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Improving healthcare decisions

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

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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

It’s Time for a Poll!

- **What stakeholder group do you represent?**

a) Industry

b) Regulatory/HTA agency

c) Academia

d) Healthcare professional

e) Other

It’s Time for a Poll!

- **In your opinion, should biosimilar value assessment be restricted to a price comparison between the biosimilar and the reference biologic?**
  - Yes
  - No

1

Teresa Barcina Lacosta

ISPOR Biosimilars SIG and its key project on biosimilar value assessment

Challenges in the Value Assessment of Biosimilars

Research Questions

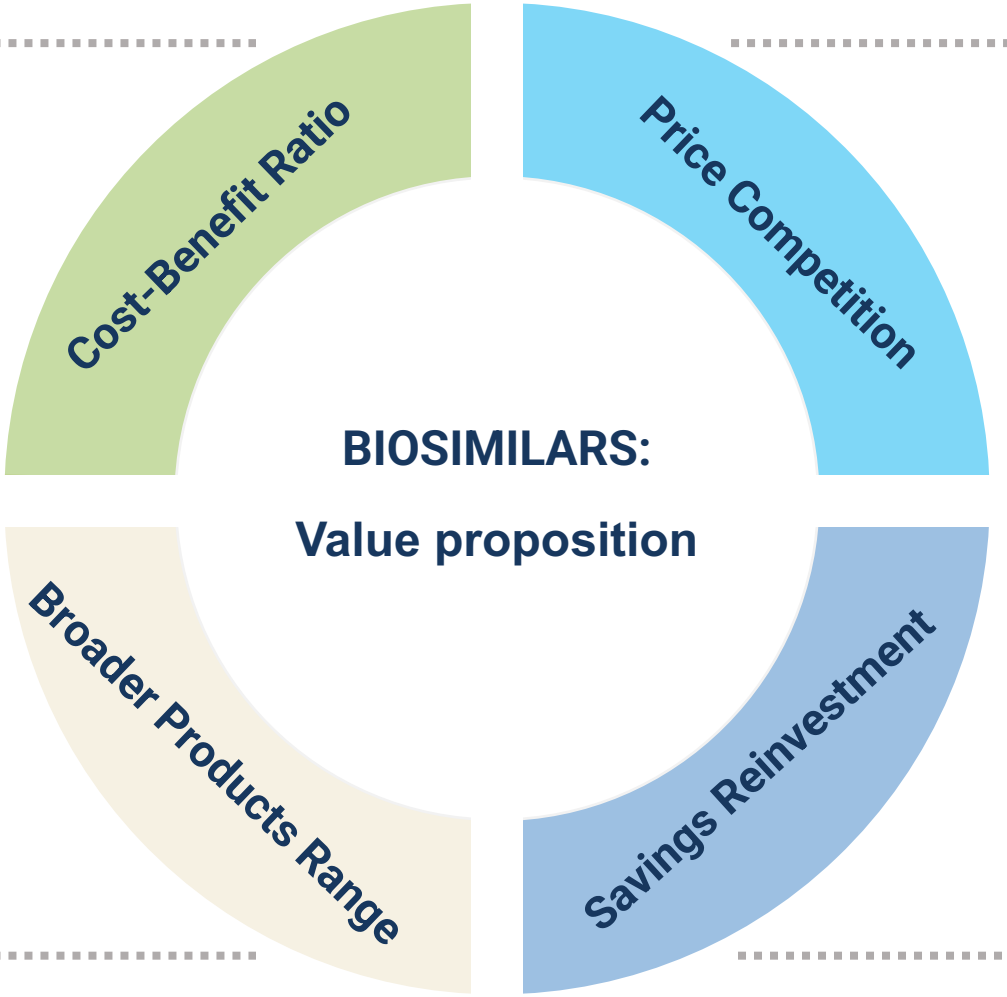
What has been the **role of HTA institutions** when it comes to assessing biosimilars value for reimbursement decision-making?

What are the **limitations** of current value assessment frameworks for biosimilars?

How can **elements of value** offered by biosimilars be integrated in economic evaluations?

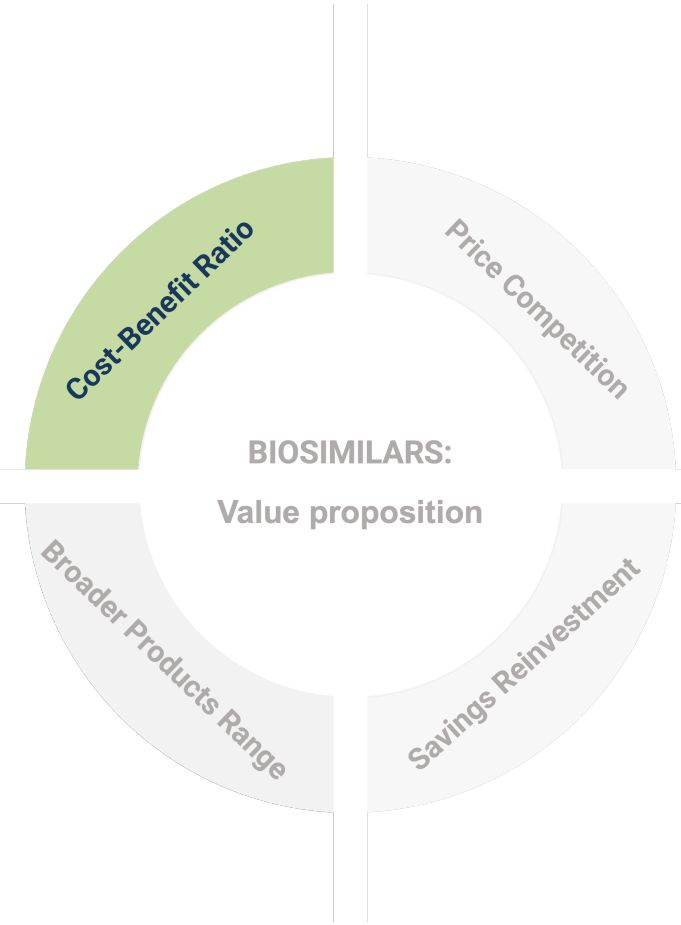
ACCESS

SAVINGS



Indications
Formulations
Admin. Devices

Quality of Care
Improvements



Benefits beyond Delivering Cost-Savings…

Cost-benefit ratio → **Reimbursement restrictions** → **ACCESS**

ACCESS → **QALY gains** → **To be considered at the HTA level?**

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

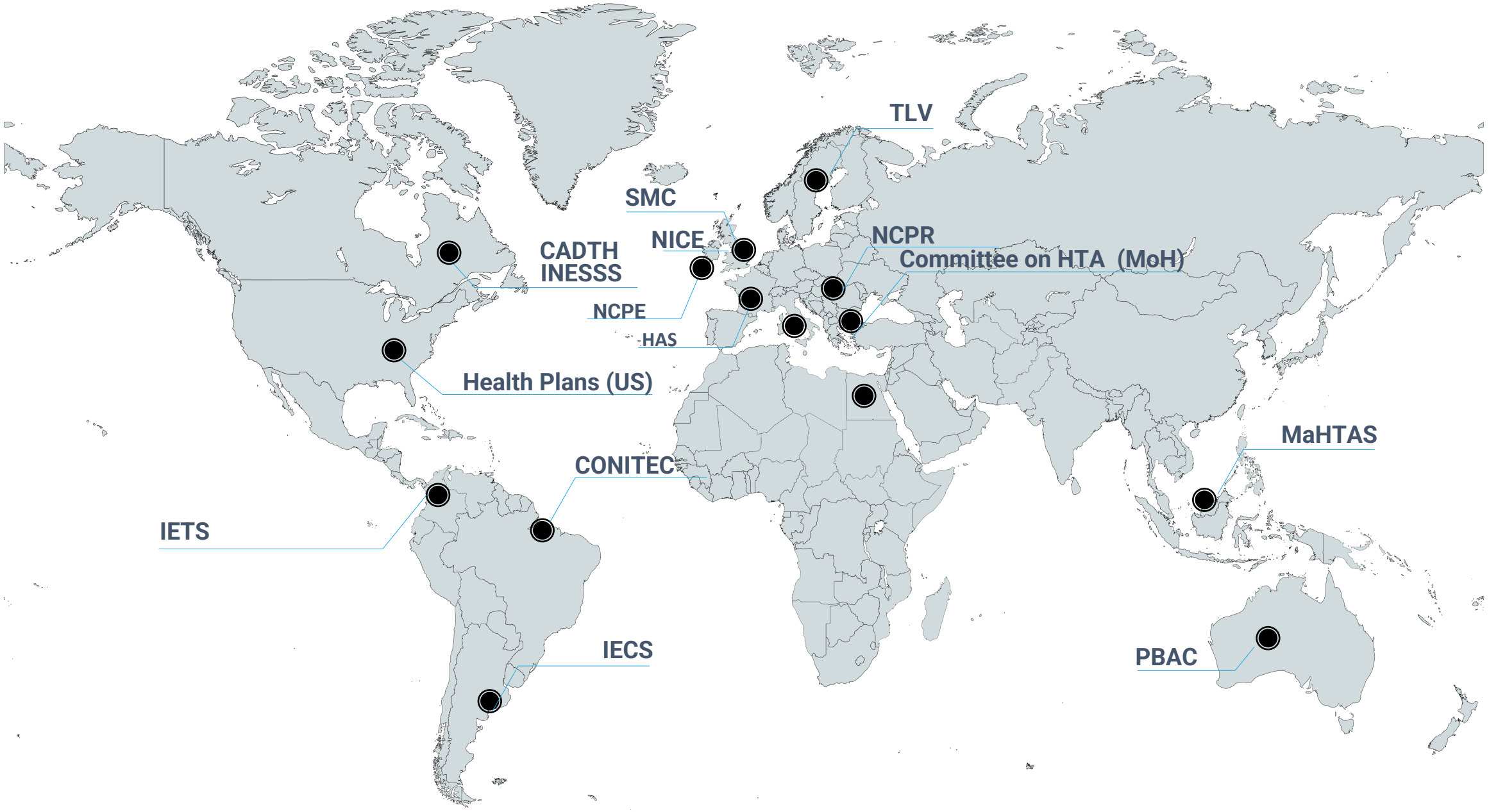
Systematic Literature Review

2

Interview with HTA Experts

Semi-structured interviews: April-August 2022

15 countries covered, 18 interviewed experts


TLV
SMC
NICE
NCPR
CADTH
INESSS
Committee on HTA (MoH)
NCPE
HAS
Health Plans (US)
MaHTAS
CONITEC
IETS
IECS
PBAC

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**

Choice of economic evaluation technique/ comparator – Diverse approaches

The originator biologic has been approved for reimbursement

→ YES →

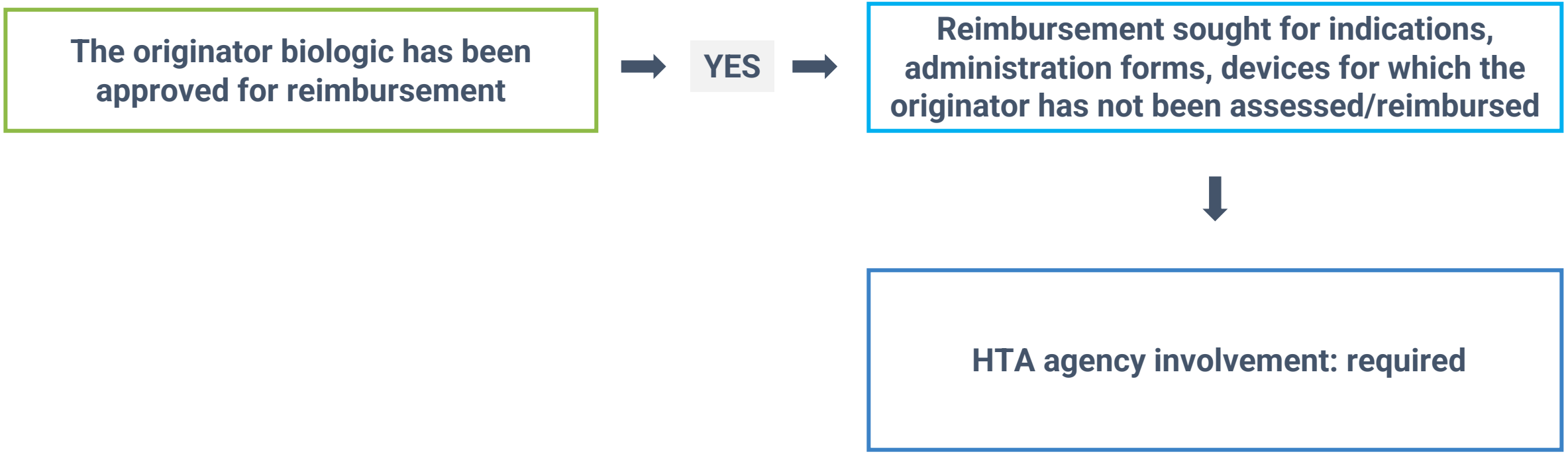
Reimbursement sought for the same indications, populations, administration forms and devices

↓

- HTA agency involvement: not required
- HTA agency involvement: required

(cost-minimization)

Choice of economic evaluation technique/ comparator – Diverse approaches



Choice of economic evaluation technique/ comparator – Diverse approaches

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

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Challenges in the Value Assessment of Biosimilars

Key considerations

- **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

2

András Inotai

Perspective of lower income countries

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

Inotai A, et al. Identifying Patient Access Barriers for Tumor Necrosis Factor Alpha Inhibitor Treatments in Rheumatoid Arthritis in Five Central Eastern European Countries. Front Pharmacol. 2020 Jun 5;11:845., **Németh, B et al** (2022). Access to high-priced medicines in lower-income countries in the WHO European Region. World Health Organization. Regional Office for Europe. https://apps.who.int/iris/handle/10665/361751.

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)

Inotai A, et al. Policy practices to maximize social benefit from biosimilars. Journal of Bioequivalence & Bioavailability. 9:467-472.

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)

Inotai A, et al. Drug policy in Central Eastern Europe – Hungary. Value in Health Regional Issues. 13: 16-22

Selection of comparator – BG practice

- 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)

Inotai A, et al. Policy practices to maximise social benefit from biosimilars. Journal of Bioequivalence & Bioavailability. 9:467-472.

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)

Harsányi A et al. Influence of biosimilar infliximab launch on the utilization pattern of biological medicines: the case of Hungary. Expert Rev Pharmacoecon Outcomes Res. 2020 Dec;20(6):653-659.

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

Inotai A, et al. How to solve financing gap to ensure patient access to patented pharmaceuticals in CEE countries? - the good, the bad, and the ugly ways. Expert Rev Pharmacoecon Outcomes Res. 19(6):627-632.

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)

Conclusion

- 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

3

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

Pharma	Approved Biosimilar	Biologic Equivalent	Biosimilars in Development
Viatris	Inflectra	Remicade	Rituxan, Humira, Neulasta, Avastin, Botox
	Ixifi	Remicade (IV)	
	Retacrit	Epogen, Procrit	
	Nivestym (Hospira)	Neupogen	
	Zirabev	Avastin	
	Trazimera	Herceptin	
	Ogivri	Herceptin	
	Hulio	Humira	
	Fulphila	Neulasta	
Coherus	Udenyca	Neulasta	Humira, Eylea, Avastin, Lucentis

Pharma	Approved Biosimilar	Biologic Equivalent	Biosimilars in Development
Amgen	Amjevita	Humira	Rituxan, Erbitux, Soliris, Eylea, Stelara
	Mvasi	Avastin	
	Avsola	Remicade	
	Kanjinti	Herceptin	
Novartis Sandoz	Zarxio	Neupogen	Remicade, Xgeva, Eylea, Avastin, Prolia
	Erelzi	Enbrel	
	Hyrimoz	Humira	
	Ziextenzo	Neulasta	
Biogen Samsung Bioepis	Imraldi	Humira	Avastin, Lucentis, Soliris, Prolia, Stelara
	Eticovo	Enbrel	
	Flixabi	Remicade	
	Ontruzant	Herceptin	

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

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It’s Time for a Poll!

- **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

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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!