aam
Association for Accessible Medicines

The Biosimilars Council
A Division of the Association for Accessible Medicines

Leading on Biosimilars

2017 AAM Biosimilars Council Conference

Biosimilar medicines: practical EU experience and perspectives

12 Sept 2017 – Adrian van den Hoven, Director General, Medicines for Europe

biosimilar medicines
A medicines for europe sector group

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Medicines for Europe Vision 2020
Our 5 pillars

Medicines For Europe
VISION


PATIENTS


QUALITY


VALUE


SUSTAINABILITY


PARTNERSHIP

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EU Biosimilar Medicines Group Membership

COMPANIES

ASSOCIATIONS

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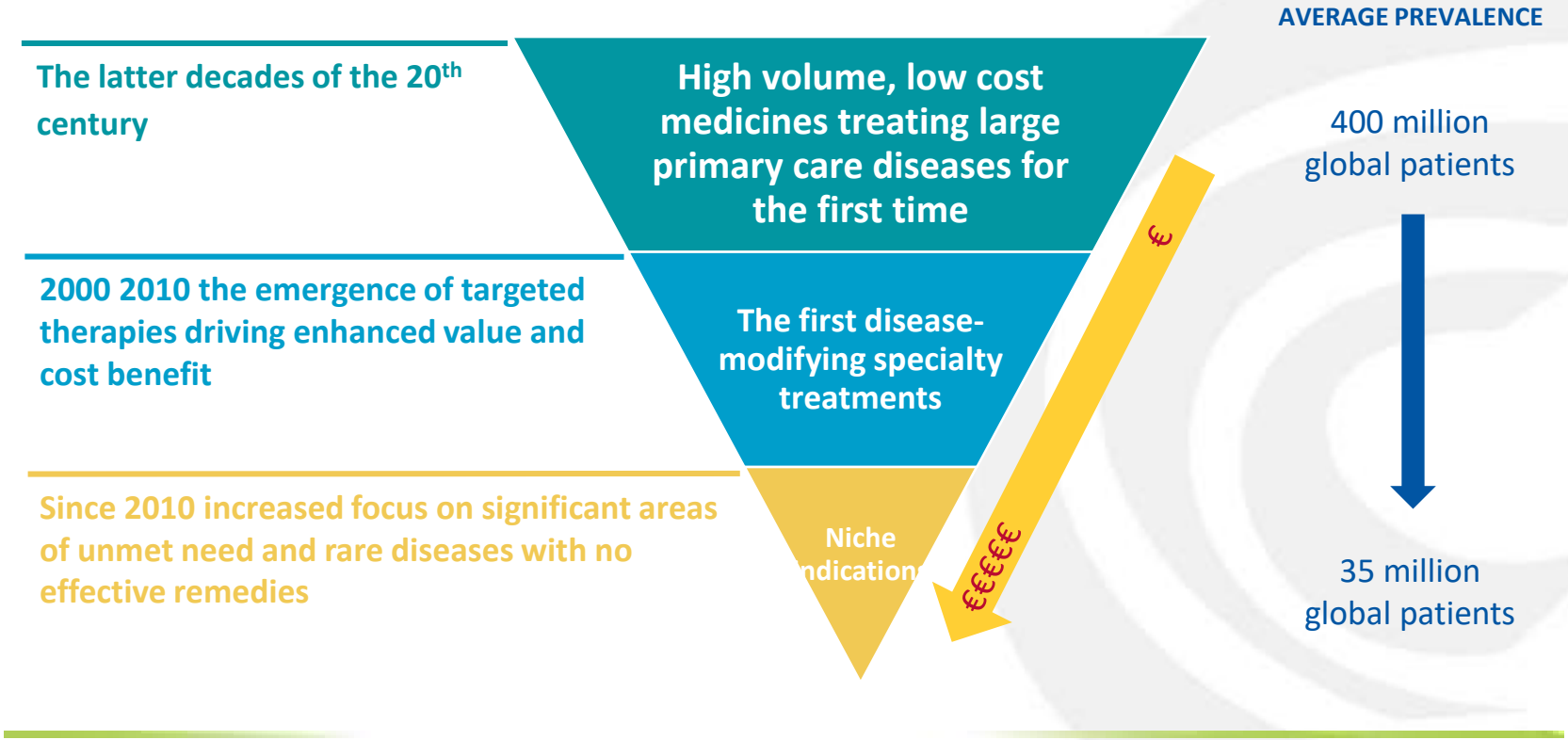
Innovative specialty medicines now are targeting smaller populations with significant unmet needs



Notes: Prevalence and Annual cost were categorised into estimated buckets; annual cost takes into account list price at time of launch.

Source: QuintilesIMS Thought Leadership Launch Excellence I and V

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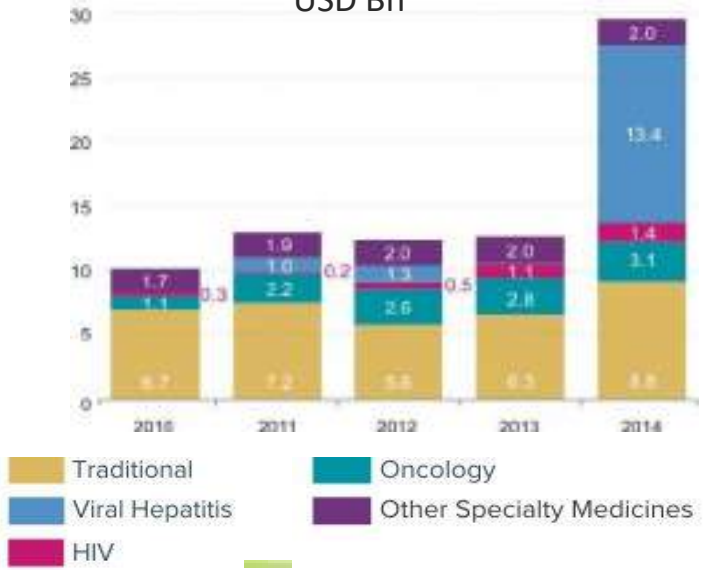
Biologicals create real issue for healthcare budgets

- Spending on new brand medicines exploded
- Biologics growth faster than total pharma growth

Is this sustainable?

Global New Brand Spending Growth

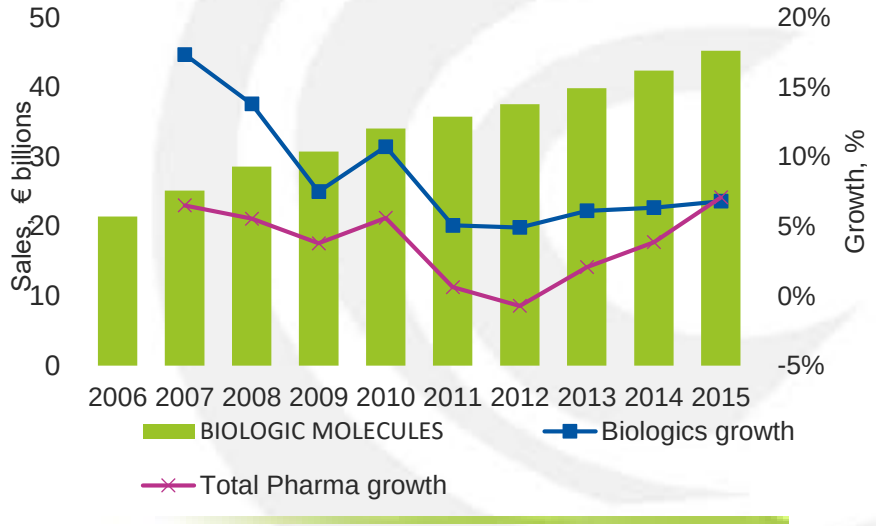
USD Bn



Source: IMS Health, R&D Focus, May 2015; MIDAS, Q4 2014, constant USD

Europe market trends

Sales and Growth



Source: IMS Health, MIDAS 2015

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Biologicals increasingly feature as key therapies

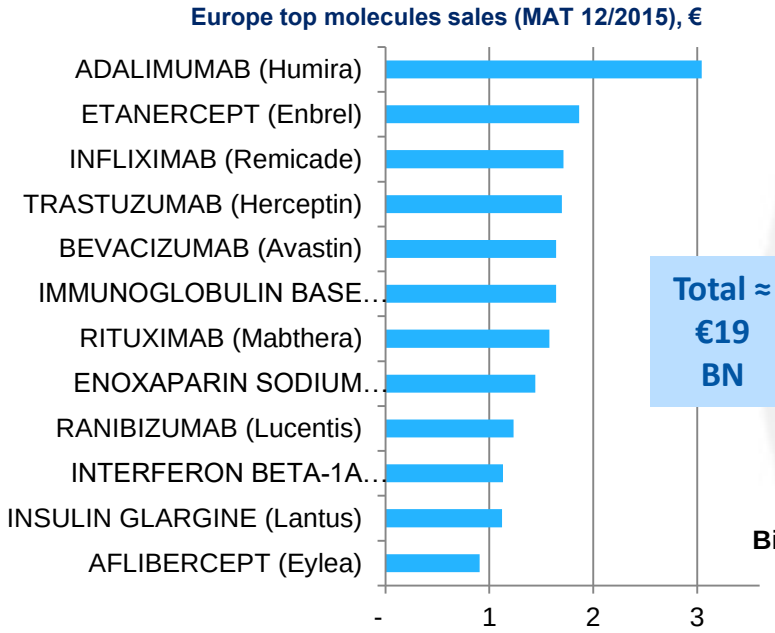
EUROPE TOP 10 PRODUCTS (SALES) 2010-16

	2010	2011	2012	2013	2014	2015	2016
1	LIPITOR	HUMIRA	HUMIRA	HUMIRA	HUMIRA	HUMIRA	HUMIRA
2	SERETIDE	SERETIDE	SERETIDE	ENBREL	ENBREL	HARVONI	HARVONI
3	HUMIRA	LIPITOR	ENBREL	SERETIDE	SERETIDE	SOVALDI	XARELTO
4	ENBREL	ENBREL	HERCEPTIN	HERCEPTIN	REMICADE	ENBREL	ENBREL
5	HERCEPTIN	HERCEPTIN	LOVENOX	REMICADE	HERCEPTIN	HERCEPTIN	HERCEPTIN
6	AVASTIN	LOVENOX	MABTHERA	AVASTIN	LOVENOX	REMICADE	SOVALDI
7	LOVENOX	REMICADE	REMICADE	MABTHERA	MABTHERA	SERETIDE	MABTHERA
8	ZYPREXA	MABTHERA	AVASTIN	LOVENOX	AVASTIN	MABTHERA	AVASTIN
9	MABTHERA	AVASTIN	SPIRIVA	LUCENTIS	LUCENTIS	AVASTIN	REMICADE
10	REMICADE	SPIRIVA	LYRICA	LYRICA	SOVALDI	LOVENOX	VIEKIRAX

Small molecule Biological

Loss of exclusivity drives biosimilar interest

Key products protection expired or losing protection by 2020



Total ≈ €19 BN

EU expiry date
2018
Expired
Expired
Expired
Expired
Expired
Expired
Expired
Expired
Expired
Expired
2020

Source: IMS Health 2016

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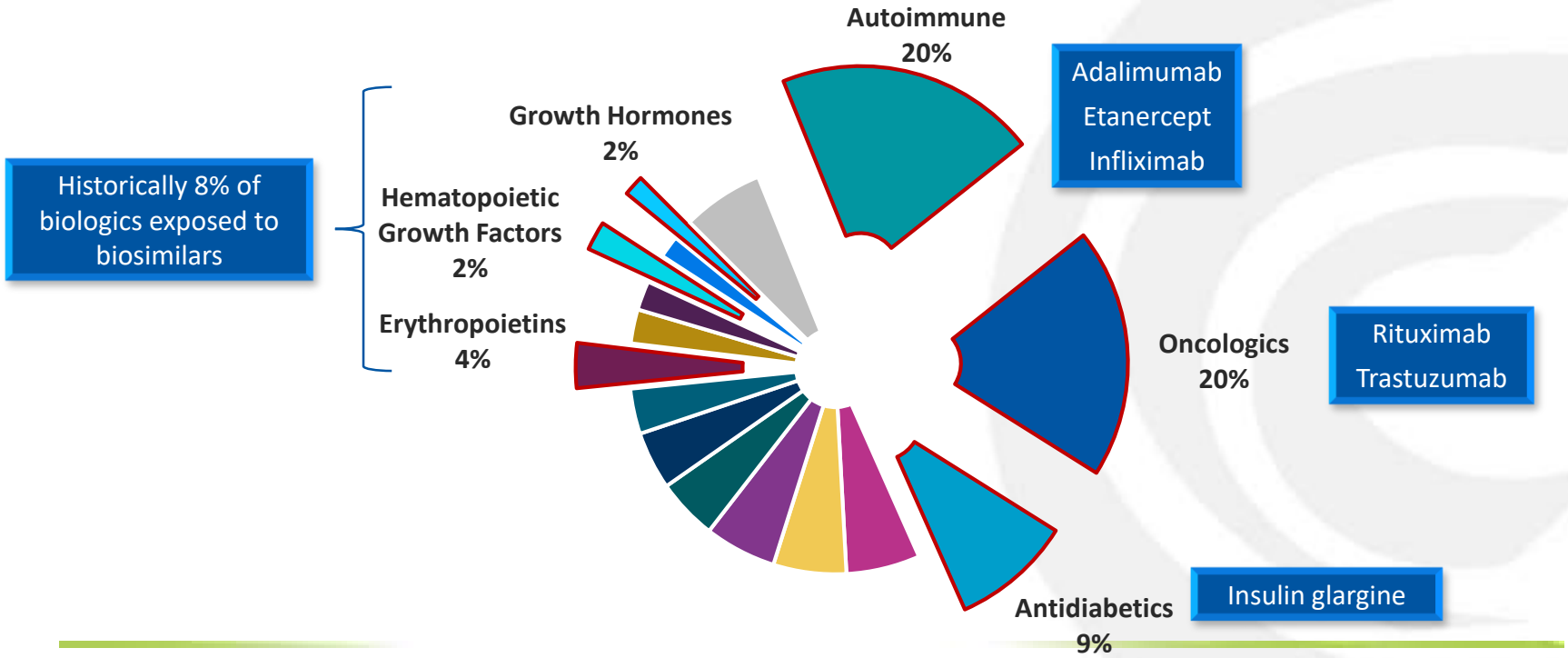
Historically biosimilar competition restricted but the future is very different

Europe

Top Biologic Therapy Areas, Europe sales (2016)



Source: QuintilesIMS MIDAS MAT Q3 2016; Europe excludes Russia and Turkey

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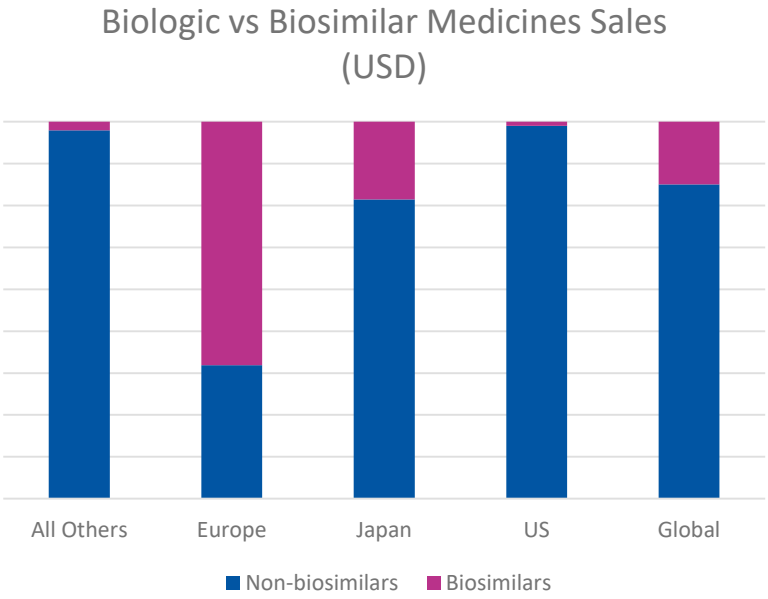
Biosimilar medicines – EU at the forefront



- 9 out of 10 biosimilar medicines sales take place in EU (2016)
- 60% of overall biological medicines sales occur in US (2016)
- **Over the last 10 years, EU cumulates nearly 100% of the use and experience with biosimilar medicines**

Source: IMS Health MIDAS MAT Q4 2016; Europe does not include Russia and Turkey

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Value proposition of biosimilar medicines

biosimilar medicines

THE BENEFITS OF BIOSIMILAR MEDICINES

LAUNCH OF BIOSIMILAR MEDICINES

REDUCTION OF TREATMENT COST

MORE PATIENTS TREATED

MORE TREATMENT OPTIONS

MORE AUTONOMY TO PRESCRIBE

MORE INVESTMENT FOR:

- HOSPITAL INFRASTRUCTURE
- CAPACITY BUILDING
- HEALTHCARE SERVICES

IMPROVED CARE AND HEALTH OUTCOMES FOR PATIENTS

+

ENSURED SUPPLY CHAIN SECURITY

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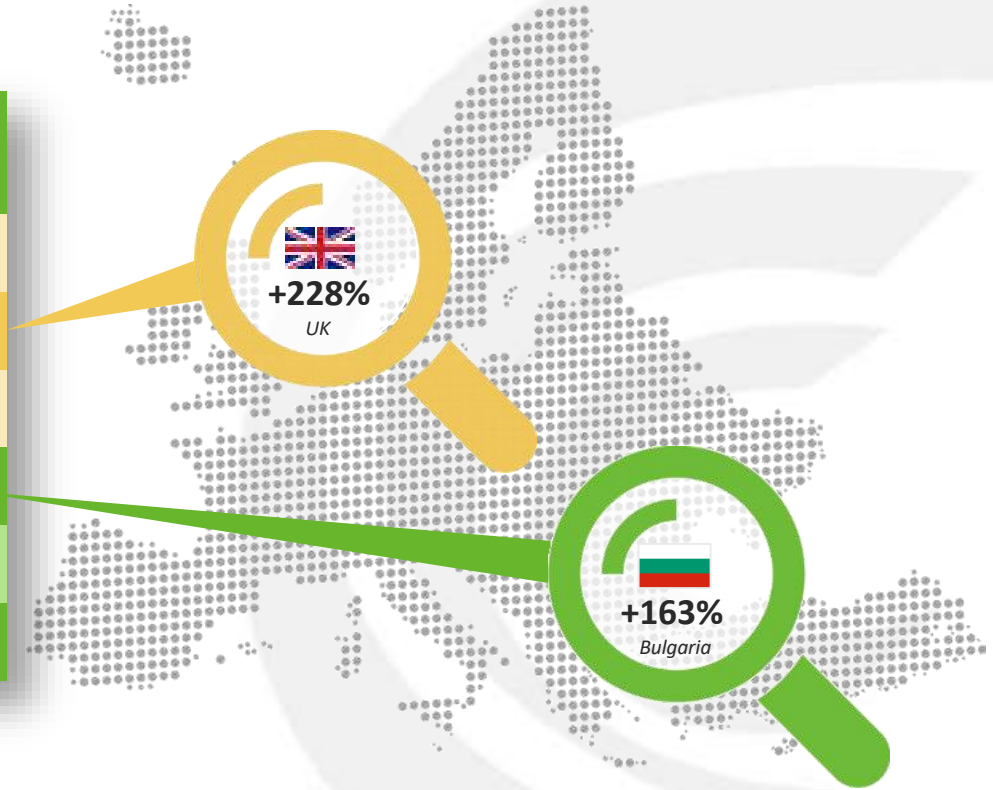
Biosimilar medicines increase patient access

Change in # of treatment days (2016 vs. year before biosimilar entrance)	
Epoetin	+66%
G-CSF (filgrastim)	+122%
Growth hormone (somatropin)	+41%
Anti-TNF (infliximab & etanercept)	+19%
Fertility (follitropin alfa)	+16%
Insulins	+19%



Source: QuintilesIMS (2017) The Impact of Biosimilar Competition in Europe

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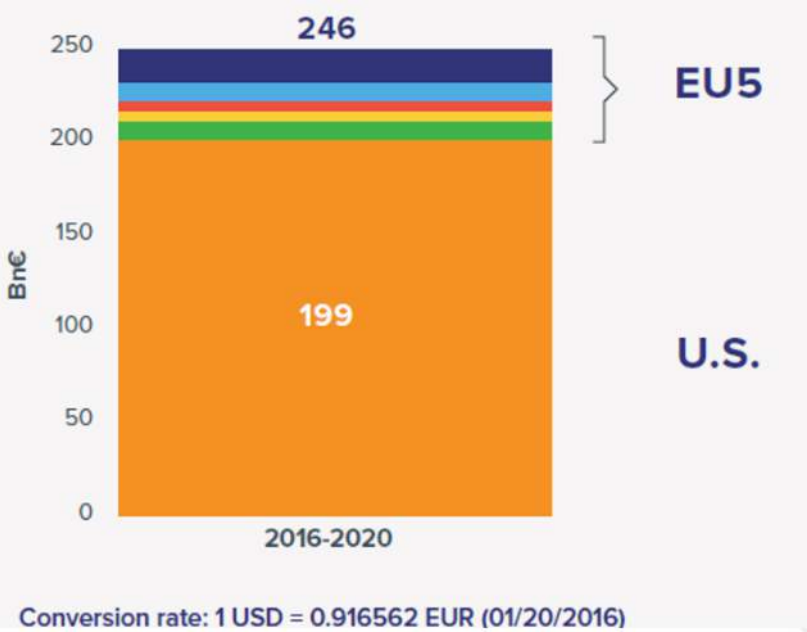
Without competition, cumulative spending in the US + EU-5 is expected to reach €246bn over 2016-2020 period

The addressable biosimilar medicines market, 2016-2020



Actual savings 2006-2016
EU-5

EUR 1.5 BN

Potential savings 2016-2020
US + EU 5
30% reduction in price per treatment

EUR 49 BN

Source: IMS Health, MIDAS, IMS Health Market Prognosis, IMS Institute for Healthcare Informatis, Dec 2015
Note: Addressable market is calculated based on projected growth of originator market without biosimilar entry. Growth rate is based on historical growth and analogue analysis. The accessible market analysis is based on Adalimumab, Insulin glargine, Etanercept, Infliximiab, Rituximab, Peg-filgrastim, Trastuzumab and Follitropin alpha.

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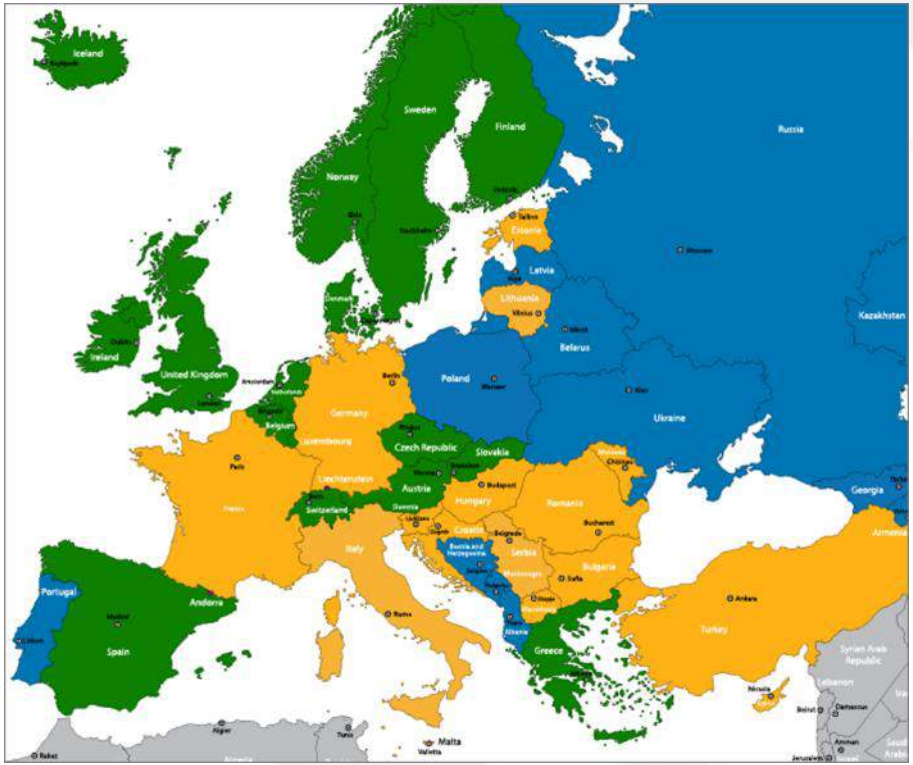
Biosimilar medicines
Opportunity to meet unmet medical needs

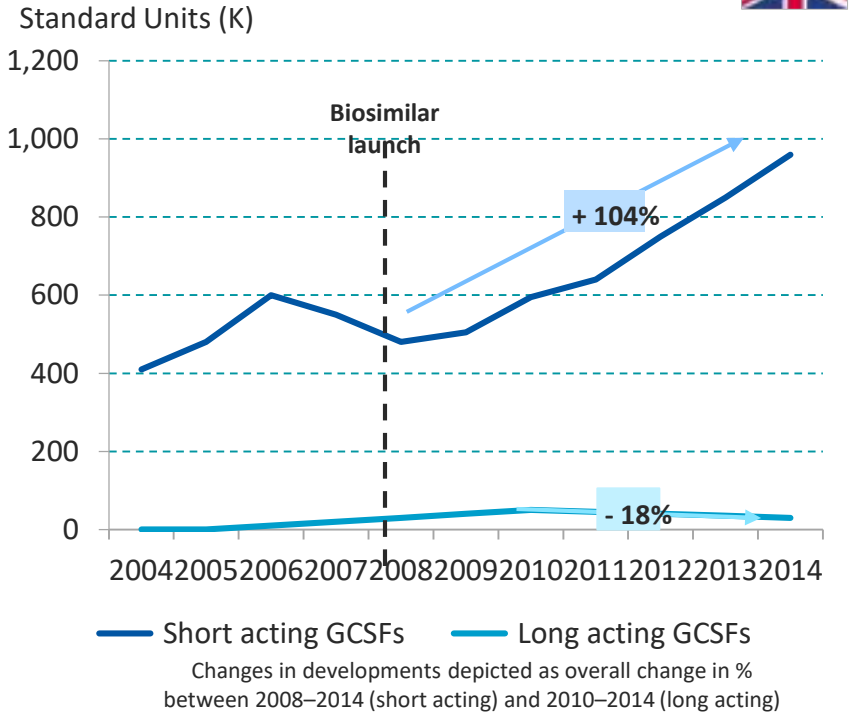
In some European countries, patients have less access to biological treatments for Rheumatoid Arthritis (RA)

- Score 0 – 3, low access
- Score 4 – 6, middle access
- Score 7 – 9, high access



Biosimilar medicines increase patient access

Filgrastim uptake in the UK



Changes in developments depicted as overall change in % between 2008–2014 (short acting) and 2010–2014 (long acting)

Source: Simon-Kucher & Partners, IMS Health, MIDAS, IMS Consulting Group, Nov 2015

- After biosimilar launch in 2008, NICE guidelines updated for improved cost-effectiveness of biosimilar filgrastim vs. alternative treatments
- G-CSF restrictions were relaxed and usage is now recommended for primary prophylaxis of neutropenia (before: secondary prophylaxis only)
- Consumption of filgrastim short-acting increased by 104% between 2009 and 2014
- **More patients access earlier in therapy cycle = Biosimilar G-CSF almost certainly improved patient outcomes**

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Biosimilar medicines increase prescribing autonomy for improved patient access

Southern healthcare region

Before: filgrastim biosimilars

- Three physicians had to approve prescription of the original product due to cost

After: filgrastim biosimilars

- Regional authorities to relax restrictions on prescribing filgrastim biosimilars for febrile neutropenia
- Prescription does not require any further authorization
- **Clinical use of G-CSF increased five-fold in the Southern Healthcare Region, driven by usage of biosimilar filgrastim**

Source: Simon-Kucher & Partners, IMS Health

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Biosimilar medicines improve treatment options

Their competitive drug acquisition cost makes it possible for biosimilar medicines to reach an acceptable ICER in situations where originator medicines cannot. Biosimilar medicines support **improved patient access to certain therapeutic** areas compared to the originator medicine

Example 1: Infliximab

Ankylosing spondylitis patients covered by EMA label

2015

2015 NICE guidance recommends **use of infliximab biosimilar medicines in** adults with non-radiographic axial spondyloarthritis

According to 2008 NICE guideline, infliximab (originator) should **not be used at all**

2008

Example 2: Epoetin

Treatment-induced anemia patients with cancer covered by EMA label

2014

According to 2014 NICE guideline, epoetin **is both clinically and cost-effective**

According to 2008 NICE guideline, epoetin is clinically effective for cancer treatment-induced anaemia, **but not cost-effective**

2008

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EU experience with biosimilar medicines

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Who decides what for biosimilar medicines in the EU?

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Scientific assessment followed by scientific opinion

No interchangeability designation

European Commission grants EU-wide marketing authorisation

Member States:

Price and reimbursement

Prescribing and substitution policies

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Over 30 EU approved biosimilar medicines

Active substance	Reference product	Biosimilar medicines
Adalimumab (2)	Humira®	Amgevita®, Solymbic®
Enoxaparin sodium (2)	Lovenox®	Inhixa®, Thorinane®
Epoetin (5)	Erypo®/Eprex®	Abseamed®, Binocrit®, Epoetin Alfa Hexal®, Retacrit®, Silapo®
Etanercept (2)	Enbrel®	Benepali®, Erelzi®
Filgrastim (7)	Neupogen®	Accofil®, Filgrastim Hexal®, Grastofil®, Nivestim®, Ratiograstim®, Tevagrastim, Zarzio®
Follitropin alfa (2)	Gonal f®	Bemfola®, Ovaleap®
Infliximab (3)	Remicade®	Flixabi®, Inflectra®, Remsima®
Insulin glargine (2)	Lantus®	Abasaglar®, Lusduna®
Rituximab (6)	MabThera®	Blitzima®, Ritemvia®, Rituzena®, Rixathon®, Riximyo®, Truxima®
Somatropin (1)	Genotropin®	Omnitrope®
Teriparatide (2)	Forsteo®	Movymia®, Terrosa®

Source: European Medicines Agency (August 2017)

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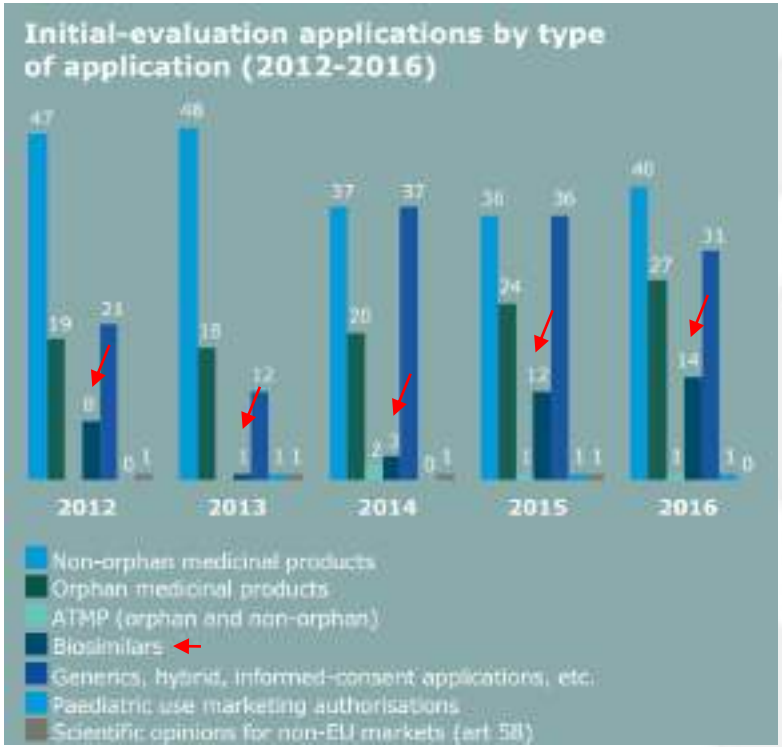
Biosimilar medicines applications: an increasing trend



Source: European Medicines Agency Annual Report 2016

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2017 pipeline: More biosimilar medicines on their way


EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

5 January 2017
EMA/4827/2017
Information Management Division

Applications for new human medicines under evaluation by the Committee for Medicinal Products for Human Use

August 2017

- 15 applications under evaluation by CHMP
  - Adalimumab (3)
  - Bevacizumab (2)
  - Infliximab (1)
  - Insulin glargine (1)
  - Pegfilgrastim (3)
  - Trastuzumab (5)
- 3 applications with positive opinion by CHMP
  - Adalimumab (1)
  - Rituximab (1)
  - Insulin lispro (1)

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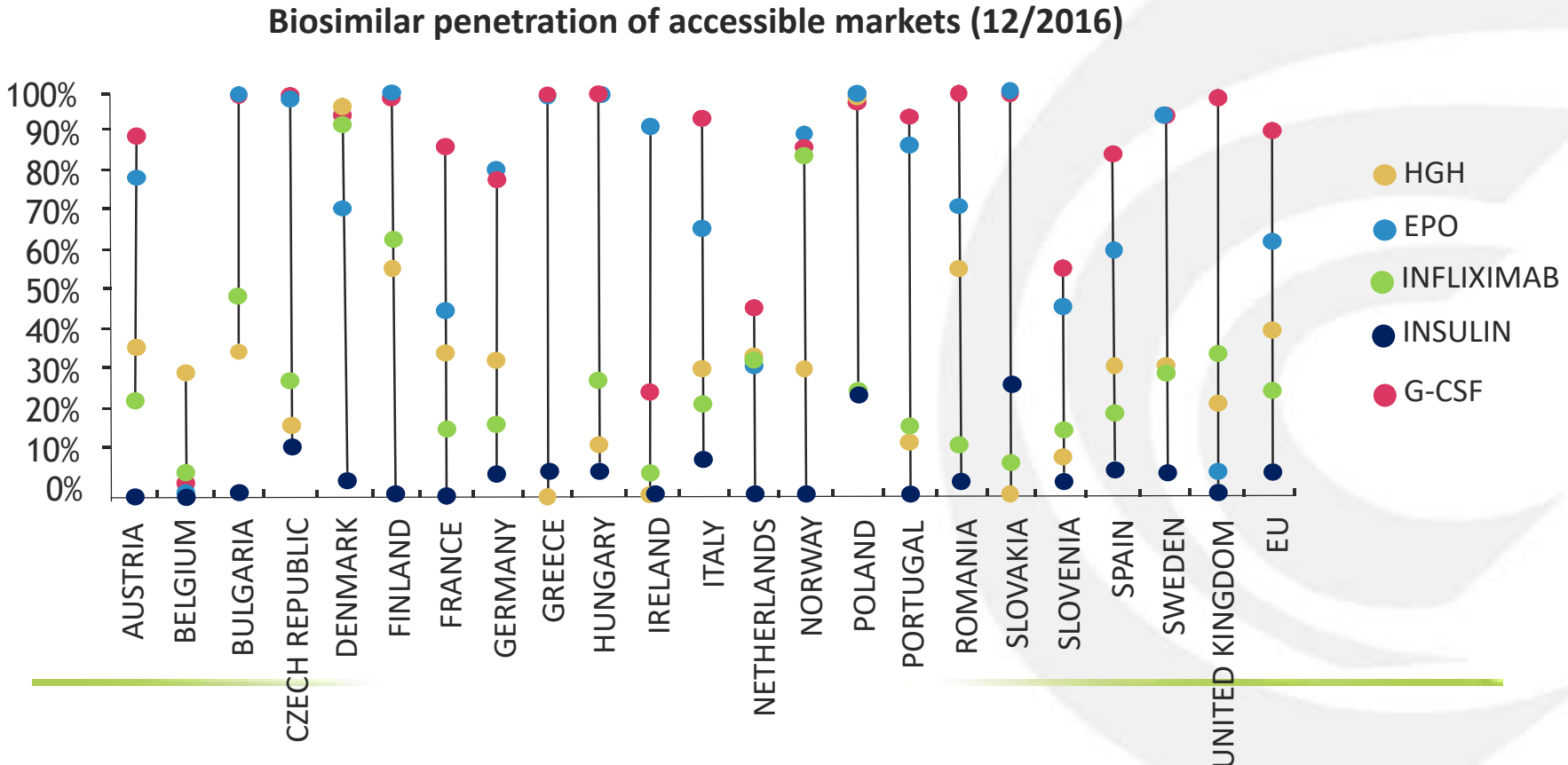
Use of biosimilar medicines varies greatly by country and therapeutic area



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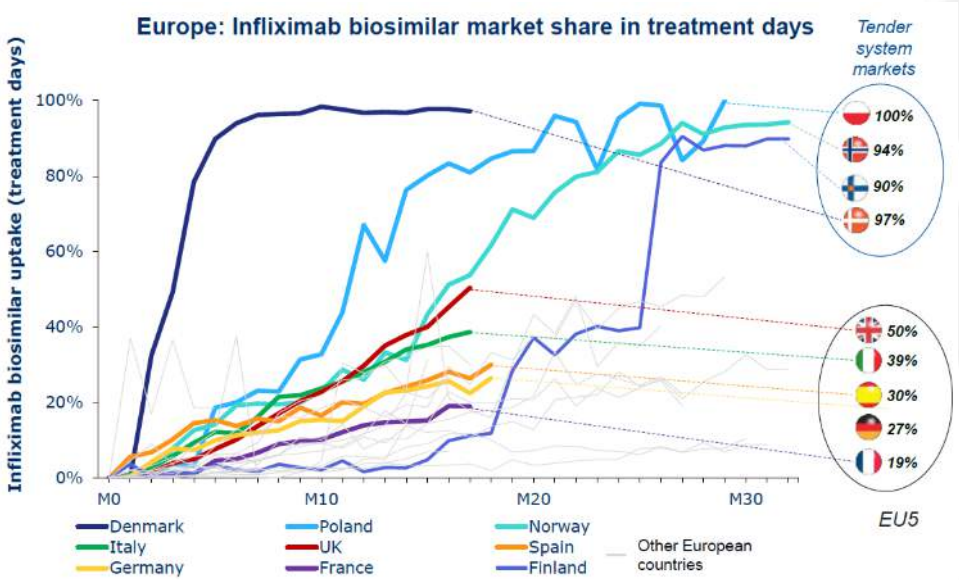
High variation in infliximab biosimilar usage, EU-5 remain behind but growing. Clinical use of biosimilar etanercept growing slightly faster



Biosimilar share (months after launch)	Denmark (M3)	Norway (M5)	Sweden (M4)	Germany (M5)	UK (M5)	Netherlands (M1)
Etanercept	85.3%	57.6%	18.0%	8.9%	6.6%	5.2%
Infliximab	49.3%	14.2%	5.8%	10.0%	7.7%	0.1%

Source: QuintilesIMS MIDAS MTH July 2016; Denmark data from MIDAS Monthly Restricted database; Latvia excluded because only biosimilar manufacturers present in market

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Large Body of Confirmatory Evidence
11 Years of Biosimilar medicines Clinical Use

Real-world experience

700 million
patient days[1]

"Over the last 10 years, the EU monitoring system for safety concerns has not identified any difference in the nature, severity or frequency of adverse effects between biosimilars and their reference medicine" [2]

Controlled experience

Source: Medicines for Europe information based on EMA Post-authorisation Safety Update Reports (PSURs); EMA – European Commission: Biosimilars in the EU – Information guide for healthcare professionals, 2017 (link)

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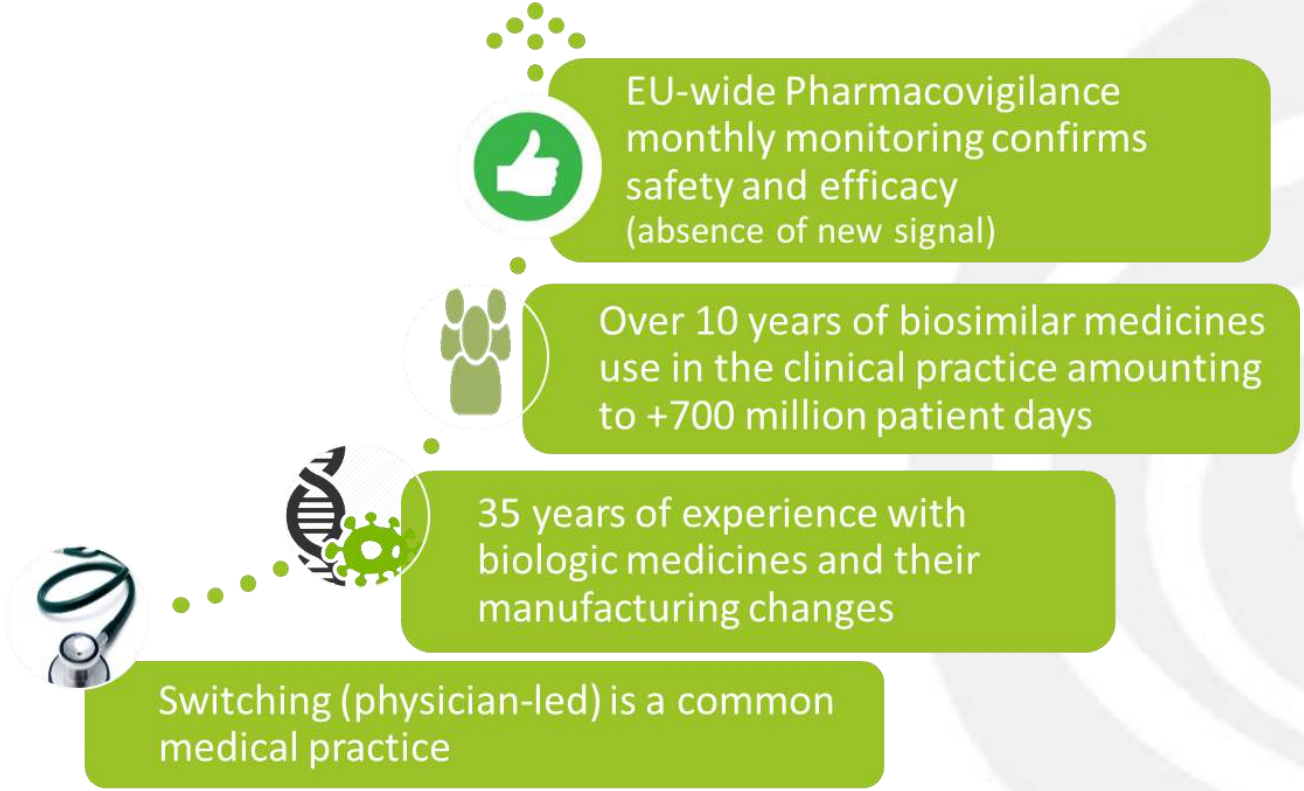
Physician-led switching has been demonstrated to be safe



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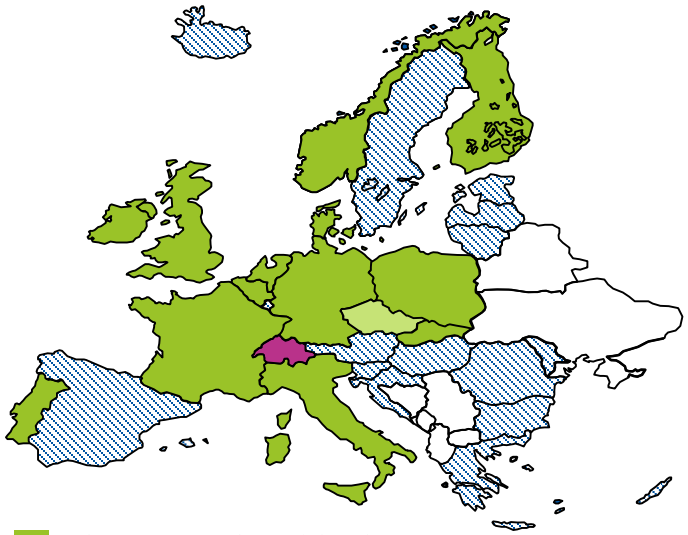
Widespread support for switching biosimilar medicines under supervision of a healthcare person

National guidance



Authorities supporting physician-led switching

Authorities advising against physician-led switching

No public position available

Source: Medicines for Europe Internal Biosimilar Mapping

Regulatory guidance


BioDrugs
DOI 10.1007/s40259-017-0210-0

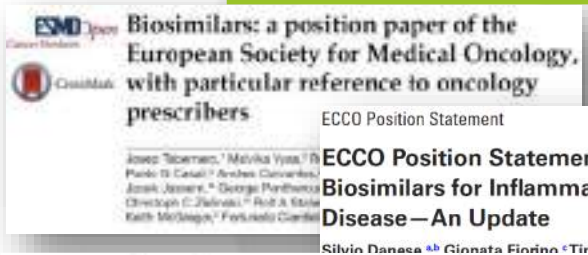
CURRENT OPINION

Interchangeability of Biosimilars: A European Perspective

Pekka Kurki[1] · Leon van Aerts[2] · Elena Wolff-Holz[3] · Thij
Venke Skibeli[5] · Martina Weise[6]

"In our opinion, switching patients from the original to a biosimilar medicine or vice versa can be considered safe."

Clinical guidance


Biosimilars: a position paper of the European Society for Medical Oncology, with particular reference to oncology prescribers


ECCO Position Statement

ECCO Position Statement on the Use of Biosimilars for Inflammatory Bowel Disease—An Update


Consensus-based recommendations for the use of biosimilars to treat rheumatological diseases

Jonathan Kay,[1] Monika M Schoels,[2] Thomas Dörner,[3] Paul Emery,[4] Tore K Kvien,[5] Josef S Smolen,[2,6] Ferdinand C Breedveld,[7] on behalf of the Task Force on the Use of Biosimilars to Treat Rheumatological Diseases

A sustainable policy framework
Multi-stakeholder approach required

- **Sustainable biosimilar medicines market?**
  - Patients
  - Prescribers
  - Payers
  - Industry

- ‘Sustainable policy framework’

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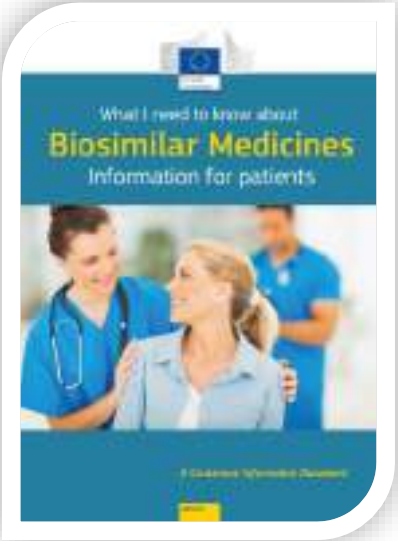
European Commission and EMA leading on stakeholder education on biosimilar medicines

What you need to know about biosimilar medicinal products
European Commission, 2013
(link)



What I need to know about biosimilar medicines – Information for patients
European Commission, 2016
(link)

Biosimilars in the EU – Information guide for healthcare professionals
EMA, 2017
(link)

The impact of biosimilar competition in Europe
QuintilesIMS, 2017
(link)

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In addition, industry supports the dissemination of information resources

[Reading List on Biosimilar Medicines]

[Overview of positions on EU physician-led switching for biosimilar medicines]

IGBA Biosimilars Communication tool kit

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Benefit sharing models: successful driver of biosimilar medicines use in clinical practice

University Hospital Southampton NHS Foundation Trust – Managed Switching

- **Managed switching program – Biosimilar infliximab for IBD**
- Team discussions with physicians – agreement with entire medical staff
- Additional staffing to implement and monitor a safe switch
- Proposed switching program discussed in detail with IBD patient panel
- Additional clinical monitoring and surveillance included at the request of patient panel
- Some of cost-savings being reinvested in improvements of patients' care
- Continuous communication with patients during switch

- 134 patients switched from originator to biosimilar infliximab, only 2 patients have requested review of the switch on medical grounds
- **Estimated savings after 4 months: £293,000**

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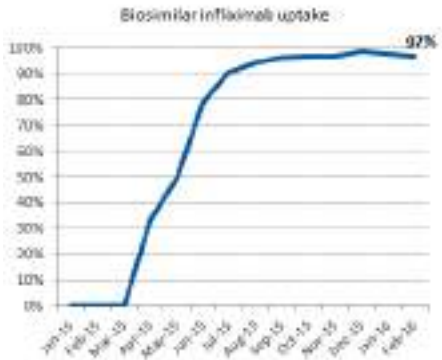
Benefit sharing: successful driver of biosimilar medicines use in clinical practice

Denmark – Good communication and direct benefits for hospitals

- All 5 regions group their tenders → National tender
- Council for Use of Expensive Hospital Medicine (RADS) makes recommendation to national tender body AMGROS
  - Expert physicians in their field included in RADS
- Savings from biosimilar medicines go back to the regional hospitals
- Clear information for patients developed by government in consultation with payers, regulators and physicians

- Attractive prices offered by companies → biosimilar infliximab won the national tender
- Change of RADS guidelines: biosimilar infliximab now first-line product for biological treatment in rheumatology/gastroenterology
- Immediate uptake of biosimilar medicine in clinical practice



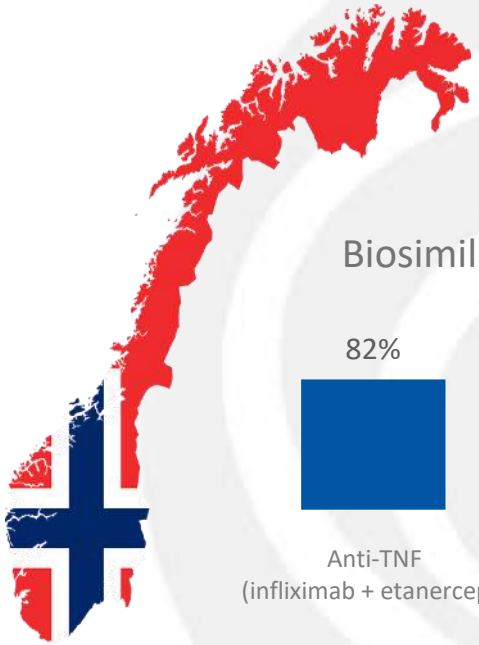
Physician incentives are essential to develop biosimilar medicines market

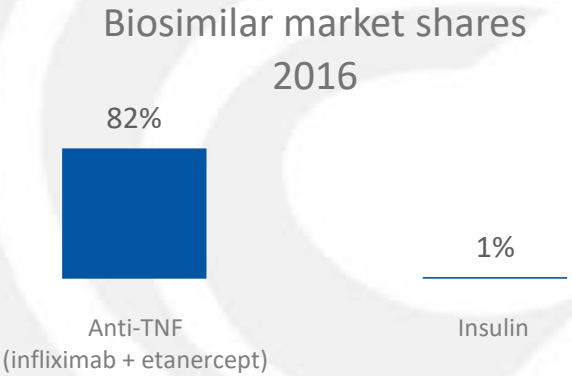
Anti-TNF
- Hospital product
- Financial incentive to prescribe biosimilar medicine

→ **Massive use of biosimilar medicines**

Insulin
- Retail product
- No financial incentive to prescribe biosimilar medicine

→ **Limited use of biosimilar medicines**





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Procurement conditions should allow multiple players on the market

Originator and biosimilar medicines compete in same lot
THERAPEUTIC EQUIVALENCE

Biosimilar medicine enters the market

Re-opening of supply agreement within 60 days

< 3 competitors
free to use single- or multi-winner tender

≥ 3 competitors
Mandatory tenders with 3 preferred products

Physicians remains in central role:

- Must prescribe preferred products (= first 3 classified in the multi-winner tender)
- Therapeutic continuity:
  - Allowed, even if medicine not 'preferred' but medical justification can be asked
  - Not allowed if the medicine did not offer to participate in the framework.

Source: http://www.gazzettaufficiale.it/eli/id/2016/12/21/16G00242/sg

Criteria for sustainable biosimilar market

A sustainable biosimilar market should deliver:

1. Long-term-savings for healthcare system due to fair erosion with adequate volume of prescribed biosimilar medicines
2. Viable business through healthy competition of several manufacturers
    1. Limited changes to pricing & market access policies over time reduce payers' efforts and increase predictability for the industry
    2. Procurement practices allow several manufacturers in the same market (e.g. by regional differentiation or multiple tender lots)
3. Physician education, communication and incentivization to ensure appropriate but cost-conscious prescribing

Source: Simon-Kucher – Policy requirements for a sustainable biosimilar market

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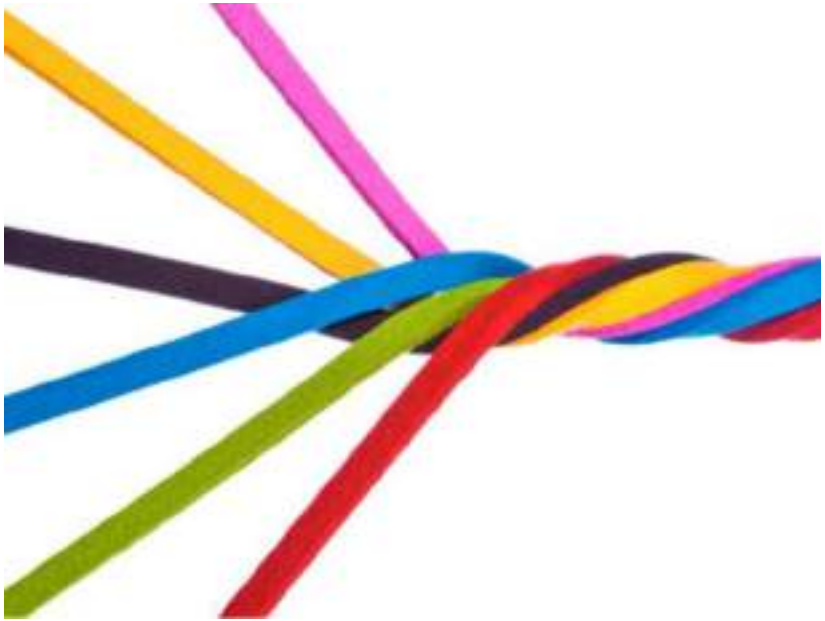
Sustainability is also supported through regulatory efficiency and convergence



- The goal pursued is identical for all: Quality, Safe & Efficacious medicines for patients
- Convergence of regulatory requirements benefits all
  - Regulators & Industry: predictability & efficiency of regulatory processes thanks to common scientific and regulatory science advances
  - Stakeholders: Clear communication and common understanding

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Regulatory Convergence consists in:

The definition of standards

The implemention of standards

Predictability of outcomes
(development and registration processes)

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Roadmap: Low hanging fruit for a streamlined international framework

1. Foreign-sourced reference product (scientifically justified)

2. Alignment of terminology (definitions):
   - Biosimilar medicines (where head-to-head comparison has been carried out)
   - Intended copy biologics

3. Removal of clinical trial requirements involving local patients

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1

Acceptance of a foreign-sourced reference product key for regulatory system efficiency

- The EMA and US FDA changed guidelines (2014 & 2015) to clarify that the reference product could be from a foreign "source" – provided it is the same as the one authorised locally, and some bridging is performed
  - Global nature of the biosimilar sector
  - Unnecessary studies and clinical trials could be waived based on science
- New US FDA Guideline on interchangeability (Jan 2017) creates uncertainty
  - Strong emphasis on clinical study programme involving the US-licensed reference product
  - Undermines the reciprocity of the now well-established single development between the EU and US and the sustainability of biosimilar medicines development

75% of EMA scientific advice procedures included a foreign-sourced reference[1]

Significant opportunity for EU/US collaboration

1. EMA, Peter Richardson

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2

Common tools are supportive of convergence and clarity of communication

95.5% product identification[1]

- While legislation will remain country specific, terminology and definitions should be common for clarity and implementation
  - Biosimilar or biosimilar medicine (biosimilarity based on comparability)
  - Intended copy biologic (other data package)
- EU naming and labelling policies
  - reflect the biosimilarity scientific concepts,
  - have a long standing track record of good traceability during use, in conjunction with batch number recording

1. EMA, Ana Hidlago Simon presentation, Biosimilar Medicines Conference, 23 March 2017

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What if …

4 Clinical study design (e.g. margins and sample size) could converge towards one agreeable standard?

Significant opportunity for EU/US (and beyond) collaboration

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Getting ready for future biosimilar medicines: integrating learnings into regulatory science

5

International regulatory dialogue on clinical requirements including for monoclonal antibodies

- Phase III clinical trials are the least sensitive part of a biosimilar monoclonal antibody development and could be waived based on strong analytical, functional and comparative PK data
- With the growing experience, a review of the clinical regulatory requirements and theoretical risks initially considered in the light of the extensive data available would be beneficial
  - What really adds value / information to the biosimilarity determination?

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WHO leads important convergence initiatives

- Post-Approval Changes guideline for biologic medicines: an important tool streamlining timelines
- The imminent launch of the Prequalification (PQ) procedure for anti-cancer (rituximab and trastuzumab) foresees:
  - A recognition of the scientific assessment for biosimilar medicines already approved by a Stringent Regulatory Authority (SRA)
  - Regulators' capacity building in the field of biosimilar medicines assessment to assess biosimilar candidates not already approved

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International dialogue plays centre role

- There are many international regulatory dialogue platforms as summarised by the EMA in ‘Connecting the Dots’
  - Eg, EMA-FDA cluster, WHO, IPRF
- Clear mandates and objectives ensure coherent progress
- We value the opportunities for industry to engage

http://www.ema.europa.eu/docs/en_GB/document_library/Brochure/2016/10/WC500214180.pdf

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Concluding Remarks

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Biosimilar medicines policies will succeed through coherent and multi-stakeholder approaches

Biosimilars in Europe: 11 years, 28 approvals, 0 safety concerns

By Dan Stanton+

10-May-2017

Last updated on 10-May-2017 at 13:35 GMT

- > 10 years safe experience with clinical use of biosimilar medicines
- Regulatory convergence helps sustainability through agile regulatory science and efficiency gains as well a in support of clear communication to stakeholders
- **Multi-stakeholder approach & benefit sharing essential** to ensure use of biosimilar medicines in clinical practice – **Physicians have an important role to play!**
- Access models and policies **vary throughout Europe** resulting in different impact – commonalities and principles apply beyond the EU
- Continued benefits in the long-term only possible if there is **healthy competition among multiple manufacturers**

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Thank you ! Questions?

The Biosimilars Council
A Division of the Association for Accessible Medicines

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