Transforming Access: The Role of Biosimilars in Advancing EML Recommendations

A 10-minute intervention on access strategy for LMICs through biosimilar integration

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Speaker Disclosure

Nuclear medicine physician with over 20 years of experience in the global pharmaceutical sector, focusing on **biosimilars since 2004** (Serono, Novartis, Amgen, Roche, Sandoz International Biopharmaceuticals, Merck Serono Biosimilars, and Organon Biosimilars)

In 2017, I joined academic partners in developing a **bevacizumab for ophthalmic use** to expand access in **LMICs**

Since 2022, I have worked ***pro bono*** to advance affordable medicines, collaborating with LMIC regulators and suppliers

In 2024, I established a **Switzerland-based platform** to support these global access efforts further

I have an intellectual and (potential) financial interest with respect to the expansion of biosimilars

WHO EML Open Session Presentation - Contents

Bevacizumab on the EML: Access, Off-Label Use & Strategic Implications

- **Bevacizumab, including quality-assured biosimilars, is listed in the EML under Section 2.1 (Ophthalmological Preparations)** — as the only anti-VEGF agent for use in **wet AMD**
- This listing refers to **off-label use**, as no other anti-VEGF product is formally approved for ophthalmology at the global level
- **No oncology indications** are included for bevacizumab in the EML, despite its broad use in cancer care
- **In countries with limited biosimilar uptake or regulatory restrictions**, there is a **risk that low-cost options are displaced by higher-cost, on-label drugs, compromising access**
- **Bevacizumab biosimilars offer a vital pathway to affordable, vision-saving care in LMICs and highly regulated markets.** But this access route remains fragile, especially when:
  - **Regulatory or supply-side barriers delay biosimilar uptake**
  - Countries **restrict off-label reimbursement**
  - **On-label commercial competitors** push for the exclusion or restriction of bevacizumab in practice

Bevacizumab biosimilars exemplify both the opportunity and the complexity of leveraging the EML for access, especially where off-label use and compounding intersect

Cost Matters: The Case for Bevacizumab in Retinal Diseases

Clinical trials using bevacizumab in ophthalmology have shown comparable safety and efficacy to branded and biosimilar anti-VEGF agents (ranibizumab, aflibercept)

It is the price that matters

The cost of **approved anti-VEGF intravitreal injections** varies significantly across regions, influenced by factors such as drug choice, healthcare systems, and availability of biosimilars. The range in Europe and the US for a single intravitreal injection:

Europe: ~€500-€1.000

US: ~$1.000-$2.000

Cost of one anti-VEGF intravitreal injection using **compounded bevacizumab:**

Europe: €50 (PLOS)

UK: £28 *(Judiciary of England and Wales, 2018)*

US: $70-$100 (Glasser)

Intravitreal Anti-Vascular Endothelial Growth Factor Cost Savings Achievable with increased Bevacizumab Reimbursement and Utilization; Glasser et al; Ophthalmology; https://doi.org/10.1016/j.ophtha.2020.06.012
Competition law and pricing among biologic drugs - the case of VEGF therapy for retinal diseases; Van de Wiele et al; 2022; https://doi.org/10.1093/jlb/lsac001
PLOS ONE | https://doi.org/10.1371/journal.pone.0197670 May 17, 2018
https://www.judiciary.uk/wp-content/uploads/2018/09/bayer-and-novartis-v-nhs-darlington-ccg-summary.pdf

Bevacizumab Pricing & the Case for Compounding in Retinal Disease

Example of retail prices for different packages/brands of bevacizumab in Germany (www.medizinfuchs 14.10.2024)

•	Avastin®	100mg	562€	400mg	1.999€
•	Mvasi®	100mg	408€	400mg	1.600€
•	Oyavas®	100mg	396€	400mg	1.555€

These are IV formulations — for retinal disease, **1.25 mg** is used per injection (**via compounding**)

*The **benefit:risk ratio** for **compounded bevacizumab** in ophthalmology is exceptionally high, especially when prepared under proper aseptic conditions. The small risk of contamination (~1 in 5,000–10,000) is **far outweighed** by the massive increase in access and affordability*

When access is constrained, the **only effective drug is the one that patients can afford**. **Compounded bevacizumab**, used safely for over two decades, delivers comparable outcomes at a fraction of the cost. Rigorous compounding standards should be promoted, not penalized, in global eye care policy

In LMICs, compounded bevacizumab reduces anti-VEGF costs by >90% while maintaining efficacy and safety

Intravitreal Anti-Vascular Endothelial Growth Factor Cost Savings Achievable with increased Bevacizumab Reimbursement and Utilization; Glasser et al; Ophthalmology; https://doi.org/10.1016/j.ophtha.2020.06.012
Avastin®/Bevacizumab Oncology Formulation: https://www.medizinfuchs.de/ Online prices in Germany 14.10.2024
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Checkpoint Inhibitors in the 2025 EML: Spotlight on Pembrolizumab

- **Checkpoint inhibitors** are being reviewed for inclusion in the **2025 EML** — a major milestone for global oncology access
- In 2024, pembrolizumab sales grew by 18% to $29.5 billion
- Pembrolizumab has **~15 clinically distinct cancer indications** at the core of its use globally
- As of April 2025, 10 (plus) companies are actively developing pembrolizumab biosimilars, according to the Spanish Biosimilars Association (BioSim)
- **Other checkpoint inhibitors** (e.g., nivolumab, atezolizumab,…) show **less biosimilar momentum** due to narrower indications and economic challenges
    - **Pembrolizumab alone controls ~60% of the global PD-1/PD-L1 inhibitor market**, making it the most logical biosimilar target

Early biosimilar uptake in countries with minimal IP barriers — a rare chance to align oncology innovation with equitable access

https://elpais.com/sociedad/2025-04-02/keytruda-el-medicamento-que-factura-tanto-como-zara-y-genera-debate-sobre-la-duracion-de-las-patentes.html?utm_source=chatgpt.com
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Biosimilar Launch Windows for Pembrolizumab: Global IP Landscape

- **Europe**
  Supplementary Protection Certificate (SPC) extends exclusivity to **July 2030**
  Pediatric extension adds 6 months → **expires January 2031**
  Biosimilar entry expected: late 2028–early 2029 for core oncology indications

- **Asia**
  Early launches likely in India and China: 2026–2027

- **Sub-Saharan Africa & MENA**
  Most countries have **no enforceable IP or data exclusivity**
  Biosimilar entry feasible: as early as 2026

- **Latin America**
  Highly **fragmented regulatory landscape**
  Brazil & Mexico: **Launch likely by 2028–2029**
  Other countries: **Possible access from 2026–2027**

*In many LMICs, pembrolizumab may face **no enforceable patents**, opening a window for earlier access, well before 2030*

https://elpais.com/sociedad/2025-04-02/keytruda-el-medicamento-que-factura-tanto-como-zara-y-genera-debate-sobre-la-duracion-de-las-patentes.html?utm_source=chatgpt.com
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U.S. IRA Impact on Pembrolizumab
Inflation Reduction Act (IRA) & Medicare Drug Price Negotiation

The bill allows **Medicare to negotiate prices for high-cost drugs with no generic or biosimilar competition**

Small Molecules	9 years post approval
Biologics	13 years post approval

IRA Timeline for Keytruda

- **FDA Approval:** September 2014
- **IRA Eligibility (13 years):** 2027
- **Price Negotiation Begins:** 2026
- **Discounted "Fair Price" (MFP) Starts:** 2028

If Selected for IRA Price Negotiation

- CMS could **cap Keytruda price** at ~$50–70K/year (vs. current list price ~$150K/year)
- Applies to **Medicare**, but may **influence private insurers**

Impact of Early Biosimilar Launch - If a biosimilar enters **before 2028**:

- **Keytruda becomes ineligible for IRA negotiation**
- **Merck avoids forced discounts**, but loses market share
- **Biosimilar competition pressures pricing across sectors**

IRA sets the stage for biosimilar competition or price regulation — but not both. Early launches shift power away from monopolies

https://www.i-mak.org/wp-content/uploads/2021/05/i-mak.keytruda.report-2021-05-06F.pdf
https://www.ajmc.com/view/cms-releases-list-of-10-drugs-subject-to-price-negotiation-under-ira?utm_source=chatgpt.com

What Europe's Experience with Adalimumab Tells Us About Pembrolizumab Biosimilars

October 18, 2018: Four adalimumab biosimilars launched simultaneously across Europe
Early discounting: ~25% below Humira
By **month 18**, discounts reached **~80%**, especially in countries with **centralized tendering** (Nordics, UK)
Countries with **centralized tenders** saw **faster, deeper price erosion**

Biosimilar **uptake was rapid**, aided by:

- Physician incentives
- Prescribing/reimbursement policies
- Competitive procurement mechanism

Implications for pembrolizumab biosimilars

- The biosimilar market dynamics have evolved significantly since the **adalimumab biosimilar launch in 2018**
- When pembrolizumab biosimilars are expected to launch in Europe, we'll likely see a more aggressive and coordinated market strategy due to:
  - Aggressive commercialization partnerships
  - Increased payer sophistication
  - No loyalty to "premium" oncology mAbs
  - Experience from past rollouts

By 2030, pembrolizumab biosimilars in Europe could cost **€20,000–€30,000 per patient per year** in public systems like the NHS and GKV

GLP-1 Therapies: From Rejection to Reconsideration — What This Means for Access

In **2023**, the WHO expert committee **did not recommend adding GLP-1 receptor agonists** for obesity, citing insufficient long-term benefit data

Weight-loss jabs at pharmacies for NHS patients (May 1st, 2025)

Why This Matters:

- GLP-1s (e.g., **semaglutide**) are now used for:
  - **Type 2 Diabetes Mellitus**
  - **Obesity management**
  - **Cardiovascular risk reduction**
- Market growth is **unprecedented**:
  - **$150 billion** projected by **2030** for injectables
  - Up to **$1 trillion globally by 2035**, including new indications (Bloomberg, Morgan Stanley, The Times)

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GLP-1 Class: Different Biologics and Small Molecule Dynamics

Peptide-based GLP-1 biologics:

- Victoza®, Saxenda® - Liraglutide injections
  - *Liraglutide's patents expired globally in 2024, and biosimilars are now entering key markets*
  - *Generic Victoza Now Available in the U.S.* 25.06.2024
  - *Biocon's biosimilar of liraglutide received approval from the UK's (MHRA) in March 2024*
- Ozempic® and Wegovy®, semaglutide injections; Rybelsus®, oral semaglutide)
  - *Whilst the core patents expire in 2026, the secondary patents are set to expire as late as 2033*
  - *China, India, Brazil: Patents will expire in 2026*
    - *Companies to launch in 2026: China: Jiuyuan Gene, Brazil: Hypera*

Small-molecule GLP-1 receptor agonists (e.g., oral semaglutide, orforglipron,…) → As of early 2025, the GLP-1 drug development pipeline includes over 150 candidates, with around 60 being small-molecule oral compounds.

- First compounds might see approval by the end of 2025

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Closing Reflections: Advancing Access through Biosimilars and Strategic Innovation

Key Considerations for the 2025 EML

- **Biosimilars** continue to offer a valuable pathway to expanding access to essential therapies
- **Targeted biosimilar development**, such as for pembrolizumab and GLP-1 receptor agonists, represents focused areas where impact may be most immediate
- **Procurement strategies** can strengthen access across health systems, including pooled purchasing and prequalification

Thank you