Vision Health Webinar

Biosimilars in Ophthalmology: International Policies and Professional Perspectives

23 March 2021 | 12:00 - 1:00 pm EDT

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Eye See You

International Federation on Ageing

This webinar is supported by an unrestricted educational grant from Bayer Canada.

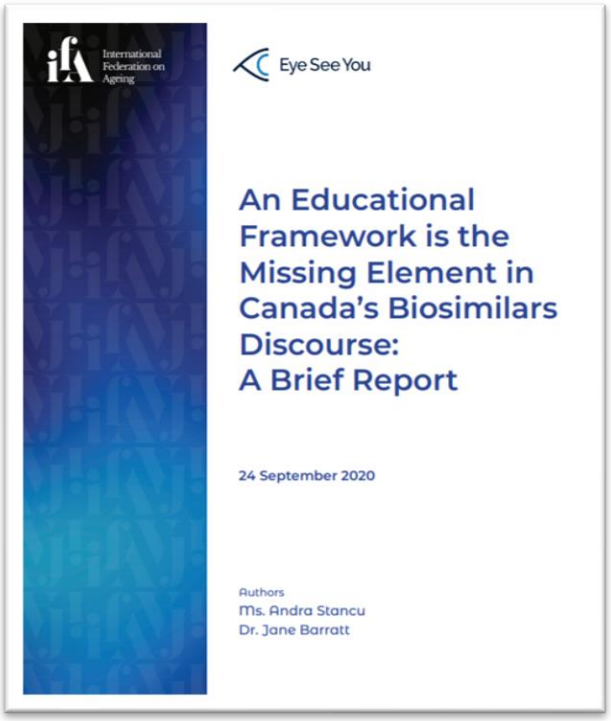
Biosimilars in Ophthalmology

Since 2016, the Eye See You program has evolved to include multiple advocacy campaigns focused around:

- Raising awareness about emerging vision-related policies;
- Facilitating timely access to educational resources regarding ophthalmic interventions;
- Connecting Canadians to experts and thought leaders in vision health;
- Creating opportunities for Canadians to engage in discourse surrounding vision health innovations.

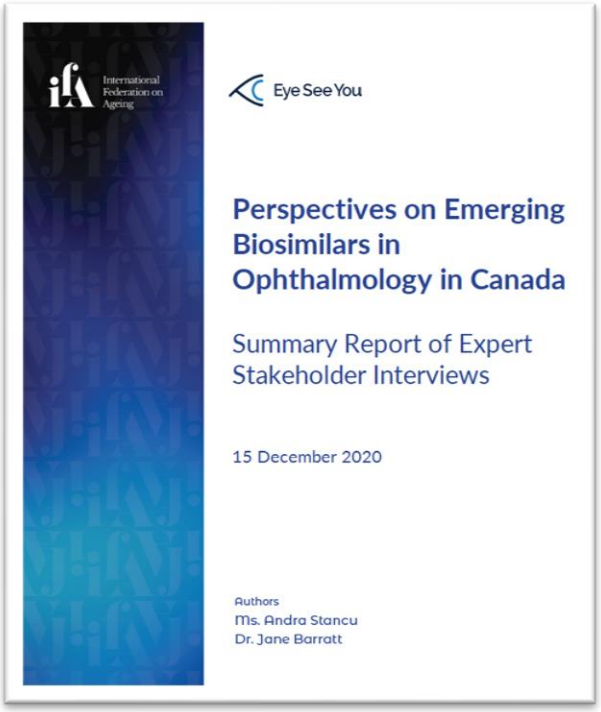
Biosimilars in ophthalmology are on Canada's horizon, however critical gaps in clinical guidelines and patient education must urgently be addressed in order to ensure emerging policies on biosimilars are founded upon person-centredness, access and safety.

Biosimilars in Ophthalmology



- Since biosimilars first entered the Canadian market in 2009, uptake has been slow in comparison to other OECD countries, with only 18 biosimilars approved to date. The Patented Medicine Prices Review Board (PMPRB) forecasts a potential $1.8 billion annual health system savings with the emergence of more biosimilars.
- While biosimilars are a relatively recent phenomenon in Canada, international experiences (in Germany, UK, Australia and Japan) provide lessons about biosimilar safety, efficacy, and implementation policies.
- Toward enabling informed consultations and decision-making between older Canadians, their caregivers and health care professionals, this report explores the urgent need to build an educational framework.

Biosimilars in Ophthalmology



Opportunities for Action:

1. Older Canadians with vision loss must be empowered to take an active role in managing their health alongside a trusted and supportive vision health team.
2. Across Canada there must be equitable access to the best quality, most appropriate and safe and effective treatments to slow or prevent blinding eye diseases.
3. Biosimilar policies must be responsive to the diverse and evolving needs of individuals across therapeutic areas to optimize health outcomes.

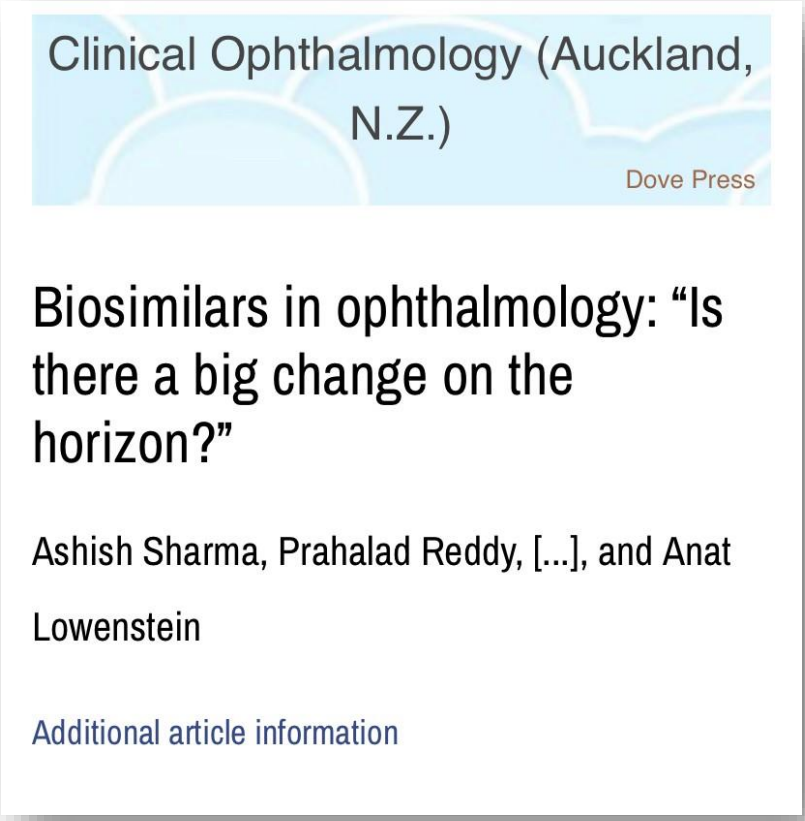
The critical perspective and guidance of vision health care providers is notably absent in the current discourse. Engagement of ophthalmologists is an important next step towards establishing clinical guidelines around the appropriate use of biosimilars in ophthalmology which may align with the WHO ICOPE and IPEC frameworks.

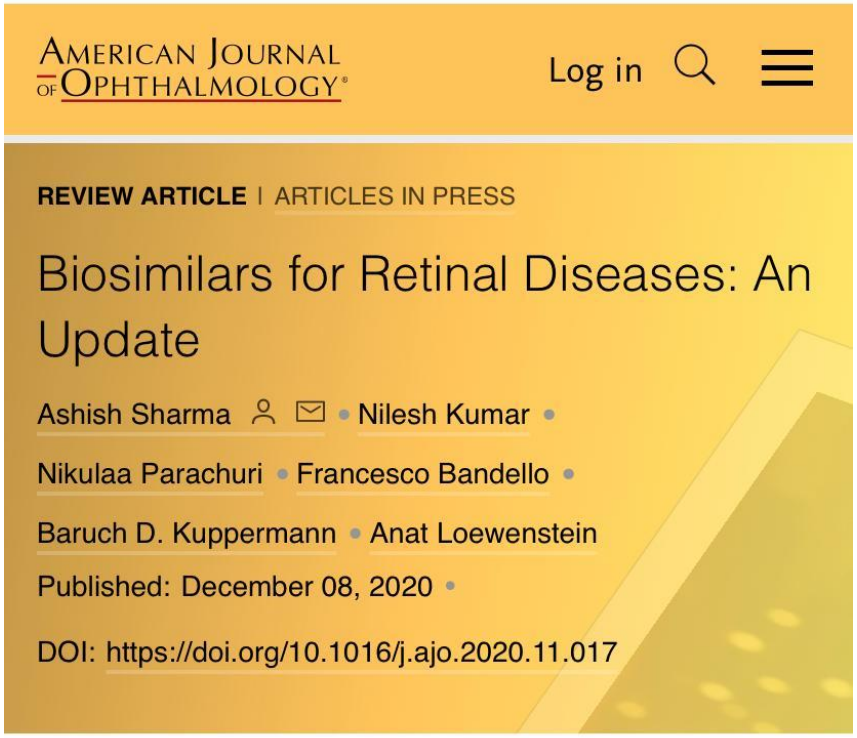
Biosimilars in Ophthalmology
International Policies and Professional Perspectives

Ashish Sharma MD

Lotus Eye Hospital and Institute, Coimbatore, TN, India

Biosimilars in Ophthalmology





Disclosures

Consultant and Speaker

- Novartis India
- Allergan Global
- Bayer India
- Intas India

Founder

- MII Ret Cam Inc

What are Biologics

The European Agency for the Evaluation of Medicinal Products (EMEA) defines biologics as '**any medicinal product containing biotechnology-derived proteins as active substance**'.

Biologics are medicines that generally come from living organisms (animals and microorganisms, such as yeast and bacteria)

Different from conventional medications (chemicals)

EMA. Guideline on similar biological medicinal products, 2005. Available: https://www. ema. europa. eu/ en/ documents/ scientific- guideline/ guideline- similar-biologicalmedicinal-products_ en. Pdf

Sharma A, Reddy P, Kuppermann BD, Bandello F, Loewenstein A. Biosimilars in ophthalmology: Is there a big change on the horizon? *OPTH*. 2018;Volume 12:2137-2143. doi:10.2147/OPTH.S180393

Examples

Biologics

Ophthalmology - Ranibizumab and Aflibercept

Conventional Medications

Ibuprofen

Biosimilars

A biosimilar is a biologic that is highly similar (**safety, purity and potency)** to, and has **no clinically meaningful differences** from, another biologic that's already approved by the FDA/EMA (known as the original biologic or reference product

Sharma A, Reddy P, Kuppermann BD, Bandello F, Loewenstein A. Biosimilars in ophthalmology: Is there a big change on the horizon? *OPTH*. 2018;Volume 12:2137-2143. doi:10.2147/OPTH.S180393

Biosimilar Vs Generic

Sharma A, Reddy P, Kuppermann BD, Bandello F, Loewenstein A. Biosimilars in ophthalmology: Is there a big change on the horizon? *OPTH*. 2018;Volume 12:2137-2143. doi:10.2147/OPTH.S180393

Why Biosimilars ?

The launch of new biosimilars over the next decade could save consumers as much as **$250 billion** and boost access to biologic treatments for an additional **1.2 million** patients by 2025.

Reference biologic - 10–15 years (1,200–2,500 million USD)

Biosimilar - 8–10 years (100–200 million USD)

Sharma A, Kumar N, Parachuri N, Bandello F, Kuppermann BD, Loewenstein A. Biosimilars for Retinal Diseases: An Update. Am J Ophthalmol. 2020 Dec 9;224:36-42.

When can Biosimilars enter a Country for its use?

Agency	Marketing Privilege of Reference Biologics
Patent of the Drug	20 years from the date of filing with additional 4 year of data privilege.
FDA	12 years of market exclusivity from the date of approval.
EMA	10 years of market exclusivity from the date of approval.
India	Biologics which are authorized in India using complete data package can be used as a Reference Biologic. In case the reference biologic is not authorized in India but is licenced and has been in wider use for more than 4 years with significant safety and efficacy data.
Korea	No guideline on marketing privilege of reference biologics.

Table 3: Market exclusivity of biosimilars under different regulatory bodies

Sharma A, Kumar N, Kuppermann BD, Bandello F, Loewenstein A. Understanding biosimilars and its regulatory aspects across the globe: an ophthalmology perspective. Br J Ophthalmol. 2020 Jan;104(1):2-7.

Biosimilars in Ophthalmology

- Reference **Ranibizumab** patent expires in 2020 (USA) and 2022 (Europe)
- Reference **Aflibercept** patent will expire in 2027 (USA &Europe).
- Both the innovator drugs aflibercept and ranibizumab come off patent in Japan and the People's Republic of China in 2022 .

GaBI Journal Editor. Patent expiry dates for biologicals: 2018 update. *GaBI J*. 2019;8(1):24-31.
Sharma A, Reddy P, Kuppermann BD, Bandello F, Loewenstein A. Biosimilars in ophthalmology: Is there a big change on the horizon? *OPTH*. 2018;Volume 12:2137-2143.
Sharma A, Kumar N, Parachuri N, Bandello F, Kuppermann BD, Loewenstein A. Biosimilars for Retinal Diseases: An Update. Am J Ophthalmol. 2020 Dec 9;224:36-42.

Upcoming Biosimilars in Ophthalmology

(Ranibizumab)

Name	Company	Stage
Razumab	Intas Pharmaceuticals Ltd, Ahmedabad, GJ, India	DGCI (2015) Approved
FYB 201	Formycon AG, Munich, and bioeq GmbH, Holzkirchen	Resubmission of BLA to USFDA (2nd half of 2020), Phase 3 completed
Xlucane	XbraneBiopharma, Sweden	Phase 3 active
SB11	Samsung Bioepis/Biogen, South Korea and USA	Phase 3 completed
Ranizurel	Reliance life sciences, India	DGCI (2020) Approved
Lupin Bosmimilar	Lupin Ltd, India	Phase 3 active
SJP-0133	Senju Pharmaceuticals, Japan	Phase 3 active
CJ-40012	CJ Healthcare, South Korea	Pre-clinical trial

Sharma A, Kumar N, Parachuri N, Bandello F, Kuppermann BD, Loewenstein A. Biosimilars for Retinal Diseases: An Update. Am J Ophthalmol. 2020 Dec 9;224:36-42.

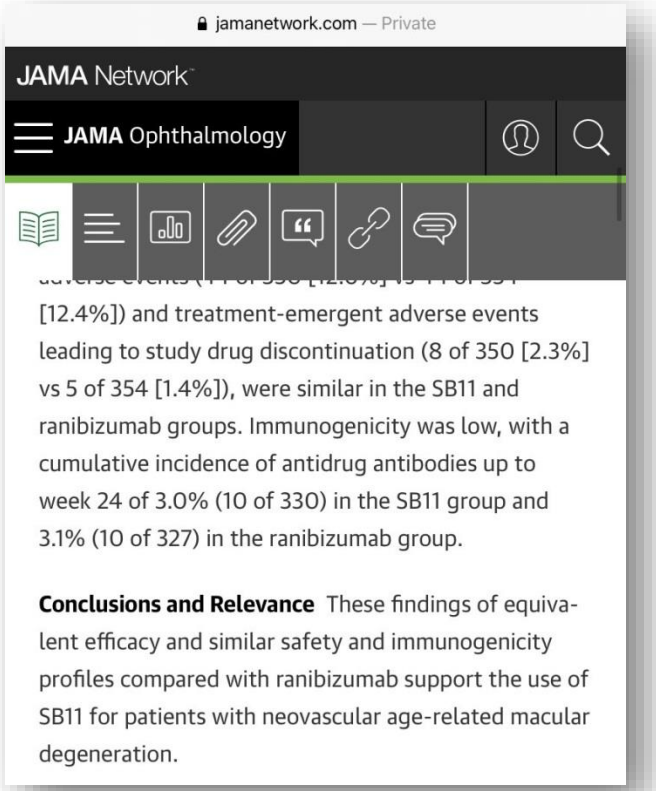
Upcoming Biosimilars in Ophthalmology

(Aflibercept)

Name	Company	Stage
M710	Momenta Pharmaceuticals and Mylan NV, Cambridge, MA.	Phase 3 active
ALT-L9	Alteogen Inc, South Korea	Phase 1 initiated
ABP-938	Amgen, USA	Phase 3 active
SB 15	Samsung Bioepis/Biogen, South Korea and USA	Phase 3 active
FYB203	Germany's Formycon	Phase 3 active
CHS-2020	CoherusBioSciences USA	Phase 3 to start in 2021

Sharma A, Kumar N, Parachuri N, Bandello F, Kuppermann BD, Loewenstein A. Biosimilars for Retinal Diseases: An Update. Am J Ophthalmol. 2020 Dec 9;224:36-42.

The Probable first Ophthalmic Biosimilar to be approved by FDA/EMA



-Woo SJ, Veith M, Hamouz J, et al. Efficacy and Safety of a Proposed Ranibizumab Biosimilar Product vs a Reference Ranibizumab Product for Patients With Neovascular Age-Related Macular Degeneration: A Randomized Clinical Trial. *JAMA Ophthalmol.* 2021;139(1):68–76. doi:10.1001/jamaophthalmol.2020.5053
-Sharma A, Kumar N, Parachuri N, Bandello F, Kuppermann BD, Loewenstein A. Biosimilars for Retinal Diseases: An Update. Am J Ophthalmol. 2020 Dec 9;224:36-42.

Approval pathway

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

2005

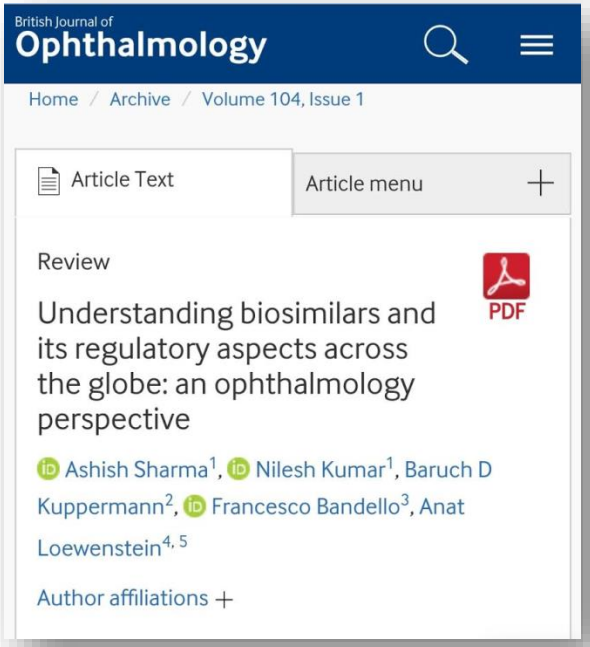
DEPARTMENT OF HEALTH & HUMAN SERVICES • USA
FDA

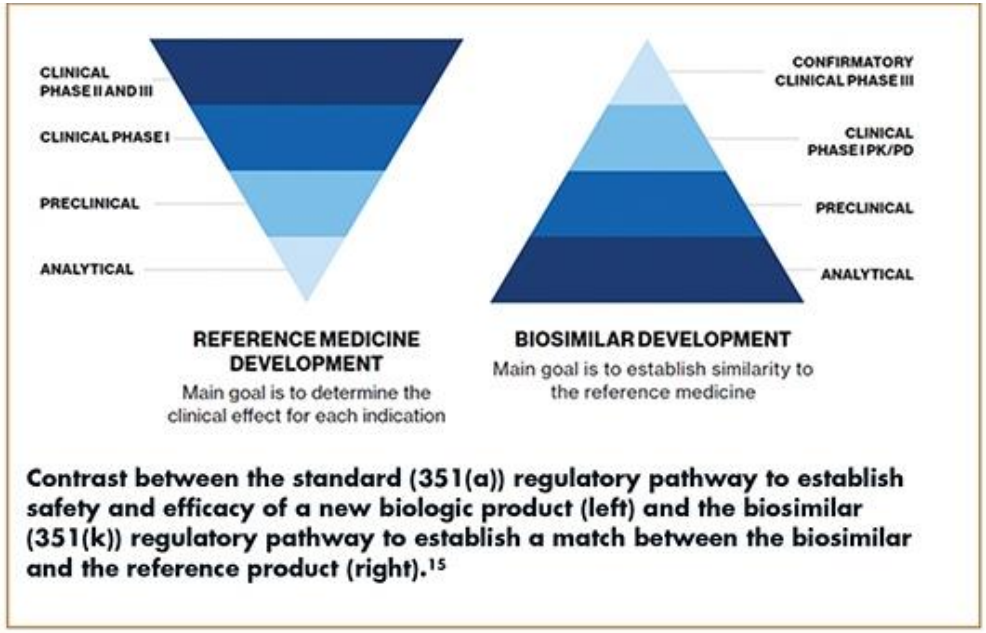
2015

Drugs Controller General of India

2012

Key differences between approval pathways for innovator biologics and biosimilars





Contrast between the standard (351(a)) regulatory pathway to establish safety and efficacy of a new biologic product (left) and the biosimilar (351(k)) regulatory pathway to establish a match between the biosimilar and the reference product (right).[15]

Pharmacovigilance

Similar to any other medicine

Common Discussion Points

Nomenclature of biosimilars

WHO came up with a unique ‘Biological Qualifier’ scheme. But consensus has not been achieved by the key marketing authorities for adopting a nomenclature.

While FDA has approved a random four-letter suffix scheme,

EMA does not feel a necessity for the suffix to be

Extrapolation of indications

- Approval for **one indication** leads to approval for all the other indications for which reference biologic is used (eg- AMD approval leads to approval for RVO, DME)
- Avoid repetition of unnecessary trial for other indications
- **Extrapolation** needs to be **supported by all the scientific evidences** generated in comparability studies (quality, non-clinical and clinical).

Interchangeability

EMA

EMA does not regulate **interchangeability, switching and substitution** of a reference medicine by its biosimilar. These fall within the remit of EU Member States.

FDA

An interchangeable product is a biosimilar that meets additional requirements outlined by the law that allows for the FDA to approve biosimilar and interchangeable medications.
There are currently no FDA-approved interchangeable medications.

India

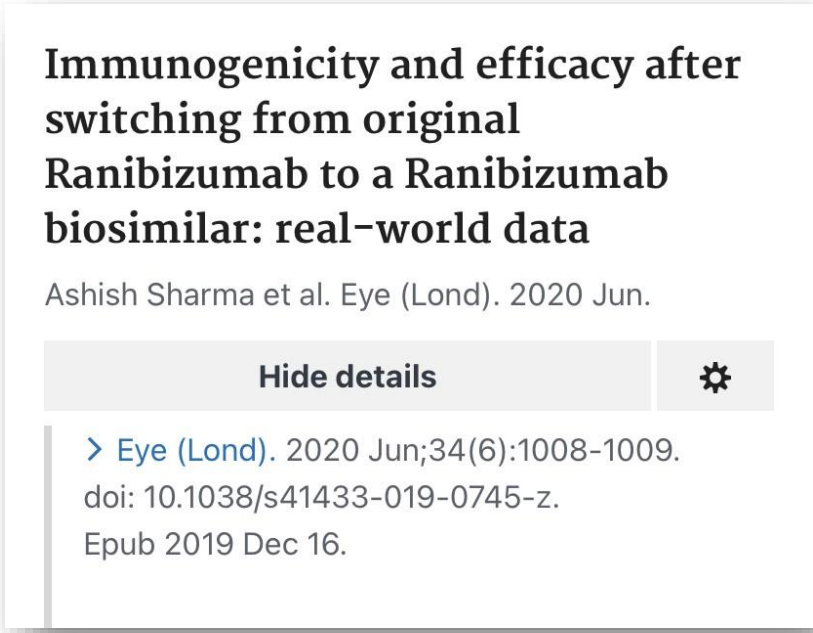
No formal guidelines
Physician decides after discussion with patients

Switching

Switching is safe

-Switching from reference drug to biosimilar
-Switching from biosimilar to reference drug
-Switching from one biosimilar to another based on the same reference drug

Further clinical studies to confirm safety of switching are considered unnecessary

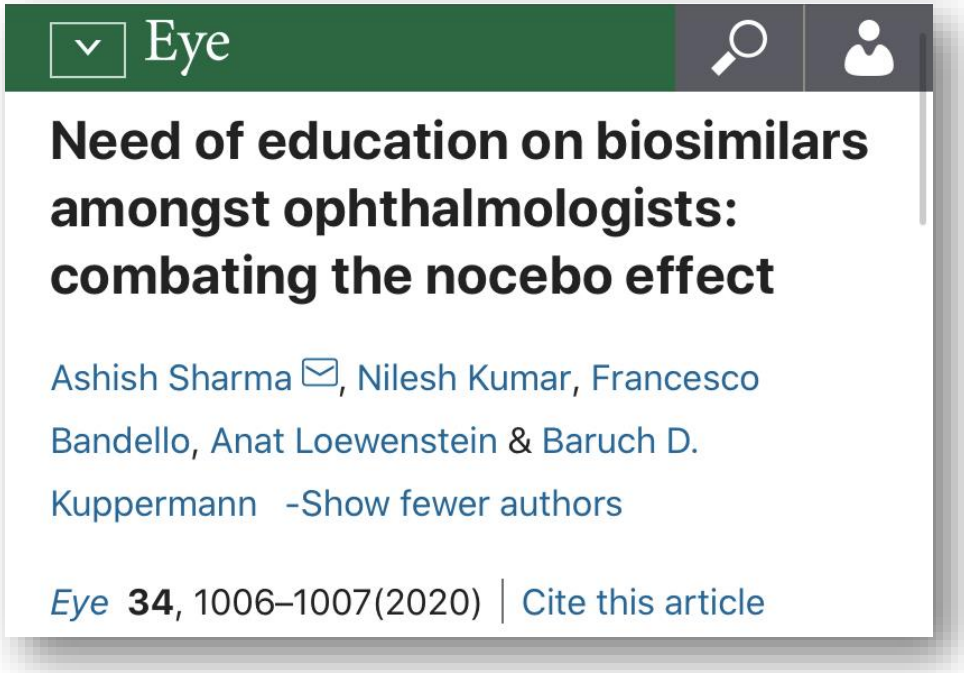


Common queries of Patients and Physicians

Common queries of physicians

- Why is the clinical trial is so short and with fewer patients (Physicians)
- Is it the same drug (Patients)
- Is it safe (Patients and Physicians)
- Will it be as effective as the Reference Drug (Patients and Physicians)

Nocebo Effect



Eye

Need of education on biosimilars amongst ophthalmologists: combating the nocebo effect

Ashish Sharma, Nilesh Kumar, Francesco Bandello, Anat Loewenstein & Baruch D. Kuppermann -Show fewer authors

Eye **34**, 1006–1007(2020) | Cite this article

Testament from EU

Over the last 10 years, the EU monitoring system for safety concerns has **not identified any relevant difference in the nature, severity or frequency of adverse effects** between biosimilars and their reference medicines.

Impact of off label Bevacizumab

The major differentiator of Biosimilar success in developing and developed world

Bevacizumab- 50-100 USD/ Inj (Aliquots with Good Compounding Pharmacy)

Ranibizumab- 2000 USD/ Inj (Single Dose Vial)

Experience from India

Journal List > Indian J Ophthalmol > v.67(8); 2019 Aug > PMC6677055

Indian Journal of Ophthalmology

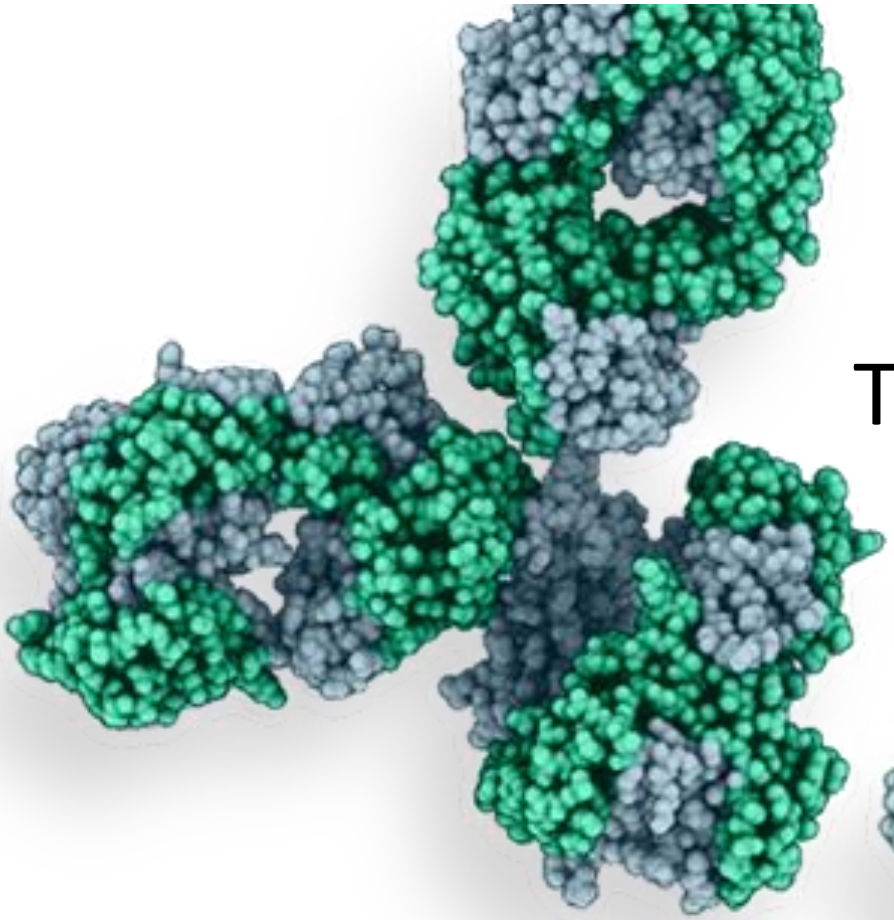
Home | Current Issue | Instructions | Submit Articles

Indian J Ophthalmol. 2019 Aug; 67(8): 1384–1385.
doi: 10.4103/ijo.IJO_430_19
PMCID: PMC6677055
PMID: 31332154

Ophthalmic biosimilars: Lessons from India

Ashish Sharma, Nilesh Kumar, Baruch D Kuppermann,[1] Bandello Francesco,[2] and Anat Lowenstein[3]

Strict Pharmacovigilance is the Key in terms of Immunogenicity



Thank you

Biosimilars in Ophthalmology: International Policies and Professional Perspectives

R. Geoff Williams, **MD FRCSC DipI ABO**
Clinical Associate Professor, University of
[illegible]y

DISCLOSURES

INVESTIGATOR

- NOVARTIS
- BAYER
- ALLERGAN
- REGENERON
- ABBOTT LABS
- ROCHE

ADVISORY BOARDS

- NOVARTIS
- BAYER
- ALCON
- VALEANT
- ALLERGAN

FINANCIAL

- MD COLLABORATE
- ARTIC DX

OBJECTIVES

- Regulatory Approval - International
- Regulatory Issues Canada
- Safety, Efficacy of Ophthalmic Biologics/Biosimilars
- Patient/Doctor/Payor Perspectives
- Future Access

Why Biosimilars?

- Similar efficacy with less cost.
- Original biologics can take 10-15 years to develop and cost 1.2-2.5B USD to develop
- Biosimilars can take 8-10 years or less and cost much less to develop 100-200 M USD
- Only one clinical study is required to compare to the biologic original to demonstrate equivalence and the biosimilar does not have to replicate the results in each indication (AMD DME RVO etc)

- Biosimilars are not as easy to produce as generic drugs are to their original drugs.
- Biosimilar makers must reverse engineer processes and therefore might come up with a different solution that may be less or possibly more effective.
- They might also be less or more safe from a immunogenicity (inflammation) perspective as well

Biosimilar Approval Process

- Europe 2005
- Japan and Korea 2009
- Canada 2010
- US and India 2012
- Global (WHO) 2009

- Razumab® (Intas Pharmaceuticals Ltd., Ahmedabad, India) was the first biosimilar to be approved worldwide starting in India
- It was approved in 2015 on the basis of a Phase 3 clinical trial involving 104 patients
- Contrast this to the studies requiring 2 separate clinical trials totaling 1200-2400 patients in registration trials for new biologics

Biosimilars in ophthalmology: "Is there a big change on the horizon?"

Clinical Ophthalmology 2018:12 2137–2143

Ashish Sharma[1]
Prahalad Reddy[1]
Baruch D Kuppermann[2]
Francesco Bandello[3]
Anat Lowenstein[4]

[1]Department of Vitreoretina, Lotus Eye Hospital and Institute, Coimbatore, Tamil Nadu, India; [2]Department of Ophthalmology, Gavin Herbert Eye Institute, University of California, Irvine, CA, USA; [3]Department of Ophthalmology, Scientific Institute San Raffaele, University Vita-Salute, Milan, Italy; [4]Division of Ophthalmology, Tel Aviv Sourasky Medical Center, Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel

Last updated: March 2015

1. Bennett CL, et al. *Lancet*. 2014;15:e594-e605. **2.** GaBI Online. Biosimilars approved in South Korea. http://www.gabionline.net/Biosimilars/ General/Biosimilars-approved-in-South-Korea. Accessed February 16, 2015. **3.** European Medicines Agency. Remsima. http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/medicines/002576/human_med_001682.jsp&mid=WC0b01ac058001d124. Accessed February 16, 2015. **4.** Health Canada. Remsima Summary Basis of Decision. http://www.hc-sc.gc.ca/dhp-mps/prodpharma/sbd-smd/drug-med/ sbd_smd_2014_remsima_160195-eng.php. Accessed February 16, 2015. **5.** GaBI Online. Biosimilar infliximab receives approval in Japan and Turkey. http://www.gabionline.net/Biosimilars/News/Biosimilar-infliximab-receives-approval-in-Japan-and-Turkey. Accessed February 16, 2015. **6.** Ropes & Gray. China announces final biosimilars guideline. http://www.ropesgray.com/news-and-insights/Insights/2015/March/China-Announces-Final-Biosimilars-Guideline.aspx. Accessed March 11, 2015.
Figure adapted from Scheinberg MA, Kay J. *Nat Rev Rheumatol*. 2012;8:430-436.

Editorial

From Biologics to Biosimilars and Biobetters – Democratization of High-end Therapeutics

Santosh G Honavar

Editor, Indian Journal of Ophthalmology,

- India was the first to approve a biosimilar in ophthalmology - **Razumab** (Intas Pharmaceuticals, Ahmedabad, India), the world's first biosimilar to ranibizumab in **2015**
- Other biosimilars are in various phases of development.

Table 1: Biosimilars relevant to ophthalmology approved in India

Innovator	Biosimilar (examples)	Indications
Bevacizumab	BevaciRel, Bevatas, Cizumab, Krabeva, Zybe	Anti-vascular endothelial growth factor
Ranibizumab	Rabumab	Anti-vascular endothelial growth factor
Adalimumab	Adfrar, Exemptia	Non-infectious uveitis
Infliximab	Infimab	Non-infectious uveitis
Tissue plasminogen activator	MiRel	Hyphema, vitreous hemorrhage, submacular hemorrhage, congenital cataract surgery etc
Rituximab	Acellbia, Maball, MabTas, Reditux, RituxiRel	Orbital inflammation, thyroid eye disease, lymphoma etc
Interferon alpha-2b	Intalfa, Reliferon, Shanferon, Zavinex	Ocular surface squamous neoplasia
Darbepoietin alpha, Epoietin alpha, Erythropoietin	Actorise, Cresp, Darbatitor, Ceriton, Epofer, Epofit, Erykine, Epotin, Erypro, Wepox, Relipoietin, Shanpoietin, Eporec, Repoitin, Zyrop	Neuroprotection
Streptokinase	Myokinase, Shankinase	Fibrin exudate, central retinal vein occlusion
Filgrastim, Peg-filgrastim	Emgrast, Fegrast, Grafeel, Neukine, Nufil, Religrast Neupeg, Pegex, Peg-grafeel	Chemotherapy-related neutropenia in ocular malignancies such as retinoblastoma

Regulatory challenges with biosimilars: an update from 20 countries

Hye-Na Kang,[1] Robin Thorpe,[2] Ivana Knezevic,[1] Mary Casas Levano,[3] Mumbi Bernice Chilufya,[4] Parichard Chirachanakul,[5] Hui Ming Chua,[6] Dina Dalili,[7] Freddie Foo,[8] Kai Gao,[9] Suna Habahbeh,[10] Hugo Hamel,[11] Gi Hyun Kim,[12] Violeta Perez Rodriguez,[13] Desi Eka Putri,[14] Jacqueline Rodgers,[15] Maria Savkina,[16] Oleh Semeniuk,[17] Shraddha Srivastava,[18] João Tavares Neto,[19] Meenu Wadhwa,[20] and Teruhide Yamaguchi[21]

Table 4. Regulatory collaboration used for biosimilar approval

Countries	Reliance: countries where the NRA approval is to be recognized	Joint review
Canada	None	• Feasibility is under discussion among the ACSS (Australia, Canada, Singapore, Switzerland) Consortium
Ghana	EU and the United States	• Economic Community of West African States (ECOWAS)[a] • WHO Collaborative Registration Procedure (CRP) and WHO Prequalification (PQ)
India[b]	Australia, Brazil, Canada, the EU, Japan, UK, and the United States	No
Iran	EU and the United States	No
Jordan[c]	Experienced regulatory authorities (e.g., the EU and the United States)	No
Malaysia	EU and the United States	No
Peru	Canada, the EU, ICH, PANDRH, the United States, and the WHO	No
Singapore	None	Feasibility is under discussion among the ACSS (Australia, Canada, Singapore, Switzerland) Consortium
Zambia	EU, the United States, and the WHO (SRA PQ procedure)	• ZAZIBONA collaborative procedure[d] • WHO PQ • Article 58 of Regulation (EC)[e]

[a] Member states of ECOWAS: Benin, Burkina Faso, Cabo Verde, Cote D'ivoire, the Gambia, Ghana, Guinea, Guinea Bissau, Liberia, Mali, Niger, Nigeria, Senegal, Sierra Leone, and Togo.
[b] In case of orphan drug.
[c] Fast-track procedure.
[d] NRAs from participating countries, namely, South Africa, Zimbabwe, Namibia, Botswana, and so on, have jointly reviewed dossiers with the Zambian NRA (Zambia Medicines Regulatory Authority).
[e] For certain products, assessment by EMA would help if Zambia Agency is cohort in the reviews under article 58 procedure.
ICH, International Council for Harmonization; PANDRH, Pan American Network for Drug Regulatory Harmonization.

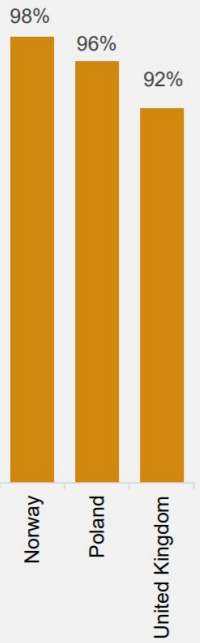
Table 8. Approach for interchangeability of biosimilars in each country participating in the survey

Countries	Automatically upon approval of the biosimilar	Depending on the clinical evidence provided by the biosimilar manufacturer	Relying on the decision made by prescribers
Canada			Yes
China			Yes
Egypt			Yes
EU			Yes
India			Yes
Indonesia			Yes
Jordan			Yes
Malaysia			Yes
Republic of Korea			Yes
Singapore			Yes
Thailand			Yes
Brazil		Yes	Yes
Ghana		Yes	Yes
Zambia		Yes	Yes
Cuba		Yes	
Peru		Yes	
Russia		Yes	
Iran	Yes		
Japan	Yes		

doi: 10.1111/nyas.14522
Ann. N.Y. Acad. Sci. xxxx (2020) 1–18

International success in biosimilar uptake is driven by high-impact policies and initiatives

The uptake of infliximab biosimilars in Norway, Poland, and the United Kingdom exceeded 90% in 2018, well above the OECD median.



Data source: IQVIA MIDAS® Database, prescription retail and hospital markets, Q4-2018. All rights reserved.

FIGURE 4.2 Select European biosimilar policies and initiatives for infliximab, Norway, Poland, and the United Kingdom, 2018

Norway	**National single-winner tender –** Physicians are required to prescribe the cheapest medicine (hospital use and some outpatient use products). **Switching –** This is allowed and common in practice. **Physician education –** The **NOR-SWITCH** study demonstrated that the infliximab biosimilar Remsima was not inferior to Remicade.
Poland	**Substitution** – Biosimilar substitution is allowed. **Tendering** – Patients are required to use the tender winning medicine. **Initiation –** Therapy-naïve patients with IBD should be initiated on the biosimilar. **Switching –** The Ministry of Health "takes the view that any exchange within the scope of drugs containing infliximab at any level of therapy is permissible."*
United Kingdom	**Initiation** – The treatment should be initiated with the cheapest available biologic medicine. **Switching** – Pilot switching programmes from Remicade to biosimilars of infliximab were found to be highly acceptable to patients and clinicians. **Guidance –** The National Health Service in England recommended that 9 out of 10 new patients should be initiated on the best value medicine within 3 months of a biosimilar launch, and at least 80% of existing patients should be switched to the best value biologic within 12 months.

* Medicines for Europe, Biosimilar Medicines Sector Group. 2019. *Positioning statements on physician-led switching for biosimilar medicines*. Brussels, Belgium.

Data source: International Policies on the Appropriate Use of Biosimilar Drugs, CADTH. Additional references were consulted for polices in Poland and the UK, see the Endnotes.

RESEARCH ARTICLE

Policies for biosimilar uptake in Europe: An overview

Evelien Moorkens[1]*, Arnold G. Vulto[2], Isabelle Huys[1], Pieter Dylst[1,3], Brian Godman[4,5], Simon Keuerleber[6], Barbara Claus[7], Maria Dimitrova[8], Guenka Petrova[8], Ljiljana Sović-Brkičić[9], Juraj Slabý[10], Robin Šebesta[11], Ott Laius[12,13], Allan Karr[14], Morgane Beck[15], Jaana E. Martikainen[16], Gisbert W. Selke[17], Susan Spillane[18,19], Laura McCullagh[18,19], Gianluca Trifirò[20], Patricia Vella Bonanno[21], Asbjørn Mack[22], Antra Fogele[23], Anita Viksna[23], Magdalena Władysiuk[24], Helder Mota-Filipe[25], Dmitry Meshkov[26], Marija Kalaba[27], Simona Mencej Bedrač[28], Jurij Fürst[29], Corrine Zara[30], Peter Skiöld[31], Einar Magnússon[32], Steven Simoens[1]

Conclusions

Most countries have put in place specific supply-side policies for promoting access to biosimilars. To supplement these measures, we propose that investments should be made to clearly communicate on biosimilars and educate stakeholders. Especially physicians need to be informed on the entry and use of biosimilars in order to create trust. When physicians are well-informed on the treatment options, further incentives should be offered to prescribe biosimilars. Gainsharing can be used as an incentive to prescribe, dispense or use biosimilars. This approach, in combination with binding quota, may support a sustainable biosimilar market.

PLOS ONE | https://doi.org/10.1371/journal.pone.0190147 December 28, 2017

Country	Biosimilar pricing in ambulatory care	Internal reference pricing	Incentives to prescribe	Substitution
Austria	First biosimilar: -38% on reference product. Second biosimilar: -15% on first biosimilar. Third biosimilar: -10% on second biosimilar. The reference product has to lower its price by 30% three months after the first biosimilar's entry into reimbursement. After the third biosimilar has entered into reimbursement, the reference product has to match the price of the cheapest available biosimilar in the Code of Reimbursement. All subsequent entries need to offer a rebate of €0.10 on the cheapest alternative. The requested percentage discount for entry into reimbursement of the first biosimilar of a given reference product was decreased in March 2017 making it easier for biosimilars to be included in the Code of Reimbursement, while the mandatory discounts for generic follower medicines were slightly increased. Before that legal reform, both groups of follower medicines had been treated equally.	Yes	Yes	No
Belgium	The price of the biosimilar is negotiated on a case per case base, where the maximum price in order to be reimbursed may not exceed the price of the reference product (class 2 reimbursement). Obligatory price reduction for the reference product when the biosimilar enters the market.	No	Yes	No
Bulgaria	The manufacturers' price of the biosimilar cannot be higher than the lowest price of the same medicine in the reference countries for Bulgaria: Romania, France, Latvia, Greece, Slovak republic, Lithuania, Portugal, Italy, Slovenia, Spain, Belgium, Czech republic, Poland, Hungary, Denmark, Finland, Estonia. Then a regressive margins scale at 3 levels exists and ceiling retail price is calculated and published officially.	Yes	No	No

Moorkens E, Vulto AG, Huys I, Dylst P, Godman B, et al. (2017) Policies for biosimilar uptake in Europe: An overview. PLOS ONE 12(12): e0190147. https://doi.org/10.1371/journal.pone.0190147
https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0190147

Country	Biosimilar pricing in ambulatory care	Internal reference pricing	Incentives to prescribe	Substitution
England (UK)	Regulated market, but free pricing by the company. Pharmaceutical price regulation scheme (PPRS): a government negotiated process for branded medicines (4–5 years) with The Association of the British Pharmaceutical Industry (ABPI). The latest PPRS negotiations have volume based pricing scheme. If total amount (£) of medicines sold is above the threshold then the government gets a rebate. Biosimilars go predominantly via hospitals, therefore primary care price or the NHS National tariff is less relevant.	No	Yes	No
France	Prices are fixed upon negotiation between pharmaceutical companies and the Economic Committee for Medicinal Products (CEPS), typically 10–20% below the price of the reference product, taking into account a range of factors including the drug's improvement in medical benefit (ASMR) rating versus therapeutic equivalents (Biosimilars are given an ASMR rating of V), the price of the drug in the rest of Europe, and sales volume forecasts.	Yes	Yes	Yes

Incentives Yes 7/15

Substitution Yes 3.5/15

REVIEW

Biosimilars for Retinal Diseases: An Update

ASHISH SHARMA, NILESH KUMAR, NIKULAA PARACHURI, FRANCESCO BANDELLO, BARUCH D. KUPPERMANN, AND ANAT LOEWENSTEIN

Am J Ophthalmol 2021;224:36–42.

- Razumab (Intas Pharmaceuticals Ltd, Ahmedabad, GJ, India)

TABLE 1. Biosimilars of Innovator Ranibizumab (Lucentis)

Product Name	Company	Stage of Development
India		
Razumab[8]	Intas Pharmaceuticals Ltd	DCGI (2015) approved
R TPR 024[9]	Reliance Life Sciences Pvt Ltd	Phase 3 completed
Lupin's ranibizumab[10]	Lupin Ltd	Phase 3 active
Europe		
FYB201[11]	Formycon AG//Bioeq, Germany	Resubmission of BLA to US FDA (second half of 2020), phase 3 completed
Xlucane[12]	Xbrane Biopharma, Sweden	Phase 3 active
South Korea		
SB11[13]	Samsung Bioepsis Co Ltd	Phase 3 active
Japan		
SJP-0133[14]	Senju Pharmaceuticals, Japan	Phase 3 active

BLA = biologics license application; DCGI = Drug Controller General of India; US FDA = United States Food and Drug Administration.

- Biosimilars of Aflibercept (Eylea) coming

TABLE 2. Biosimilars of Innovator Aflibercept (Eylea)

Product Name	Company	Stage of Development
USA		
MYL-1701P/M710[15]	Mylan Inc/Momenta Pharmaceuticals, Inc	Phase 3 active
ABP-938[16]	Amgen	Phase 3 active
CHS-2020[17]	Coherus BioSciences	Phase 3 to start in 2021
Europe		
FYB203[18]	Formycon AG/Bioeq, Germany	Phase 3 active
South Korea		
SB15[19]	Samsung Bioepsis Co Ltd	Phase 3 active

OBJECTIVES

- Regulatory Issues International
- **Regulatory Issues Canada**
- Safety, Efficacy of Ophthalmic Biologics/Biosimilars
- Patient/Doctor/Payor Perspectives
- Future Access

Patents and the USMCA (NAFTA 2.0)

- On December 10, 2019, Canada, the United States and Mexico signed the Protocol of Amendment to the Agreement between the United States of America, the United Mexican States and Canada, commonly referred to as the USMCA.
- The USMCA specifies that a Party shall provide adjustment of the term of a patent to compensate for Patent Office delays in issuing patents. Patent term adjustment may accrue if a patent issues more than five years from the date the application is filed, or three years after examination is requested, whichever is later.
- The United States has had such provisions in its patent laws for some 20 years, but patent term adjustment to compensate for Patent Office delay will be entirely new to Canadian patent law.
- Canada must implement its obligations under this provision within 4.5 years of the date the USMCA enters into force.
- Bill C-4 was introduced in the Canadian Parliament on January 29, 2020, a necessary step towards ratification of the USMCA.

Biosimilars Approved in Canada

Biosimilars approved by Health Canada

Thus far in 2020, Health Canada has approved seven biosimilars of six innovator products. This brings the total Health Canada approvals to 25 biosimilars of 12 innovator products. Below is a complete list:

	Biosimilar	Manufacturer and year of approval	Review time (from filing to the earlier of approval and IP hold, where available)	Medicinal ingredient	Marketed?
1	OMNITROPE	Sandoz, 2009	748 days	somatropin	yes
2, 3	REMSIMA/INFLECTRA	Celltrion, Hospira 2014	427 days	infliximab	yes (INFLECTRA)
4	BASAGLAR	Eli Lilly, 2015	356 days	insulin glargine	yes
5	GRASTOFIL	Apotex, 2015	1039 days[4]	filgrastim	yes
6	BRENZYS	Samsung Bioepis, 2016	358 days	etanercept	yes
7	ERELZI	Sandoz, 2017	353 days	etanercept	yes
8	ADMELOG	Sanofi-aventis, 2017	351 days	insulin lispro	yes
9	RENFLEXIS	Samsung Bioepis, 2017	793 days	infliximab	yes
10	HADLIMA, HADLIMA PUSHTOUCH	Samsung Bioepis, 2018	432 days	adalimumab	no
11	LAPELGA	Apotex, 2018	349 days	pegfilgrastim	yes
12	MVASI	Amgen, 2018	358 days	bevacizumab	yes
13	FULPHILA	Mylan, 2018	754 days	pegfilgrastim	yes
14	TRUXIMA	Celltrion, 2019	335 days	rituximab	yes
15	OGIVRI	BGP Pharma, 2019	356 days	trastuzumab	yes
16	ZIRABEV	Pfizer, 2019	336 days	bevacizumab	yes
17	TRAZIMERA	Pfizer, 2019	348 days	trastuzumab	yes
18	HERZUMA	Celltrion, 2019	324 days	trastuzumab	yes
19	OSNUVO	Avir Pharma, January 2020	637 days	teriparatide	no
20	KANJINTI	Amgen, February 2020	920 days	trastuzumab	yes
21	AVSOLA	Amgen, March 2020	351 days	infliximab	yes
22	NIVESTYM	Pfizer, April 2020	345 days	filgrastim	yes
23	ZIEXTENZO	Sandoz, April 2020	336 days	pegfilgrastim	yes
24	RIXIMYO	Sandoz, April 2020	795 days	rituximab	yes
25	RUXIENCE	Pfizer, May 2020	344 days	rituximab	yes

According to Health Canada's annual report, revised September 1*, Health Canada approved eight biosimilar submissions in the 2019/2020 fiscal year, which runs from April 1, 2019 to March 31, 2020, and 11 in the fiscal year prior to that. Some of these are likely on IP hold.

Regulatory

On December 10, 2019, Canada, the United States and Mexico signed the Protocol of Amendment to the Agreement between the United States of America, the United Mexican States and Canada (commonly referred to as the USMCA) (see our article here). While the original USMCA, signed in 2018, required a Party to provide a data protection term for biologics of at least ten years from the date of first marketing approval, the final USMCA does not include this requirement. Current Canadian data protection law provides an eight-year data protection term (with a possible six-month paediatric extension) for both biologics and small molecule drugs.

12	MVASI	Amgen, 2018	358 days	bevacizumab

16	ZIRABEV	Pfizer, 2019	336 days	bevacizumab

CHARTBOOK
National Prescription Drug Utilization Information System
NPDUIS

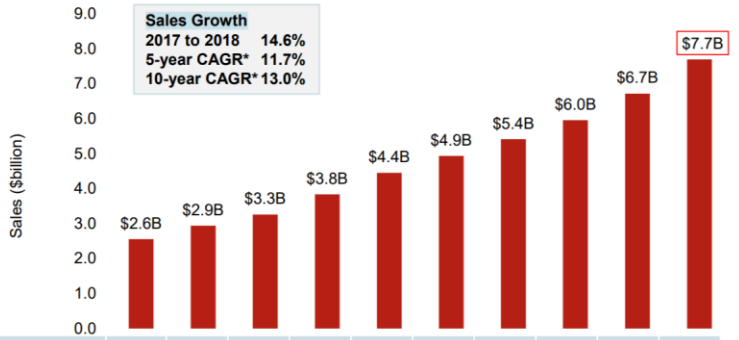
Patented Medicine Prices Review Board

Conseil d'examen du prix des médicaments brevetés

Canada

- Biol[illegible] gro[illegible] pharmaceutical market. Sales of biologic medicines in Canada have tripled over the last decade, increasing by 14.6% in the last year
- The first biosimilar was introduced in Canada in 2009. By 2018, a total of nine biologic medicines had one or more biosimilars approved for sale in Canada, offering the promise of lower prices and market competition. However, biosimilar sales only amounted to $146 million in 2018 or 1.9% of the $7.7 billion biologic market.

Sales of biologic medicines in Canada, 2009 to 2018



	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Biologic share of pharmaceutical sales	13.5%	15.1%	17.2%	19.9%	22.7%	24.0%	24.7%	25.9%	27.4%	30.1%
Biologic sales per capita	$76	$86	$95	$110	$127	$139	$151	$164	$183	$208
Biosimilar sales ($million)	**<$0.1**	**$0.1**	**$0.9**	**$2.0 (0.1%)**	**$3.3 (0.1%)**	**$4.3 (0.1%)**	**$5.7 (0.1%)**	**$12.5 (0.2%)**	**$60.8 (0.9%)**	**$146.3 (1.9%)**

Note: Includes all prescription biologics and insulin biologics sold in Canada as of 2018.
* CAGR, compound annual growth rate.
Data source: IQVIA MIDAS® Database, prescription retail and hospital markets, 2018.

Patented Medicine Prices Review Board

CHARTBOOK

National Prescription Drug Utilization Information System

NPDUIS

Patented Medicine Prices Review Board

Conseil d'examen du prix des médicaments brevetés

Canada

FIGURE 1.1 Biologic medicine share of total pharmaceutical sales, OECD, 2018

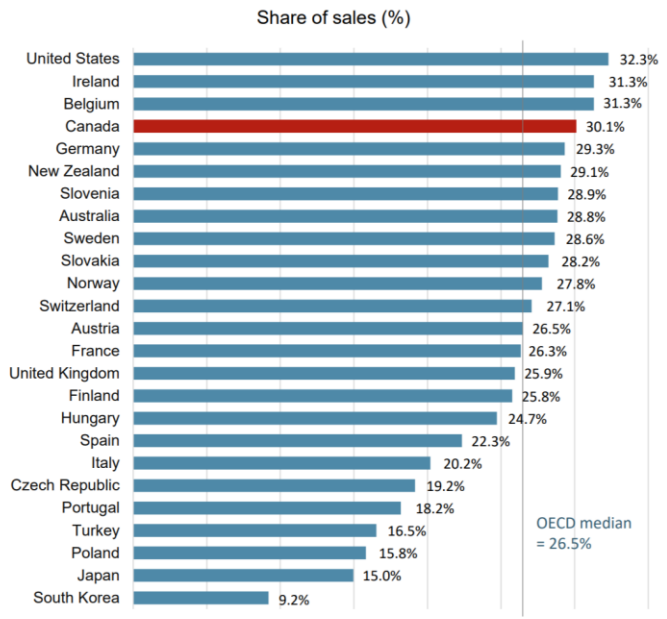
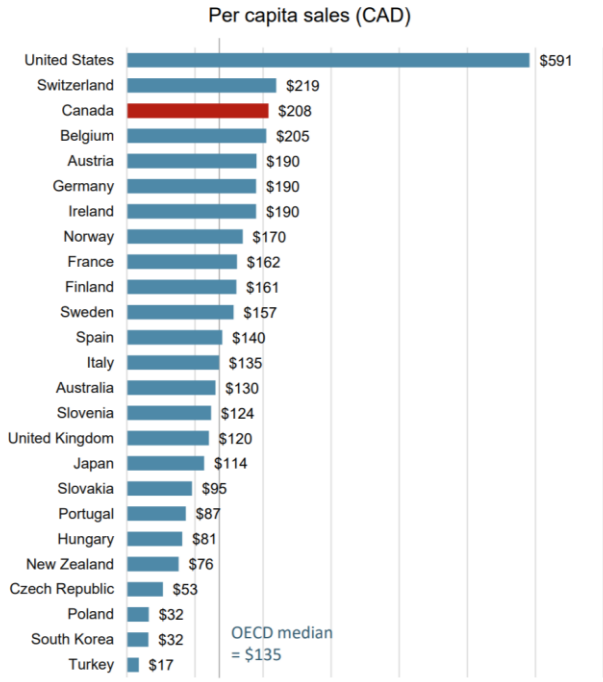


FIGURE 1.2 Per capita sales of biologic medicines, OECD, 2018



CHARTBOOK

National Prescription Drug Utilization Information System

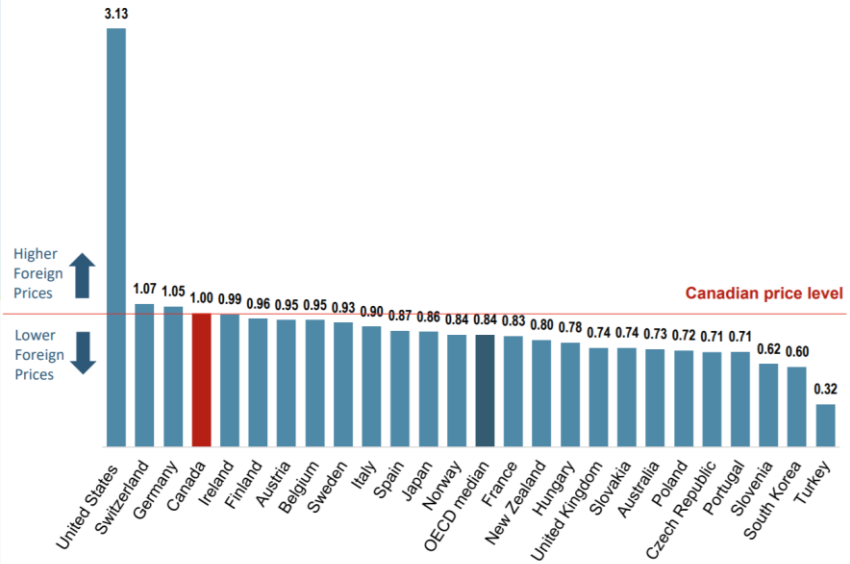
NPDUIS

Patented Medicine Prices Review Board

Conseil d'examen du prix des médicaments brevetés

Canada

FIGURE 1.3 Average bilateral foreign-to-Canadian price ratios for originator biologics, OECD, 2018



CHARTBOOK

National Prescription Drug Utilization Information System

NPDUIS

Patented Medicine Prices Review Board

Conseil d'examen du prix des médicaments brevetés

Canada

Canada lags behind Europe in the number of biosimilars approved and marketed

By the end of 2018, Health Canada had approved biosimilars for 9 of the 15 biologic medicines, and 5 of these had recorded sales in Canada. By comparison, biosimilars for all 15 medicines were approved in Europe, and there were recorded sales for all but 2.

In 2019, biosimilars for trastuzumab and rituximab were approved by Health Canada and recorded first sales. In addition, first sales were recorded for three other biosimilar medicines: bevacizumab, insulin lispro, and pegfilgrastim.

TABLE 3.1 Initial biosimilar approvals and market availability in Europe, the US, and Canada as of Q4-2018

Medicine (originator biologic)	Europe		US		Canada	
	Approval	First sales	Approval	First sales	Approval	First sales
Infliximab (Remicade)	Sept-13	Q4-2013	Apr-16	Q4-2016	Jan-14	**Q1-2015**
Adalimumab (Humira)	Mar-17	Q4-2018	Sept-16		May-18	
Etanercept (Enbrel)	Jan-16	Q1-2016	Aug-16		Aug-16	**Q4-2016**
Trastuzumab (Herceptin)	Nov-17	Q2-2018	Dec-17			
Insulin glargine (Lantus)	Sept-14	Q2-2015	Dec-15*	Q4-2016	Sept-15	**Q1-2016**
Rituximab (MabThera/Rituxan)	Feb-17	Q2-2017	Nov-18			
Filgrastim (Neupogen)	Sept-08	Q4-2008	Mar-15	Q3-2015	Dec-15	**Q2-2016**
Bevacizumab (Avastin)	Jan-18		Sept-17		Apr-18	
Epoetin alfa (Eprex/Erypo)	Aug-07	Q4-2007	May-18	Q3-2018		
Insulin lispro (Humalog)	Jul-17	Q4-2017	Dec-17*	Q1-2018	Nov-17	
Enoxaparin† (Clexane/Lovenox)	Sept-16	Q1-2017	N/A	N/A		
Pegfilgrastim (Neulasta)	Sept-18	Q4-2018	Jun-18	Q3-2018	Apr-18	
Somatropin (Genotropin)	Apr-06	Q2-2006	May-06*	Q1-2007	Apr-09	**Q3-2009**
Teriparatide (Forsteo/Forteo)	Jan-17		*			
Follitropin alfa (GONAL-f)	Sept-13	Q2-2014				
Total	**15**	**13**	**12**	**7**	**9**	**5**

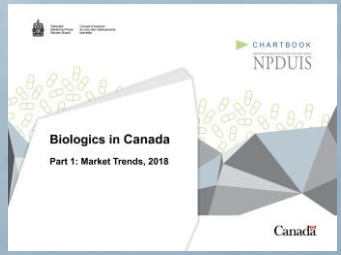
* Approved or will be approved via 505(b)(2) pathway in the United States.

† Lovenox was not approved under a Biologic License Application in the US. While generic versions of the originator medicine have been approved under the FDA's Abbreviated New Drug Application, they are not reflected in this analysis.

Data source: US Food and Drug Administration (FDA), European Medicines Agency (EMA), and Health Canada databases. IQVIA MIDAS® Database, prescription retail and hospital markets, 2018. All rights reserved.

Factors that may influence biosimilar uptake in Canada

Factor	Description
Interchangeability	**In Canada, as in most countries, biosimilars are not interchangeable with the reference biologic** ▪ The decision to prescribe a biosimilar or switch an existing patient to the biosimilar version rests primarily with the prescribing physician ▪ Not all biosimilars are approved for the same indication(s) as the originator biologic ▪ Payers can play a significant role by encouraging the use of biosimilars through preferential reimbursement policies
Payer policies	**Most Canadian public payers have implemented policies of reimbursing the biosimilar for naïve patients – with limited impact,** as nothing prevents the physician from prescribing a different brand-name medicine
Switching	**Switching from an ongoing biological treatment to an approved biosimilar has not been encouraged in Canada until recently** ▪ New initiatives include biosimilar switching policies in British Columbia and Alberta, and the biosimilar transition program offered by Green Shield
Maintaining market share	**Strategies/initiatives undertaken by the manufacturer of the originator biologic that may limit the uptake of biosimilars:** ▪ Free reference biologics reportedly offered to hospitals, where treatment is often initiated ▪ Exclusivity agreements with third-party infusion clinic networks ▪ Fees to specialists for administering the medicine ▪ Patient Support Programs: offer services like access to clinics and reimbursement navigation

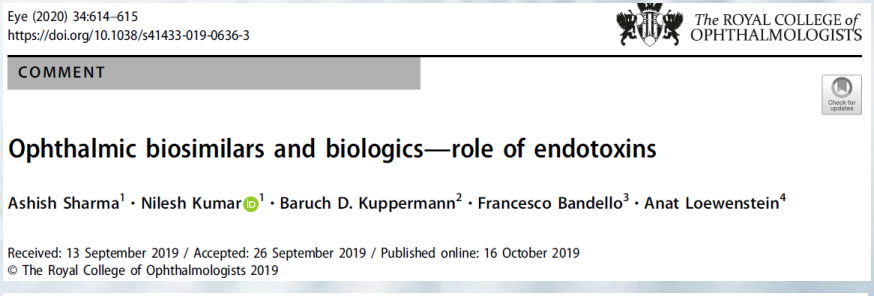


OBJECTIVES

- Regulatory Issues International
- Regulatory Issues Canada
- **Safety, Efficacy of Ophthalmic Biologics/Biosimilars**
- Patient/Doctor/Payor Perspectives
- Future Access

Safety of Biosimilars

- Endotoxin-induced uveitis (EIU) is the sterile inflammation of the uveal tissue of the eye following an exposure to lipopolysaccharides of the Gram-negative bacterial cell wall. These endotoxins are intrinsic in origin as the biologics involve cell cultures to produce the molecule
- Immunogenicity has been reported with all biologics
- Immunogenicity may be related to the molecule as well as any toxins related to the manufacturing process
- Immunogenicity is also highly individual meaning that some patients may be more prone as well as some biologics have a different immunogenicity profile

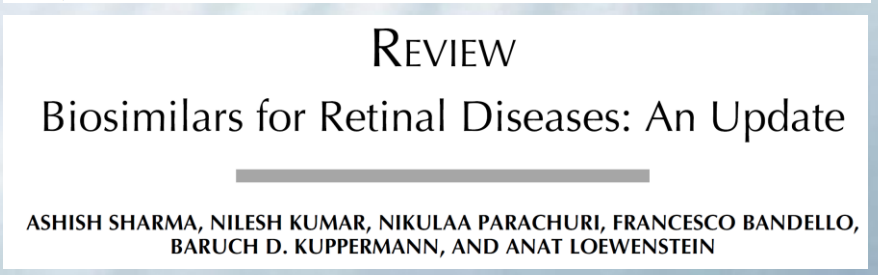

Eye (2020) 34:614–615
https://doi.org/10.1038/s41433-019-0636-3
The ROYAL COLLEGE of OPHTHALMOLOGISTS

COMMENT

Ophthalmic biosimilars and biologics—role of endotoxins

Ashish Sharma[1] · Nilesh Kumar[1] · Baruch D. Kuppermann[2] · Francesco Bandello[3] · Anat Loewenstein[4]

Received: 13 September 2019 / Accepted: 26 September 2019 / Published online: 16 October 2019


REVIEW

Biosimilars for Retinal Diseases: An Update

ASHISH SHARMA, NILESH KUMAR, NIKULAA PARACHURI, FRANCESCO BANDELLO, BARUCH D. KUPPERMANN, AND ANAT LOEWENSTEIN

Am J Ophthalmol 2021;224:36–42.

Ophthalmic biosimilars and biologics—role of endotoxins

Ashish Sharma[1] · Nilesh Kumar[1] · Baruch D. Kuppermann[2] · Francesco Bandello[3] · Anat Loewenstein[4]

Eye (2020) 34:614–615

- Endotoxin-induced uveitis (EIU) is the sterile inflammation the eye following an exposure to lipopolysaccharides of the Gram-negative bacterial cell wall.
- Endotoxins are produced in culture as the biologics involve cell cultures
- Sterile endophthalmitis (inflammation) has been reported in all anti-VEGF formulations
- Infectious endophthalmitis is still the more severe complication (incidence of 0.029–0.058%)

- Biologics such as ranibizumab and aflibercept are produced from mammalian cell lines
- DARPins (Abicipar) are produced from bacterial cells (E. coli) and thus may have a higher propensity to have intrinsic endotoxins.
- Abicipar was withdrawn because of intraocular inflammation rates within the studies despite a new formulation that was tested in the MAPLE trial
- Brolucizumab has received FDA approval, is also produced from microbial cell

The Nocebo Effect

Eye (2020) 34:1006–1007
https://doi.org/10.1038/s41433-019-0722-6

The ROYAL COLLEGE of OPHTHALMOLOGISTS

COMMENT

Need of education on biosimilars amongst ophthalmologists: combating the nocebo effect

Ashish Sharma[1] · Nilesh Kumar[1] · Francesco Bandello[2] · Anat Loewenstein[3] · Baruch D. Kuppermann[4]

Received: 4 November 2019 / Revised: 12 November 2019 / Accepted: 19 November 2019 / Published online: 29 November 2019

The **placebo effect** is the **positive effect** on a person's health experienced after taking a **substance that should have no effect**.

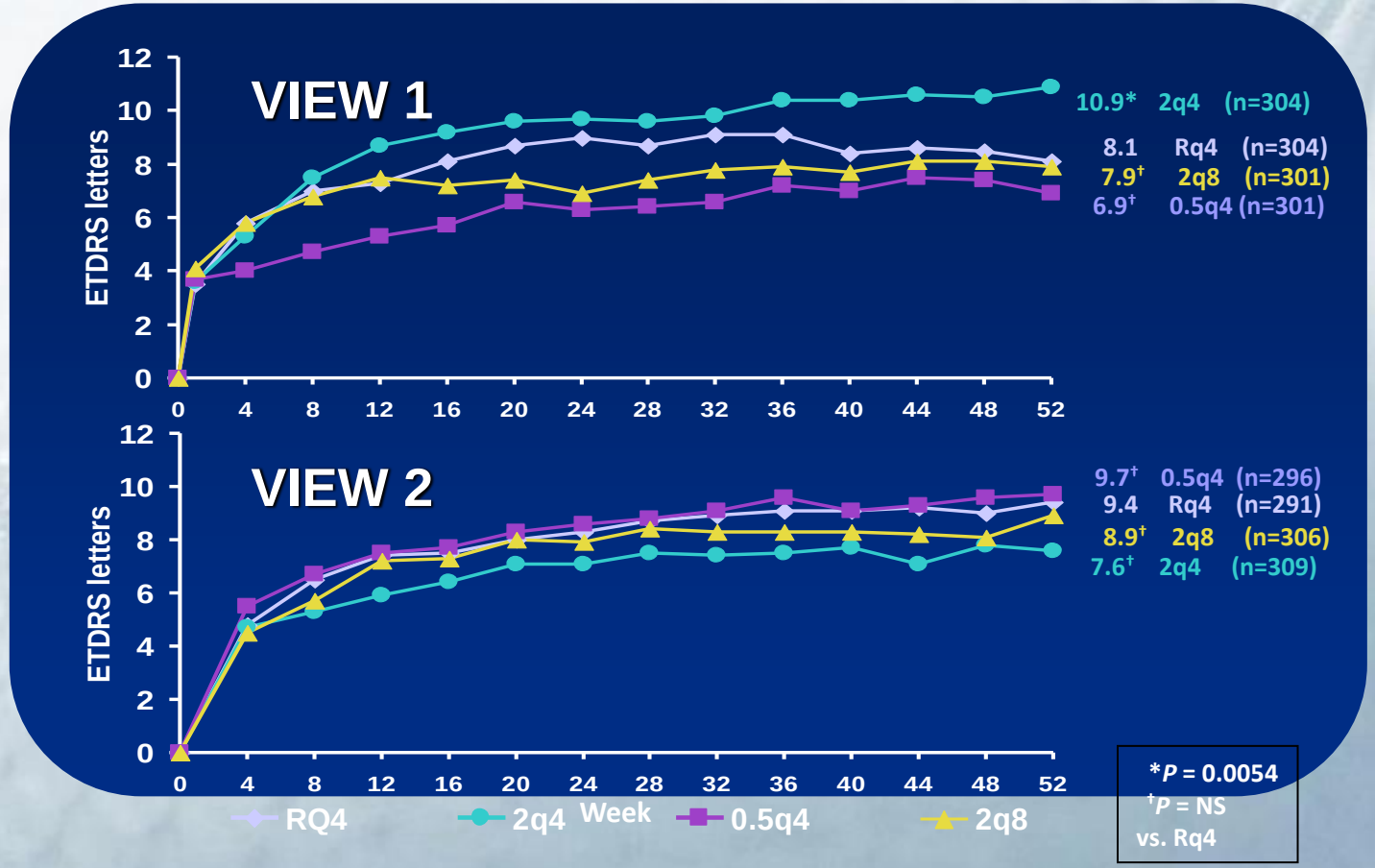
The **nocebo effect** is the **negative perception** effect on patients and health care providers that a substance that should have the same effect (ie biosimilar vs biologic) **is inferior**

OBJECTIVES

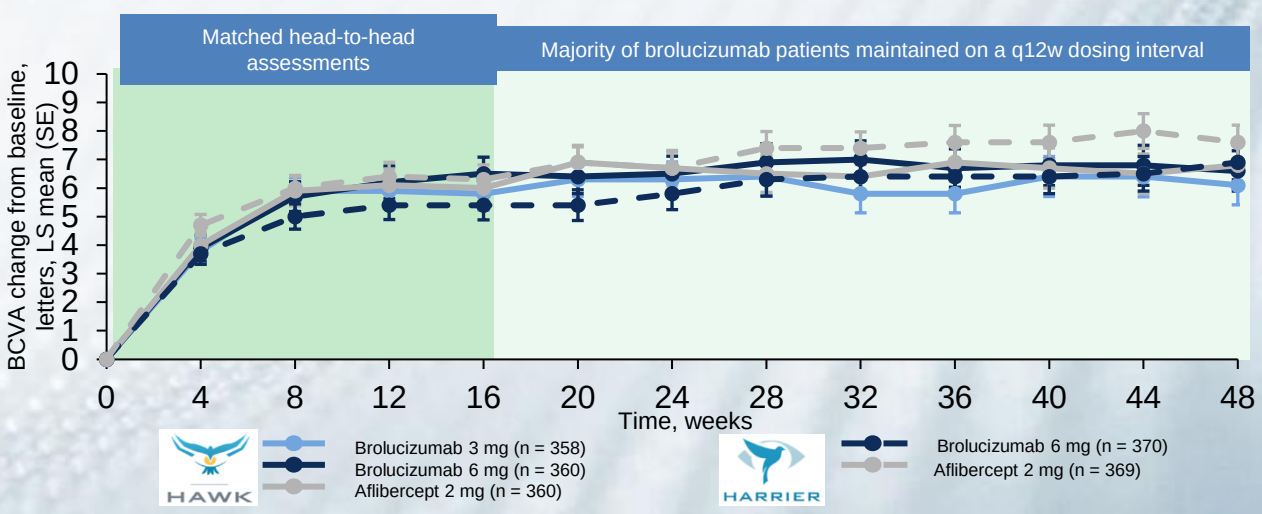
- Regulatory Issues International
- Regulatory Issues Canada
- Safety, Efficacy of Ophthalmic Biologics/Biosimilars
- **Patient/Doctor/Payor Perspectives**
- Future Access

VIEW 1 & 2 (Aflibercept)

Mean Change in Visual Acuity to 1 year Compared to Baseline



Brolucizumab achieved robust and consistent visual gains and a majority of patients maintained on a q12w dosing interval

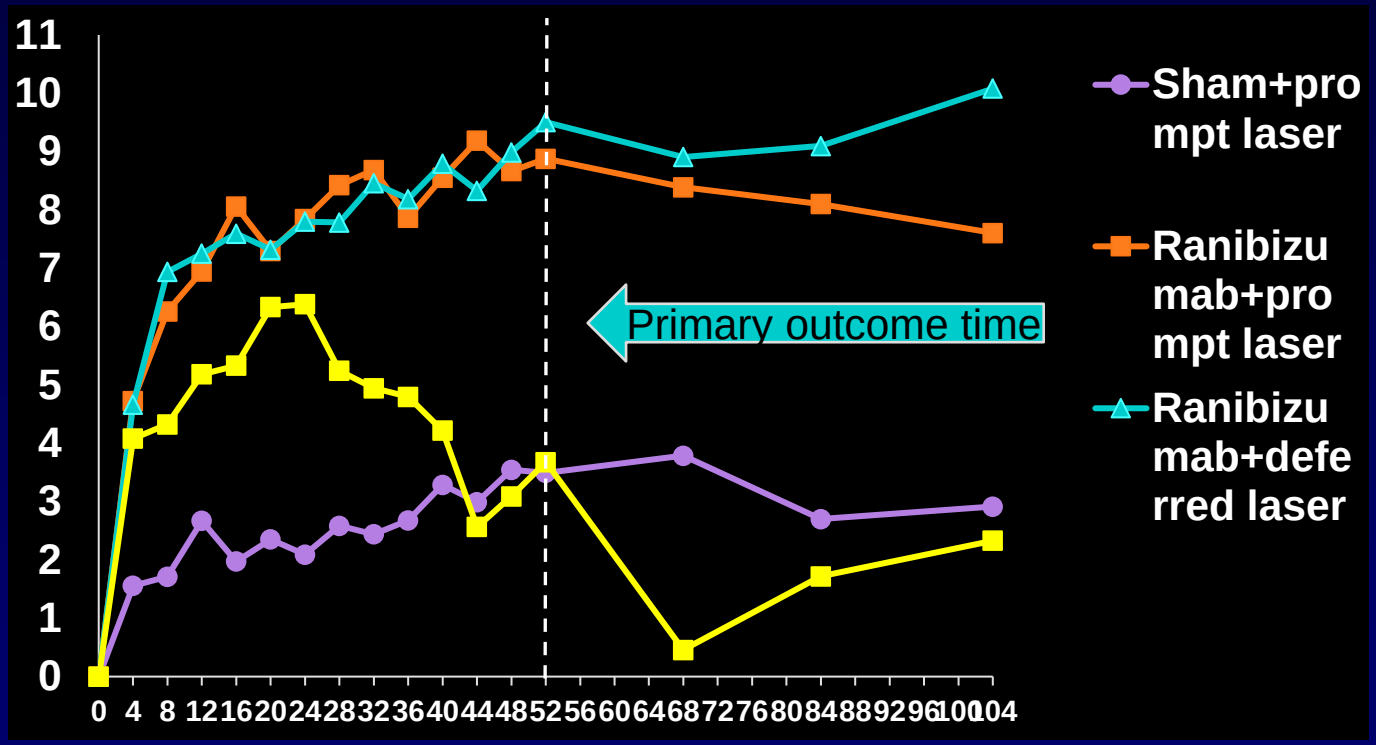


	Treatment	Patients maintained on an exclusive q12w interval at Week 48
HAWK	Brolucizumab 3 mg (n = 358)	52% [95% CI (46.0, 56.6)]
	Brolucizumab 6 mg (n = 360)	57% [95% CI (51.9, 62.4)]
HARRIER	Brolucizumab 6 mg (n = 370)	52% [95% CI (46.9, 57.4)]

LS, least squares.

Dugel PU, et al. AAO 2017 [Oral presentation]; Alcon Research Ltd. Data on file (Phase 3 FIR 2017).

Mean Change in Visual Acuity* at Follow-up Visits



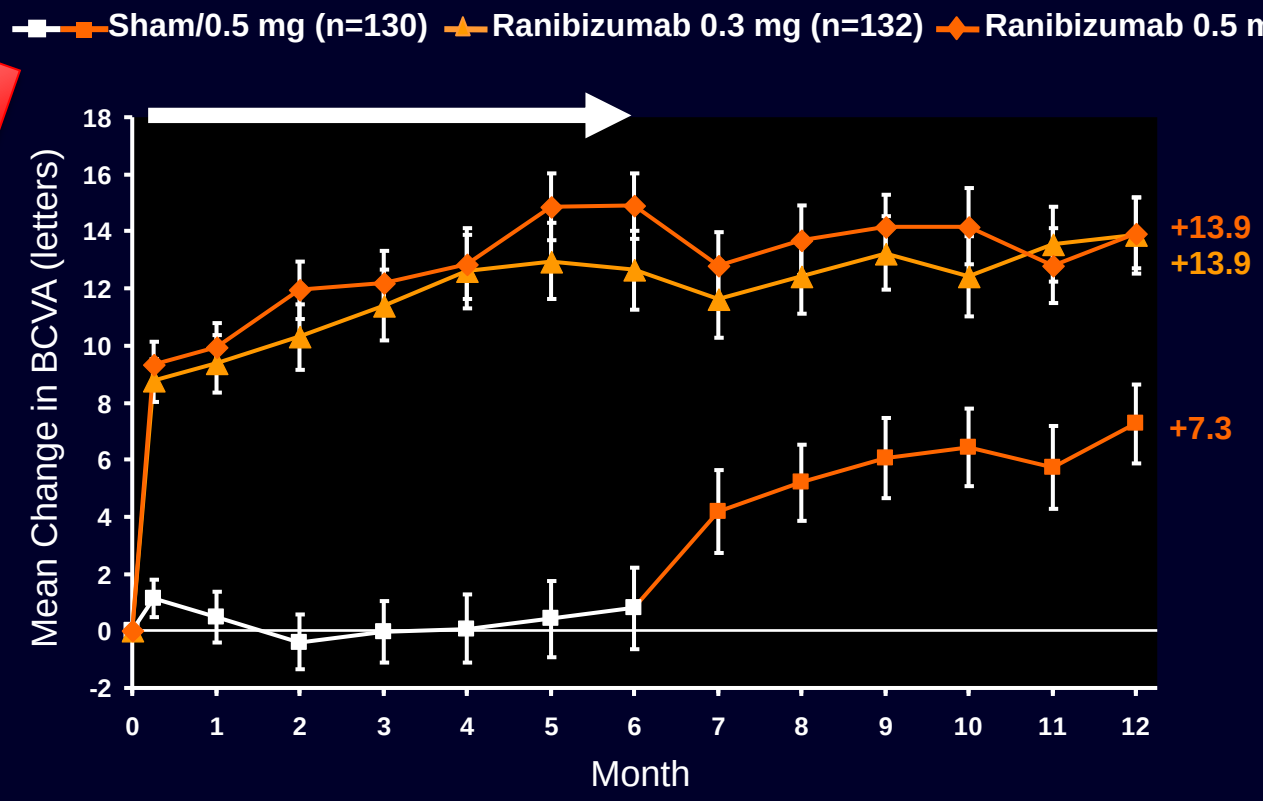
Protocol I

* Values that were ±30 letters were assigned a value of 30

P-values for difference in mean change in visual acuity from sham+prompt laser at the 52-week visit: ranibizumab+prompt laser <0.001; ranibizumab+deferred laser <0.001; and triamcinolone+prompt laser=0.31.

Visual Acuity Endpoint:

Mean Change from Baseline in BCVA Score Over Time



Note: Vertical bars are ±1 standard error of the mean.

OBJECTIVES

- Regulatory Issues International
- Regulatory Issues Canada
- Safety, Efficacy of Ophthalmic Biologics/Biosimilars
- Patient/Doctor/Payor Perspectives
- **Future Access**

The Global Landscape on Interchangeability of Biosimilars

Anurag S. Rathore , James G. Stevenson , Hemlata Chhabra & Chinmoyee Maharana

To cite this article: Anurag S. Rathore , James G. Stevenson , Hemlata Chhabra & Chinmoyee Maharana (2021): The Global Landscape on Interchangeability of Biosimilars, Expert Opinion on Biological Therapy, DOI: 10.1080/14712598.2021.1889511

To link to this article: https://doi.org/10.1080/14712598.2021.1889511

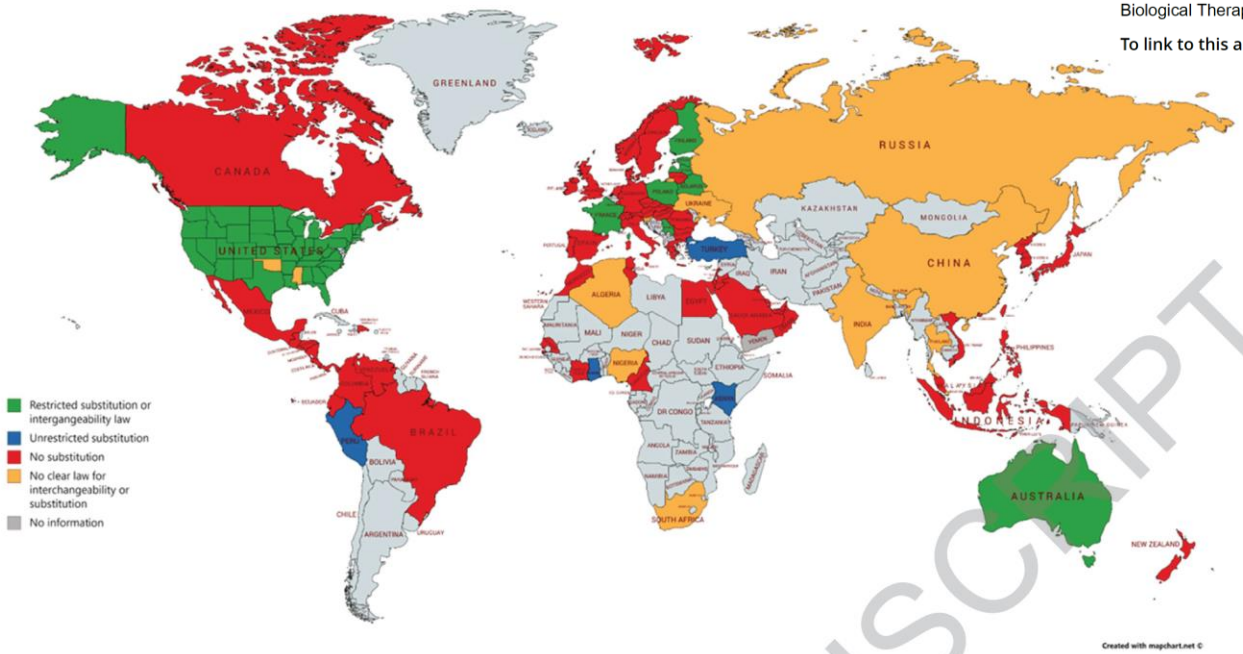


Fig 5

Switching is referred to when a physician decides to exchange one medicine with another recognized to be therapeutically equivalent.

Substitution implies replacing one drug for another at the pharmacy without requiring consultation with the prescriber or the patient.

Generic substitution of small molecule drugs is commonly used today and has been a significant contributor to the fact that around 90% of prescriptions dispensed today in the US are generics

Strategies to achieve fairer prices for generic and biosimilar medicines

Price Regulation
Regulatory Harmonization
Clinical Guidelines
Prevent delays
Switch studies
Public education
Advocacy Campaigns

Table 1 | Actions required to lower drug prices and broaden access

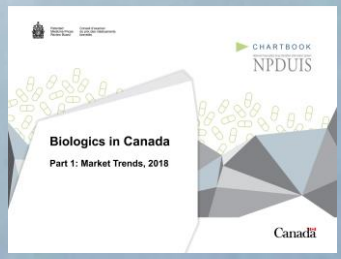
Stakeholder	Goal	Potential strategies	How governments (or other bodies) could facilitate these strategies
Government, through ministries, departments, and agencies	Sustain and improve health and wellbeing of its citizens	• Ensure quality of medicines on the market • Price regulation, including regulation of supply chain mark-ups; reimbursement decisions • Implement compulsory licences • Provide a legal and policy framework to conduct procurement • Provide incentives to influence provider behaviour both positively (eg rewards) or negatively (penalties) or by providing feedback (eg monitoring prescribing behaviour) • Provide information and education activities to patients	• Regulatory convergence and harmonisation: bodies like the European Medicines Agency and similar regulatory harmonisation initiatives in Africa can reduce the burden of marketing authorisation reviews • Procure World Health Organization prequalified products • Grant priority review to first generic • Carefully evaluate which pricing policies to implement and how to conduct tenders so that prices are fair and sustainable, products are of high quality, and manufacturers are not driven out of the market
Health payers	Provide quality and affordable healthcare services and products to their insured patients	• Use of bargaining power to obtain fairer prices • Direct patients to more cost effective products through financial incentives (eg lower or no co-payments) and education/information work • Provide incentives to influence provider behaviour both positively (eg rewards) or negatively (penalties) or by providing feedback (eg monitoring prescribing behaviour)	• Develop clinical guidelines and formularies in close collaboration with the relevant medical group; use a bottom-up rather than top-down approach built around increasing access in policy development • Organise information and educational activities
Pharmaceutical industry	Produce medicines that improve patients' health and generate value for shareholders	• Price medicines with affordability and health system sustainability in mind • Offer tiered pricing based on country's income level and income distribution • Originator—grant a voluntary licence • Generic—take advantage of voluntary licences through patent pool to produce lower cost generics	• Regulate pharmaceutical promotion and competition • Implement regulations that prevent delaying entry of generic medicines • Create patent pools (eg medicines patent pool) to facilitate use of voluntary licences
Prescribers (doctors and other authorised prescribers)	Improve health outcomes of their patients	• Follow clinical guidelines • Prescribe the most cost effective treatment tackling the patient's needs • Seek evidence based independent information on medicines	• Engage doctors as partners and work together to find solutions around concerns affecting generic and biosimilar use • Involve doctors in "switch studies" • Impose prescription quota (ie generics or biosimilars must account for a certain share of total volume of medicines prescribed)
Dispensers (pharmacists and other professionals authorised to dispense— eg, pharmacy technicians)	Deliver good services and products to patients Make a profit	• Substitute a branded medicine with a generic where allowed, inform patient about least expensive option, educate patient about safety and bioequivalence of generic and biosimilar medicines	• Provide financial incentives to dispense lower cost generic and biosimilar • Require dispensers to inform about (availability of) lower priced generic or biosimilar • Provide information to patients, especially important when substituting from one generic or biosimilar to another • Impose dispensing quota (ie generics or biosimilars must account for a certain share of total dispensed)
Patient and civil society	Access to quality assured affordable medicines	• Request generic substitution in countries where this is voluntary • Advocacy campaigns: eg. access to HIV/AIDS and hepatitis C medicines • Buyers' clubs or drug buying networks (eg, FixHepC) which help patients to import medicines for individual use from countries where they are available at a lower price	• Conduct information campaigns for the public • Work with prescribers and dispensers to inform and educate patients about the safety and efficacy of generics and biosimilars

Biosimilar Initiatives in Canada

Given the high cost of biologics in Canada, biosimilars offer the potential for important savings. Recently, Canadian payers have undertaken a number of initiatives to increase biosimilar uptake, which are outlined in the table below.

The second part in the *Biologics in Canada* chartbook series will explore the potential for increased biosimilar savings in more detail.

Payer		Initiative
Public payers	Quebec	Quebec only reimburses the lowest priced version of infliximab.
	Manitoba	New patients are required to try two Tier 1 medicines before being reimbursed for a Tier 2 medicine; Tier 1 biologic medicines have been determined to be the most cost-effective.
	British Columbia	In 2019, British Columbia became the first Canadian province to initiate a switch to biosimilar medicines for patients covered under the PharmaCare program. Under the policy, patients using Enbrel, Remicade, and Lantus for specific indications are required to switch to the biosimilar.
	Alberta	Alberta announced that all patients taking Enbrel, Remicade, Lantus, Neupogen, Neulasta, and Copaxone for indications ranging from rheumatoid arthritis to diabetes and multiple sclerosis will be required to switch to the biosimilar.
Private payers		Green Shield Canada (GSC) initiated a pilot program in 2018. The program targeted patients taking Remicade and Enbrel for three rheumatic conditions and reduced reimbursement to the biosimilar price. Under the program, the patient could switch to the biosimilar or remain on the biologic and pay the cost difference. Since then, GSC has opened its biosimilar transition program to any sponsor who wishes to take part.



Extreme regulations to lower drug prices mean Canada will get fewer new drugs

Opinion: Severe price cuts would clearly discourage pharmaceutical manufacturers from launching new drugs in Canada

Brett Skinner and Nigel Rawson

Special to Financial Post

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- Ottawa has doubled down on the fantasy that government can legislate lower drug prices without causing unintended consequences.
- The federal government is expanding the regulatory powers of the Patented Medicine Prices Review Board (PMPRB).
- The PMPRB evidently believes that with new regulatory tools it can ascertain what the correct prices should be. The guidelines are more extreme than drug pricing policies in other countries. It is not too much of a stretch to say that the new regime reflects Soviet-style thinking on price controls.
- The authors applied the new regulations to a hypothetical new medication for a rare disorder and found that the price ceilings that resulted could be 45 to 84 per cent below existing levels. Such severe price cuts would clearly discourage pharmaceutical manufacturers from launching new drugs in Canada.
- The new regulations change the reference countries. The international benchmark is now biased because the group of 11 countries is arbitrarily stacked with lower-priced jurisdictions. According to the board, higher-priced markets like the U.S. and Switzerland are out because they differ from Canada regarding price controls, GDP per capita, population and new medicines.
- According to the board, higher-priced markets like the U.S. and Switzerland are out because they differ from Canada regarding price controls, GDP per capita, population and new medicines. But for three of the four criteria, the U.S. and Switzerland were as similar to Canada as Norway, Sweden and France which are now in.
- Lower-priced markets experienced fewer new drug launches.
- That the new Patented Medicine Prices Review Board regulations will reduce the availability of new medicines in Canada is consistent both with the evidence and with common sense.

Balancing the Playing Field

What does the Government want?

What does the Payor/Insurer want?

What does the patient want?

What does the physician want?

What role does the pharmacist play?

What does the Originator Pharmaceutical Company want?

What does the Biosimilar Company want?

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