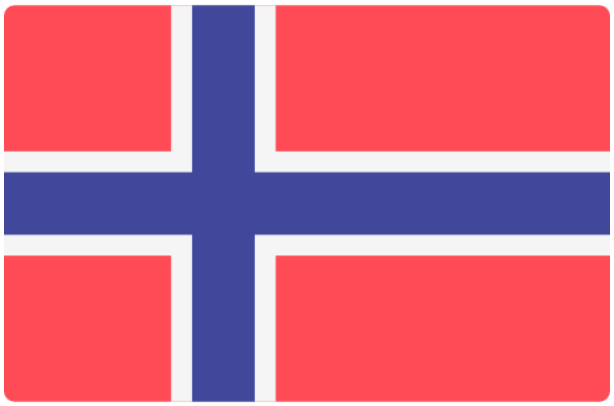
Unlocking the Potential of Biosimilars

A Roadmap for Biosimilar Policy Sustainability

Biosimilar Policy Landscape & Sustainability Assessment

Norway



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Introduction

The adoption of biosimilars can offer significant benefits to stakeholders yet has not been a uniform and equal process across countries. Biosimilar uptake has shown large discrepancies across (and sometimes within) countries.[i, ii] For example, in 2020 the uptake of infliximab biosimilars was 89% in the UK versus 6% in Japan.[iii] Biosimilar utilization can also vary significantly within countries. For example, in a 2021 US study, practice setting (outpatient hospital department vs office practice, and for-profit vs not-for-profit) was found to be a key driver in biosimilar use.[iv] A country's policy environment likely affects the variation in biosimilar success. Assessing the current biosimilar policy landscape and the extent to which current policies support long-term sustainability for biosimilars is critical to understanding the drivers of success, inefficiency and risk areas of biosimilars in any given country.

Methodology

This study presents a global analysis of the biosimilar-specific policies across a wide range of countries. Country-specific policy landscapes are summarised according to an assessment framework of nine policy areas depicted in **Table 1**. Country-specific desk research was conducted to draft policy landscapes and were subsequently validated through 1:1 interviews with country experts.

Table 1 - Policy area assessment framework

	**Manufacturing and R&D**	Policies incentivising local/regional manufacturing or investing in biosimilar R&D
	**Regulatory Approval**	Policies ensuring streamlined or accelerated regulatory pathways at national or regional level
	**Health Technology Assessment**	Policies allowing for reduced or differentiated HTA requirements for biosimilars
	**Pricing & Reimbursement**	Policies mandating price reductions for biosimilars or originator products or affecting reimbursement
	**Contracting**	Policies governing purchasing, including national/sub-national tendering and procurement of biosimilars
	**Biosimilar Education & Understanding**	Policies or initiatives supporting biosimilars education
	**Prescribing**	Policies affecting physician uptake and prescribing
	**Dispensing**	Policies at pharmacy level affecting dispensing of biosimilars
	**Monitoring**	Policies ensuring monitoring of safety and efficacy of biosimilars

Source: CRA

During 1:1 interviews, a sustainability assessment of each policy area was conducted to provide a 'biosimilar sustainability rating'. Based on a literature review, a scorecard was developed and tested with biosimilar policy experts. The scorecard summarises the potential multi-stakeholder benefits of biosimilars using a 5-point 'star rating' scale. (See **Table 2**). In addition to country-specific documents, a cross-country summary and global analysis of the long-term sustainability of biosimilar policies is published in the White Paper 'Unlocking the Potential of Biosimilars: A Global Roadmap for Biosimilar Policy Sustainability'.[v]

Table 2 – 5-point 'star rating' scale

★★★★★	The policy area is considered to be sustainable **for all stakeholders**
★★★★☆	Some **minor areas** for improvement were identified to result in a fully sustainable environment, however no unsustainable policies impact the area
★★★☆☆	Some **major areas** for improvement were identified to result in a fully sustainable environment, however no unsustainable policies impact the area
★★☆☆☆	There are sustainable policies in place which are being negated by the **presence of unsustainable policies** in the same/different policy area
★☆☆☆☆	The (lack of) policies in place are considered to **actively contribute to an unsustainable policy environment** for the majority of stakeholders

Source: CRA

Summary

	**Manufacturing** and R&D	No specific manufacturing and R&D policies were identified in Norway. Around 90% of total market is supplied by manufacturers from 3 foreign countries, as there are no producers of biosimilars in Norway.	★★★★★	Biosimilars are held to the same manufacturing standards as originator products therefore quality is maintained. Manufacturing can begin before originator LoE facilitating supply at launch while still observing the full exclusivity period of the originator product.
	**Regulatory Approval**	As a member of the European Economic Area (EEA) Norway follows the regulation (EC) No 726/2004 for centralized marketing authorization from the European Parliament	★★★★☆	Current evidence requirements are slightly streamlined and therefore can result in slightly faster access to biosimilars. However, recent research indicates that comparative clinical studies are not required for all biosimilar products and reducing the need for this evidence and/or implementing formally accelerated timelines could offer further regulatory efficiencies.
	**Health Technology Assessment**	Biosimilars are not required to undergo an HTA assessment. Only a price submission is required for access.	★★★★★	Lack of HTA requirements accelerates biosimilars access and avoid potential delays regarding bureaucracy.
	**Pricing & Reimbursement**	Biosimilar list prices are set through free-pricing mechanisms provided the list price does not exceed originator price levels. Inpatient biosimilar net prices are subsequently determined through tenders. Outpatient biosimilars are subject to progressive price discounts which increase over time considering both the level of market competition and the AIP and turnover of drugs during their commercialisation. In both cases, net prices are kept confidential.	**Inpatient:** ★★★★★ **Outpatient:** ★★★★☆	Free pricing without exceeding the originator's price ensures cost savings upon biosimilar entry and encourages price competition driven by market dynamics. Further net price discounts are applied through tendering mechanisms (see 'contracting'). Free pricing without exceeding the originator's price ensures cost savings upon biosimilar entry and encourages price competition driven by market dynamics. Moreover, applying lower discounts to biosimilars vs small molecule generics indicates there is recognition of their differences. However, the use of progressive discounts bound to the level of competition and product turnover can decrease predictability for manufacturers already in the market.
	**Contracting**	In the inpatient setting, public tender procedures run nationally with regional health	**Inpatient:** ★★★☆☆	Multi-winner contracts have recently been introduced in Norway to expand competition

		authorities (RHAs) input and are awarded predominantly on price. Tenders include all products that prescribing physicians deem to be clinically equivalent products (i.e. products placed equally within treatment guidelines, including originators) for a given indication. Past supply shortages have led to the establishment of multi-winner tenders, although price still governs the awarding In the outpatient setting, biosimilars are contracted and distributed by three main pharmacy chains and price negotiations are kept confidential	**Outpatient:** ★★★★☆	which, based on feedback gathered in this research, can help to avoid supply shortages. Moreover, a national tendering approach that allows for additional regional and specialist input ensures multi-stakeholder input in decision making. However, considering factors beyond price for contract awarding could further improve perception of biosimilars, and inclusion of originators in tenders might affect innovation and R&D in the long-term. Direct price negotiations with manufacturers have resulted in broad access to biosimilars and good uptake. However, individual negotiations to provide access to biosimilars can be an inefficient contracting route.
	**Biosimilar Education & Understanding**	NoMa's educational efforts have focused on HCP education to promote the perception that all biologics have batch-dependent variations	★★★★★	Governmental efforts to promote health education has managed to dramatically change HCPs negative perception and boost biosimilar access and competition, driving considerable cost savings
	**Prescribing**	Physicians need to follow a ranking established for drugs when prescribing. This ranking is developed by the Sykehusinnkjøp HF based on price and tendering. Pre tendering procedures receive input from HCPs. Physicians need to provide valuable clinical reasons to prescribe medicines not being the first-choice recommendation, but they are allowed to do so	★★★★★	Prescribing policies in the country have managed a high uptake of biosimilars and driven high-cost savings. Physicians' input to tendering procedures ensures that formulary lists consider clinical perspective, and clinical rationale still needs to be provided when other products are preferred
	**Dispensing**	Automatic substitution in Norway allowed from July 2021, although inclusion of products in the substitution list is considered on an individual basis. INN prescribing used in the country	★★★★☆	Individual analysis of products for substitution ensures clinical perspective considered before automatic substitution is applied. Periodic substitution lists to boost uptake coupled with educational campaigns have generally ensured sustainable access for biosimilars, although a transparent and traceable system with multi-stakeholder input is required.
	**Monitoring**	The monitoring system implemented in Norway assigns a unique identifying number	★★★★☆	Monitoring system tracing batch-dependent AE can improve the understanding of biosimilars'

		to each batch of biosimilars. This identifier is directly noted onto the patient's health record upon dispensing of drugs.AE registration is based on the individual HCP to do so.		value and provide a fast system to control their access if issues arise. AE monitoring could be improved through easier and faster systems for HCPs to register an individual patients AE

Key Successes, Areas for Improvement & Risk Areas

Key Biosimilar Policy Successes
▲ Efforts by the Norwegian government have resulted in high biosimilar market penetration
▲ Allowance of product substitution on an individual, product-by-product basis ensures that physicians retain a good level of autonomy and decision making power over prescribing decisions. Similarly, physician input to tendering lists further supports this
Key Biosimilar Policy Areas for Improvement
► While some tenders still allow for single winners, there has been increased consideration of multiple (typically two) winner tenders in the country which could be expanded
► AE monitoring could be improved through easier and faster systems for HCPs to register an individual patients AE
Key Biosimilar Policy Risks
▼ Tenders awarded to single winners leave an open door for potential supply shortages and delivery problems, as has already been observed in the country in a couple of occasions.
▼ The important weight that price takes in tender awarding allows for substantial price discounts, which could disincentivise participation and lead to reduced levels of competition. However, this might not be the situation in the future.
Key Biosimilar Policy Priorities to Achieve Long-Term Sustainability in Norway
1. TBD

Policy Landscape Assessment

Manufacturing and R&D

Manufacturing Exemption Waiver

The manufacturing of biosimilars (and generics) can begin prior to the expiry of the originator's patent exclusivity in a similar manner to that permitted by EU legislation. However, and also equal to the EU regulation, biopharmaceutical products can be covered by more than one patent family – e.g., by compound, process, formulation, use.

Norway has in general very little pharmaceutical production. Currently, no biological drugs including biosimilar drugs are produced in Norway. It is recently claimed from the new government that they want more production, including biological drugs, in Norway.

No specific manufacturing and R&D policies for biosimilars were identified in Norway. Around 90% of the total pharmaceutical market in the country is supplied between three main foreign manufacturers.

Regulatory Approval

Streamlined evidence requirements

Norway, as member of the European Economic Area (EEA) together with Iceland and Liechtenstein follows the regulation (EC) No 726/2004 for centralized marketing authorization from the European Parliament.[vi]

The centralised procedure for granting regulatory approval of biosimilars was first introduced by the EMA in 2004 (Regulation n. 726/2004).[vii, viii] The Committee for Medicinal Products for Human Use (CHMP) regulates the authorization of biologics. The process aims at **providing enough evidence to demonstrate a high degree of similarity between the biosimilar and its reference product.** Therefore, no data needs to be acquired in terms of clinical benefit, as this is already provided by the reference product.[ix]

The process to demonstrate biosimilarity consists of three different steps. Firstly, thorough physic-chemical and biological analyses are developed to demonstrate proper quality of the product, as well as its toxicology. This is followed by a second step of non-clinical (pre-clinical) trials to compare pharmacodynamics and pharmacokinetics. The final step aims at demonstrating clinical comparability between the biosimilar and the reference product, and is developed via clinical trials to demonstrate safety, efficacy and immunogenicity.[x,xi]

Immunogenicity data needs to be collected for one year before the CHMP allows marketing authorisation, and maintained later on for long-term pharmacovigilance purposes.[xii] Immunogenicity factors are listed in the guidelines (e.g., anti-drug antibodies (ADAs)) but risk assessments are encouraged to be developed on a product-specific basis, as immunogenicity is hard to foresee.[xiii] **Extrapolation of indications is permitted by the EMA once biosimilarity has been demonstrated for at least one, when the scientific justification is granted**.[xiv]

Health Technology Assessment

No biosimilar HTA requirements

In Norway, biosimilars are not required to undergo an HTA assessment. Only a price submission is required for access.[xv] This does not apply in those cases where originators are not reimbursed for a given indication, in which case biosimilars need to undergo HTAs.

Pricing & Reimbursement

Reference pricing

Price of medicinal drugs in Norway are calculated based on the maximum Pharmacy Purchase Price (*Norwegian: apotekens inköpspris*, AIP) and the maximum Pharmacy Selling Price (*Norwegian: apotekens utförsäljningspris, AUP*).[xvi] **External reference pricing is used to set the AIP for newly developed drugs (i.e. originators) in Norway**. In the case of biosimilars, the AIP cannot exceed the price of the reference originator product and, within this limitation, biosimilar prices are set via free-pricing mechanisms by the manufacturers.[xvii] In addition, reimbursement of biosimilars is not only based on the originator price, but also on any other biosimilars already existing for the molecule.[xviii]

Progressive price discounts

The original price discount set for outpatient biosimilars when they enter the market is not static. It keeps increasing with time and as the market competition gets higher.[xix] Such discounts take into account the *AIP* and the turnover of drugs during a certain amount of time after their commercialization. When the turnover (measured through *AUP*) of biologic drugs or biosimilars exceeds a certain value, further discounts apply.[xx] Price revisions can only happen at the earliest 12 months after the last price cut has been made. The thresholds applied are as follows:

- 60% discount for biological and bioequivalent medicinal products if the turnover exceeds NOK 15 million
- 75% discount for biological and bioequivalent medicinal products if the turnover exceeds NOK 30 million
- 80% discount if the turnover exceeds NOK 100 million.

The discounts applied for biological and bioequivalent medicinal products are lower than the discounts applied to generic products (69%, 88% and 90% respectively) indicating that there is recognition that biosimilar products should be treated differently to small molecule generics.

Contracting

Scope of contracts

In Norway, tenders for inpatient biosimilars are run when a specific therapeutic area or indication is considered by clinical specialists to have a sufficient number of clinically equal products available for its

treatment in the inpatient setting, this includes products even with different INNs. [xxi] **Public tender procedures are run nationally but have input from the hospital level through regional health trusts (RHTs).** There are four RHTs funded by the government, which teamed up to build the **organizations for buy for hospital and health** (Norwegian: *Sykehusinnkjøp HF Divisjon legemidler,* old LIS). The responsibility of the LIS is to procure pharmaceuticals for specialised health services and to conduct price negotiations for new drugs on behalf of the four RHTs. To do this, the LIS needs to align hospital preferences with supplier agreements, taking into consideration preferred drugs by hospitals for its recommendations to the buyers. .[xxii] On the other hand, biopharmaceuticals for the outpatient setting are contracted and distributed by three main pharmacy chains and price negotiations are kept confidential, although steep price reductions are obtained in the end.

Single-winner contracts

Biosimilars have been involved in national annual tenders in Norway since 2015, when infliximab first entered the market.[xxiii] The tendering process in Norway allows a single winner, resulting in high price discounts from originators. However, the **Norwegian Pharmaceutical Industry Association (LMI) has proposed the winning of two suppliers in tendering contracts with guaranteed market shares.[xxiv]**

Contract decision criteria

Since equal clinical performance is a requirement for drugs to enter the tender and no comparative added values are expected there, contracts are awarded **mostly on price criteria, although** prices are no longer published in Norway since 2017.[xxv] Tendering is organised by the Sykehusinnkjøp HF and allows for large price reductions, even going higher than 60%. This system, in conjunction with other initiatives in Norway, has resulted in a **market share of biosimilars to increase to up to 95%.**

Contract length

The length of tenders is 12-24 months.[xxvi]

Biosimilar Education & Understanding

HCP educational programs

It has been reported that most Norwegian GPs had an “anti-biosimilar understanding” approach that was presenting a decisive barrier for the proper adoption of biosimilars in the country.[xxvii] NoMa’s efforts have focused on HCP education to promote the perception that all biologics have batch-dependent variations and, therefore, not only biosimilars present differences from their originator.[xxviii]

In addition, the EMA’s official webpage includes information about biosimilars and document to properly educate HCPs. Such documents were last updated in September 2019 and are currently available in 23 different languages. The information has been created gathering opinions from EU scientific experts (e.g., Doctors, nurses, pharmacists).[xxix, xxx]

Patient educational programs

Patients in Norway are believed to be less sceptical about biosimilars, although, equally to generics, there are still concerns about switching from originators despite efforts from the Norwegian government such as the commissioning of the NOR-SWITCH study was commissioned in 2017.[xxxi]

Additional to the online documents available in the EMA's webpage, other patient-friendly resources are available. An animated video was created, also in a wide scope of languages, clarifying key factors for these medicines for patients.[xxxii] The European Commission has also created manuals to raise patient awareness around biosimilars.[xxxiii]

Prescribing

Non-medical switching

Switching is not compulsory in the country, although physicians need to **follow a ranking established for drugs when prescribing. This ranking is developed by the LIS based on price and tendering**. This leads to a big market share from biosimilars, as they are normally the least expensive option. When necessary, physicians can prescribe medicines which are not first choice (but they have to be on the list).

In 2017, the **NOR-SWITCH study** was commissioned by the Norwegian government to **develop an efficacy and safety comparison of infliximab biosimilar with its reference product**. The results from the trial established no difference between the two molecules, confirming non-inferiority of biosimilars.[xxxiv] This study was actually run to demonstrate the possibility of drug switching for future policy and decision-making, although the study itself did not test for multiple switching, therefore the evidence provided was still considered limited. Currently, **the NoMA leaves for physicians and hospitals the decision for switching from reference products to their biosimilars, always requiring the physician to inform the patient.**[xxxv]

Dispensing

Automatic substitution

The law regulating automatic substitution in Norway was updated in July 2021 to allow and partly enforce biosimilar substitution. The NoMA proposed in 2012 the inclusion of biosimilars in the substitution list to be added in the Pharmacy act.[xxxvi] The substitution list, which includes all types of drugs and is updated monthly and available at the NoMA's webpage, is implemented to allow for automatic substitution at the pharmacy level and have now started to include biosimilar products (e.g., insulin glargine and follitropin alpha). The inclusion of products in the substitution list is evaluated individually by a committee of experts, although the used criteria are unknown.

Monitoring

Pharmacovigilance measures

The monitoring system implemented in Norway assigns a unique identifying number to each batch of biosimilars. This identifier is directly noted onto the patient's health record upon dispensing of drugs. This allows a straight-forward tracing of any batch-dependent adverse side effects or immunogenicity.[xxxvii] However, AE reporting among physicians is poorly regulated, resulting in low levels of tracing despite robust systems being in place.

Bibliography

i Rémuzat, C., et al. (2017). "Key drivers for market penetration of biosimilars in Europe". Available at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5328350/

ii Barbier, L. (2021). "Sustainable biosimilar competition". Available at https://limo.libis.be/primo-explore/fulldisplay?docid=LIRIAS3601109&context=L&vid=Lirias&search_scope=Lirias&tab=default_tab&lang=en_US&fromSitemap=1

iii Kim, Y. et al (2020). "Uptake of Biosimilar Infliximab in the UK, France, Japan, and Korea: Budget Savings or Market Expansion Across Countries?". Available at https://www.frontiersin.org/articles/10.3389/fphar.2020.00970/full#:~:text=The%20share%20of%20infliximab%20biosimilar,point%20in%20the%20data%20set.

iv Boswell Dean, E., Johnson, P. and Bond, A.M. (2021). "Physician, Practice, and Patient Characteristics Associated With Biosimilar Use in Medicare Recipients". Available at https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2775641

[v] Charles River Associates (2022). "Unlocking the potential of Biosimilars: A Global Roadmap for Biosimilar Policy Sustainability". Available at https://www.biosimilarsroadmap.com.

[vi] Moorkens et al. (2017) "*Policies for biosimilar uptake in Europe: An overview*". Available at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5746224/pdf/pone.0190147.pdf

[vii] European Medicines Agency (EMA). (n.d.). "Biosimilars in the EU – Information guide for healthcare professionals". Available at https://www.ema.europa.eu/en/documents/leaflet/biosimilars-eu-information-guide-healthcare-professionals_en.pdf

[viii] European Medicines Agency (EMA). (n.d.). "Biosimilar medicines: marketing authorisation". Available at https://www.ema.europa.eu/en/human-regulatory/marketing-authorisation/biosimilar-medicines-marketing-authorisation#2.-steps-prior-to-submitting-the-application-section

[ix] Gherghescu et al. (2021). "*An overview of regulatory approvals by the EMA and FDA*". Available at https://www.mdpi.com/1999-4923/13/1/48/pdf

[x] Gherghescu et al. (2021). "*An overview of regulatory approvals by the EMA and FDA*". Available at https://www.mdpi.com/1999-4923/13/1/48/pdf

[xi] Biosimilar Medicines. (2016). "*Biosimilar medicines handbook*". Available at https://www.medicinesforeurope.com/wp-content/uploads/2016/04/BIOSIMILAR-MEDICINES-HANDBOOK_INT_web_links2.pdf

[xii] Medicines Evaluation Board. (n.d.). "Biosimilar medicinal product". Available at https://english.cbg-meb.nl/topics/mah-biosimilar-medicinal-product

[xiii] Kurki, P. (2019). "Compatibility of immunogenicity guidance by the EMA and the US FDA". Available at https://pubmed.ncbi.nlm.nih.gov/30672313/

[xiv] CHMP. (2014). "Guideline on similar biological medicinal products". Available at https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-similar-biological-medicinal-products-rev1_en.pdf

[xv] GaBI (2017). "What pricing and reimbursement policies to use for off-patent biologicals in Europe? – results from the second EBE biological medicines policy survey". Available at http://gabi-journal.net/what-pricing-and-reimbursement-policies-to-use-for-off-patent-biologicals-in-europe-results-from-the-second-ebe-biological-medicines-policy-survey.html

[xvi] Lovdata. (2009) "*Regulations on medicinal products (medicines regulations)*". Available at https://lovdata.no/dokument/SF/forskrift/2009-12-18-1839/KAPITTEL_13#%C2%A712-15

[xvii] Moorkens et al. (2017) "*Policies for biosimilar uptake in Europe: An overview*". Available at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5746224/pdf/pone.0190147.pdf

[xviii] IQVIA. (2020) "*White Paper Advancing Biosimilar Sustainability in Europe*". Available at https://www.iqvia.com/insights/the-iqvia-institute/reports/advancing-biosimilar-sustainability-in-europe

[xix] Pant et al. (2018) "*International policies on the appropriate use of biosimilar drugs*". Available at https://www.cadth.ca/sites/default/files/pdf/es0333_international-policies-on-use-of-biosimilar-drugs.pdf

[xx] Lovdata. (2009) "*Regulations on medicinal products (medicines regulations)*". Available at https://lovdata.no/dokument/SF/forskrift/2009-12-18-1839/KAPITTEL_13#%C2%A712-15

[xxi] IMS. Institute for Healthcare Informatics. (2016) "*Delivering on the Potential of Biosimilar Medicines. The Role of Functioning Competitive Markets*". Available at https://www.medicinesforeurope.com/wp-content/uploads/2016/03/IMS-Institute-Biosimilar-Report-March-2016-FINAL.pdf

[xxii] JHPOR. (2014). "*Drug procurement cooperation (LIS) – Norwegian tender system to reduce cost of expensive medicines*". Available at https://www.jhpor.com/article/1312-drug-procurement-cooperation-lis---norwegian-tender-system-to-reduce-cost-of-expensive-medicines

[xxiii] GaBI. (2015) "*Norway, biosimilars in different funding systems. What works?*" Available at http://gabi-journal.net/norway-biosimilars-in-different-funding-systems-what-works.html

[xxiv] HIS Markit. (2018) "*Norwegian pharma industry calls for tendering and IRP reforms*". Available at https://ihsmarkit.com/research-analysis/norwegian-pharma-industry-calls-for-tendering-and-irp-reforms.html

[xxv] Barbier, L., et al. (2021) "*Off-patent biologicals and biosimilars tendering in Europe – A proposal towards more sustainable practices*". Available at https://www.mdpi.com/1424-8247/14/6/499

[xxvi] Moorkens et al. (2017) "*Policies for biosimilar uptake in Europe: An overview*". Available at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5746224/pdf/pone.0190147.pdf

[xxvii] AJMC. (2017) "*Learning from the Norwegian experience with Biosimilars*". Available at https://www.centerforbiosimilars.com/view/learning-from-the-norwegian-experience-with-biosimilars

[xxviii] Madsen, S. (2018) "*Regulation of biosimilars and success factors for uptake in clinical practice*". Available at https://www.afmps.be/sites/default/files/content/biosimilar_brussels_2018-02-08.pdf

[xxix] ESMO. (2019). "*EMA guide on biosimilars for healthcare professionals available now in 23 official EU languages*". Available at https://www.esmo.org/oncology-news/ema-guide-on-biosimilars-for-healthcare-professionals-available-now-in-23-official-eu-languages

[xxx] European Medicines Agency (EMA) (n.d.) "Biosimilar medicines: Overview". Available at https://www.ema.europa.eu/en/human-regulatory/overview/biosimilar-medicines-overview#regulatory-guidance-section

[xxxi] Madsen, S. (2018) "*Regulation of biosimilars and success factors for uptake in clinical practice*". Available at https://www.afmps.be/sites/default/files/content/biosimilar_brussels_2018-02-08.pdf

[xxxii] GaBI Online (2021). "*Education for biosimilars in Europe and the US*". Available at https://gabionline.net/reports/Education-for-biosimilars-in-Europe-and-the-US

[xxxiii] European commission. (2016). "*What I need to know about biosimilar medicines – Information for patients*". Available at https://ec.europa.eu/docsroom/documents/26643

[xxxiv] Jorgensen, K.K., et al. (2017) "*Switching from originator infliximab to biosimilar CT-P13 compared with maintained treatment with originator infliximab (NOR-SWITCH): a 52-week, randomized, double-blind, non-inferiority trial*". Available at https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(17)30068-5/fulltext

[xxxv] Pant et al. (2018) "*International policies on the appropriate use of biosimilar drugs*". Available at: https://www.cadth.ca/sites/default/files/pdf/es0333_international-policies-on-use-of-biosimilar-drugs.pdf

[xxxvi] Mondaq. (2012) "*Norway: automatic substitution of biologicals in Norway*". Available at https://www.mondaq.com/life-sciences-biotechnology-nanotechnology/206788/automatic-substitution-of-biologicals-in-norway

[xxxvii] AJMC. (2017) "*Learning from the Norwegian experience with Biosimilars*". Available at https://www.centerforbiosimilars.com/view/learning-from-the-norwegian-experience-with-biosimilars

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