Current Approaches for Biosimilars Value Assessment and Reimbursement Decision Making –
Mapping HTA Practices Internationally

ISPOR 2022 Europe Conference
Forum organized by the ISPOR Biosimilars SIG
Meet the speakers

Steven Simoens  
PhD in Economics  
KU Leuven (Belgium)

Teresa Barcina Lacosta  
PhD Candidate in Pharmacy  
KU Leuven (Belgium)

András Inotai  
PhD in Pharmacoconomics  
Semmelweis University (Hungary)

Alexander Gee  
Senior Director, Pricing and Market access  
Parexel International (UK)
Conflicts of Interest Statements

- **Steven Simoens**, PhD. Senior full professor in Health Economics, KU Leuven (Belgium)
  Founder of the KU Leuven MABEL Fund. Dr. Steven Simoens has been involved in research activities conducted for Amgen, Celltrion, Hospira, Mundipharma, MSD, Sandoz and Pfizer

- **Teresa Barcina**, PharmD. PhD candidate in Pharmaceutical Sciences, KU Leuven (Belgium)
  No conflicts of interest to disclose

- **András Inotai**, PhD, Dr. Habil. Associate professor at Center for Health Technology Assessment, Semmelweis University (Hungary). Principal researcher, Syreon Research Institute (Hungary)
  Employee of Syreon Research Institute. Dr. András Inotai has worked on multiple research projects related to biosimilars, for which Syreon Research Institute received funding from Egis Pharmaceuticals PLC and Medicines for Europe.

- **Alexander Gee.** Senior Director, Pricing and Market access at Parexel International (US)
  Employee at Parexel International
Aim of today’s Forum

- Describe characteristics of value assessment frameworks for biosimilars used across jurisdictions
- Identify current limitations of these frameworks
- Open a discussion between panelists and the audience on challenges related to the value assessment of biosimilars
Agenda

- ISPOR Biosimilars Special Interest Group and its key project on biosimilar value assessment
- Perspective of Central and Eastern European Countries
- US perspective
- Discussion with the audience
How to participate in interactive polling?
It’s Time for a Poll!

What is your country of residence?

a) Higher income European country (incl. Western and Northern Europe)
b) Lower income European country (incl. Central and Eastern Europe)
c) USA/Canada
d) Other
What stakeholder group do you represent?

a) Industry  
b) Regulatory/HTA agency  
c) Academia  
d) Healthcare professional  
e) Other
In your opinion, should biosimilar value assessment be restricted to a price comparison between the biosimilar and the reference biologic?

- Yes
- No
Teresa Barcina Lacostea

ISPOR Biosimilars SIG and its key project on biosimilar value assessment
Challenges in the Value Assessment of Biosimilars

Research Questions

- What has been the role of HTA institutions when it comes to assessing biosimilars value for reimbursement decision-making?
- What are the limitations of current value assessment frameworks for biosimilars?
- How can elements of value offered by biosimilars be integrated in economic evaluations?
BIOSIMILARS: Value proposition

- Cost-Benefit Ratio
- Price Competition
- Broader Products Range
- Savings Reinvestment

Indications
Formulations
Admin. Devices

Access
Savings

Quality of Care Improvements
Benefits beyond Delivering Cost-Savings...

- Cost-benefit ratio
- Reimbursement restrictions

To be considered at the HTA level?

QALY gains

ACCESS
Challenges in the Value Assessment of Biosimilars

1. Systematic Literature Review
   - Information retrieval: Sept 24th 2021; 288 records
   - Databases: PubMed, EMBASE, WOS Core Collection, EBSCOhost, ISPOR and CDR databases

2. Interview with HTA Experts
Challenges in the Value Assessment of Biosimilars

1. Systematic Literature Review

2. Interview with HTA Experts
   - Semi-structured interviews: April-August 2022
   - 15 countries covered, 18 interviewed experts
Value Assessment of Biosimilars: Gaps and Challenges Identified

- Choice of appropriate economic evaluation technique and of appropriate comparator
- Approach to biosimilar value assessment in biologic-naïve and biologic-experienced populations
- Lack of clarity as to how biosimilar value assessment can account for potential ‘nocebo’ effects
- Approach to filling the clinical evidence gap for indications granted based on evidence extrapolation
- Management of uncertainty and role of managed entry agreements
- Valorization of expanding access to treatment
- Valorization of value-added services
The originator biologic has been approved for reimbursement

YES

Reimbursement sought for the same indications, populations, administration forms and devices

- HTA agency involvement: not required
- HTA agency involvement: required (cost-minimization)
Choice of economic evaluation technique/comparator – Diverse approaches

The originator biologic has been approved for reimbursement

YES

Reimbursement sought for indications, administration forms, devices for which the originator has not been assessed/reimbursed

HTA agency involvement: required
The originator biologic has been approved for reimbursement

NO

Full economic evaluation conducted

Comparator: should not be the originator, but a reimbursed product
Approach to biosimilar value assessment in different patient populations

Limited interest to adopt a non-treatment-naïve population perspective and to:

- Incorporate real world data regarding safety of switching
- Model potential impact of ‘nocebo’ effects on adherence
Approach to filling the clinical evidence gap for indications granted based on evidence extrapolation

HTA agencies/payers generally accept the principle of extrapolation

- When doubts remained, a reassessment of evidence was conducted at the HTA level

Approach to managing residual clinical uncertainties

- Limited role of Managed Entry Agreements (high-implementation costs for limited added-value in the case of biosimilars)
Valorization of expanding access to treatment

- Relevant question from HTA perspective: what is the mechanism that has led/can lead to greater access?

Valorization of value-added services

- Challenging to account for these services at the HTA level, due to the generally regional/local nature of these offers

- Greater chance to account for services that lead to lower hospital visits/ healthcare infrastructure needs
Value Assessment of Biosimilars: Gaps and Challenges Identified

- Choice of appropriate **economic evaluation technique** and of appropriate **comparator**
- Approach to biosimilar value assessment in **biologic-naïve** and **biologic-experienced** populations
- Lack of clarity as to how biosimilar value assessment can account for potential ‘**nocebo**’ effects
- Approach to filling the clinical evidence gap for **indications** granted based on **evidence extrapolation**
- **Management of uncertainty** and role of managed entry agreements
- Valorization of **expanding access** to treatment
- Valorization of **value-added services**
Challenges in the Value Assessment of Biosimilars

- **Divergence of value assessment processes/criteria** across and within countries
- Trend towards **streamlined value assessment processes** (HTA agencies progressively less involved)
- In cases where HTA agencies’ involvement and full economic evaluations are required, **methodological guidance specific to biosimilars is missing**
- **Limited flexibility** to account for adherence-related factors and patient preferences, value-added services, QALY gains generated as a result of biosimilars expanding access to treatments
General features of lower income countries

- New medicines at international launch prices are often not cost-effective
- Limited HTA capacities – stronger emphasis on BI
- New medicines are available with volume restrictions (inc. price volume agreements)
- Transparency of decisions is more limited
- Poorer health status – societies pay higher penalties for suboptimal decisions
- Salaries of physicians are lower – potentially stronger ties to additional funding from pharmaceutical companies
- No specific HTA document exists for biosimilars (HU, BG), general HTA guidelines applicable
Selection of comparator – HTA principles

- Policy relevant comparator of biosimilars
  - Off-patent originator (if reimbursed)
  - Older (small molecule?) standard reimbursed therapy (if biosimilar introduces the biological INN first in the country)

Selection of comparator – HU practice

- Implicit preference by authorities to apply a CMA for biosimilars
  - Pharmaceutical companies offer price cut vs the originator (even if it is not reimbursed/available only with individual funding request (IFR))

- Sometimes originator is available on an IFR program/named patient basis (it still has a ‘price’, the biosimilar offers some ‘discount’ but necessarily not as much as in terms of public price as requested in the normal pathway)
  - Why is the originator not reimbursed? There is less strict HTA criteria (for high priced medicines) in case of individual reimbursement, also reimbursement on named patient basis often transforms later into formal reimbursement (suboptimal pathway)

- Comparator selection: what is considered relevant by local HTA guideline may be different compared to what is considered relevant by Technology Assessment Committee on the NHIFA (issue partly resolved since the 2021 revision of HTA guideline requesting a scenario analysis for IFR comparator)
Only reimbursed comparator is accepted

If the off-patent original is not reimbursed, the old reimbursed therapy will be the accepted comparator, even if this necessitates full economic evaluation (with modelling)
Selection of type of economic evaluation – HTA principles

- Cost comparison/Cost minimization (CMA)
- Full economic evaluation (CEA/CUA)
Selection of type of economic evaluation – HU practice

- **Scenarios**
  - Biosimilar applications with simplified track - does not even reach the HTA office
  - Biosimilars are assessed by HTA office only if they are first as an INN (i.e. they are getting reimbursed before the originator product)
  - HTA office/NHIF try to enforce CMA for biosimilars (in the case of marginal health gain), CUA may be used if biosimilar is not (bio)equivalent to the originator (and there is meaningful difference in health gain)

- **Challenge:** evergreening practice of originators – different drug form
  - If bioequivalence can be demonstrated, CMA is acceptable
  - Physicians with strong financial ties to originator manufacturers may be more open to evergreening/using patented medicines (as proven by high original share in some INNs)

Selection of type of economic evaluation – BG practice

- **Scenarios**
  - INN with the same dose and drug form – reference price is calculated (cost comparison/CMA)
  - INN with different drug form – bioequivalence calculated, CMA applicable
  - If there are differences in the outcomes demonstrated by clinical trials, a full economic evaluation (CEA/CUA) is performed
  - If no comparative data exists, indirect comparison is performed
Population effect – biosimilars can alleviate access restrictions

- New medicines (incl. biosimilars) at international launch price are often not cost effective in lower income CEE countries
- Payers often consider BI more important than CE
- To meet budget constraints new medicines are often introduced with volume restrictions
- Biosimilar with more affordable price can alleviate volume restrictions

Population effect – biosimilar can alleviate access restrictions

HU
- From an HTA perspective, this benefit generated by biosimilars would be considered as double counting, unless a biosimilar increases patient access not through its lower price but through lower healthcare infrastructure needs.

BG
- NHIF determines the patient’s eligibility criteria which should be fulfilled to initiate biologics.
- Reimbursed medicines are available for all patients who meet the eligibility criteria.
- (-> <- comparison of utilization of high income vs. CEE countries. N.b. Biosimilars may also increase access by making new treatments available also at an earlier stage.)
In lower income countries value assessment of biosimilars follows international HTA principles

- Type of economic evaluation

However, in some cases individual ‘pragmatic’ solutions are applied that are different from international ‘state-of-art’ HTA principles (e.g. comparator selection)

Politically sensitive areas: access to high priced medicine

- What explains the difference in terms of standardized drug utilization vs. high income countries?

Topics with limited relevance/priority from CEE HTA perspective: nocebo effect, value added services
Alexander Gee
US perspective
Despite increasingly favorable dynamics, there are still some clear limitations to biosimilar uptake

- Strong market demand is driven by need for cost savings, leading to incentives to use and favorable reimbursement policies
- There is increasing knowledge of and experience with biosimilars from all stakeholders
- Growing biosimilar competition will continue to drive costs down
- Interchangeability and biosimilar nomenclature issues can create friction
- Currently, there is a lack of consistency as some health plans prioritize coverage for specific biosimilars, others retain the originator, and yet others do not differentiate
  - This has created a fragmented market with varying levels of uptake
Biosimilar competition is increasing with key US players developing robust biosimilar portfolios

<table>
<thead>
<tr>
<th>Pharma</th>
<th>Approved Biosimilar</th>
<th>Biologic Equivalent</th>
<th>Biosimilars in Development</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amgen</td>
<td>Amjevita</td>
<td>Humira</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mvasi</td>
<td>Avastin</td>
<td></td>
</tr>
<tr>
<td>Novartis</td>
<td>Avsola</td>
<td>Remicade</td>
<td></td>
</tr>
<tr>
<td>Sandoz</td>
<td>Kanjinti</td>
<td>Herceptin</td>
<td></td>
</tr>
<tr>
<td>Biogen</td>
<td>Zaxipto</td>
<td>Neupogen</td>
<td></td>
</tr>
<tr>
<td>Samsung Bioepis</td>
<td>Erelzi</td>
<td>Enbrel</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Hyrimoz</td>
<td>Humira</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Zierentz</td>
<td>Neulasta</td>
<td></td>
</tr>
<tr>
<td>Coherus</td>
<td>Imraldi</td>
<td>Humira</td>
<td>Avastin, Lucentis, Soliris, Prolia</td>
</tr>
<tr>
<td></td>
<td>Elicovo</td>
<td>Enbrel</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Flixabi</td>
<td>Remicade</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ontuzant</td>
<td>Herceptin</td>
<td></td>
</tr>
<tr>
<td>Biogen</td>
<td>Ogivri</td>
<td>Herceptin</td>
<td></td>
</tr>
<tr>
<td>Samsung Bioepis</td>
<td>Hulio</td>
<td>Humira</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fulphila</td>
<td>Neulasta</td>
<td></td>
</tr>
<tr>
<td>Viatris</td>
<td>Inflectra</td>
<td>Remicade</td>
<td>Rituax, Humira, Neulasta, Avastin, Avastin, Botox</td>
</tr>
<tr>
<td></td>
<td>Ixifi</td>
<td>Remicade (IV)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Retacrit</td>
<td>Epogen, Procrit</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Nivestym (Hospira)</td>
<td>Neupogen</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Zirabev</td>
<td>Avastin</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Trazimera</td>
<td>Herceptin</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ogivri</td>
<td>Herceptin</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Hulio</td>
<td>Humira</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fulphila</td>
<td>Neulasta</td>
<td></td>
</tr>
<tr>
<td>Coherus</td>
<td>Udenyca</td>
<td>Neulasta</td>
<td>Humira, Eylea, Avastin, Lucentis</td>
</tr>
</tbody>
</table>
Biosimilar adoption will be driven by demonstrating comparable clinical outcomes, market access, reducing patient burden and competitive delivery.

- Clinical Data
- Dosing Interval
- Insurance Coverage
- Drug Delivery
- Patient Financial Burden
Several of the strategies used by originators, to gain or protect share in biosimilar markets, may become leveraged by biosimilars as competition increases.

- Formulation and Drug Delivery
- Commercial and GTM Strategy
- Pricing and Payer Strategy
- Evidence Generation
- Patient Support
- Biobetters
Q&A
Value Assessment of Biosimilars: Gaps and Challenges Identified

- Choice of appropriate economic evaluation technique and of appropriate comparator
- Approach to biosimilar value assessment in biologic-naïve and biologic-experienced populations
- Lack of clarity as to how biosimilar value assessment can account for potential ‘nocebo’ effects
- Approach to filling the clinical evidence gap for indications granted based on evidence extrapolation
- Management of uncertainty and role of managed entry agreements
- Valorization of expanding access to treatment
- Valorization of value-added services
Please rank the relevance of the identified challenges:

1. Choice of economic evaluation technique/comparator
2. Assessing biosimilars value in distinct populations (naïve/ experienced)
3. Accounting for potential ‘nocebo’ effects
4. Filling clinical evidence gaps regarding indications extrapolation
5. Integrating RWD to manage residual clinical uncertainties
6. Valorization of expanding access to treatments
7. Valorization of value-added services
Sign up to join our Special Interest Group!

1. Visit the ISPOR home page – [www.ispor.org](http://www.ispor.org)
2. Select “Member Groups”
3. Select “Special Interest Groups”
4. Click on “Biosimilars”
5. Select “Join a Special Interest Group”

> For more information about our group email biosimilarsig@ISPOR.org
Thank You!