Globalization of Biosimilars

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Outline of the presentation

- Milestones for biosimilar developments
  - Current situation
  - Benefits of Globalization
  - Shiny side vs Grey areas
    - Strategies
  - Critics of Biosimilars
  - Future prospects
How will globalization of biosimilars take place

Why Globalization?

Is it really needed?

Who will benefit the most?

What ‘price’ are we ready to pay for development of biosimilars?
Growth of Biological products
Developmental milestones

• 1996: FDA issued first comparability Guidelines for interchangeability Biologics
• 2004: EMA develops legislation for guidelines on biosimilars
• 2006: First biosimilar available (Omnitrope)
• 2009: BPCIA authorized FDA to oversee an abbreviated pathway for biosimilar approval
• 2010: Canada, S. Africa, Japan biosimilar guidelines
• 2012: Three draft guidelines by FDA in public domain
• 2014 July: FDA accepts first application for Biosimilars
• Sept 2014: FDA issues purple book
The patent cliff (highlighted in Yellow)
Biosimilars market is highly fragmented

- Top ten players represent < 15% of market
- Market shares of biosimilars is < 5% as compared to innovator biologics
- Distribution unequal
Biosimilar products

1. **Recombinant non-glycosylated proteins**
   - G-CSF), interferon, and human growth hormone (Largest)

2. **Recombinant glycosylated proteins**
   - erythropoietin, monoclonal antibodies, and follitropin.

3. **Recombinant peptides**
   - Glucagon, calcitonin

Monoclonal Antibody, Insulin, and Interferon market will exhibit the fastest growth by 2018
Biosimilar market is segmented

- Oncology, - largest and fastest-growing segment
- Blood disorders,
- Growth hormonal deficiency,
- Chronic and autoimmune disorders, and
- Others (female infertility, hypoglycemia, myocardial infarction, postmenopausal osteoporosis, and chronic kidney failure).
Biosimilars are segmented...cont.d

- Not all that goes off-patent is pursued
- Some like Erythropoietin (EPO) have many takers
  - (In Spain EPO 50% ; while GH around 5%)
- Monoclonal antibodies (Mab) represent a more complex manufacturing pattern
How different regions are greeting biosimilars

Biosimilars available in 50 countries all over the world

**Eager**
1. Europe (EMA)
2. Asia
3. Australia

**Cautious**
1. US (FDA)
2. Canada (PBRER ICH)

Non-originator biologics dominate in some countries: termed “Pharmerging Markets”
- Algeria
- Argentina
- Brazil
- China
- Colombia
- Egypt
- India
- Indonesia
- Mexico
- Pakistan
- Russia
- Turkey
What's Red-Hot...

What's Not...
Regulatory points to look out

- FDA proposes to assess applications as
  - Not similar
  - Similar
  - Highly similar
  - Highly similar with fingerprint-like similarity:

- Interchangeability

- Data exclusivity and patents
First edition published by FDA in July 2014

1. Divided in two parts
   - Center for Drug Evaluation and Research (CDER)
   - Center for Biologic Evaluation and Research (CBER)

2. Information on biologic substitutes
   - BLA number
   - Product name
   - Proprietary name
   - Date of licensure
   - Date of First licensure
   - Reference product
   - Interchangeability
Shiny side

• Biologics/ Biosimilars outperforming
• Covers variety of disease
• Offer novel treatment strategy
• Provide revenue in billions
• Overcoming of Patent cliff
• Cover for rising health care costs
Grey areas

- **Biosimilar**
  - Safety concerns –
  - Efficacy issues

- **Regulatory**
  - Lack of guidelines regarding interchangeability
  - Manufacturing similarity ≠ Biosimilar

- **Pharma Co**
  - Need of large investment;
  - High gestation periods

- **Physicians**
  - Apprehension
  - Lack of experts
### EMA Biosimilar Applications Rejections & Withdrawals

<table>
<thead>
<tr>
<th>Biosimilar vs Innovator</th>
<th>Year</th>
<th>Differences</th>
<th>Consequence</th>
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<tbody>
<tr>
<td>Alpheon (interferon alpha 2a) vs. Roferon-A®</td>
<td>2006</td>
<td>• Differences identified between the two medicines (such as impurities)</td>
<td>• CHMP recommended that Alpheon be refused marketing authorization</td>
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<td></td>
<td></td>
<td>• Non-validated finished product evaluation process</td>
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<td></td>
<td></td>
<td>• Lack of stability data</td>
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<td>Human Rapid Marvel, Human Long Marvel and Human 30/70 Insulins vs. Humulin® S, I and M3 Insulins, respectively</td>
<td>Feb 2008</td>
<td>Clinical differences in rates of lowering blood sugar levels - “Trend in favor of Humulin”</td>
<td>Marvel withdrew its applications for marketing authorizations</td>
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<tr>
<td></td>
<td></td>
<td>• Inadequate submission of active/finished product process</td>
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<td></td>
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<td>• Non-validated manufacturing process</td>
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Factors deciding growth in a particular market/country

• Policy of Government/ Regulatory body
• Market size
• Distribution: Retail/ hospital
• Scope of incentives
• Physician/consumers
What favors biosimilar growth

- A strategic location - Market
- Favourable economic climate
- Strong government support
- Technological leadership
- A pool of world-class researchers and experts
Positive strategies

• Pharmaceutical co:
  – Investment
  – Marketing skills
  – Partnerships

• Researchers:
  – Clinical development
  – Analytical

• Regulatory bodies: Clear regulatory policies

• Physicians: Awareness among practitioners
• Taiwan government: unveiled the availability of a $1.9 billion biotechnology venture capital fund

• Sandoz invested & gained
  – shown tremendous growth

• Merck tried to manufacture biosimilars for Enbrel; expecting its patent expiry in 2012.... But Amgen got patent protected till 2028
• Draft guidelines for biosimilars announced by Dept of biotechnology in asso with CDSCO
• Over 20 products approved by GEAC
• More than 250 brands available
• Various clinical trials being conducted on biosimilars (GEAC with permission from DCGI approves clinical trials)
<table>
<thead>
<tr>
<th>Product In India</th>
<th>Company</th>
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<tbody>
<tr>
<td></td>
<td>Bharat Biotech</td>
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<tr>
<td>Enbrel</td>
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<tr>
<td>EPO</td>
<td>Pipe</td>
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<td>G - CSF</td>
<td>Pipe</td>
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<td>GH</td>
<td>Pipe</td>
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<tr>
<td>Insulin</td>
<td>Pipe</td>
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<td>Interferon</td>
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*Pipe = In Pipeline; Appr = Approved*
Critics of developments of Biosimilars
Viewed as hindrance in new drug development

Abbotts case: petition against biosimilar approval to FDA

Flip-flop policy of Amgen

Concern about Safety issues

Skepticism among physicians
Way forward

- Establish clear pathways for regulatory approval
- Innovation in pharmacovigilance trials
- Investment in market: Huge opportunity
- Establish partnership with international industry leaders
- Export of products
Things to Look forward to...

- FDA approval process to the two biosimilar applications...
- Whether FDA accepts more applications...
- How (& when) Interchangeability is defined..
- After-effects of overcoming patent-cliff...
- Reach to consumers??
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Thank You