The Advent of Biosimilars in Canada: Balancing Short Term Opportunity and Long-Term Sustainability

Bruno Mäder, Merck Canada Inc.

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Outline

• What is a biologic? What is a biosimilar?
• The cost of biologics in Canada
• Biosimilars: Balancing the short-term opportunity and long-term sustainability
• Conclusions
Merck and Samsung Bioepis Biosimilars
Development and Commercialization Agreement

Goal of Merck-Samsung Bioepis collaboration is to develop and commercialize a full portfolio of biosimilars, which may address healthcare system needs worldwide.
What is a Biologic?
What is a Biosimilar?
What are Biologics?

**BIOLOGIC**: Medicinal product made by or derived from living organisms

The Complexity of Biologics versus Small Molecules

Biologics are on average: $\approx$100- to 1,000-fold larger than small-molecule drugs

What is a Biosimilar?

World Health Organization:

• A biotherapeutic product which is similar in terms of quality, safety and efficacy to an already licensed reference biotherapeutic product.¹

Health Canada:

• A ‘Subsequent Entry Biologic’ is a biologic drug that enters the market subsequent to a version previously authorized in Canada, and with demonstrated similarity to a reference biologic drug.²

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Generics vs Biosimilars Development and Approval:

<table>
<thead>
<tr>
<th>Health Canada Approval Requirements</th>
<th>GENERICS</th>
<th>BIOSIMILARS</th>
</tr>
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<tbody>
<tr>
<td>• Bioequivalence¹ (comparative bioavailability)</td>
<td></td>
<td>• Chemistry &amp; Manufacturing²</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Physiochemical and biological characterization²</td>
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<tr>
<td></td>
<td></td>
<td>• Non-clinical data (in vitro, animals)²</td>
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<tr>
<td></td>
<td></td>
<td>• Clinical data (pharmacokinetics, efficacy, safety, tolerability, immunogenicity)²</td>
</tr>
</tbody>
</table>

| Development Cost | $2 - $5 M³ | > $100 M³ |
| Development Time | 2 to 3 years³ | > 5 years³ |

2. Guidance for sponsors: information and submission requirements for subsequent entry biologics (SEBs). In: Drugs and health products. Ottawa: Health Canada; 2010
3. Henry G. Grabowski, Rahul Guha and Maria Salgado, Regulatory And Cost Barriers Are Likely To Limit Biosimilar Development And Expected Savings In The Near Future, Health Affairs, 33, no.6 (2014):1048-1057
“All truth passes through three stages. First, it is ridiculed. Second, it is violently opposed. Third, it is accepted as being self-evident.”

Arthur Schopenhauer, German philosopher (1788 – 1860)
“The arguments currently being raised against biosimilar substitution are similar to arguments used against traditional generic drug substitution following the passage of the Hatch-Waxman Act in 1984.

...Generic prescription drugs are now broadly viewed as completely safe and an appropriate substitution for the brand-name version, and now represent 86 percent of U.S. prescriptions. The widespread availability and acceptance of generic drugs has also resulted in substantial savings to the healthcare system.”

L. PURVIS, AARP PUBLIC POLICY INSTITUTE. 2014\(^1\)

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Health Canada Requirements for the Approval of Biosimilars are Rigorous

- Analytical Techniques
- Physicochemical Properties
- Biological Activity
- Immunological Properties
- Purity and Impurities
- Specifications
- Stability
- Manufacturing Process
- In Vitro Studies
- In Vivo Studies (Animals)
- Pharmacokinetic Studies
- Pharmacodynamic Studies
- Clinical Efficacy and Safety Trials
- Risk Management Plan
- Pharmacovigilance Plan

Guidance for sponsors: Information and Submission Requirements for Subsequent Entry Biologics - March 5, 2010
Assessing Originator Biologics and Products of Manufacturing Drift

Originator Development¹

- Human Studies
  - PK, PD, safety, efficacy, immunogenicity
- Functional Assays
  - In vitro binding, potency
- Analytical Studies
  - Biochemical, structural, purity

Products of Manufacturing Drift²

Originator molecule variations that arise from manufacturing drift require functional and analytical studies to ensure bioequivalence³

PK, pharmacokinetic; PD, pharmacodynamics


Biosimilar Assessment Resembles that of Products of Manufacturing Drift

Biosimilar development is similar to that of products of manufacturing drift, but additionally assesses results in human studies.

PK, pharmacokinetic; PD, pharmacodynamics
Post-Approval Manufacturing Process Changes Are Common

Number of Process Changes After Approval\textsuperscript{1–9}

Post-Approval Manufacturing Process Changes: 47 For Remicade®

Five Types of Manufacturing Process Changes For Remicade® Since EMA Approval 1999¹

1. Growth media changes
2. Purification changes
3. Manufacturing site changes
4. Manufacturing changes to the finished product
5. Manufacturing changes to the active substance

Total: 47

The Cost of Biologics in Canada
Biologics: The Most Significant and Fastest-Growing Segment of Canada’s Pharmaceutical Spending

- $5.5B - 24% of the entire Canadian market for pharmaceuticals (MAT Aug 2014)*
- 12% growth in last year while the total market was up only 3%*
- Four of the top five selling brands in Canada are biologics.*

Top Selling Brands in Canada - MAT August 2015 Sales (Millions)²

<table>
<thead>
<tr>
<th>Brand</th>
<th>Sales (Millions)</th>
<th>% Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>REMICADE (JANSSEN PHARMA)</td>
<td>869</td>
<td>(+14.6%)</td>
</tr>
<tr>
<td>HUMIRA (ABBVIE)</td>
<td>561</td>
<td>(+17.3%)</td>
</tr>
<tr>
<td>LUCENTIS (NOVARTIS PHARMA)</td>
<td>489</td>
<td>(+4.6%)</td>
</tr>
<tr>
<td>HARVONI (GILEAD SCIENCES)</td>
<td>377</td>
<td>(Launched in Oct ‘14)</td>
</tr>
<tr>
<td>ADVAIR (GLAXO SMITHKLINE)</td>
<td>351</td>
<td>(-0.3%)</td>
</tr>
<tr>
<td>ENBREL (AMGEN)</td>
<td>345</td>
<td>(+2.4%)</td>
</tr>
</tbody>
</table>

*The statements, findings, conclusions, views, and opinions contained and expressed in this publication are based in part on data obtained under license from IMS Health Canada Inc. concerning the following information service(s): IMSight, Canadian Drug Store & Hospital Purchases Audit (August through December 2014), PharmaFocus 2018, and PharmaStat (Inflectra and Remicade, February through August 2015) specific to the Biosimilar market. All Rights Reserved. The statements, findings, conclusions, views, and opinions contained and expressed herein are not necessarily those of IMS Health Canada Inc. or any of its affiliated or subsidiary entities.
2014: An Unprecedented Year for New Product Launches

Note: Number inside each bar represents the number of products launched in that respective year.
* Zaxine was launched prior to 2014 but its sales dollars were added to the 2014 new product launches.

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Biosimilars: Balancing the Short-term Opportunity and Long-term Sustainability
CANADA: A Young Biosimilar Industry

- 19 biosimilars since 2006
- Substantial long-term R.W. clinical experience
- Inflectors® and Remsima® in some countries since 2010 and key EU markets Feb ’15
- National pharmacare schemes and Tendering
- Hospital based
- Low/ no patient support

- 4 brands of biosimilars (first in 2012)
- Hospital Based
- Low / no patient support
- Low price for branded products /defined discount post exclusivity

- Three biosimilars approved since 2009: Omnitrope®, Inflectra®, Basaglar®
- No filgrastim or epoetin biosimilars yet
- Minimal clinical experience
- Retail based vs Hospital in Europe and Korea
- 50/50 public:private market
- High cost of entry: Patient Support Programs

- 1st biosimilar approved March 6, 2015: Zarxio® (filgrastim-sndz)
The European Experience: Cost-Lowering Impact of Biosimilars Introduction

Evolution of medicine price for accessible EPO market

# Originator Biologics With Biosimilars in Development

<table>
<thead>
<tr>
<th>Drug (Brand Name)</th>
<th>Private Sales - Canada (MAT Sept 2015)</th>
<th># Biosimilars in Development (Global)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Humira®</td>
<td>$248 M</td>
<td>13</td>
</tr>
<tr>
<td>Enbrel®</td>
<td>$126 M</td>
<td>21</td>
</tr>
<tr>
<td>Remicade®</td>
<td>$316 M</td>
<td>9</td>
</tr>
<tr>
<td>Lantus®</td>
<td>$70 M</td>
<td>5</td>
</tr>
<tr>
<td>Rituxan®</td>
<td>$12 M</td>
<td>30</td>
</tr>
<tr>
<td>Avastin®</td>
<td>$7 M</td>
<td>14</td>
</tr>
<tr>
<td>Herceptin®</td>
<td>$408 M</td>
<td>24</td>
</tr>
<tr>
<td>Neulasta®</td>
<td>$49 M</td>
<td>14</td>
</tr>
<tr>
<td>Lucentis®</td>
<td>$37 M</td>
<td>2</td>
</tr>
<tr>
<td>Aranesp®</td>
<td>$5 M</td>
<td>4</td>
</tr>
<tr>
<td>Neupogen®</td>
<td>$26 M</td>
<td>52</td>
</tr>
</tbody>
</table>

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2. Subsequent Entry Biologics — Emerging Trends in Regulatory and Health Technology Assessment Frameworks, Environmental Scan, CADTH, Issue 43, January 2014 (Table 4, Page 12)
Originators now more focused on protecting brands even after loss of exclusivity.

Pressure Forces on Biosimilar entry into Canada

Physician Acceptance

Patient Support Programs
Balancing Short Term ‘Easy fix’ vs Long-Term Sustainability

- Costs of originator brands
- Immediate Savings
  - Reimbursement policies
  - Originator responses
  - Physician response
- Long-term Savings

Biosimilars
Examples of International Policies to Encourage Biosimilar Use

 Specific targets or quotas for physician and sickness funds for biosimilars.¹

 NICE draft guidance states that treatment should be started with the least expensive drug.²

 The Pharmaceutical Benefits Scheme has set out an Access and Sustainability Package, which includes a goal of investing AUD20 million to raise awareness of and confidence in biosimilars among health professionals and consumers.³

Establishing a Sustainable Biosimilar Industry

Real World Clinical Experience

Education

Sustainable Pricing

Criteria and/or Policy Development

Sustainable Biosimilar Industry
Conclusions

• The cost of biologics represents a substantive and growing portion of total drug spending in Canada

• Biosimilars may represent an opportunity to achieve cost reductions for private drug benefit plans, which supports overall sustainability and affordability.

• Now is the time to establish a foundation for an emerging biosimilar industry that offers continuing benefits to all stakeholder groups in both the short and long term.