Why Are Biosimilars Important? Opportunities and Challenges

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What is Biosimilar?

Biosimilar medicines: variability of global definitions

EMA	A biological medicinal product that **contains a version of the active substance of an already authorized product** (reference medicinal product) in the EEA (European Economic Area)
US FDA	A biological product that is **highly similar to** a US-licensed **reference product notwithstanding minor differences in clinically inactive components**, and for which there are **no clinically meaningful differences** between the biological product and the reference product in terms of **safety, purity, and potency** of the product
WHO	A biotherapeutic product that is **similar in terms of quality, safety, and efficacy** to an already licensed reference product

EEA, European Economic Area; EMA, European Medicines Agency; FDA, US Food and Drug Administration; WHO, World Health Organization.

Source: EMA, 2015; FDA, 2015b; WHO, 2016

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Mapping of the biosimilars regulatory landscape across the globe

EEA, European Economic Area; EMA, European Medicines Agency; FDA, US Food and Drug Administration; WHO, World Health Organization.

Source: Krishnan et al., 2015; WHO, 2016

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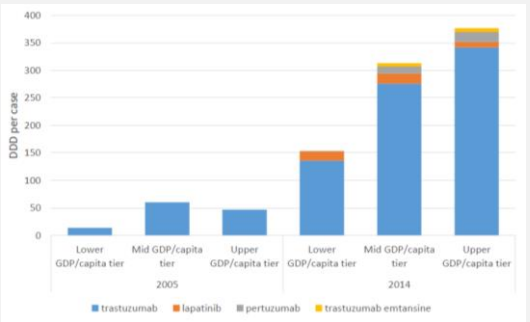
What are the main benefits that biosimilar medicines bring to the healthcare system?

Biosimilar medicines: objectives of pharmaceutical policies

- *Disinvestment aspect:* Reduce health care expenditure without compromising health outcomes → **sustainability of health care financing**
- *Investment aspect:* Increase population health gain by improved patient access without increasing health expenditure → **health improvement**

Inotai A, Csanádi M, Vitezic D, Francetic I, Tesar T, Bochenek T, Lorenzovici L, Dylst P, Kaló Z. Policy Practices to Maximise Social Benefit from Biosimilars. Journal of Bioequivalence & Bioavailability. 2017. 9. 467-472.

European uptake of HER2+ drugs indicates access restrictions in lower income countries



Source: Jönsson B, Hofmarcher T, Lindgren P, Wilking N. Comparator report on patient access to cancer medicines in Europe revisited. IHE Rep. 2016;4:228.

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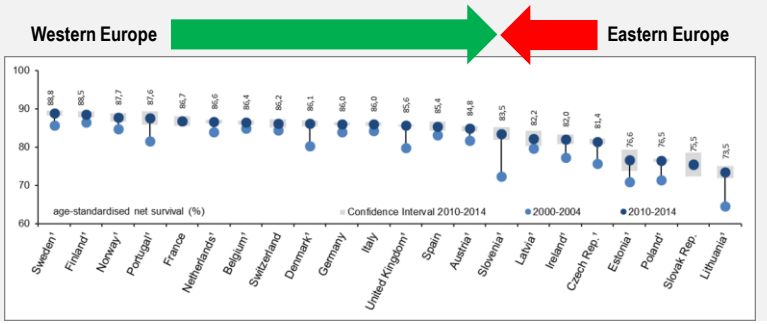
European data on breast cancer five-year net survival indicates greater unmet need for biologicals in lower income countries



Source: OECD Health Statistics 2017
http://dx.doi.org/10.1787/888933603982

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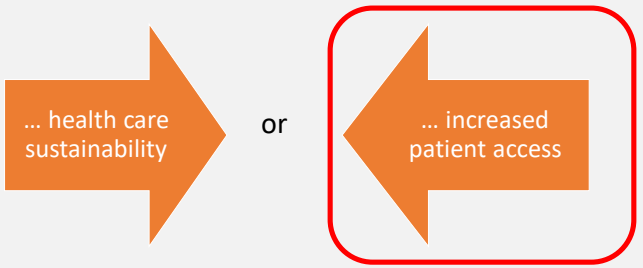
Learnings from the case study: Biosimilar medicines are game changer for …



To reduce health gap between higher and lower income countries

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Value proposition of biosimilar medicines

	Originator is reimbursed without access limits to patients	**Originator is reimbursed with access limits to patients**	**Originator is not reimbursed**
Value proposition	savings in drug budget	health gain (by increased patient access) without the need for extra budget	health gain (by creating patient access) with relatively minor increase in drug budget
Decision context	Disinvestment	Re-investment of savings	Investment

Ref: Inotai A, Csanádi M, Vitezic D, Francetic I, Tesar T, Bochenek T, Lorenzovici L, Dylst P, Kaló Z. Policy Practices to Maximise Social Benefit from Biosimilars. Journal of Bioequivalence & Bioavailability. 2017. 9. 467-472.

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What are the current challenges of biosimilar uptake in middle income countries?

I. Fear of immunogeneicity

Single switch to biosimilars: real concern or just hype based on scientific literature?

- 41 non-empirical papers stated hypothetical risk without any empirical justification (e.g. clinical trial data)
- 12 empirical papers indicated that switching to biosimilars is not accompanied by increased risk of immunogenicity, significant adverse events, loss of efficacy according to current clinical evidence

Prevention of switching to biosimilars in fear of these reasons seems to be disproportional

- Short term consequences: may harm improved patient access
- Long term consequences: may harm long term sustainability of health care (assuming increasing share of expenditure on biologic drugs)

However, hypothetical risk should not be disregarded, pharmacovigilance system should be strengthened

Ref: Inotai A, Prins C, Csanádi M, Vitezic D, Codreanu C, Kaló Z. Is there a reason for concern or is it just hype? – A systematic literature review of the clinical consequences of switching from originator biologics to biosimilars. Expert Opin Biol Ther. 2017. 17. 8. 915-926.

II. Acceptance of international scientific evidence
Why regulators in some countries still question what has been answered in other countries?

- There is no need to repeat for regulators what has already been confirmed by others (e.g. in Denmark or Norway). This is especially true for lower income countries
- It is not realistic that for a global industry, each country has to re-create its own pool of supportive evidence from scratch.
- Mutualisation of of evidence generation is essential in the European Union. However, good practice sharing or information exchange platform for EU member states is missing.
- European Public Assessment Reports (EPARs) and EPAR public summaries are a fundamental resource of information.

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III. Attempts of originators for product differentiation
Behind the subcutaneous trastuzumab hype: evaluation of benefits and their transferability based on scientific literature

- 42 articles included in the review to compare intravenous (IVT) and subcutaneous trastuzumab (SCT) forms

- Statistical test results were rarely reported; the similarity of adverse event profiles of SCT and IVT could not be validated.
- Potential time savings for patients due to subcutaneous administration was not validated in CEE settings, where patient's waiting time for treatment administration is fairly long.
- Standard patient reported outcome instruments were rarely used to confirm the preference of patients/health care professionals to SCT over IVT.
- Feasibility of self/home administration of SCT, especially in case of concomitant intravenous chemotherapies, was not considered.
- **Cost comparisons did not consider 1) either price erosion of IVT or 2) the incremental cost of potential differences in adverse events**

Ref: Inotai A, Ágh T, Karpenko AW, Zemplényi A, Kaló Z. Behind the Subcutaneous Trastuzumab Hype: Evaluation of Benefits and Their Transferability to Central Eastern European Countries. Expert Rev Pharmacoecon Outcomes Res. 2019. 19. 2. 105-113.

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What can be done by policymakers to maximize social benefit from biosimilars in middle income countries?

Investment to health by increased utilisation of biosimilars

Objective:

- Treatment naive patients: in financing protocols biosimilars are first line therapies (even before other patented originator biologicals)
- Maintenance patients: single switch to biosimilars under medical supervision

Policies to maximise societal benefit of biosimilars: European lessons

Regulatory and public administration of biosimilar medicines	Expedited price and reimbursement process to facilitate timely market entry
	Administrative tools and policy measures to incentivize use of more affordable biosimilars
	Acceptance of international data generated in other EU member states based on existing or new information exchange platform among regulators
Reimbursement and financing protocols	Multisource biologic medicines should be first line biologic therapy for all patients. More expensive patented biologic medicines with no proven significant clinical benefit compared to biosimilar medicines should be only second line options.
	Single switch of patients from original biologic medicine to more affordable biosimilar alternative under medical supervision should be mandated after patent expiry.
	No separate reimbursement categories for 1) biosimilars and 2) original biological or its modified formulation (e.g. subcutaneous vs. intravenous), unless the modified formulation has proven benefits to patients or health care payers
Patient education	Physicians should not only be informed about scientific evidence on biosimilars but also guided on how to educate appropriately their patients on these medicines.

Ref: Inotai A, Csanádi M, Petrova G, Bochenek T, Tesar T, York K, Fuksa L, Kostyuk A, Lorenzovici L, Egyed K, Kaló Z. Patient Access, Unmet Medical Need, Expected Benefits And Concerns Related To Utilisation of Biosimilars In Eastern European Countries. BioMed Research International. 2018. 9597362. 9.