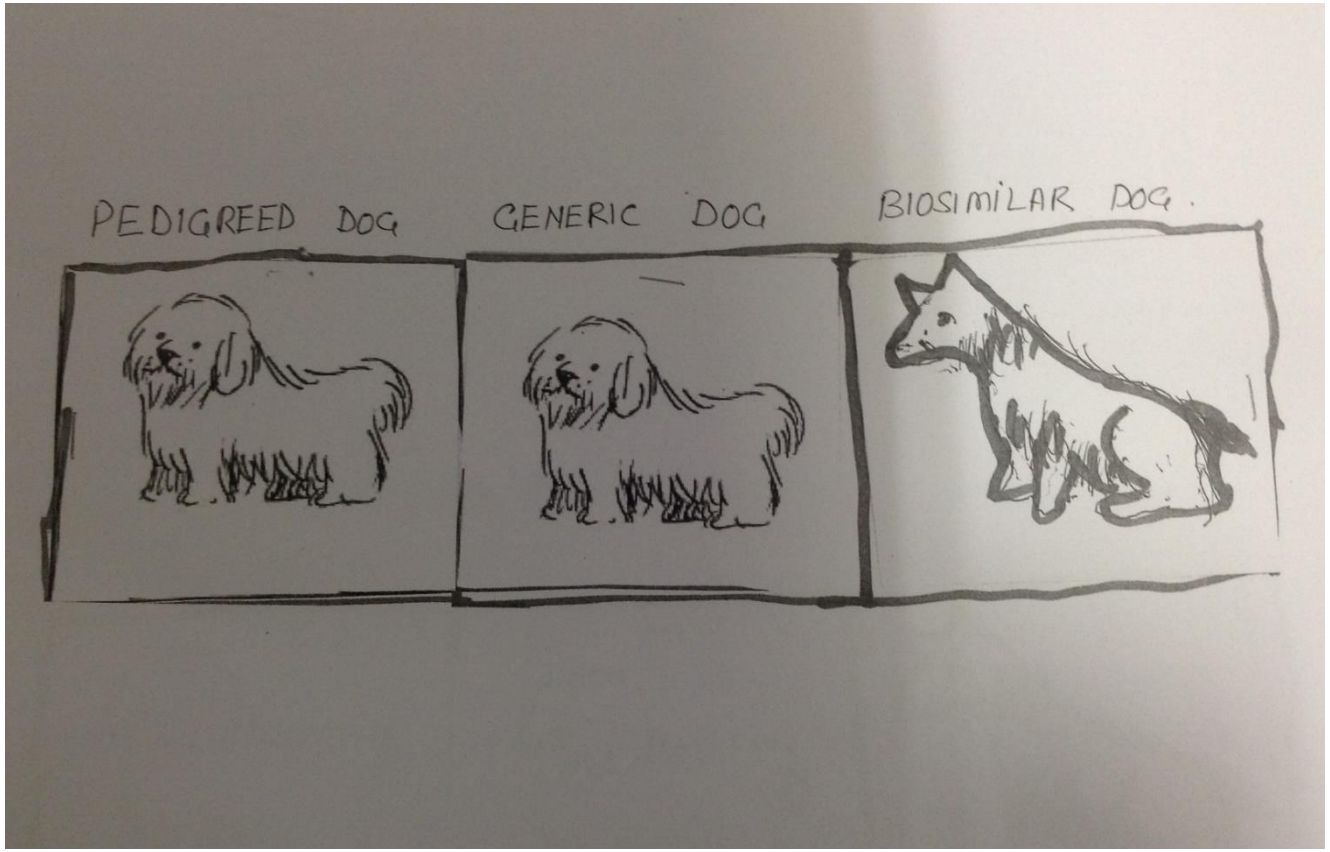
What are Biosimilars?

Biosimilars are a less expensive copy of Biological Products.

Unlike Bioequivalent Generics, Biosimilars are similar to original Biological Products but not an exact copy.

Biosimilars are complex heterogeneous molecules manufactured using living cells.

Generics vs Biosimilars



Generics vs Biosimilars

BIOSIMILAR

A typical Biologic drug consists of more than 20,000 atoms, about 1000 times the size of common small molecule drug.

Biosimilar are complex macromolecules containing amino acids strings.

Biosimilars contains micro heterogeneities caused by glycosylation and other post-translational modifications.

Replication of originator molecule is nearly impossible due to complex manufacturing Process.

GENERICS

A small molecule Generic drug, like Aspirin is made up of only 21 atoms.

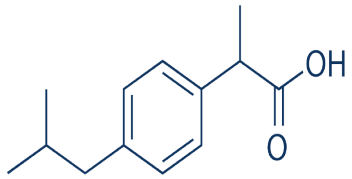
Generics of small synthetic molecules.

Due to smaller size, structure and impurities are well defined.

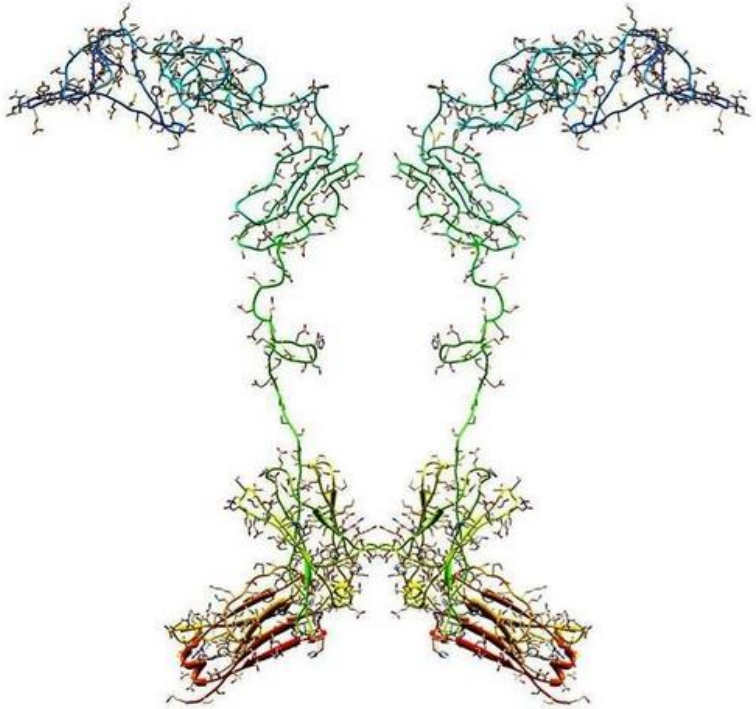
Replication of originator molecule is easy due to simple structure.

Generics vs Biosimilars

SMALL MOLECULE GENERIC DRUG



BIOSIMILAR BIOLOGICAL PRODUCT



Biosimilars vs Interchangeable

Biosimilar	Interchangeable
Approved based on showing high similarity with already approved Reference Product.	In addition to meeting biosimilar standards, they are expected to produce same clinical results as reference product in any given patient.
Can only be prescribed by Healthcare Provider.	May be substituted with reference product by pharmacist without intervention of Healthcare provider.

EU Regulatory Framework

3 Overarching Guidance's

- Guideline on Similar Biological Medicinal Products containing Biotechnology-derived Proteins as Active Substance: Quality Issues (Revision 1): Effective December 2014.
- Guideline on Similar Biological Medicinal Products (Revision 1): Effective 30 April 2015.
- Guideline on Similar Biological Medicinal Products containing Biotechnology-derived Proteins as Active Substance: Non-clinical and Clinical Issues (Revision 1): Effective 01July 2015.

Several Product Specific Guidance.

Guidance's have undergone revisions.

US Regulatory Framework

The Biologics Price Competition and Innovation Act (BPCI Act) of 2009 was signed into law on March 29, 2010 and is similar to Hatch-Waxman Act that establishes an abbreviated approval pathway for Generic Drugs (Generic version of small molecule drugs).

BPCI Act creates an abbreviated Licensure Pathway for Biological products shown to be Biosimilar to or interchangeable to FDA licensed Reference products, i.e. less than a full complement of product specific preclinical and clinical data is required for Licensure.

US Regulatory Framework

FDA issued Following 3 Final Guidance's similar to EU overarching guidance's in 2015.

- Quality Considerations in Demonstrating Biosimilarity of a Therapeutic Protein Product to a Reference Product (Effective April 2015).
- Scientific Considerations in Demonstrating Biosimilarity to a Reference Product (Effective April 2015).
- Biosimilars: Questions and Answers Regarding Implementation of the Biologics Price Competition and Innovation Act of 2009 (Effective April 2015).

FDA also issued 4 draft guidance's.

One draft guidance and proposed rule on naming convention.

Definition of Biosimilar Biological Product

Different names, classifications and definitions in different countries.

FDA Guidance define:

- “Biosimilars are the biological product, highly similar to the FDA approved Reference Product notwithstanding minor differences in clinically inactive components and
- “There are no clinically meaningful differences between the biological product and the Reference Product in terms of the Safety, Purity and Potency of the Product”.

Goal is to demonstrate Bio-similarity between proposed and reference product, not to independently establish safety and efficacy of proposed product.

General Requirements for Submissions

BLA Submission requires scientific data showing that the biological product:

- Is biosimilar to reference product.
- Has the same mechanism of action, conditions of use, route of administration, dosage form and strength as reference product.
- Comprehensive characterization and comparison at quality level should provide a basis for reduction in the non-clinical and clinical data.
- A final determination of Biosimilarity is based on totality of the evidence: combination of quality, non-clinical & clinical evaluation.
- Manufacturing Facility must also meet FDA standards.

Biosimilar Now: Existing Biosimilar

Approved Biosimilars in EU

Omnitrope (Somatropin) was the first Biosimilar approved in EU in 2006.

EMA has approved 21 Biosimilars within following product class:

- Human Growth Hormone
- Granulocyte Colony Stimulating Factor
- Erythropoiesis Stimulating Agent
- Insulin
- Tumor Necrosis Factor (TNF) Inhibitor

Two Biosimilar approvals have been withdrawn, leaving 19 approved Biosimilars in Europe.

Biosimilar in US

On March 06, 2015, US FDA approved Zarxio, the first Biosimilar product in US.

Sandoz Inc's Zarxio is Biosimilar to Amgen's Neupogen (Filgrastim), which was originally licensed in 1991.

Zarxio is approved for the same indications as Neupogen.

For this approval, FDA has a placeholder nonproprietary name for this product as "filgrastim-sndz".

Biosimilar Future: Emerging Biosimilars

Two Major Biosimilar Market Growth Drivers

Healthcare Cost Saving

- Biologic Drugs are 20 times costlier than small molecule Drugs.
- Biosimilars are about a third less costly than originator Drugs.

Biologic Patent Expiration

- Through 2015, about 45 Biologic Drugs worth more than $65 Billion in Global Sales will Lose Patent Protection.
- Through 2020, about $100 Billion in Global Sales will Lose Patent Protection.

"You the guy who asked for the least expensive generic alternative?"

Biologics increasing as key Therapies

Global top 10 Biological products from 2009 to 2014:

- ENBREL
- REMICADE
- HUMIRA
- LANTUS
- MABTHERA
- AVASTIN
- NOVOMIX
- AVONEX
- HERCEPTIN
- COPAXON

All of them will lose patent protection by 2020.

US Biosimilar Market Opportunity

US has largest market opportunity for Biosimilars around the globe.

US patients use more Biologics than any other country.

Only one approved Biosimilar, which was approved in 2015, as compared to many in EU and ROW.

Current Biosimilar market is worth $ 2.0-2.5 Billion.

By 2020 Biosimilar sales are predicted to reach $25.0 Billion.

Main Players looking to Penetrate US Market

Innovator Companies

Amgen

Pfizer

Boehringer Ingelheim

Generic Companies

Hospira

Sandoz

Teva

Emerging Market Players/CMO

Lonza

Biocon

Celltrion

Other Players

Samsung Biologics

FujiFilm

US Biosimilar Challenges

Regulatory Framework Need to be fully established:

- 3 Final Regulatory Guidance issued recently.
- 4 other guidance are in draft stage.
- Draft Guidance for naming convention was issued recently.

Manufacturing Complexity:

- Complexity of Production and Purification Process.
- Higher Pre-clinical and Clinical Cost.

Transition of Stakeholders (Healthcare Providers, payers, Patients, Pharmacists etc.) from Innovator Biologics to Biosimilar Medicine:

- Biosimilar are not exact copy as generics, therefore fear based on safety and efficacy exists. Need to Build Learning curve on Biosimilars
- Biosimilars are not granted automatic substitution.

Global Biosimilar Challenges

Automated Substitution of Originators with Biosimilars

Switching of Originator Drug with Biosimilar Drug and vice versa

Naming of Biosimilar Drugs

Summary

Biosimilar Drugs are different from Generic Drugs.

Establishing a high degree of similarity in quality between the Biosimilar and the Reference product is the key in the regulatory approval of Biosimilar.

Biosimilars present a opportunity of better patient access and lower cost for biological products.

Biosimilars presents lucrative market opportunity in US.

Final Thoughts

Prices of Biosimilar are only 30% lower than innovator drugs as compared to Generics which are about 80-90% lower than innovator drugs.

Benefit is still significant as Biologic product tend to have very high price, which is about 20 times more than small molecule drug.

Once Biosimilar are fully established and more experience is gained in development, will it be possible to bring the cost of Biosimilar medicine further down?

BIOSIMILAR DRUGS ARE CATCHING UP FAST