White Paper

The Impact of Biosimilar Competition in Europe

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Introduction

‘The Impact of Biosimilar Competition in Europe’ report describes the effects on price, volume, and market share following the arrival of biosimilar competition in Europe. The report consists of: observations on competitive markets, and a set of Key Performance Indicators (KPIs) to monitor the impact of biosimilars in 23 European markets.

The report has been a long-standing source of information on the status of the biosimilars market. This iteration has been delayed due to the COVID-19 pandemic across the globe and has provided an opportunity to provide full-year 2019 data, and an additional data point (June 2020 MAT) which incorporates the impact on patients in Europe across major therapeutic areas to 30th June 2020. The direct impact of which is visible in the Low Molecular Weight Heparin (LMWH), and Fertility (somatropin) markets.

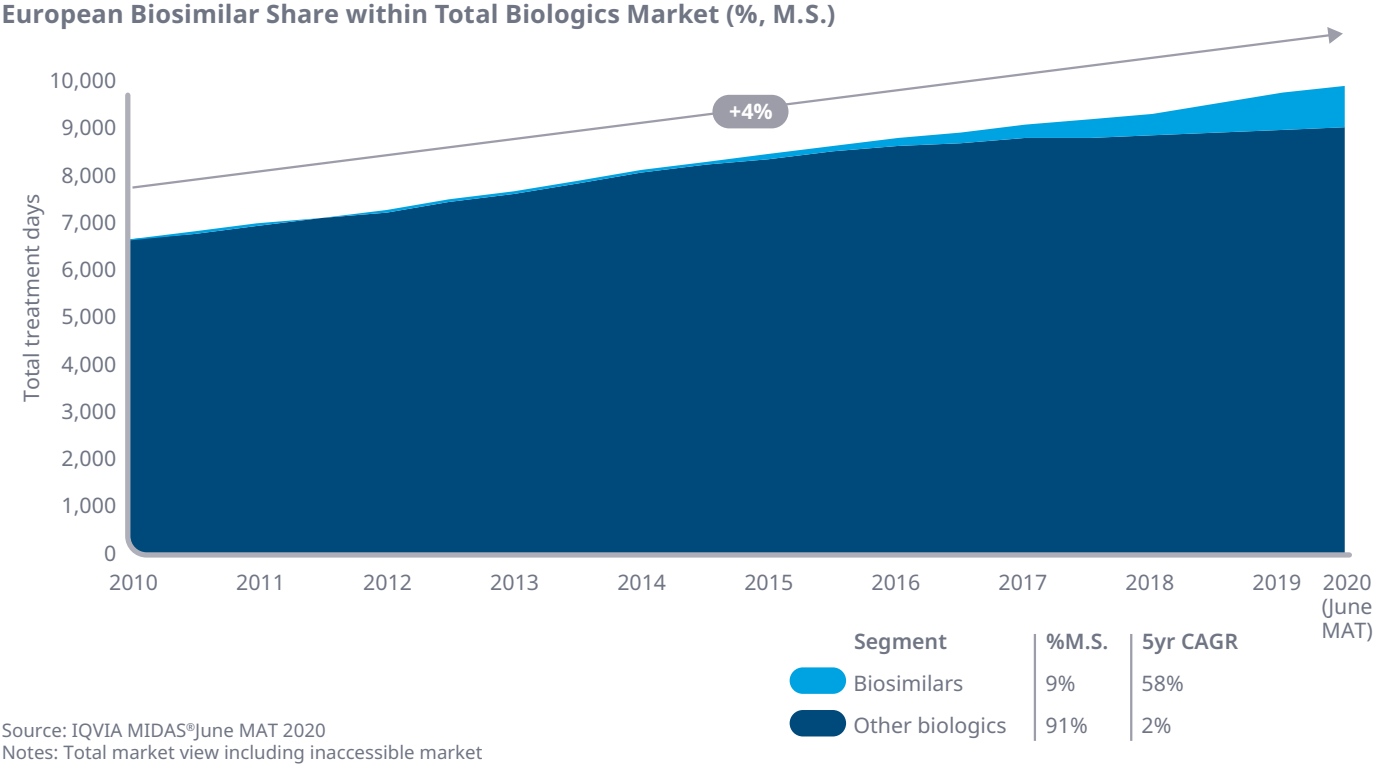
This report has been prepared by IQVIA at the request of the European Commission services with initial contributions on defining the KPIs from EFPIA, Medicines for Europe, and EuropaBio. The observations have been developed solely by IQVIA based on the data and analyses performed. The information and views set out in this report are those of its authors and are not to be attributed to, nor necessarily reflect the views of the European Commission or any of its services.

The European Medicines Agency (EMA) has a central role in setting the rules for biosimilar submissions, approving applications, establishing approved indications and monitoring adverse events, and if necessary, issuing safety warnings.
We have, when appropriate, quoted their information and statements.

Key observations

Biologic medicines have reached €8.4 billion, and represent 9%* of the total biologics market in 2020. However, their growth is dramatic (~60% year-on-year). IQVIA's "5 Observations on the Impact of Biosimilar Competition" for 2020 reflects upon the historic learnings, current progress, and future potential of biosimilar competition in this emergent market.

European Biosimilar Share within Total Biologics Market (%, M.S.)



Source: IQVIA MIDAS®June MAT 2020
Notes: Total market view including inaccessible market

1. SAVINGS: BIOSIMILAR COMPETITION CONTINUES TO OFFER OPPORTUNITIES TO MAKE HEALTHCARE SAVINGS

There are two components of price savings to consider when assessing the impact of biosimilars. The first is the visible price saving at list-price level, and the second is the confidential discount. In combination, these two elements allow countries to reduce their overall budgets, invest in innovation, and increase biologic usage.

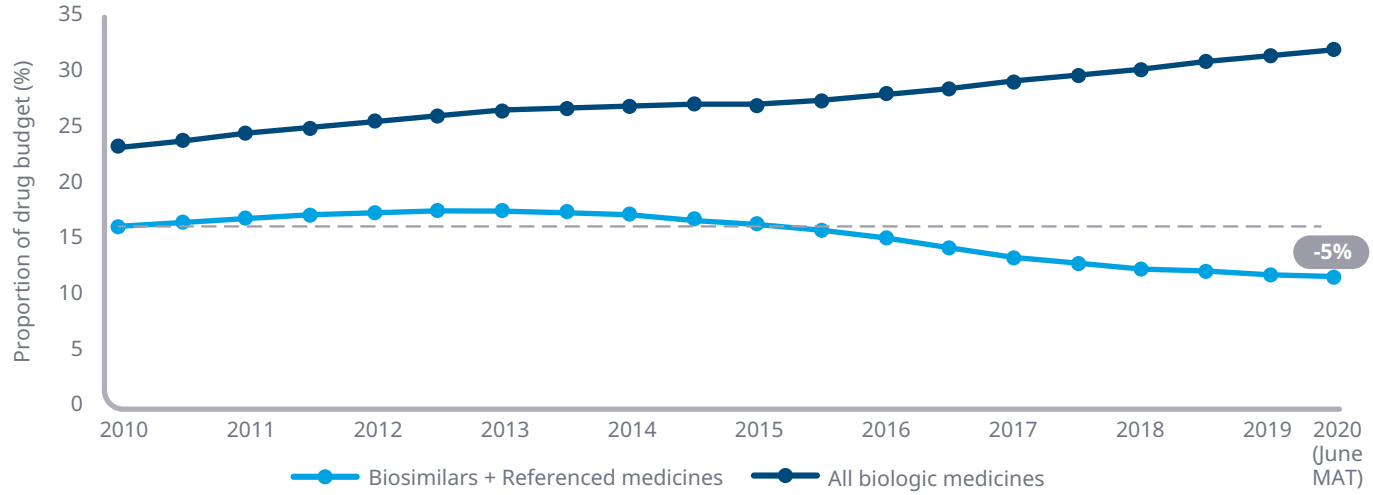
1.1 Visible savings on list prices have reduced drug budgets by around 5% since 2014

In different markets, we see highly variable 'visible' list price reductions (HGH -14%; EPO -67%; GCSF -56%; Anti-TNF -17%; Insulins -7%; Fertility -44%; LMWHs -27%; Oncology -12%). The variation is dependent on the system and product, and are much smaller than the confidential rebates.

In the exhibit below, list price changes in the 'accessible'[1] market have reduced the cost of markets with biosimilar competition by almost 1/3, showing the potential that biosimilar competition has to produce transparent savings. This impact is offset by the increase spend on other biological medicines (without biosimilar competition), and is likely even more significant.

[1] Accessible market refers to the combined contribution of the referenced, biosimilar, and non-referenced medicines. Refer to methodology section for full definitions, and further details.
It is noted that measuring market shares in value, regardless of applicable measurement challenges when it comes to capturing net prices, may yield a lower share for biosimilars as value-based pricing incentives imply unit prices per DDD will be lower for repeat-use products in chronic indications. However, the latter products will represent higher volumes of total DDD aggregates.

Biologic Accessible Medicines as a Proportion of the Total Drug Budget (Rx only)



Source: IQVIA MIDAS® June MAT 2020 (Rx only)

Notes: Biologic accessible market includes: referenced medicines, non-referenced medicines, and biosimilar molecule sales at list price (excluding rebates and discounts) in local currency Euros between 2010 and 2020.

1.2 Confidential savings could offer a further 5-10% saving to the overall drug budget

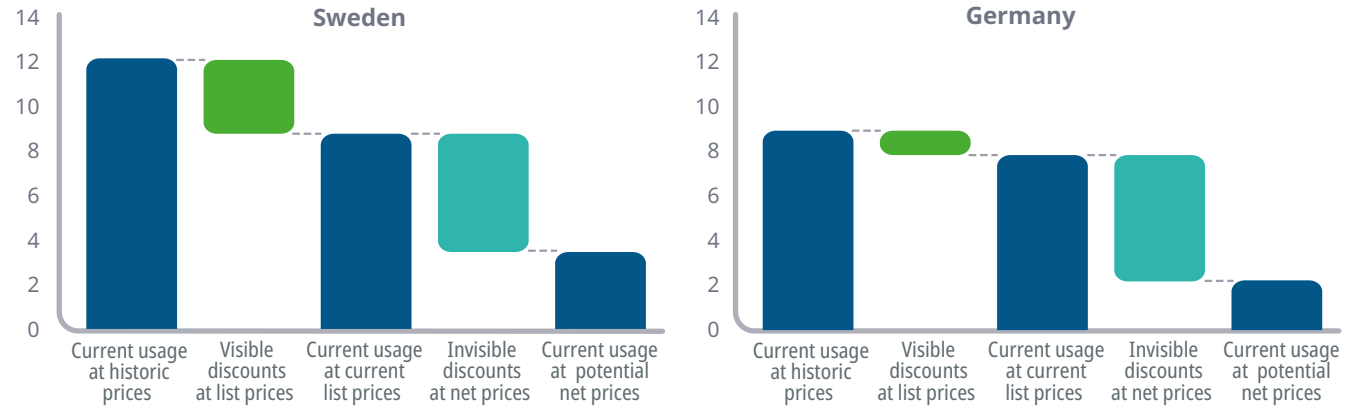
The second segment to consider is confidential rebates. Rebates and confidential discounts can be between 10% - 90% of the list price dependant on maturity or market structure. Rebates and commercial discounts to payers are commercially sensitive and it is not unusual to see variation even at a sub-national level. However, confidential discounts may come with drawbacks that in the longer run may paradoxically hamper competition in the market. Diminished price transparency may imply potential market entrants do not readily understand the effective market price at which they could compete. Further, managed entry agreements ideally incorporate a form of horizon to ensure that commitments under the MEA do not to inhibit competition by follow-on products.

The level of true savings is influenced by several factors, such as: original list price within a country, how tendering is set-up, implementation, and use.

The exhibit below shows: list price reductions, data from IQVIA's hospital panels, and public information on rebates, to create an estimate of savings potential. The methodology is based on net prices observed in countries where transparency exists (e.g. public announcements, and transparent hospital systems) and on the ability for other markets to achieve similar net prices.

Two example markets are chosen with: reliable net price reduction figures (Sweden), and where low list price reductions likely hide high confidential discounting (Germany). The model shows a hypothetical perspective on a real situation.*

Visible and Potential Confidential Discounts (% of Drug Budget)



Source: Modeling based on IQVIA MIDAS® June MAT 2020, and public sources

*It is stressed that these savings are relative to an assumed projection and to some extent may not have materialized as market volume may have shifted to protected follow-on biologics (see section 3).

The overall savings potential is not solely dependent on the size of the rebates. It is heavily influenced by price reduction, and the countries' level of usage in the first place to make a substantial saving. Countries with historically low usage will struggle to achieve significant savings.

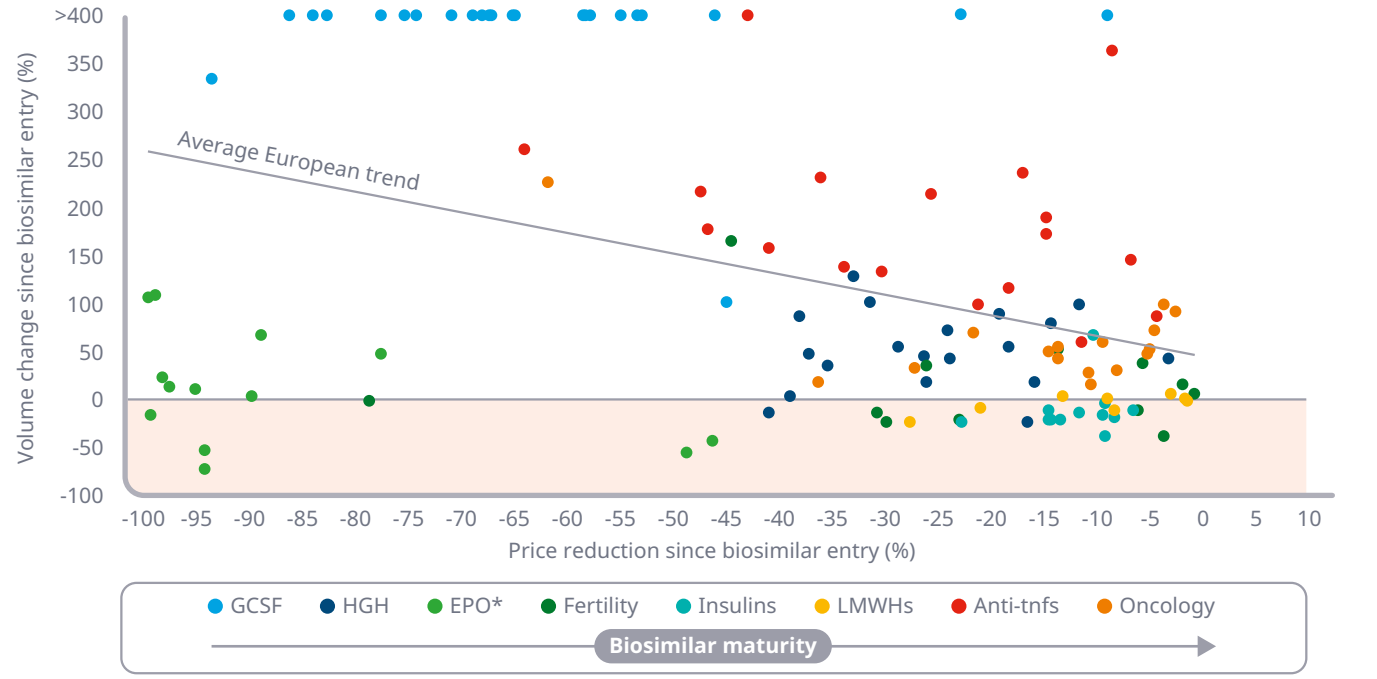
2. USAGE: SOME COUNTRIES ARE NOT INCREASING USAGE DESPITE PRICE REDUCTIONS

One of the core assumptions for the impact of biosimilar competition is that 'lower prices should result in more patients treated'. This is not always the case, and in many instances the reverse is seen as fewer patients are treated after biosimilar introduction.

2.1 Lower cost of treatment does not automatically increase access

In most cases lower prices do increase usage. By viewing the relationship between cost and volume for the major therapeutic segments it becomes clear that there are many instances where a lower price has not translated into increased volume. In 21% of cases, lower prices have resulted in a lower volume of patients treated after biosimilar entry. This phenomenon is relevant to insulins (12 countries), LMWHs (6 countries), EPO (5 countries), Fertility (6 countries), and a few cases in HGH (2 countries).

Relationship Between Falling List Prices and Increased Access in Europe (%, TDs)



Source: IQVIA MIDAS® June MAT 2020

Notes: *EPO accessible market includes Aranesp (darbepoetin alfa) which is a significantly lower cost product that the other referenced medicines. This results in the overall price category appearing artificially low.

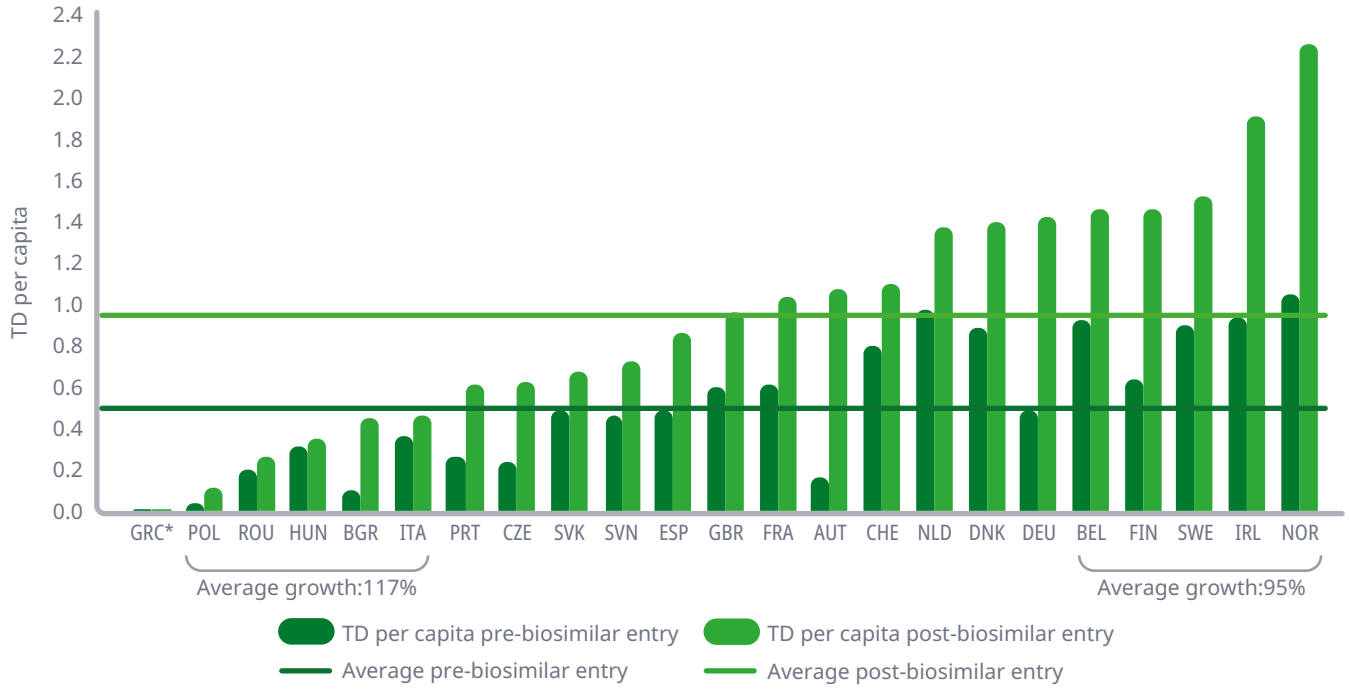
These cases are not specific to a region, and are found in major EU5 markets, Nordic markets, and Central & Eastern European Markets. The most significant examples include Hungary, Romania, and France where >80% list price discounts are seen, coupled with volume reductions of 10% - 20%. It could be argued that this is to support the increased usage of another treatment, but only if the same number of patients were treated. These products saw significant growth in newer areas indicating a shift in treatment patterns. By contrast, GCSFs (as the oldest running class of medicines accessible to biosimilars) have seen vast growth over the 14-years of biosimilar competition.

This could be the movement of patients in the insulin market to the inaccessible segment, and safety considerations related to EPO, as well as the additional more complex to measure considerations such as changes in prescription policies.

2.2 Countries with high growth may still have low usage

One of the persistent expectations of biosimilar competition has been that in countries with a low starting usage per capita a lower cost would increase the usage. Analysing the anti-TNF class, it is important to separate 'high growth' from 'high usage'. Many markets with low usage of the originator biologic often see high growth upon biosimilar-entry, but are starting from a very low base (often 30%-50% below the average volume per capita). Growth is undeniably positive, but this perspective is required as the average growth rate for the bottom 5 markets[2] is higher than the top-5 markets by 25% despite remaining far below average levels.

Anti-TNFs: Understanding High Growth in Access Despite Low Usage for Key Markets (TD/capita)



Source: IQVIA MIDAS® MAT June 2020

Notes: Chart represents the accessible anti-TNF market (only referenced, biosimilars, non-referenced medicines). Non-accessible medicines are excluded from this analysis. Greece contains only retail panel data.

Markets must be compared to suitable analogues to ensure a fair comparison. For example, Bulgaria experienced 348% growth in treatment days per capita to 0.46, but still remains below the pre-biosimilar average (0.51). Similarly, growth rates for other markets such as Sweden do not take into account the high base or the above average starting position. It is important here to acknowledge the Nordic markets who have highlighted that it is possible to have high usage, and increase further. The raw data shows certain cases where this is driven by the origionator and not the biosimilar directly which in certain situations. Progress is strong in many markets, but low usage is still present and further progress can be achieved.

In most cases this is the status quo. There is an outlier where low growth can be a positive sign. In the case of Herceptin (trastuzumab), there are reports that the majority of patients have already been treated with the originator molecule and as such the opportunity to increase access is not present. This presents further complexity when viewing the impact of biosimilar competition in that market as the accessible market appears high but has low growth potential.

[2] Excluding Greece due to the IQVIA MIDAS® data panel only covering the retail market in Greece, making it unrepresentative for the purposes of comparison.

3. STRATEGY: THE VARIATION OF ORIGINATORS RESPONSE TO PROTECTION EXPIRY

A major impact of biosimilar competition in Europe is the change in the response of the originator manufacturer. In Europe, originator biologic manufacturers defend against biosimilar competition using various means; with second generation products, reformulations, dosing improvements, supporting devices, and/or competing on price.

3.1 Originators focus on the accessible market to retain market share

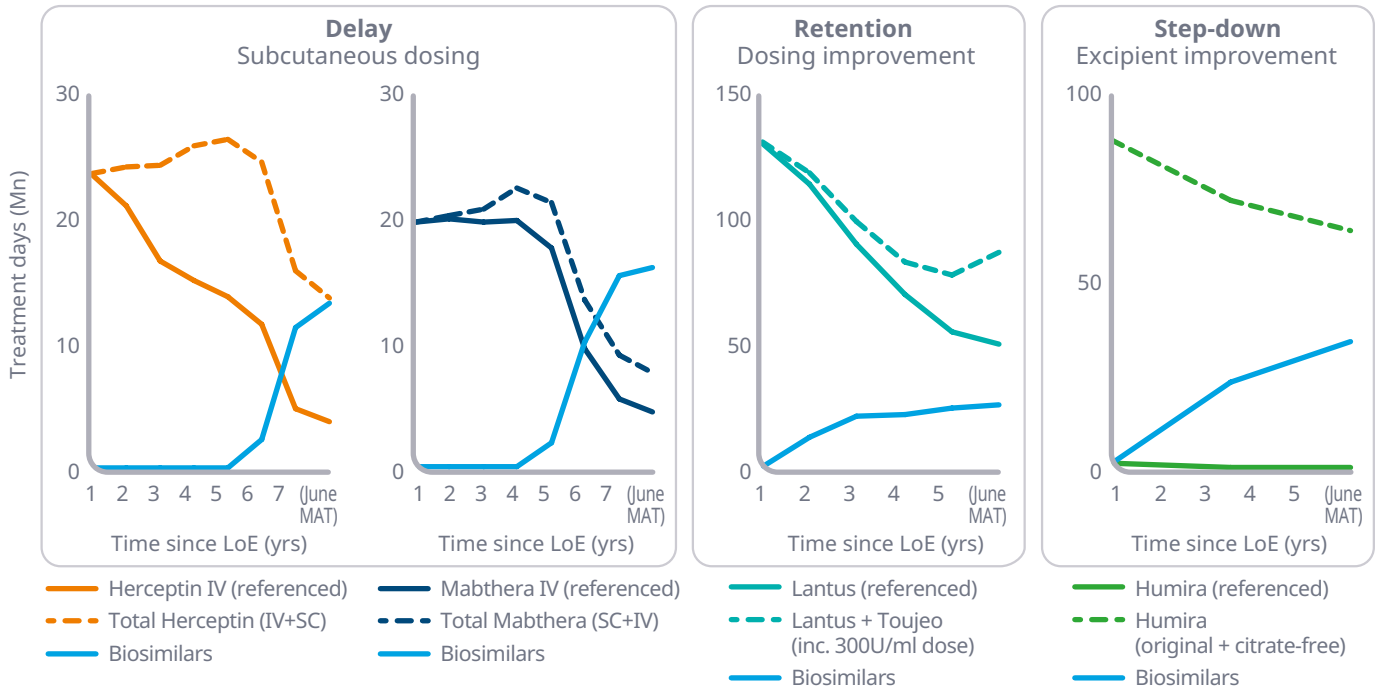
In the past decade, manufacturers have explored strategies to minimise the impact from competition with variable degrees of success. The originator manufacturers for the largest biologic medicines have used a variety of strategic methods, and notably price competition. Using recent examples, originator molecules experience several interesting dynamics:

i. **delayed** drop in market share as biosimilars enter the market introducing subcutaneous formulations

ii. **retention** of historic market share post-protection expiry with dosing changes

iii. **step-down** in market share with product enhancements

Recent examples of market retention by originators



Source: IQVIA MIDAS®MAT June 2020

Notes: Curves are normalized to allow comparison. After protection expiry, only a portion of the product is categorised as 'referenced' as innovation and additional protection is afforded to the product through alternative administration, excipients, or dosing.

However, determining the 'most effective' originator defence strategy at an aggregate level is too simple in an increasingly complex market. In reality, the success of a strategy is dependent on many factors that are specific to the molecule, country, and the ecosystem. Strategies that work well in one market may perform poorly in others as healthcare systems are highly differentiated in their approaches.

4. POLICY: SEVERAL MODELS CAN WORK TO SUPPORT COMPETITIVE MARKETS

Country policies have direct implications for how well markets can operate and polices related to biologics and biosimilars are often updated or amended. It is important to understand the nuances of each market, their policies, potential hurdles, and unique systems to deliver long-term value to patients across Europe.

4.1 Countries took different approaches to leverage biosimilar competition

Across Europe many countries have been categorised in detail.[3] The major areas for comparison are related to the regulatory landscape, awareness, incentives, pricing rules, and purchasing mechanisms. By viewing these elements, it becomes clear that success is not a simple one-size fits all approach and is dependent on how the country is organised. The exhibit below compares:

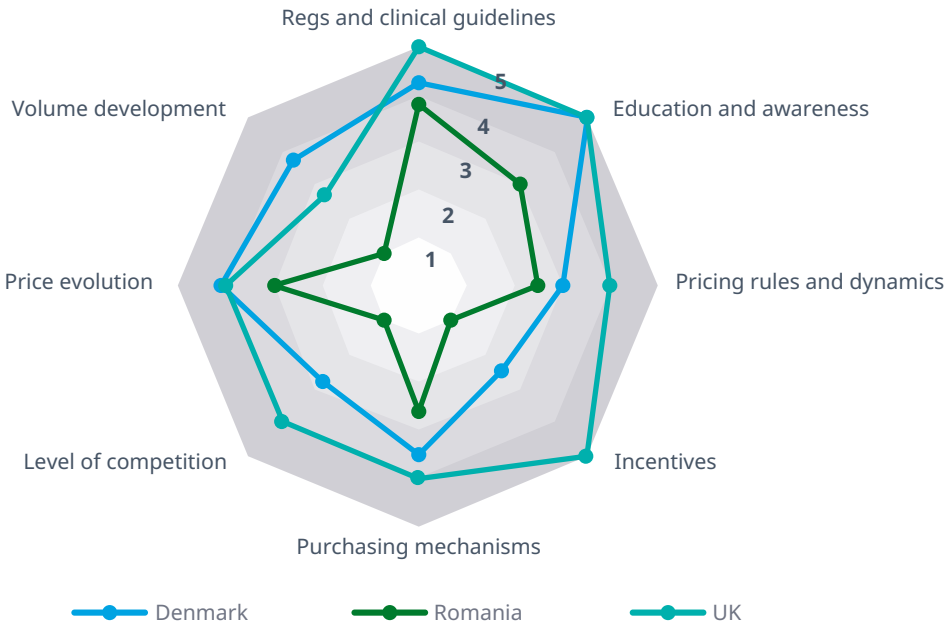
i. a strong system without equivalent benefits from biosimilar competition (UK)

ii. one of the best-in-class markets for savings and increasing access (Denmark)

iii. an immature market for biosimilars with areas for policy improvement (Romania)

The exhibit shows the strengths and weaknesses and creates a unique fingerprint for the market.
For example, incentives for prescribing biosimilars may not always translate directly to volume development as other limiting factors are at play, depending on the national context. Sometimes, the implementation by the prescriber and translating savings into a real impact through benefit sharing are more efficient in creating volume development. Many different elements must come together to support a market that can benefit from the impact of biosimilar competition effectively.

Illustrative example of approaches to biosimilar competition (Q1 2020)



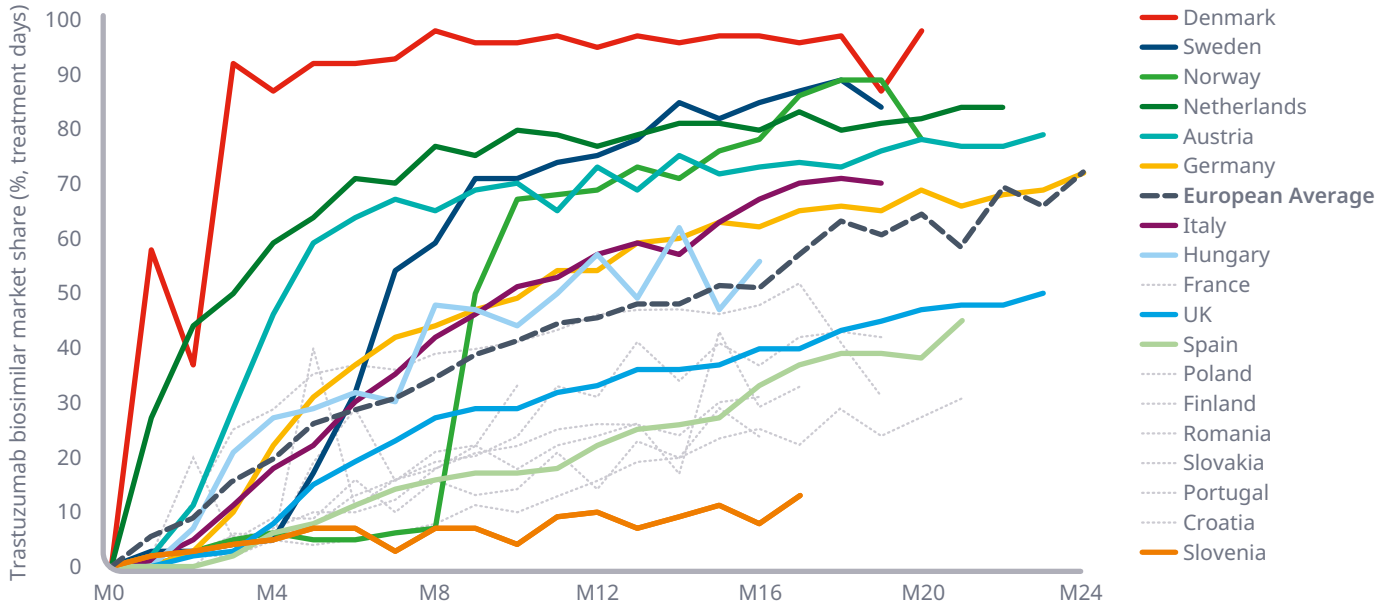
[3] Medicines for Europe: Biosimilar Scorecards 2020 covering 12 Markets (Denmark, France, Germany, Hungary, Italy, Netherlands, Norway, Poland, Romania, Spain, Sweden, United Kingdom).

4.2 Equivalent polices must be compared to see the true biosimilar competition

Uptake curves only show part of the impact of competition. As introduced in observation 3.1 and 4.1, interpretation of commercial strategies and international medicines policies is a complex task. Using the example of Herceptin (trastuzumab), we demonstrate that comparing equivalent markets is critical to form reliable conclusions on the progress of markets.

When comparing biosimilar uptake of Herceptin (trastuzumab), a pan-European comparison should not be shown. Some countries chose to move to the originator in subcutaneous form rather than pursue an IV biosimilar-focussed strategy. The originator manufacturer, Roche, focussed on an evolved treatment strategy, and indirect costs of IV-administration, rather than competing in the IV space directly on price. In the exhibit below, countries with >50% market share of originator in subcutaneous form in 2020 are noted with grey dotted lines and excluded from comparison. Note, this does not apply to all countries with low uptake, some countries simply have poor implementation.

Trastuzumab: Equivalent Country Comparisons (%, MS)



Source: IQVIA MIDAS® MAT 2020 June MAT

Notes: Countries with over 50% market share of the originator Herceptin (trastuzumab) SC form are shown in dotted lines.
Those with full colour lines represent markets which have not focussed on the originators new innovation, and instead focus on the biosimilar uptake.
Includes SC & IV trastuzumab biosimilars. Countries in the exhibit are listed by overall trastuzumab biosimilar market share ranging from high to low.

This strategy was deemed economically feasible by different countries, linked to tenders, hospital or clinic costs, and prioritisation with many calculating this as the best option. The impact of biosimilar competition is the ability for countries to make these choices on their terms, and be right in either case.

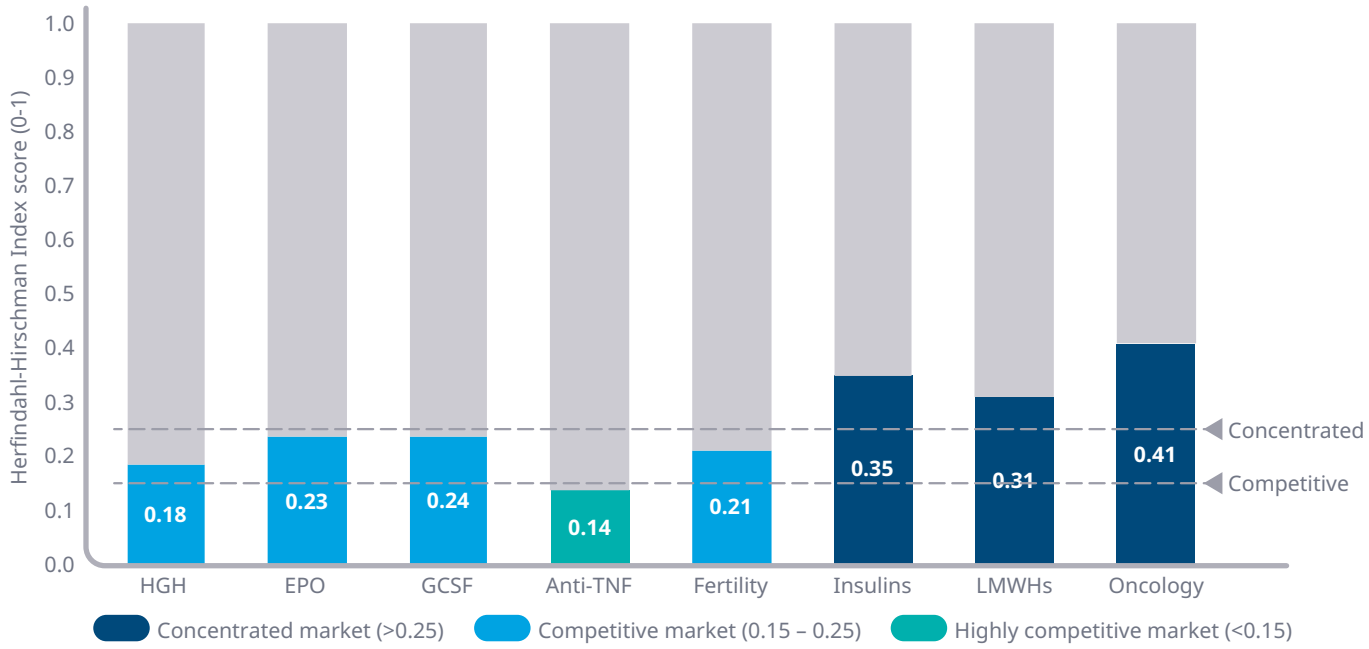
4.3 Dynamic competition is the key to ensuring long-term benefits from biosimilar competition

As European markets mature, metrics to view markets must also develop. The market concentration (as defined by the Herfindahl-Hirschman Index) in the exhibit below shows the competitiveness of the therapy classes with biosimilars.

For new biosimilars to be developed and to maintain price competition, several competitors must stay active in the market. In the long-term, a highly concentrated market means that only a few companies can participate in a tender. The eventually means poor price competition and comes with all the associated risks of reliance on one company. The trend has moved towards volumes being split between several companies in multi-winner tenders.

The anti-TNF market has faced significant biosimilar competition and is a market containing 3 referenced medicines, whereas the more recent classes (insulins, LMWHs, and oncology medicines) are in the process of maturing into competitive markets.

Total market concentration (Herfindahl-Hirschman Index)



Source: IQVIA MIDAS® and EMA EPAR Marketing Authorisation Holders

Notes: Agencies generally consider markets in which the HHI is between 0.15 and 0.25 points to be moderately concentrated, and consider markets in which the HHI is in excess of 2.5 points to be highly concentrated. However, high levels of protection exist in the less mature markets such as LMWHs and oncology. Total market covered within the ATC classes in the scope of this report.

The complexity of biologic molecules acts as a natural barrier to entry for the creation of biosimilar medicines, and this can be seen in the competitive landscape of the KPIs shown the report. Focusing on biosimilar uptake alone is no longer suitable. The importance of competition by originator medicines is part of the success of biologic molecules post-protection expiry, and it is an imperative to support markets by ensuring sustainable competition long-term.

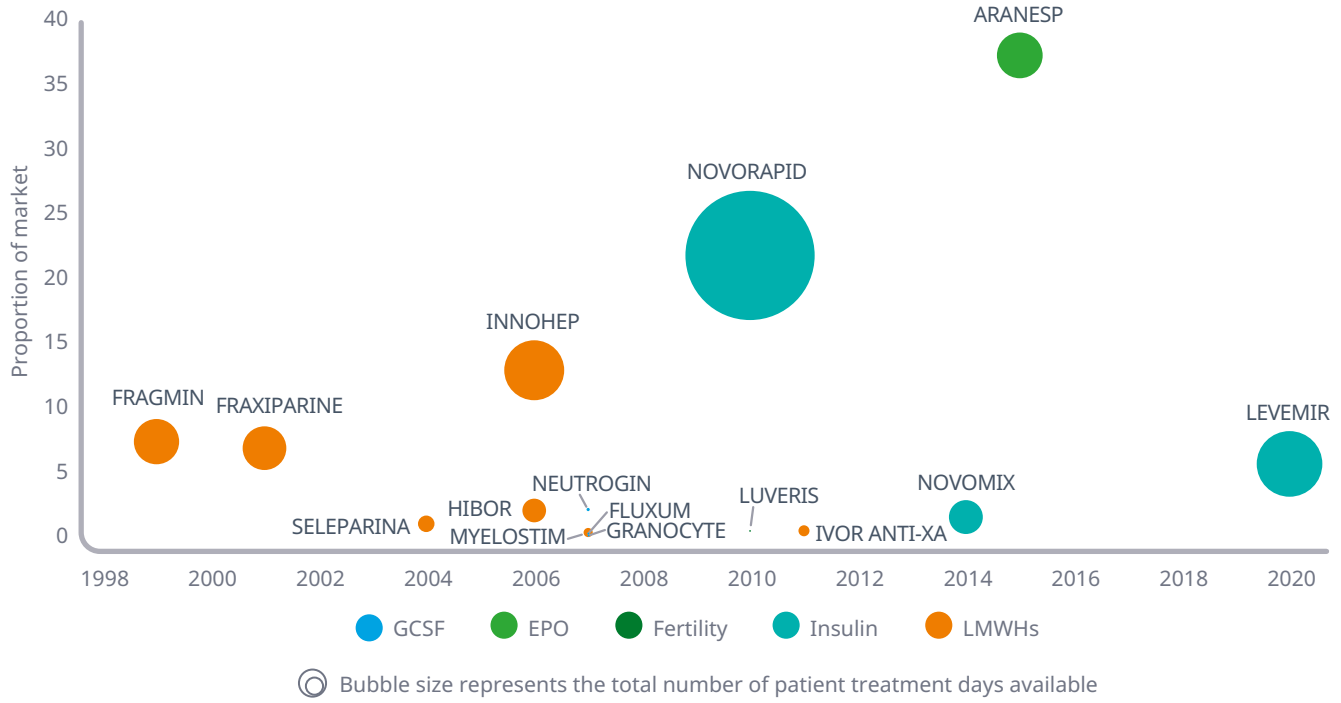
5. FUTURE: THE REAL IMPACT OF BIOSIMILAR COMPETITION IS JUST BEGINNING

In the past, a small number of large products dominated the loss of exclusivity (LOE) opportunity. Almost 75% of the biologic opportunity between 2013-2018 was driven by 5 high-value products: Mabthera, Herceptin, Enbrel, Remicade, and Humira. However, starting in the next 4-5 years, the number of biologic expiries increases dramatically.

5.1 There is historical opportunity still available for biosimilar competition

There are several 'non-referenced'[4] products in the major therapy classes. The most notable is Aranesp (darbepoetin alfa), which does have molecules in late-stage development and biosimilars approved only in APAC markets.[5] The product has a significant share of the total market for EPOs (~40%), and biosimilar competition here would be beneficial as low volume growth is noted in section 2.1.

Non-referenced Biosimilars by Class



Source: IQVIA MIDAS® June 2020 MAT
Notes: Each of these molecules is categorised in the 'non-referenced' market according to IQVIA MIDAS and ARK Patent Intelligence

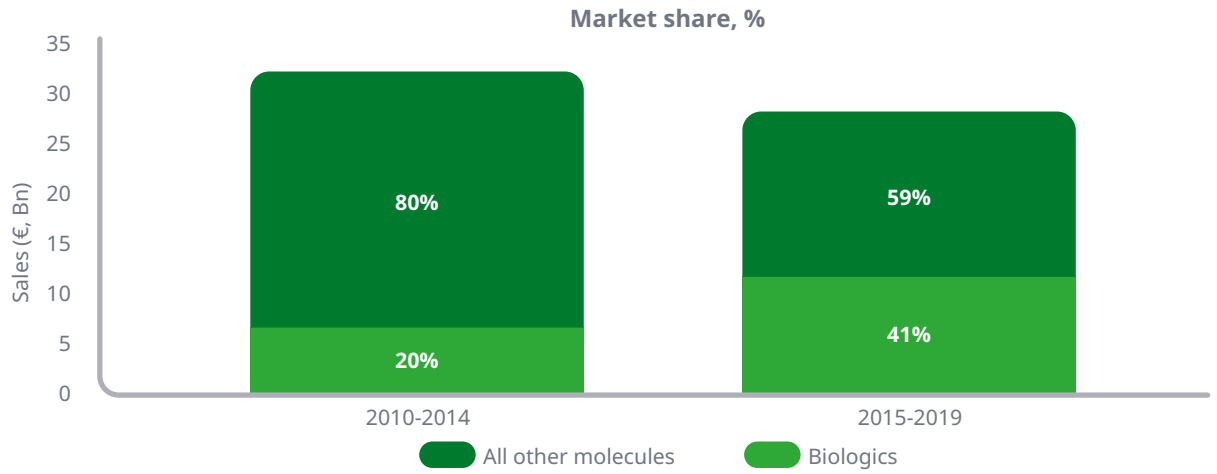
5.2 Biologic LOEs are growing in potential impact, now and in the future

Biologic LOEs have grown in importance in the last 10 years from 20% to 41% of the total opportunity. This was due to the loss of protection of the world's highest value products: Humira, Enbrel and Remicade. Of all products with LOE in the past 10-years, biologics have become of increased importance. Estimates suggest that this figure will remain around 40% throughout the next 10-years due to the high number of biologic launches.

[4] Non-referenced refers to a medicine which has lost its protection status, without an EMA-approved biosimilar. Refer to methodology section for full definitions, and further details.

[5] IQVIA Pipeline Intelligence (November 2020)

Total Loss of Opportunity by Segment

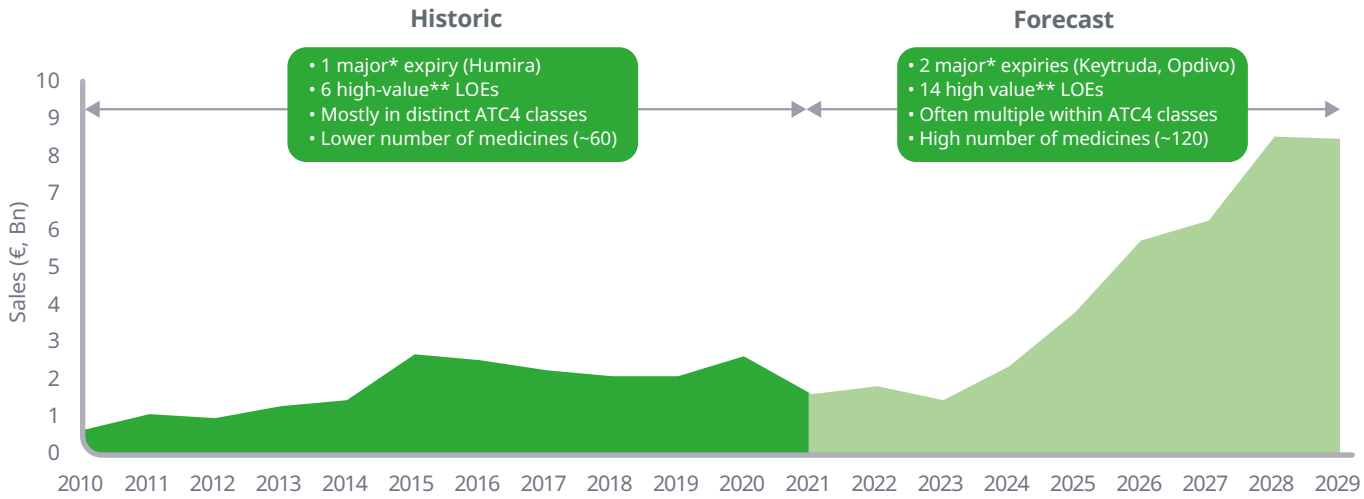


Source: IQVIA MIDAS® Q4 2019 (accessed Nov 2020), IQVIA Ark Patent Intelligence
Notes: The IP for biologicals can involve multiple patents and patent timelines for each individual product and therefore it is difficult to give an exact date for patent expiry for biologicals. It should be noted that these results are estimates as determined from IQVIA MIDAS® and ARK Patent Intelligence where available. Rx only, covering 23 European markets.

5.3 Twice as many products will lose protection in the next ten years

Historically, the majority of biologic opportunity has come from a small number of high-value products. In the next 4-5 years there is a paradigm shift to a period where 3 times the number of products will begin to lose exclusivity. These products are smaller in value, and represent smaller patient populations, however, major LOEs for PD-1 inhibitors (Opdivo and Keytruda) are also present. These are the only molecules forecast to equal (or exceed) Humira's sales.

Biologic Loss of Exclusivity



Source: IQVIA MIDAS® Q4 2019 (accessed Nov 2020), IQVIA Ark Patent Intelligence, IQVIA ForecastLink for data post-2020
Notes: The IP for biologicals can involve multiple patents and patent timelines for each individual product and therefore it is difficult to give an exact date for patent expiry for biologicals. It should be noted that these results are estimates as determined from IQVIA MIDAS® and ARK Patent Intelligence where available. Rx Biologics in 23 European countries.
Definitions: *Major molecules = sales >3Bn€ at LOE-1; **High value molecules = sales >1Bn€ at LOE-1

In the near-term (2021-2023), we will see a minor reduction in biologic LOE opportunity. There is an opportunity to use this period to focus on realising the full potential of biosimilar savings from expired biologics, ahead of the next major period of biologic LOE. Most systems are labour intensive, and preparation for biosimilar competition is not as simple as preparation for generic competition. The imperative is to increase preparedness for the volume of expiries, support launch excellence across multiple markets, and ensure systems are in place to maximise the impact of biosimilar competition rapidly. This will likely require adjusted or new approaches to biosimilar development and market access to allow strong competition with products that have lower value and smaller patient populations.

Methodology

The indicators are intended to give a broad overview of the uptake and the implications on price and volume evolution after introduction of biosimilar medicines. There are differences in perspective between payers, providers, and different types of manufacturers. In focusing on the payer perspective, there are caveats that should be considered when interpreting the results:

- **Pricing and discounts:**
  the report is based on publicly available list prices. Discounting occurs, especially in contracting with hospitals and in countries using tenders for biological drug procurement, which can lead to larger price fluctuations than is visible through the reported IQVIA data.

- **Approved indications and efficacy:**
  not all products in a specific product group in the accessible, non-accessible or total market have the same approved indications and can have differences in efficacy and individual patient outcomes. Biosimilars normally receive the same indications as the referenced products and are expected to have the same safety and efficacy.

- **Volume estimates:**
  the pack volumes reported are based on IQVIA collected data which may have been unknowingly impacted by issues such as parallel exporting. The volumes have been converted to daily doses using the published World Health Organization (WHO) defined daily doses (DDD) which can introduce bias. Consumption measures are therefore not adjusted for clinical practice guidelines, patient characteristics, indications for which the molecule is used, or other factors that may result in different volumes utilised on a per patient Treatment Day basis.

- **Long-term vs. one-off use:**
  hospital-only vs. retail: no distinction is made in this report between biologicals for long term (repeat use) and one-off use, nor between hospital-only and retail products, although competitive conditions and scope for biosimilar uptake are likely to differ in the various scenarios.

- **Protection expiry:**
  The intellectual property for biologicals can involve multiple patents, patent timelines, data exclusivity, and litigation for each individual product and therefore it is difficult to give an exact date for protection expiry for biologicals. It should be noted that these results are estimates as determined from IQVIA MIDAS® and ARK Patent Intelligence where available, and historical products are cross-referenced to public sources.

Other definitions found within the report include:

- **Launch date:**
  date of first recorded sales of Biosimilar Medicinal Product in the country. Products can be approved in Europe prior to this date but it is not recorded as such.

- **Price indicators:**
  Price: the price level used is gross ex-manufacturer price (list price), which values the product at the level that the manufacturer sells out, without considering rebates or discounts. Price evolution: price per Treatment Day (TD) in 2020 (June MAT) versus year before biosimilar entry.

- **Volume indicators:**

  Volume: volume is measured in Treatment Days (also known as Defined Daily Dose) which is a measure of the average dose prescribed as defined by the WHO.

  Biosimilar market share: number of biosimilar treatment days as a share of (i) biosimilar + referenced product(s) volume, (ii) accessible market volume and (iii) total market volume.

  Volume evolution: number of Treatment Days in 2020 (June MAT) versus year before biosimilar entry.

  Volume per capita 2020 (June MAT): number of Treatment Days consumed in 2020 (June MAT) normalised by population size (World Bank data).

  Volume per capita year before biosimilar entrance: number of Treatment Days consumed the year before the entrance of biosimilars, normalised by population size.

The following terms are used throughout this segment of the report:

TOTAL MARKET: Products within the same ATC code	**ACCESSIBLE MARKET**	**Referenced Medicinal Product:** Original product, granted market exclusivity at the start of its life, exclusivity has now expired, and the product has been categorised as referenced by having a biosimilar with an EMA-approved marketing authorisation available on a European market.	
		Non-Referenced Medicinal Product: Original product, granted market exclusivity at the start of its life, exclusivity has now expired1, and the product has never been categorised as a Referenced Medicinal product by receiving EMA-approved marketing authorisation.	
		Biosimilar Medicinal Product: Product, granted regulatory approval, demonstrating similarity to the Reference Medicinal Product in terms of quality characteristics, biological activity, safety and efficacy.	
	NON-ACCESSIBLE MARKET	**Non-accessible category:** products within the same ATC4 code as the accessible category products. These are typically second-generation products; this category may include products with different dosing schedules and / or route of administration to those in the accessible category, and have valid protection status.	

Country and therapy area KPIs

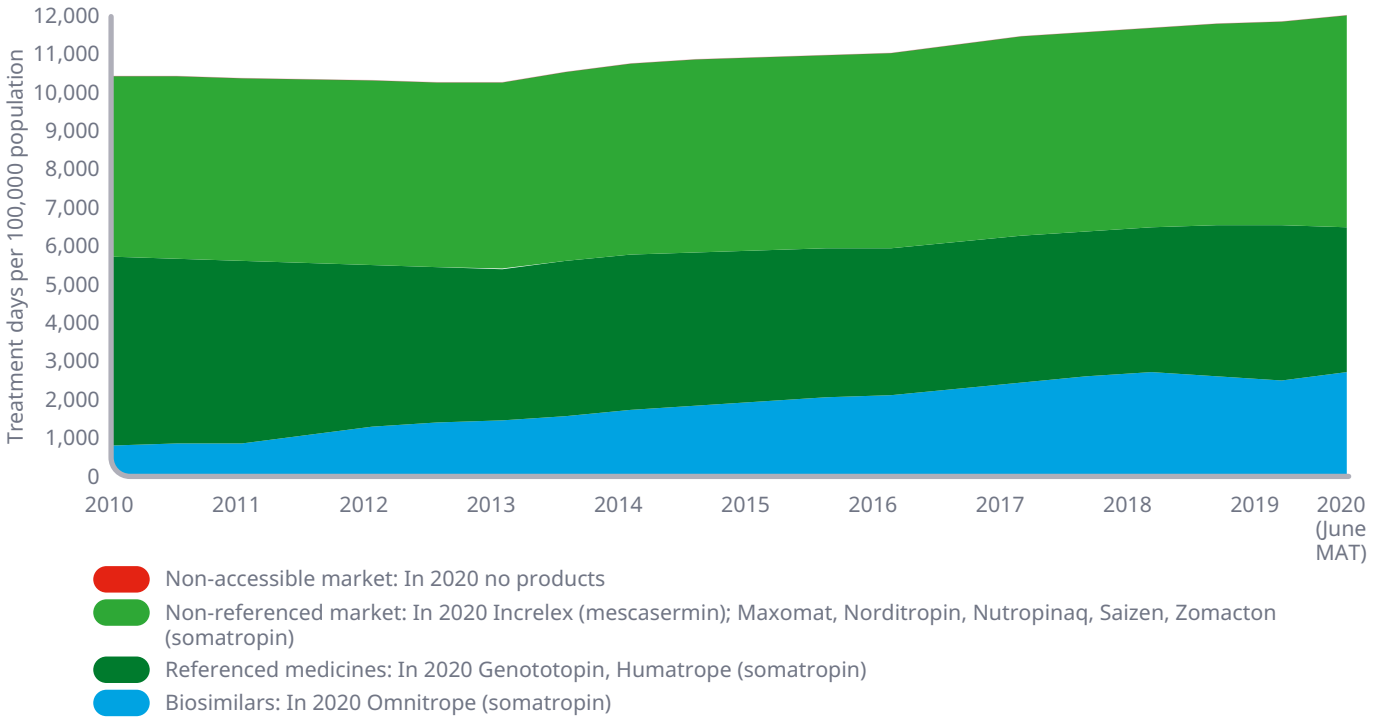
Human growth hormone (HGH)

HGH also known as somatropin, is a peptide hormone that stimulates growth, cell reproduction and regeneration in humans. It is used to treat growth disorders in children and growth hormone deficiency in adults.

HGH MARKET DEVELOPMENT

Protection has expired for the major molecule in this class Humatrope (somatropin). The figure below reflects the existence of 2nd-generation products that are not classified as biosimilars, nor have protection status, and as such are not able to be classified within the 'referenced medicines' category.

HGH Market Development



ADDITIONAL INFORMATION ABOUT HGH MEDICINES

Subcutaneous injection is typically used to administer Human Growth Hormone treatment. The dosage of administration should be individualised for each patient, with a weight-based regimen. The duration of treatment, usually a period of several years, will depend on maximum achievable therapeutic benefit.

HGH approved indications

NAMING		CLASSIFICATION										INDICATIONS								
MOLECULE	PRODUCT	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020 (JUNE MAT)	ANEMIA FOR CHEMOTHERAPY PATIENTS	ADULT GROWTH HORMONE DEFICIENCY	TURNER SYNDROME	GROWTH FAILURE DUE TO CHRONIC RENAL INSUFFICIENCY (CRI)	SGA - SMALL FOR GESTATIONAL AGE	PWS - PRADER-WILLI SYNDROME	IDIOPATHIC SHORT STATURE	SHOX - SHORT-STATURE HOMEBOX-CONTAINING GENE DEFICIENCY	NOONAN SYNDROME
SOMATROPIN	GENOTROPIN HUMATROPE OMNITROPE MAXOMAT* NORDITROPIN NUTROPINAQ SAIZEN ZOMACTON	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●

● Non-accessible market ● Non-referenced market ● Referenced medicines ● Biosimilars

* MAXOMAT has been discontinued

Selected KPIs to Illustrate Volume Share, Price Evolution, and Volume Evolution in Selected European Countries

		AU	BE	BU	CZ	DK	FI	FR	DE	GR*	HU	IE	IT	NL	NO	PL	PT	RO	SK	SL	ES	SE	CH	UK	EU
MARKET SHARE TD (2020, JUNE MAT)	Biosimilar vs Referenced product	35%	32%	52%	24%	98%	57%	43%	46%	0%	23%	0%	47%	42%	3%	46%	36%	67%	0%	15%	34%	53%	30%	31%	41%
	Biosimilar vs Accessible market	10%	21%	52%	8%	75%	15%	18%	22%	0%	10%	0%	26%	22%	3%	46%	19%	41%	0%	7%	22%	36%	5%	13%	23%
	Biosimilar vs Total market	10%	21%	52%	8%	75%	15%	18%	22%	0%	10%	0%	26%	22%	3%	46%	19%	41%	0%	7%	22%	36%	5%	13%	23%
PRICE PER TD (2020 JUNE MAT/YR BEFORE BS ENTRY)	Biosimilar and Referenced product	-16%	-23%	-26%	-27%	27%	-31%	-19%	2%	-16%	-18%	-9%	-25%	-37%	-30%	75%	-49%	-24%	-13%	-37%	-19%	-42%	-33%	-14%	-22%
	Biosimilar Accessible market	-6%	-24%	-26%	-31%	12%	-38%	-18%	6%	-16%	-16%	-11%	-24%	-35%	-26%	78%	-39%	-33%	-3%	-37%	-19%	-41%	-28%	-14%	-17%
	Total market	-6%	-24%	-26%	-31%	12%	-38%	-18%	6%	-16%	-16%	-11%	-24%	-35%	-26%	78%	-39%	-33%	-3%	-37%	-19%	-41%	-28%	-14%	-17%
VOLUME TD (2020, JUNE MAT/YR BEFORE BS ENTRY)	Biosimilar and Referenced product	7%	59%	21%	80%	71%	17%	28%	131%	-23%	-10%	66%	99%	30%	131%	162%	30%	280%	39%	53%	91%	-15%	-24%	21%	47%
	Biosimilar Accessible market	119%	43%	19%	102%	-28%	87%	54%	195%	-23%	19%	100%	71%	35%	44%	164%	4%	127%	43%	47%	88%	-15%	55%	80%	51%
	Total market	119%	43%	19%	102%	-28%	87%	54%	195%	-23%	19%	100%	71%	35%	44%	164%	4%	127%	43%	47%	88%	-15%	55%	80%	51%
	TD per capita	0.08	0.13	0.03	0.16	0.10	0.11	0.15	0.16	0.00	0.06	0.08	0.11	0.11	0.18	0.11	0.05	0.05	0.09	0.08	0.18	0.12	0.10	0.07	0.10
	TD/capita (Yr before BS entrance)	0.03	0.09	0.02	0.08	0.15	0.06	0.10	0.05	0.00	0.05	0.04	0.06	0.08	0.13	0.04	0.04	0.02	0.06	0.06	0.09	0.15	0.06	0.04	0.06
	First Recorded sales of Biosimilars	2008	2009	2012	2010	2011	2008	2007	2006	2015	2012	2006	2007	2008	2011	2008	2014	2008	2013	2010	2007	2007	2010	2007	2006

* Only retail panel data is available for Greece

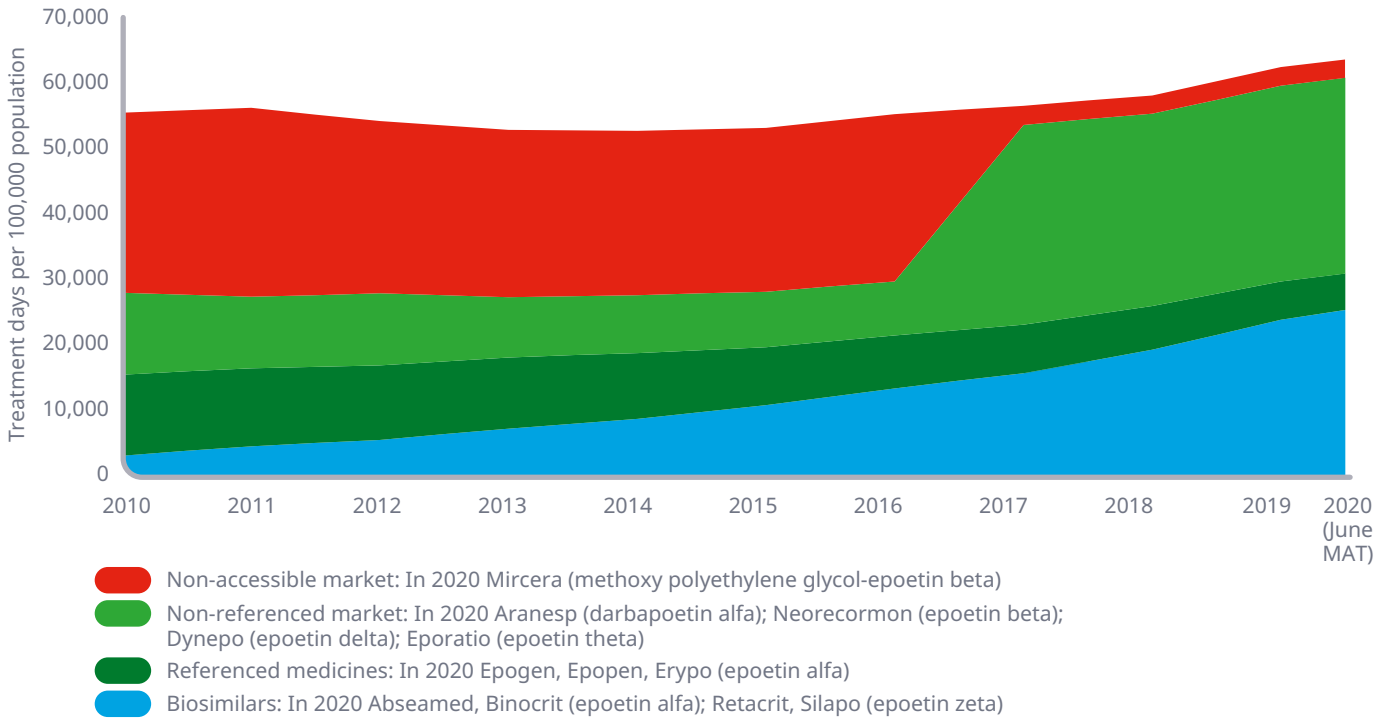
Epoetin (EPO)

EPO is a form of human erythropoietin produced by recombinant technology, with the same amino acid sequence and mechanism of action as endogenous erythropoietin. Its major functions are to promote the differentiation and development of red blood cells and to initiate the production of haemoglobin, the molecule within red blood cells that transports oxygen.

EPO MARKET DEVELOPMENT

Protection expired for a significant molecule in this class, Aranesp (darbepoetin alfa). The figure below reflects this shift from the molecule as a non-accessible product, to one that is now open to biosimilar competition but is yet to be referenced.

EPO Market Development



EPO Approved Indications

NAMING		CLASSIFICATION											INDICATIONS					DOSING/ADMINISTRATION	
MOLECULE	PRODUCT	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020 (JUNE MAT)	ANEMIA FOR CHEMOTHERAPY PATIENTS	ANEMIA FOR PATIENTS WITH CKD*	PREVENTING ANEMIA IN PREMATURE BABIES	ANEMIA IN ADULTS WITH MDS	REDUCTION OF ALLOGENIC TRANSFUSION EXPOSURE IN ORTHAPEDIC SURGERY	PATIENT TYPE** (ADULT OR PEDIATRIC)	FREQUENCY
DARBEPOETIN ALFA	ARANESP	●	●	●	●	●	●	●	●	●	●	●	●	●			●	Both	3 x per week
EPOETIN ALFA	ABSEAMED BINOCRIT EPOGEN EPOPEN ERYPO	● ● ● ● ●	● ● ● ● ●	● ● ● ● ●	● ● ● ● ●	● ● ● ● ●	● ● ● ● ●	● ● ● ● ●	● ● ● ● ●	● ● ● ● ●	● ● ● ● ●	● ● ● ● ●	● ● ● ● ●	● ● ● ● ●		● ● ● ●	● ● ● ● ●	Both	3 x per week
EPOETIN BETA	NEORECORMON	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	Both	3 x per week
EPOETIN DELTA	DYNEPO***	●	●	●	●								●	●	●			Both	3 x per week
EPOETIN THETA	EPORATIO	●	●	●	●	●	●	●	●	●	●	●	●	●				Adult	3 x per week
EPOETIN ZETA	RETACRIT SILAPO	● ●	● ●	● ●	● ●	● ●	● ●	● ●	● ●	● ●	● ●	● ●	● ●	● ●				Both	3 x per week
METHOXY POLYETHYLENE GLYCOL-EPOETIN BETA	MIRCERA	●	●	●	●	●	●	●	●	●	●	●		●				Adult	Every 2 weeks

● Non-accessible market ● Non-referenced market ● Referenced medicines ● Biosimilars

* Anaemia for patients with Chronic kidney disease

** Subcutaneous injection is typically used for chemotherapy patients. Intravenous injection is typically used for patients with kidney problems and for patients who are going to donate their own blood.

*** Dynepo has been discontinued

Selected KPIs to Illustrate Volume Share, Price Evolution, and Volume Evolution in Selected European Countries

		AU	BE	BU	CZ	DK	FI	FR	DE	GR*	HU	IE	IT	NL	NO	PL	PT	RO	SK	SL	ES	SE	CH	UK	EU
MARKET SHARE TD (2020, JUNE MAT)	Biosimilar vs Referenced product	80%	13%	100%	82%	40%	100%	74%	87%	83%	100%	100%	86%	31%	83%	100%	92%	98%	100%	74%	90%	97%	24%	14%	82%
	Biosimilar vs Accessible market	35%	9%	80%	50%	15%	84%	57%	79%	83%	56%	19%	83%	11%	45%	93%	28%	79%	71%	51%	80%	31%	7%	8%	69%
	Biosimilar vs Total market	23%	2%	57%	24%	0%	14%	22%	52%	77%	29%	6%	72%	2%	1%	19%	20%	47%	56%	17%	51%	20%	1%	3%	40%
PRICE PER TD (2020 JUNE MAT/YR BEFORE BS ENTRY)	Biosimilar and Referenced product	-90%	10%	-69%	5%	1063%	13%	-99%	-99%	-100%	-99%	-76%	-100%	216%	96382%	534%	3310%	-93%	-84%	-56%	-98%	-98%	-60%	58%	-67%
	Biosimilar Accessible market	-90%	61%	-78%	9%	444%	37%	-99%	-99%	-99%	-98%	-94%	-100%	41%	65338%	536%	932%	-94%	-89%	-46%	-95%	-98%	-49%	-19%	-67%
	Total market	-89%	-48%	-41%	173%	-91%	-57%	-99%	-98%	-48%	-24%	-88%	-97%	-25%	3459%	111%	1309%	-96%	-90%	-64%	-92%	-95%	-70%	-60%	-59%
VOLUME TD (2020, JUNE MAT/YR BEFORE BS ENTRY)	Biosimilar and Referenced product	5%	-14%	131%	386%	-93%	2109%	41%	295%	547%	56%	55%	254%	-74%	-71%	5040%	208%	96%	348%	-19%	102%	9%	-47%	162%	153%
	Biosimilar Accessible market	4%	-14%	48%	118%	-98%	-36%	-17%	109%	285%	24%	-52%	106%	-59%	-89%	14%	143%	-72%	66%	-44%	10%	14%	-54%	23%	36%
	Total market	-20%	34%	59%	222%	-5%	34%	8%	96%	174%	6%	-14%	54%	-18%	21%	263%	10%	-59%	12%	16%	4%	-3%	19%	69%	31%
	TD per capita	0.73	0.69	0.38	0.29	0.46	0.45	0.97	0.75	0.06	0.38	0.42	1.27	0.42	0.24	0.10	0.49	0.12	0.50	0.60	0.72	0.44	0.39	0.40	0.64
	TD/capita (Yr before BS entrance)	0.92	0.52	0.24	0.09	0.48	0.33	0.90	0.38	0.02	0.36	0.49	0.83	0.52	0.20	0.03	0.45	0.30	0.45	0.52	0.69	0.45	0.33	0.23	0.48
	First Recorded sales of Biosimilars	2008	2014	2011	2011	2010	2008	2009	2007	2008	2009	2008	2008	2009	2008	2009	2010	2009	2010	2009	2009	2008	2009	2009	2007

* Only retail panel data is available for Greece

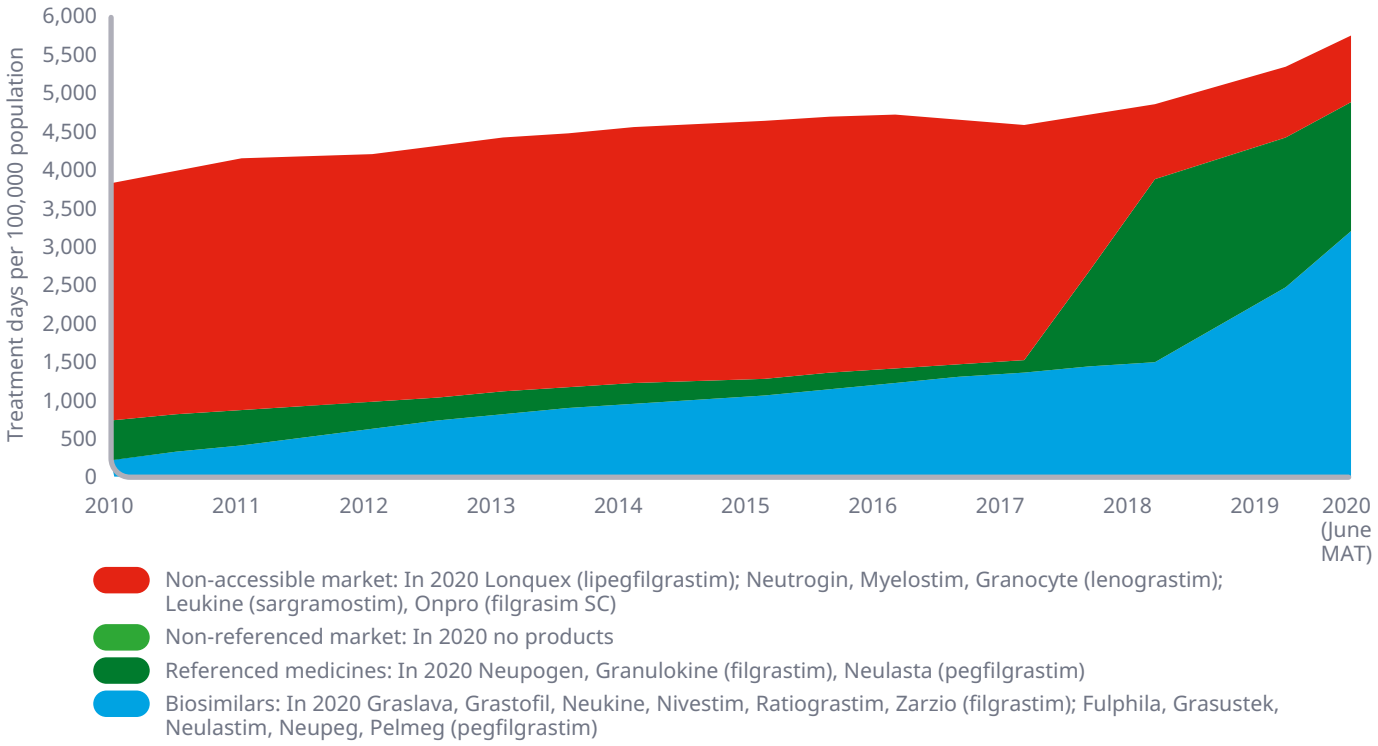
Granulocyte-colony stimulating factor (GCSF)

G-CSF is a glycoprotein that stimulates the bone marrow to produce granulocytes and stem cells and release them into the bloodstream. G-CSF is used prophylactically with certain cancer patients accelerate recovery from neutropenia after chemotherapy, allowing higher-intensity treatment regimens.

GCSF MARKET DEVELOPMENT

Protection expired for a significant molecule in this class, Neulasta (pegfilgrastim). The figure below reflects this shift from the molecule as a non-accessible product with protection, to one that is now open to biosimilar competition and has been referenced within the same year by a significant number of biosimilars.

GCSF Market Development



ADDITIONAL INFORMATION ABOUT G-GCSF MEDICINES

Subcutaneous injection typically used to administer G-CSF daily for 5-7 days, starting 72hrs after completion of chemotherapy or bone marrow transplantation, with the exception of pegfilgrastim and lipegfilgrastim which are long acting G-CSF and therefore administered once only at least 24 hrs after completion of each chemotherapy cycle.

GM-CSF (Granulocyte macrophage colony-stimulating factor) Sargramostim and Molgramostim are given daily, most often as a subcutaneous injection (under the skin) but can also be given directly into a vein (intravenous, IV).

GSCF Approved Indications

NAMING		CLASSIFICATION											INDICATIONS					
MOLECULE	PRODUCT	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020 (JUNE MAT)	CYTOTOXIC CHEMOTERAPY ASSOCIATED WITH FEBRILE INDUCED NEUTROPENIA	NEUTROPENIA INDUCED BY ACUTE MYELOID LEUKEMIA	BONE MARROW TRANSPLANTATION FOR NON MYELOID MALIGNANCY INDUCED NEUTROPENIA	MOBILISATION OF PERIPHERAL BLOOD PROGENITOR CELLS (PBPCS)	SEVERE CHRONIC NEUTROPENIA (SCN) WITH DIAGNOIS OF CONGENITAL, CYCLIC, OR IDIOPATHIC NEUTROPENIA	NEUTROPENIA PREVENTION AND TREATMENT IN PATIENTS WITH HIV
FILGRASTIM	GRANULOKINE GRASALVA GRASTOFIL NEUKINE NEUPOGEN NIVESTIM RATIOGRASTIM ZARZIO	● ● ● ●	● ● ● ●	● ● ● ●	● ● ● ●	● ● ● ●	● ● ● ●	● ● ● ●	● ● ● ●	● ● ● ●	● ● ● ●	● ● ● ●	● ● ● ● ● ● ● ●	● ●	● ● ● ● ● ● ● ●	● ● ● ● ● ● ● ●	● ● ● ● ● ● ● ●	● ● ● ● ● ● ● ●
LENOGRASTIM	GRANOCYTE MYELOSTIM NEUTROGIN	● ● ●	● ● ●	● ● ●	● ● ●	● ● ●	● ● ●	● ● ●	● ● ●	● ● ●	● ● ●	● ● ●	● ● ●		● ● ●	● ● ●		
LIPEGFILGRASTIM	LONQUEX					●	●	●	●	●	●	●	●					
MOLGRAMOSTIM	LEUCOMAX	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●		
PEGFILGRASTIM	NEULASTA ONPRO NEULASTIM NEUPEG PELMEG GRASUSTEK FULPHILA	●	●	●	●	●	●	●	●	● ● ● ● ●	● ● ● ● ●	● ● ● ● ● ●	● ● ● ● ● ● ●					
SARGRAMOSTIM	LEUKINE	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●		

● Non-accessible market ● Non-referenced market ● Referenced medicines ● Biosimilars

Selected KPIs to Illustrate Volume Share, Price Evolution, and Volume Evolution in Selected European Countries

		AU	BE	BU	CZ	DK	FI	FR	DE	GR*	HU	IE	IT	NL	NO	PL	PT	RO	SK	SL	ES	SE	CH	UK	EU
MARKET SHARE TD (2020, JUNE MAT)	Biosimilar vs Referenced product	55%	4%	41%	80%	100%	46%	66%	47%	90%	96%	12%	79%	65%	98%	82%	79%	87%	78%	34%	90%	92%	24%	93%	65%
	Biosimilar vs Accessible market	55%	4%	41%	80%	100%	46%	66%	47%	90%	96%	12%	79%	65%	98%	82%	79%	87%	78%	34%	90%	92%	24%	93%	56%
	Biosimilar vs Total market	46%	3%	30%	56%	89%	36%	61%	37%	89%	93%	11%	70%	48%	94%	68%	79%	87%	56%	30%	88%	92%	24%	83%	56%
PRICE PER TD (2020 JUNE MAT/YR BEFORE BS ENTRY)	Biosimilar and Referenced product	-75%	-58%	-74%	-71%	-58%	-68%	-67%	-53%	-69%	-78%	-58%	-46%	-65%	-55%	-84%	-93%	-67%	-83%	-86%	-45%	-65%	-53%	-9%	-56%
	Biosimilar Accessible market	-75%	-58%	-74%	-71%	-58%	-68%	-67%	-53%	-69%	-78%	-58%	-46%	-65%	-55%	-84%	-93%	-67%	-83%	-86%	-45%	-65%	-53%	-9%	-54%
	Total market	-61%	-38%	-75%	-60%	-28%	-49%	-42%	-32%	-51%	-69%	-22%	-22%	-39%	-26%	-78%	-82%	-67%	-70%	-79%	-32%	-43%	-23%	7%	-38%
VOLUME TD (2020, JUNE MAT/YR BEFORE BS ENTRY)	Biosimilar and Referenced product	781%	1175%	2616%	1183%	888%	892%	1814%	1118%	2667%	599%	888%	430%	936%	2605%	576%	335%	973%	1563%	1314%	101%	552%	488%	438%	732%
	Biosimilar Accessible market	781%	1175%	2616%	1183%	888%	892%	1814%	1118%	2667%	599%	888%	430%	936%	2605%	576%	335%	973%	1563%	1314%	101%	552%	488%	438%	870%
	Total market	112%	143%	2234%	594%	77%	81%	78%	259%	-61%	67%	70%	16%	12%	204%	237%	-23%	915%	638%	383%	-32%	67%	73%	96%	97%
	TD per capita	0.11	0.11	0.04	0.03	0.07	0.10	0.09	0.09	0.01	0.06	0.09	0.04	0.04	0.08	0.06	0.03	0.03	0.06	0.09	0.02	0.04	0.04	0.03	0.06
	TD/capita (Yr before BS entrance)	0.05	0.04	0.00	0.00	0.04	0.05	0.05	0.02	0.02	0.04	0.05	0.03	0.03	0.03	0.02	0.04	0.00	0.01	0.02	0.04	0.02	0.03	0.01	0.03
	First Recorded sales of Biosimilars	2009	2011	2009	2010	2009	2009	2009	2008	2009	2009	2009	2009	2009	2009	2009	2010	2009	2009	2009	2009	2009	2009	2008	2008

* Only retail panel data is available for Greece

Anti-tumour necrosis factor (ANTI-TNF)

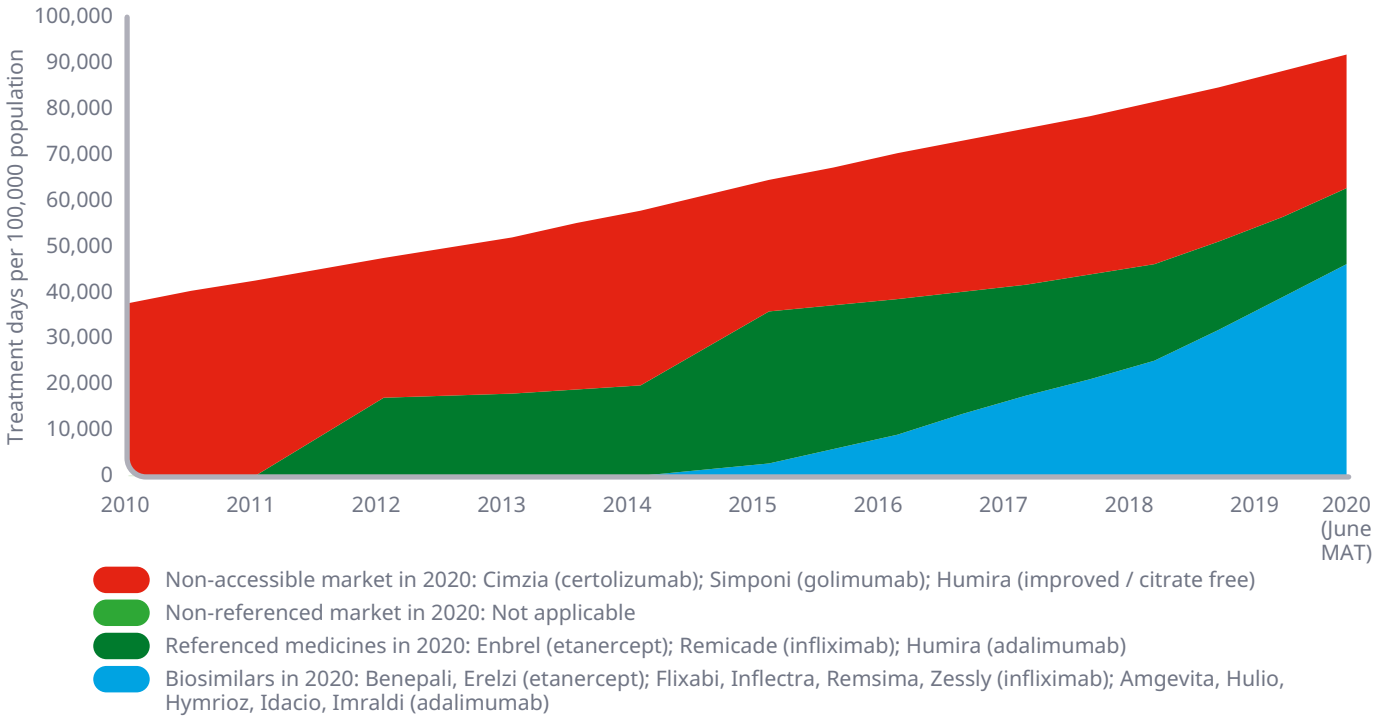
Anti-TNF drugs are a class of drugs that are used to treat inflammatory conditions such as Rheumatoid Arthritis (RA), Ankylosing Spondylitis, Psoriatic Arthritis, Juvenile Arthritis, Crohn's Disease, Ulcerative Colitis, Psoriasis and Hidradinitis Suppurativa. These drugs are able to reduce inflammation and stop disease progression.

TNF is a chemical produced by the immune system that causes inflammation in the body. In healthy individuals, excess TNF in the blood is blocked naturally, but in those who have conditions like RA, higher levels of TNF in the blood lead to more inflammation, joint destruction and persistent symptoms. Anti-TNF agents can alter the disease's effect on the body by controlling inflammation in joints, gastrointestinal tract and skin.

ANTI-TNF MARKET DEVELOPMENT

Protection for Mabthera and Herceptin expired a number of years prior to biosimilar entry. This chart reflects the period in which these products were non-referenced.

ANTI-TNF Market Development



ADDITIONAL INFORMATION ABOUT ANTI-TNF MEDICINES

In this section we report insights from biosimilars on the market in Europe for two Anti-TNF molecules: infliximab and etanercept. The EMA approved the first infliximab biosimilars in September 2013, and the first etanercept biosimilar in January 2016. The EMA has also approved several rituximab biosimilars, however these have been considered separately in the Oncology section of the report. The Anti-TNF market is unique as it has two referenced products with different biosimilar molecules. The market shares and price/volume evolution figures refer to the total Anti-TNF market, therefore, include all products within each category. This means, for example, in markets where only infliximab biosimilars have launched, the "biosimilar versus referenced product" market share will still represent the biosimilar market share of all the biosimilars and referenced products on the market (including Enbrel).

ANTI-TNF Approved Indications

NAMING		CLASSIFICATION											INDICATIONS											DOSING	
MOLECULE	PRODUCT	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020 (JUNE MAT)	RA	JIA	PSA	AS	AS WITHOUT RADIOGRAPHIC EVIDENCE	CD (ADULT / PEDIATRIC)	UC (ADULT / PEDIATRIC)	PPS	HS	UV	FREQUENCY	ROUTE (SUBQ / IV)	CITRATE FREE (Y/N)
ADALIMUMAB	HUMIRA HUMIRA (citrate free) AMGEVITA HULIO HYRIMOZ IMRALDI IDACIO	●	●	●	●	●	●	● ●	● ●	● ● ● ● ● ● ●	● ● ● ● ● ● ●	● ● ● ● ● ● ●	○ ○ ○ ○ ○ ○ ○	○ ○ ○ ○ ○ ○ ○	○ ○ ○ ○ ○ ○ ○	○ ○ ○ ○ ○ ○ ○	○ ○ ○ ○ ○ ○ ○	○ ○ ○ ○ ○ ○ ○	○ ○ ○ ○ ○ ○ ○	○ ○ ○ ○ ○ ○ ○	○ ○ ○ ○ ○ ○ ○	○ ○ ○ ○ ○ ○ ○	Every 2 weeks	SC SC SC SC SC SC SC	N Y Y N N Y
CERTOLIZUMAB PEGOL	CIMZIA	●	●	●	●	●	●	●	●	●	●	●	○		○	○		○		○			Monthly	SC	n/a
ETANERCEPT	ENBREL BENEPALI ERELZI	●	●	●	●	●	●	● ●	● ●	● ●	● ●	● ●	○ ○ ○	○ ○ ○	○ ○ ○	○ ○ ○				○ ○ ○			Once or twice weekly	SC SC SC	n/a n/a n/a
GOLIMUMAB	SIMPONI	●	●	●	●	●	●	●	●	●	●	●	○		○	○							Monthly	SC	n/a
INFLIXIMAB	REMICADE* REMSIMA INFLECTRA FLIXABI ZESSLY	●	●	●	● ●	● ●	● ●	● ●	● ●	● ●	● ●	● ●	○ ○ ○ ○ ○		○ ○ ○ ○ ○	○ ○ ○ ○ ○				○ ○ ○ ○ ○			Every 8 weeks	IV BOTH IV	n/a n/a n/a n/a n/a

● Non-accessible market ● Non-referenced market ● Referenced medicines ● Biosimilars

*Protection expired earlier in some markets, resulting in the appearance of biosimilars prior to the formal EU protection expiry. Notes: RA = rheumatoid arthritis, JIA = Juvenile idiopathic arthritis; PsA = Psoriatic arthritis; AS = Ankylosing spondylitis; CD = Crohn's disease; UC = ulcerative colitis; PPs = plaque psoriasis; HS = Hidradenitis Suppurativa; Uv = Uveitis

Selected KPIs to Illustrate Volume Share, Price Evolution, and Volume Evolution in Selected European Countries

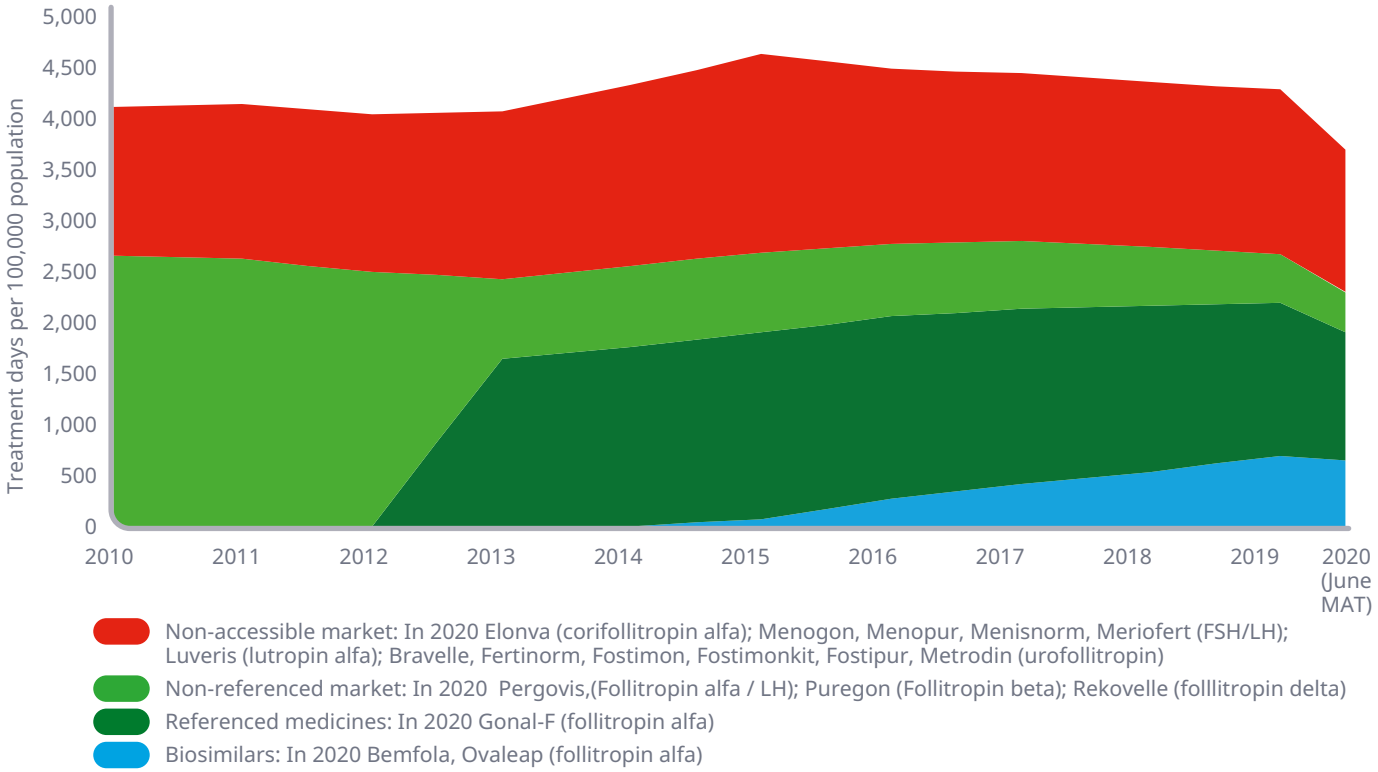
		AU	BE	BU	CZ	DK	FI	FR	DE	GR*	HU	IE	IT	NL	NO	PL	PT	RO	SK	SL	ES	SE	CH	UK	EU
MARKET SHARE TD (2020, JUNE MAT)	Biosimilar vs Referenced product	37%	26%	18%	45%	96%	38%	48%	61%	0%	4%	41%	64%	59%	74%	71%	47%	21%	12%	40%	49%	56%	20%	31%	41%
	Biosimilar vs Accessible market	37%	26%	18%	45%	96%	38%	48%	61%	0%	4%	41%	64%	59%	74%	71%	47%	21%	12%	40%	49%	56%	20%	13%	23%
	Biosimilar vs Total market	30%	24%	15%	40%	88%	32%	43%	52%	0%	4%	37%	55%	56%	67%	60%	43%	19%	11%	36%	44%	52%	16%	13%	23%
PRICE PER TD (2020 JUNE MAT/YR BEFORE BS ENTRY)	Biosimilar and Referenced product	-43%	-30%	-23%	-36%	-7%	-26%	-34%	-8%	2%	7%	-17%	-4%	-18%	-15%	-64%	-47%	-11%	-21%	-47%	-15%	-41%	-33%	-14%	-22%
	Biosimilar Accessible market	-43%	-30%	-23%	-36%	-7%	-26%	-34%	-8%	2%	7%	-17%	-4%	-18%	-15%	-64%	-47%	-11%	-21%	-47%	-15%	-41%	-28%	-14%	-17%
	Total market	-42%	-36%	-24%	-42%	-19%	-33%	-40%	-20%	-8%	-8%	-25%	-13%	-26%	-20%	-61%	-51%	-21%	-31%	-48%	-24%	-46%	-28%	-14%	-17%
VOLUME TD (2020, JUNE MAT/YR BEFORE BS ENTRY)	Biosimilar and Referenced product	607%	133%	888%	232%	146%	215%	139%	362%	126%	68%	235%	87%	115%	191%	261%	217%	61%	98%	178%	171%	158%	-24%	21%	47%
	Biosimilar Accessible market	607%	133%	888%	232%	146%	215%	139%	362%	126%	68%	235%	87%	115%	191%	261%	217%	61%	98%	178%	171%	158%	55%	80%	51%
	Total market	563%	58%	348%	168%	58%	131%	69%	189%	-20%	12%	103%	29%	41%	116%	168%	133%	28%	39%	55%	79%	70%	55%	80%	51%
	TD per capita	1.08	1.46	0.46	0.63	1.41	1.47	1.04	1.43	0.00	0.36	1.91	0.47	1.37	2.26	0.11	0.62	0.26	0.68	0.72	0.87	1.52	1.11	0.97	0.91
	TD/capita (Yr before BS entrance)	0.16	0.93	0.10	0.24	0.89	0.64	0.62	0.49	0.01	0.32	0.94	0.36	0.97	1.05	0.04	0.26	0.21	0.49	0.47	0.48	0.90	0.81	0.60	0.48
	First Recorded sales of Biosimilars	2015	2015	2014	2013	2015	2013	2015	2015		2014	2014	2015	2015	2013	2014	2013	2014	2014	2015	2015	2015	2016	2015	2013

* Only retail panel data is available for Greece

Fertility (FOLLITROPIN ALFA)

Gonadotropin preparations are drugs that mimic the physiological effects of gonadotropins, used therapeutically primarily as fertility medication for ovarian hyperstimulation and reversal of an ovulation. For the purpose of this report, only Follicle-Stimulating Hormones (FSH) and Luteinizing Hormone (LH) preparations were considered.

Fertility Market Development



Fertility Approved Indications

NAMING		CLASSIFICATION											INDICATIONS					DOSING/ADMINISTRATION	
MOLECULE	PRODUCT	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020 (JUNE MAT)	INFERTILITY	HYPOGONADISM	ANOVULATION	OVULATION INDUCTION	REPRODUCTIVE TECHNIQUES, ASSISTED	ROUTE (SUBQ/IV/IM)	FREQUENCY
CORIFOLLITROPIN ALFA	ELONVA	●	●	●	●	●	●	●	●	●	●	●	●					SC	Patient specific
FOLLICLE-STIMULATING HORMONE / LUTEINISING HORMONE	MENOGON MENOPUR MERIOFERT*	● ●	● ●	● ●	● ●	● ●	● ●	● ● ●	● ● ●	● ● ●	● ● ●	● ● ●	● ● ●		●	●	● ●	SC/IM SC SC	Daily Daily Daily
FOLLITROPIN ALFA	GONAL-F BEMFOLA OVALEAP	●	●	●	● ● ●	● ● ●	● ● ●	● ● ●	● ● ●	● ● ●	● ● ●	● ● ●	● ● ●	● ●	● ●		● ●	All All All	Daily Daily Daily
FOLLITROPIN ALFA / LUTEINISING HORMONE	PERGOVERIS	●	●	●	●	●	●	●	●	●	●	●	●					All	Daily
FOLLITROPIN BETA	PUREGON	●	●	●	●	●	●	●	●	●	●	●	●	●				SC	Patient specific
FOLLITROPIN DELTA	REKOVELLE	●	●	●	●	●	●	●	●	●	●	●	●			●	●	SC	Daily
LUTROPIN ALFA	LUVERIS	●	●	●	●	●	●	●	●	●	●	●	●			●		All	Daily
UROFOLLITROPIN	BRAVELLE FOSTIMON FOSTIMONKIT FOSTIPUR METRODIN	● ● ● ● ●	● ● ● ● ●	● ● ● ● ●	● ● ● ● ●	● ● ● ● ●	● ● ● ● ●	● ● ● ● ●	● ● ● ● ●	● ● ● ● ●	● ● ● ● ●	● ● ● ● ●	● ● ● ● ●		●	● ● ● ● ●	● ●	SC/IM IM IM SC SC/IM	Daily Daily Daily Daily Daily

● Non-accessible market ● Non-referenced market ● Referenced medicines ● Biosimilars

*Also know as Fertinorm, Mensiorm (Poland)

Selected KPIs to Illustrate Volume Share, Price Evolution, and Volume Evolution in Selected European Countries

		AU	BE	BU	CZ	DK	FI	FR	DE	GR*	HU	IE	IT	NL	NO	PL	PT	RO	SK	SL	ES	SE	CH	UK	EU
MARKET SHARE TD (2020, JUNE MAT)	Biosimilar vs Referenced product	0%	55%	0%	12%	25%	24%	35%	39%	28%	90%	0%	39%	0%	31%	36%	37%	4%	53%	25%	45%	27%	5%	30%	34%
	Biosimilar vs Accessible market	0%	35%	0%	8%	21%	19%	27%	20%	18%	84%	0%	28%	0%	27%	23%	27%	3%	52%	22%	30%	27%	4%	29%	23%
	Biosimilar vs Total market	0%	19%	0%	6%	12%	12%	19%	16%	10%	67%	0%	16%	0%	16%	11%	17%	2%	25%	16%	18%	16%	2%	13%	16%
PRICE PER TD (2020 JUNE MAT/YR BEFORE BS ENTRY)	Biosimilar and Referenced product	58%	-5%	184%	-70%	-36%	-37%	-61%	-58%	-11%	-86%	-34%	-31%	-50%	-40%	65%	-13%	-28%	-26%	-65%	-32%	-48%	-2%	9%	-44%
	Biosimilar Accessible market	-26%	-6%	-30%	-13%	10%	-6%	-31%	-44%	-2%	-79%	32%	-3%	12%	9%	69%	6%	7%	18%	-1%	-23%	8%	61%	86%	-18%
	Total market	-42%	-7%	52%	24%	25%	7%	-9%	15%	22%	-69%	35%	7%	30%	6%	26%	50%	65%	30%	19%	1%	-1%	49%	52%	15%
VOLUME TD (2020, JUNE MAT/YR BEFORE BS ENTRY)	Biosimilar and Referenced product	86%	48%	52%	39%	44%	64%	13%	176%	6%	13%	59%	-39%	-9%	151%	39%	34%	45%	86%	61%	3%	73%	-14%	10%	23%
	Biosimilar Accessible market	35%	38%	-23%	53%	-4%	-12%	-13%	165%	16%	-2%	17%	-38%	0%	40%	18%	-4%	61%	52%	5%	-21%	21%	-15%	9%	12%
	Total market	103%	1%	-66%	7%	-28%	-34%	-30%	73%	-24%	-21%	-18%	-45%	-24%	2%	-13%	-26%	-8%	-16%	-29%	-37%	-20%	-38%	-24%	-17%
	TD per capita	0.01	0.04	0	0.06	0.07	0.03	0.06	0.06	0.02	0.03	0.08	0.04	0.05	0.06	0.02	0.02	0.01	0.02	0.04	0.05	0.07	0.03	0.01	0.04
	TD/capita (Yr before BS entrance)	0	0.04	0.01	0.05	0.1	0.04	0.09	0.04	0.02	0.04	0.09	0.07	0.07	0.06	0.02	0.03	0.02	0.03	0.06	0.08	0.08	0.05	0.02	0.05
	First Recorded sales of Biosimilars	2014	2015	2016	2015	2014	2014	2015	2014	2016	2015	2016	2015	2016	2014	2015	2015	2016	2016	2015	2015	2014	2018	2014	2014

* Only retail panel data is available for Greece

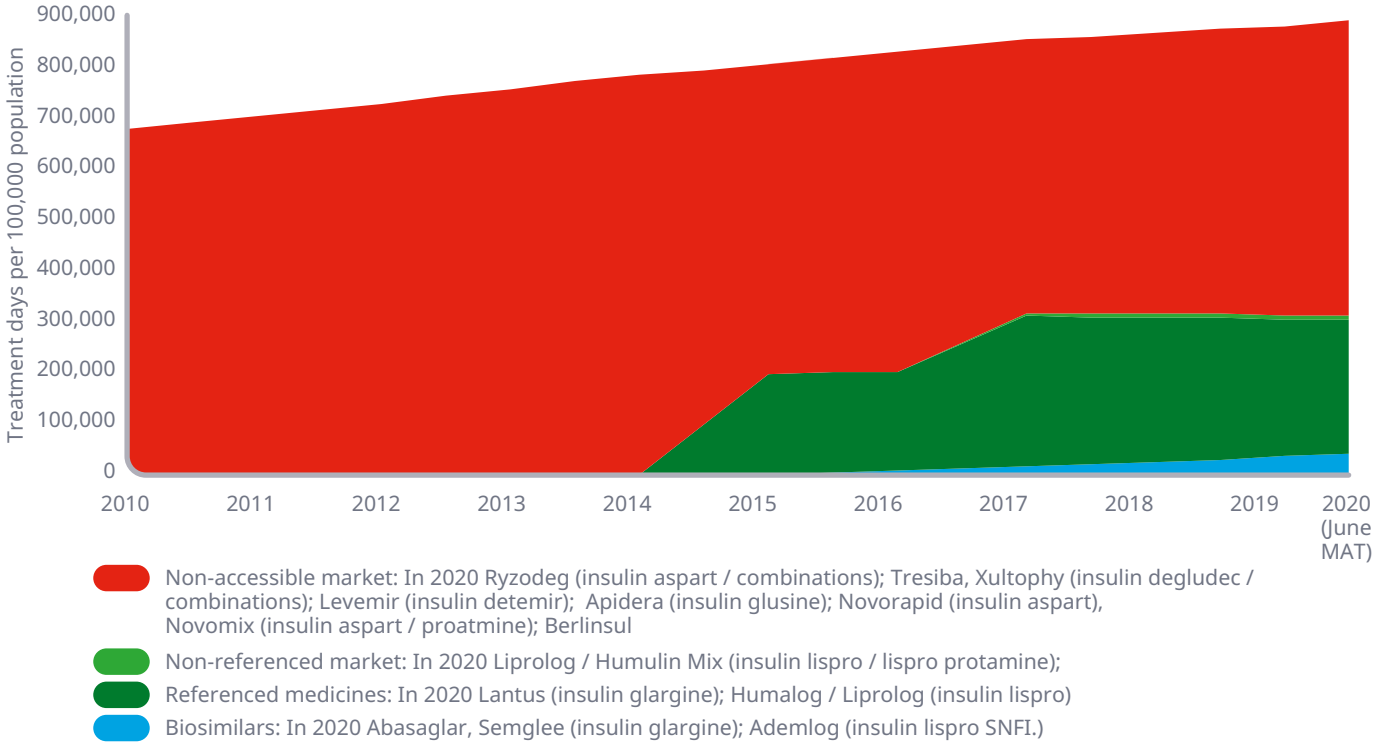
Insulins

Recombinant human insulin is a form of insulin made from recombinant DNA that is identical to human insulin; used to treat diabetics who are allergic to preparations made from beef or pork insulin.

INSULIN MARKET DEVELOPMENT

Protection for the referenced product was lost in 2015, with biosimilars entering the market shortly after, although a significant proportion of the market still remains in the in-accessible segment due to protection.

Insulin Market Development



ADDITIONAL INFORMATION ABOUT INSULIN MEDICINES

Insulin preparations differ mainly by their kinetic/pharmacodynamic profiles. They are usually classified as rapid- (faster acting than soluble human insulin), short- (e.g. soluble human insulin), intermediate- (NPH /Neutral Protamine Hagedorn insulin, e.g. human isophane insulin), and long-acting preparations (insulins with action profiles significantly longer than NPH insulin). They are used alone or as free mixtures or premixed preparations of rapid/short-acting insulin and intermediate/long-acting (biphasic) insulin in various proportions.

Regular insulin is a short-acting insulin and is generally injected subcutaneously (SubQ) 2-5 times daily within 30-60 minutes before a meal. In conventional regimen the total daily insulin dose is administered as a mixture of rapid/short-acting and intermediate-acting insulins in 1-2 injections. In intensive regimen the total daily dose is administered as 3 or more injections or by continuous subcutaneous infusion to cover basal and pre-meal bolus insulin requirements.

Insulin Approved Indications

NAMING		CLASSIFICATION											INDICATIONS	DOSING/ADMINISTRATION	
MOLECULE	PRODUCT	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020 (JUNE MAT)	DIABETES MELLITUS	FREQUENCY	MODE OF ACTION
INSULIN ASPART	NOVORAPID	●	●	●	●	●	●	●	●	●	●	●	●	before every meal	Fast-acting
INSULIN ASPART#INSULIN ASPART PROTAMINE	NOVOMIX	●	●	●	●	●	●	●	●	●	●	●	●	before every meal	Fast-acting
INSULIN ASPART#INSULIN DEGLUDEC	RYZODEG				●	●	●	●	●	●	●	●	●	daily	Fast-acting
INSULIN DEGLUDEC	TRESIBA				●	●	●	●	●	●	●	●	●	daily	Long-acting
INSULIN DEGLUDEC / LIRAGLUTIDE	XULTOPHY					●	●	●	●	●	●	●	●	daily	Long-acting
INSULIN DETEMIR	LEVEMIR	●	●	●	●	●	●	●	●	●	●	●	●	twice a day	Long-acting
INSULIN GLARGINE	LANTUS ABASAGLAR SEMGLEE	●	●	●	●	●	● ● ●	● ● ●	● ● ●	● ● ●	● ● ●	● ● ●	● ● ●	daily daily daily	Long-acting Long-acting Long-acting
INSULIN GLARGINE / LIXISENATIDE	SOLIQUA								●	●	●	●	●	daily	Long-acting
INSULIN GLULISINE	APIDRA	●	●	●	●	●	●	●	●	●	●	●	●	before every meal	Fast-acting
INSULIN HUMAN*	BERLINSULIN GENSULIN HUMULIN INSUMAN**	● ● ● ●	● ● ● ●	● ● ● ●	● ● ● ●	● ● ● ●	● ● ● ●	● ● ● ●	● ● ● ●	● ● ● ●	● ● ● ●	● ● ● ●	● ● ● ●	determined by physician determined by physician once/twice a day determined by physician	Short-acting Short-acting Short-acting Fast-acting
INSULIN LISPRO	HUMALOG/LIPROLOG ADMELOG	●	●	●	●	●	●	●	● ●	● ●	● ●	● ●	● ●	before every meal before every meal	Fast-acting Fast-acting
INSULIN LISPRO#INSULIN LISPRO PROTAMINE	HUMALOG / LIPROLOG MIX	●	●	●	●	●	●	●	●	●	●	●	●	determined by physician	Fast-acting

● Non-accessible market ● Non-referenced market ● Referenced medicines ● Biosimilars

* Country specific molecules include Polhumin R, and other low use products ** Insuplant was replaced by Insuman in 2012

Notes: Exubera was withdrawn by Pfizer in 2007 and has been removed from the table

Selected KPIs to Illustrate Volume Share, Price Evolution, and Volume Evolution in Selected European Countries

		AU	BE	BU	CZ	DK	FI	FR	DE	GR*	HU	IE	IT	NL	NO	PL	PT	RO	SK	SL	ES	SE	CH	UK	EU
MARKET SHARE TD (2020, JUNE MAT)	Biosimilar vs Referenced product	0%	4%	11%	10%	18%	13%	7%	11%	16%	11%	0%	17%	30%	4%	32%	11%	7%	32%	8%	15%	35%	1%	9%	13%
	Biosimilar vs Accessible market	0%	4%	9%	9%	18%	13%	7%	11%	16%	10%	0%	17%	30%	4%	30%	11%	7%	30%	7%	15%	34%	1%	9%	13%
	Biosimilar vs Total market	0%	1%	1%	2%	3%	4%	3%	4%	6%	1%	0%	8%	8%	1%	10%	4%	2%	9%	1%	6%	10%	0%	3%	4%
PRICE PER TD (2020 JUNE MAT/YR BEFORE BS ENTRY)	Biosimilar and Referenced product	-3%	-21%	-14%	-8%	-9%	-23%	-11%	-2%	-12%	-21%	-19%	-14%	-17%	-8%	-29%	-10%	-10%	-14%	-21%	-24%	-17%	-3%	-10%	-7%
	Biosimilar Accessible market	16%	-14%	51%	7%	-9%	-23%	-8%	4%	1%	-9%	-14%	-12%	-14%	-6%	-10%	14%	3%	2%	17%	-13%	-9%	2%	8%	2%
	Total market	31%	14%	66%	37%	7%	-15%	6%	15%	36%	41%	3%	16%	8%	22%	38%	1%	23%	34%	52%	4%	9%	36%	28%	20%
VOLUME TD (2020, JUNE MAT/YR BEFORE BS ENTRY)	Biosimilar and Referenced product	-1%	-15%	0%	33%	-16%	-23%	-15%	163%	-4%	-29%	-18%	-9%	-9%	-9%	168%	50%	15%	25%	-1%	-6%	9%	-24%	-5%	32%
	Biosimilar Accessible market	-17%	-22%	-37%	8%	-16%	-23%	-19%	121%	-24%	-37%	-21%	-15%	-11%	-11%	68%	13%	-3%	4%	-33%	-20%	-4%	-27%	-21%	15%
	Total market	-16%	2%	-25%	18%	2%	1%	7%	79%	1%	-3%	6%	0%	-7%	12%	-25%	21%	9%	-4%	-24%	-4%	-3%	-3%	-15%	16%
	TD per capita	4.52	6.66	4.41	9.00	6.61	11.63	6.66	20.53	7.05	8.98	4.85	5.68	8.25	7.54	4.98	6.87	5.71	6.22	6.40	6.67	9.18	4.35	6.17	8.70
	TD/capita (Yr before BS entrance)	5.41	6.56	5.89	7.61	6.50	11.50	6.20	11.45	6.95	9.21	4.56	5.69	8.91	6.75	6.66	5.67	5.23	6.47	8.45	6.98	9.50	4.47	7.29	7.47
	First Recorded sales of Biosimilars	2017	2016	2015	2015	2015	2015	2016	2015	2016	2015	2016	2016	2015	2015	2015	2016	2016	2015	2016	2015	2015	2015	2015	2015

* Only retail panel data is available for Greece

Oncology

Monoclonal Antibody Antineoplastic agents use monoclonal antibodies (mAb) to bind monospecifically to certain cells or proteins to treat cancer. The objective is that this treatment will stimulate the patient's immune system to attack those cells.

Considering that the primary indications used for Mabthera and rituximab biosimilars are in Oncology, and since IQVIA sales and treatment day volume cannot be split by indication, rituximab market dynamics are only considered in this separate Oncology section, within the Monoclonal Antibody Antineoplastic class alongside major oncology products with biosimilar competition: trastuzumab and bevacizumab.

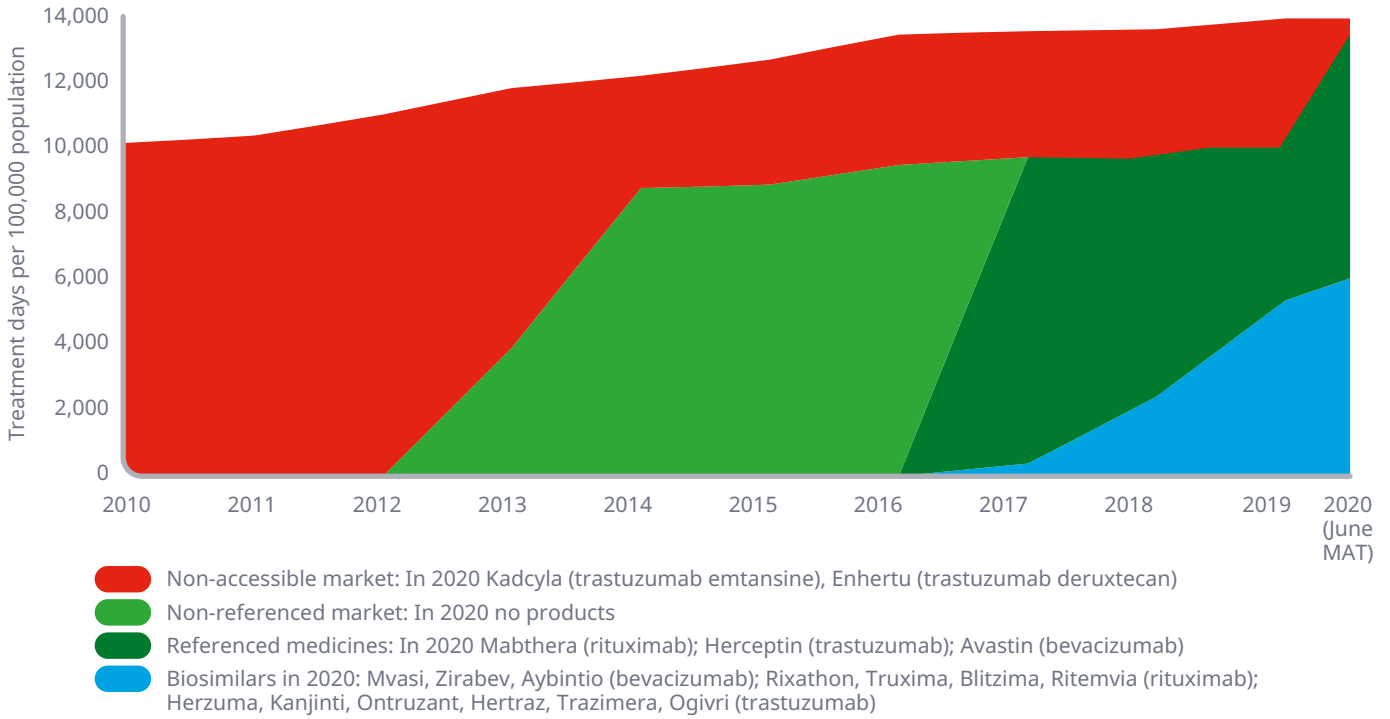
In this market the non-accessible products are classified by identifying products which have a similar mechanism of action, and are used for similar indications to rituximab. There are both IV and SC forms of Mabthera available, but because the biosimilar is only available in IV form, Mabthera IV is classified as the referenced product, and Mabthera SC is classified as a non-referenced product.

WHO DDD's are not available for products in this class, so rituximab and trastuzumab DDD's were calculated using IQVIA Oncology Dynamics data (MAT Dec 2017), accounting for the dosing and length of the treatment cycle in EU5. For other products in the class, the DDD's were calculated using EMA dosing information.

ONCOLOGY MARKET DEVELOPMENT

Protection for Mabthera and Herceptin expired a number of years prior to biosimilar entry. This chart reflects the period in which these products were 'non-referenced'. In contrast, Avastin had approved biosimilars in Europe before protection expiry. There are no recorded sales, but this is recorded, and Avastin is classified accurately as 'non-accessible' until its protection status expires.

Oncology Market Development



Oncology Approved Indications

NAMING		CLASSIFICATION											INDICATIONS									DOSING	
MOLECULE	PRODUCT	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020 (JUNE MAT)	FL, DLBC (NON-GL)	CLL	MC	HER-2+ BC	METASTATIC GC	RCC	NSCLC	EOC	PPC	ROUTE (SUBQ / IV)	FREQUENCY
BEVACIZUMAB*	AVASTIN MVASI ZIRABEV AYBINTIO	●	●	●	●	●	●	●	●	●	●	●			●			●	●	●	●	IV IV IV IV	2 - 3 week cycles (indication/ combination dependant)
RITUXIMAB**	MABTHERA RIXATHON TRUXIMA BLITZIMA RITEMVIA	●	●	●	●	●	●	●	●	●	●	●	●	●								SC/IV IV IV IV IV	3 week cycles
TRASTUZUMAB	HERCEPTIN HERZUMA KANJINTI ONTRUZANT HERTRAZ TRAZIMERA OGIVRI	●	●	●	●	●	●	●	●	●	●	●				●	●					SC/IV IV IV IV IV IV IV	3 week cycles
TRASTUZUMAB EMTANSINE	KADCYLA				●	●	●	●	●	●	●	●				●						IV	3 week cycles
TRASTUZUMAB DERUXTECAN	ENHERTU											●				●						IV	3 week cycles

● Non-accessible market ● Non-referenced market ● Referenced medicines ● Biosimilars

*Note: no sales for any biosimilar of bevacizumab are recorded by IQVIA MIDAS® during the time period in the report. Although, sales are visibile for bevacizumab in Germany in July 2020. Products with an EMA marketing authorisation granted prior to Avastin's loss of exclusivity are captured, however, Avastin does not transition to a 'referenced' medicine until a biosimilar has positive marketing authorisation and protection expires. Products are only included with a positive EMA marketing authorisation granted before 30th June 2020 for the purposes of this report.

** Indicatied for non-oncology indications such as rheumatoid arthritis, Granulomatosis with polyangiitis and microscopic polyangiitis. ...Pemphigus vulgaris.

FL = follicular lymphoma, DLBC = Diffuse large B-cell lymphoma, MC = metastatic carcinoma, GC = gastic cancer, RCC = renal cell carcinoma, NSCLC = non-small cell lung cancer, EOC = epithelial ovarian cancer, PPC = Primary peritoneal cancer

Selected KPIs to Illustrate Volume Share, Price Evolution, and Volume Evolution in Selected European Countries

		AU	BE	BU	CZ	DK	FI	FR	DE	GR*	HU	IE	IT	NL	NO	PL	PT	RO	SK	SL	ES	SE	CH	UK	EU
MARKET SHARE TD (2020, JUNE MAT)	Biosimilar vs Referenced product	52%	4%	3%	67%	74%	27%	40%	49%	0%	32%	16%	52%	72%	70%	20%	30%	12%	24%	20%	36%	64%	12%	61%	45%
	Biosimilar vs Accessible market	52%	4%	3%	67%	74%	27%	40%	49%	0%	32%	16%	52%	72%	70%	20%	30%	12%	24%	20%	36%	64%	12%	61%	40%
	Biosimilar vs Total market	49%	4%	3%	67%	72%	26%	39%	47%	0%	31%	16%	50%	70%	69%	20%	28%	6%	24%	20%	34%	62%	11%	59%	39%
PRICE PER TD (2020 JUNE MAT/YR BEFORE BS ENTRY)	Biosimilar and Referenced product	-5%	-2%	-3%	-62%	-13%	2%	-21%	-14%	0%	2%	-10%	-8%	-9%	14%	-36%	-14%	8%	-4%	-27%	-5%	-3%	-11%	0%	-12%
	Biosimilar Accessible market	-5%	-2%	-3%	-62%	-13%	2%	-21%	-14%	0%	2%	-10%	-8%	-9%	14%	-36%	-14%	8%	-4%	-27%	-5%	-3%	-11%	0%	-17%
	Total market	-7%	-12%	-9%	-63%	-17%	-2%	-21%	-15%	0%	-6%	-13%	-12%	-15%	9%	-38%	-13%	73%	-10%	-29%	-9%	-4%	-13%	0%	-19%
VOLUME TD (2020 JUNE MAT/YR BEFORE BS ENTRY)	Biosimilar and Referenced product	47%	93%	100%	227%	55%	46%	69%	41%	0%	62%	16%	31%	60%	51%	18%	49%	-86%	73%	33%	52%	27%	28%	-1%	42%
	Biosimilar Accessible market	47%	93%	100%	227%	55%	46%	69%	41%	0%	62%	16%	31%	60%	51%	18%	49%	-86%	73%	33%	52%	27%	28%	-1%	59%
	Total market	-6%	39%	17%	141%	14%	12%	7%	-4%	0%	-6%	-8%	-5%	24%	25%	1%	22%	-86%	-1%	14%	19%	9%	-2%	-6%	16%
	TD per capita	0.16	0.21	0.12	0.25	0.18	0.17	0.18	0.19	0.00	0.11	0.14	0.13	0.16	0.15	0.06	0.11	0.01	0.10	0.13	0.15	0.14	0.16	0.10	0.16
	TD/capita (Yr before BS entrance)	0.17	0.15	0.10	0.10	0.15	0.15	0.16	0.20	0.00	0.11	0.15	0.14	0.13	0.12	0.06	0.09	0.05	0.11	0.12	0.13	0.13	0.17	0.11	0.13
	First Recorded sales of Biosimilars	2017	2018	2018	2018	2017	2018	2017	2017		2018	2017	2017	2017	2017	2018	2017	2018	2018	2018	2017	2018	2018	2017	2017

* Only retail panel data is available for Greece

Low-molecular-weight heparin (LMWH)

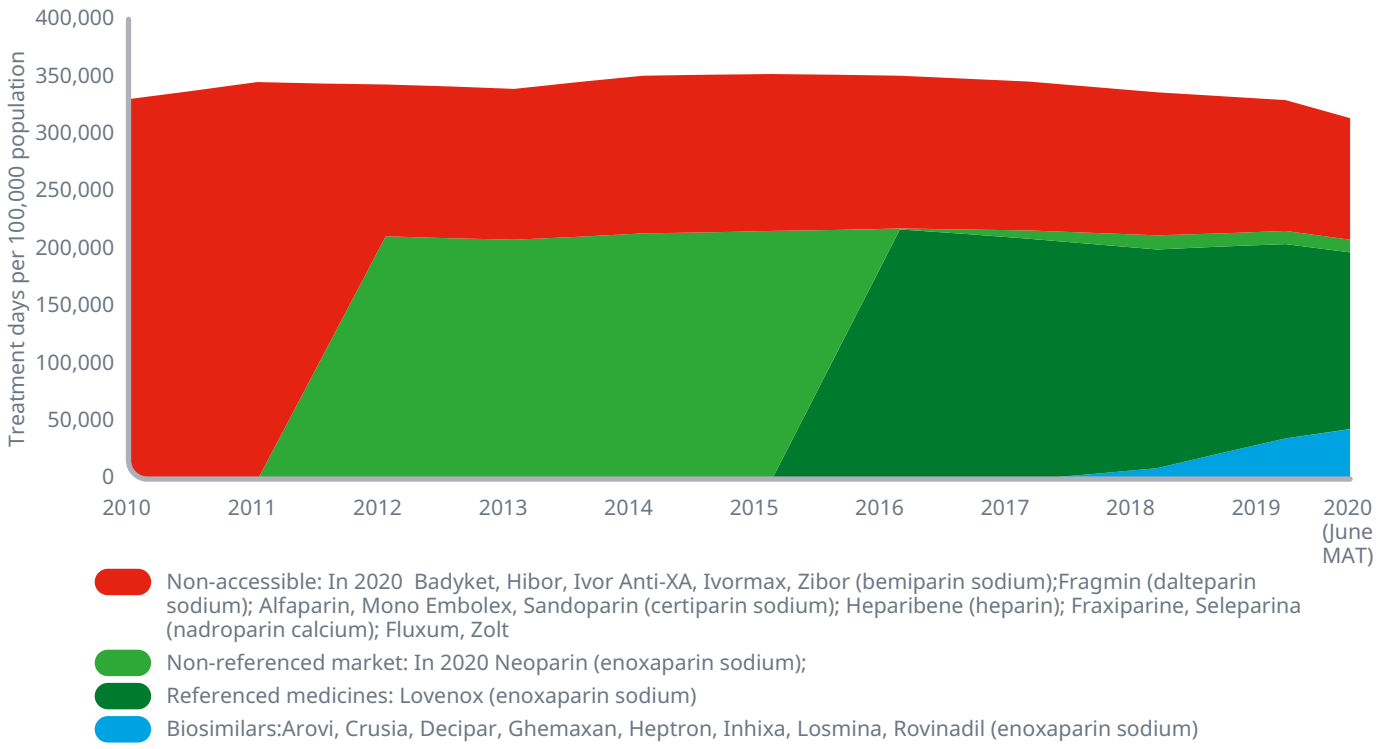
Low-Molecular-Weight Heparin (LMWH) is a class of anticoagulant medications. They are used in the prevention of blood clots, treatment of venous thromboembolism (deep vein thrombosis and pulmonary embolism) and in the treatment of myocardial infarction. LMWH is obtained by fractionation of polymeric heparin. Many LMWH products are on the market, each similar in structure but created using different initial chemical procedures e.g. Enoxaparin is created using alkaline beta-eliminative cleavage of the benzyl ester of heparin.

Two Enoxaparin Sodium biosimilars (Inhixa and Thorinane) were authorised by the EMA in 09/2016. IQVIA MIDAS® sales only started to be reported for these biosimilars in 2017. By 2018, only 6 of the 23 cohort countries showed biosimilar usage (Austria, France, Germany, Italy, Spain, and UK). Now in 2020 is the first year the market has been included within 'The Impact of Biosimilar Competition' report as a milestone 10 of the 23 markets can now be included.

LMWH MARKET DEVELOPMENT

Protection for Lovenox expired a number of years prior to biosimilar entry. This chart reflects the period in which these product was 'non-referenced'.

LMWH Market Development



LMWH Approved Indications

NAMING		CLASSIFICATION											INDICATIONS			
MOLECULE	PRODUCT	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020 (JUNE MAT)	DEEP VEIN THROMBOSIS TREATMENT AND PROPHYLAXIS	PULMONARY EMBOLISM	ATRIAL THROMBUS	BRIDGING THERAPY PRIOR TO STARTING WARFARIN
EMIPARIN SODIUM	BADYKET HIBOR IVOR ANTI-XA IVORMAX ZIBOR	●	●	●	●	●	●	●	●	●	●	●	●	●		
CERTOPARIN SODIUM	ALFAPARIN MONO EMBOLEX SANDOPARIN	●	●	●	●	●	●	●	●	●	●	●	●	●		
DALTEPARIN SODIUM	FRAGMIN	●	●	●	●	●	●	●	●	●	●	●	●			
ENOXAPARIN SODIUM	LOVENOX NEOPARIN INHIXA AROVI CRUSIA DECIPAR GHEMAXAN HEPTRON LOSMINA ROVINADIL	●	●	●	●	●	●	●	●	●	●	●	●			●
HEPARIN	HEPARIBENE	●	●	●	●	●	●	●	●	●	●	●	●	●	●	
NADROPARIN CALCIUM	FRAXIPARINE SELEPARINA	●	●	●	●	●	●	●	●	●	●	●	●	●		
PARNAPARIN	FLUXUM ZOLTAR	●	●	●	●	●	●	●	●	●	●	●	●	●		
REVIPARIN	CLIVARIN CLIVARINA	●	●	●	●	●	●	●	●	●	●	●	●	●		
TINZAPARIN	INNOHEP	●	●	●	●	●	●	●	●	●	●	●	●	●		●

● Non-accessible market ● Non-referenced market ● Referenced medicines ● Biosimilars

Selected KPIs to Illustrate Volume Share, Price Evolution, and Volume Evolution in Selected European Countries

		AU	BE	BU	CZ	DK	FI	FR	DE	GR*	HU	IE	IT	NL	NO	PL	PT	RO	SK	SL	ES	SE	CH	UK	EU
MARKET SHARE TD (2020, JUNE MAT)	Biosimilar vs Referenced product	40%	0%	0%	0%	64%	4%	8%	23%	0%	0%	0%	33%	0%	0%	0%	40%	0%	0%	0%	35%	0%	0%	47%	22%
	Biosimilar vs Accessible market	40%	0%	0%	0%	64%	4%	8%	23%	0%	0%	0%	33%	0%	0%	0%	40%	0%	0%	0%	35%	0%	0%	47%	21%
	Biosimilar vs Total market	33%	0%	0%	0%	1%	3%	4%	18%	0%	0%	0%	29%	0%	0%	0%	38%	0%	0%	0%	26%	0%	0%	26%	14%
PRICE PER TD (2020 JUNE MAT/YR BEFORE BS ENTRY)	Biosimilar and Referenced product	-73%				10742%	-57%	-37%	-50%				-23%			-55%	-87%				-21%			23%	-27%
	Biosimilar Accessible market	-26%				10778%	39%	49%	21%				44%			-33%	-32%				39%			76%	42%
	Total market	-41%				-1%	-4%	1%	-14%				23%			-2%	-37%				-12%			-13%	-6%
VOLUME TD (2020, JUNE MAT/YR BEFORE BS ENTRY)	Biosimilar and Referenced product	-24%				-53%	1%	0%	-11%				-14%			13%	-2%				4%			7%	8%
	Biosimilar Accessible market	-24%				-53%	1%	0%	-11%				-14%			-1%	-8%				4%			7%	7%
	Total market	-22%				3%	-1%	-5%	-19%				-22%			-7%	-1%				4%			-4%	7%
	TD per capita	3.94	3.13	0.97	3.56	1.31	2.47	3.91	5.19	2.28	4.98	1.58	2.80	1.07	2.08	3.27	1.86	1.34	4.84	2.44	3.53	1.48	2.04	1.84	3.17
	TD/capita (Yr before BS entrance)	5.04				1.27	2.50	4.12	6.43				3.57			3.51	1.89				3.41			1.92	2.97
	First Recorded sales of Biosimilars	2018				2019	2020	2018	2017				2017			2019	2019				2018			2017	2017

* Only retail panel data is available for Greece

Appendix

Table 1: EMA List of Approved Biosimilars (July 2020)

MEDICINE NAME	INTERNATIONAL NON-PROPRIETARY NAME (INN) / COMMON NAME	THERAPEUTIC AREA	ATC CODE	MARKETING AUTHORISATION HOLDER/ COMPANY NAME	MARKETING AUTHORISATION DATE
INSULIN ASPART SANOFI	insulin aspart	Diabetes Mellitus	A10AB05	sanofi-aventis groupe	25/06/2020
NEPEXTO	etanercept	Arthritis, Rheumatoid, Arthritis, Juvenile Rheumatoid, Arthritis, Psoriatic, Spondylarthropathies, Spondylitis, Ankylosing, Psoriasis	L04AB01	Mylan IRE Healthcare Limited	20/05/2020
RUXIENCE	rituximab	Leukemia, Lymphocytic, Chronic, B-Cell, Arthritis, Rheumatoid, Microscopic Polyangiitis, Pemphigus	L01XC02	Pfizer Europe MA EEIG	1/04/2020
AMSPARITY	adalimumab	Arthritis, Rheumatoid, Arthritis, Juvenile Rheumatoid, Psoriasis, Arthritis, Psoriatic, Spondylitis, Ankylosing, Uveitis, Colitis, Ulcerative, Crohn Disease, Hidradenitis Suppurativa	L04AB04	Pfizer Europe MA EEIG	13/02/2020
CEGFILA (PREVIOUSLY PEGFILGRASTIM MUNDIPHARMA)	pegfilgrastim	Neutropenia	L03AA13	Mundipharma Corporation (Ireland) Limited	19/12/2019
GRASUSTEK	pegfilgrastim	Neutropenia	L03AA13	Juta Pharma GmbH	20/06/2019
KROMEYA	adalimumab	Arthritis, Rheumatoid, Arthritis, Juvenile Rheumatoid, Psoriasis, Arthritis, Psoriatic, Spondylitis, Ankylosing, Uveitis, Colitis, Ulcerative, Crohn Disease	L04AB04	Fresenius Kabi Deutschland GmbH	2/04/2019
IDACIO	adalimumab	Arthritis, Rheumatoid, Arthritis, Juvenile Rheumatoid, Psoriasis, Arthritis, Psoriatic, Spondylitis, Ankylosing, Uveitis, Hidradenitis Suppurativa, Colitis, Ulcerative, Crohn Disease	L04AB04	Fresenius Kabi Deutschland GmbH	2/04/2019
ZIRABEV	bevacizumab	Colorectal Neoplasms, Breast Neoplasms, Carcinoma, Non-Small-Cell Lung, Carcinoma, Renal Cell, Uterine Cervical Neoplasms	L01XC07	Pfizer Europe MA EEIG	14/02/2019
OGIVRI	trastuzumab	Stomach Neoplasms, Breast Neoplasms	L01XC03	Mylan S.A.S	12/12/2018
ZIEXTENZO	pegfilgrastim	Neutropenia	L03AA13	Sandoz GmbH	22/11/2018
PELMEG	pegfilgrastim	Neutropenia	L03AA13	Mundipharma Corporation (Ireland) Limited	20/11/2018
FULPHILA	pegfilgrastim	Neutropenia	L03AA13	Mylan S.A.S	20/11/2018
PELGRAZ	pegfilgrastim	Neutropenia	L03AA13	Accord Healthcare S.L.U.	21/09/2018
UDENYCA	pegfilgrastim	Neutropenia	L03AA13	ERA Consulting GmbH	21/09/2018
HULIO	adalimumab	Hidradenitis Suppurativa, Psoriasis, Crohn Disease, Uveitis, Arthritis, Rheumatoid, Colitis, Ulcerative, Spondylitis, Ankylosing, Arthritis, Psoriatic	L04AB04	Mylan S.A.S.	16/09/2018
HYRIMOZ	adalimumab	Hidradenitis Suppurativa, Crohn Disease, Arthritis, Juvenile Rheumatoid, Uveitis, Arthritis, Rheumatoid, Colitis, Ulcerative, Spondylitis, Ankylosing, Skin Diseases, Papulosquamous, Arthritis, Psoriatic	L04AB04	Sandoz GmbH	26/07/2018
HEFIYA	adalimumab	Hidradenitis Suppurativa, Spondylitis, Ankylosing, Psoriasis, Arthritis, Juvenile Rheumatoid, Uveitis	L04AB04	Sandoz GmbH	26/07/2018
HALIMATOZ	adalimumab	Hidradenitis Suppurativa, Psoriasis, Arthritis, Juvenile Rheumatoid, Uveitis, Arthritis, Rheumatoid, Spondylitis, Ankylosing, Arthritis, Psoriatic	L04AB04	Sandoz GmbH	26/07/2018
TRAZIMERA	trastuzumab	Stomach Neoplasms, Breast Neoplasms	L01XC03	Pfizer Europe MA EEIG	26/07/2018
ZESSLY	infliximab	Arthritis, Psoriatic, Psoriasis, Crohn Disease, Arthritis, Rheumatoid, Colitis, Ulcerative, Spondylitis, Ankylosing	L04AB02	Sandoz GmbH	18/05/2018
KANJINTI	trastuzumab	Stomach Neoplasms, Breast Neoplasms	L01XC03	Amgen Europe B.V.	16/05/2018
SEMGLEE	insulin glargine	Diabetes Mellitus	A10AE04	Mylan S.A.S	23/03/2018
HERZUMA	trastuzumab	Stomach Neoplasms, Breast Neoplasms	L01XC03	Celltrion Healthcare Hungary Kft.	8/02/2018
MVASI	bevacizumab	Carcinoma, Renal Cell, Peritoneal Neoplasms, Ovarian Neoplasms, Breast Neoplasms, Carcinoma, Non-Small-Cell Lung, Fallopian Tube Neoplasms	L01XC07	Amgen Technology (Ireland) UC	15/01/2018
ONTRUZANT	trastuzumab	Stomach Neoplasms, Breast Neoplasms	L01XC03	Samsung Bioepis NL B.V.	15/11/2017
CYLTEZO	adalimumab	Hidradenitis Suppurativa, Arthritis, Psoriatic, Psoriasis, Crohn Disease, Arthritis, Juvenile Rheumatoid, Uveitis, Arthritis, Rheumatoid, Colitis, Ulcerative, Spondylitis, Ankylosing	L04AB04	Boehringer Ingelheim International GmbH	10/11/2017

MEDICINE NAME	INTERNATIONAL NON-PROPRIETARY NAME (INN) / COMMON NAME	THERAPEUTIC AREA	ATC CODE	MARKETING AUTHORISATION HOLDER/ COMPANY NAME	MARKETING AUTHORISATION DATE
IMRALDI	adalimumab	Hidradenitis Suppurativa, Psoriasis, Crohn Disease, Uveitis, Arthritis, Rheumatoid, Arthritis, Colitis, Ulcerative, Spondylitis, Ankylosing, Arthritis, Psoriatic	L04AB04	Samsung Bioepis NL B.V.	24/08/2017
INSULIN LISPRO SANOFI	insulin lispro	Diabetes Mellitus	A10AB04	sanofi-aventis groupe	18/07/2017
BLITZIMA	rituximab	Lymphoma, Non-Hodgkin, Leukemia, Lymphocytic, Chronic, B-Cell	L01XC02	Celltrion Healthcare Hungary Kft.	13/07/2017
RITEMVIA	rituximab	Lymphoma, Non-Hodgkin, Microscopic Polyangiitis, Wegener Granulomatosis	L01XC02	Celltrion Healthcare Hungary Kft.	13/07/2017
RITUZENA (PREVIOUSLY TUXELLA)	rituximab	Lymphoma, Non-Hodgkin, Microscopic Polyangiitis, Leukemia, Lymphocytic, Chronic, B-Cell, Wegener Granulomatosis	L01XC02	Celltrion Healthcare Hungary Kft.	13/07/2017
ERELZI	etanercept	Arthritis, Psoriatic, Psoriasis, Arthritis, Juvenile Rheumatoid, Arthritis, Rheumatoid, Spondylitis, Ankylosing	L04AB01	Sandoz GmbH	23/06/2017
RIXIMYO	rituximab	Lymphoma, Non-Hodgkin, Arthritis, Rheumatoid, Microscopic Polyangiitis, Wegener Granulomatosis	L01XC02	Sandoz GmbH	15/06/2017
RIXATHON	rituximab	Lymphoma, Non-Hodgkin, Arthritis, Rheumatoid, Leukemia, Lymphocytic, Chronic, B-Cell, Wegener Granulomatosis, Microscopic Polyangiitis, Pemphigus	L01XC02	Sandoz GmbH	15/06/2017
SOLYMBIC	adalimumab	Arthritis, Psoriatic, Spondylitis, Ankylosing, Crohn Disease, Colitis, Ulcerative, Hidradenitis Suppurativa, Psoriasis, Arthritis, Rheumatoid	L04AB04	Amgen Europe B.V.	22/03/2017
AMGEVITA	adalimumab	Arthritis, Psoriatic, Colitis, Ulcerative, Arthritis, Juvenile Rheumatoid, Spondylitis, Ankylosing, Psoriasis, Crohn Disease, Arthritis, Rheumatoid	L04AB04	Amgen Europe B.V.	21/03/2017
TRUXIMA	rituximab	Lymphoma, Non-Hodgkin, Arthritis, Rheumatoid, Wegener Granulomatosis, Leukemia, Lymphocytic, Chronic, B-Cell, Microscopic Polyangiitis	L01XC02	Celltrion Healthcare Hungary Kft.	17/02/2017
MOVYMIA	teriparatide	Osteoporosis	H05AA02	STADA Arzneimittel AG	11/01/2017
TERROSA	teriparatide	Osteoporosis	H05AA02	Gedeon Richter Plc.	4/01/2017
LUSDUNA	insulin glargine	Diabetes Mellitus	A10AE04	Merck Sharp & Dohme B.V.	3/01/2017
INHIXA	enoxaparin sodium	Venous Thromboembolism	B01AB05	Techdow Pharma Netherlands B.V.	15/09/2016
THORINANE	enoxaparin sodium	Venous Thromboembolism	B01AB05	Pharmathen S.A.	14/09/2016
FLIXABI	infliximab	Spondylitis, Ankylosing, Arthritis, Rheumatoid, Crohn Disease, Colitis, Ulcerative, Arthritis, Psoriatic, Psoriasis	L04AB02	Samsung Bioepis NL B.V.	26/05/2016
BENEPALI	etanercept	Arthritis, Psoriatic, Arthritis, Rheumatoid, Psoriasis	L04AB01	Samsung Bioepis NL B.V.	13/01/2016
ACCOFIL	filgrastim	Neutropenia	L03AA02	Accord Healthcare S.L.U.	17/09/2014
ABASAGLAR (PREVIOUSLY ABASRIA)	insulin glargine	Diabetes Mellitus	A10AE04	Eli Lilly Nederland B.V.	9/09/2014
BEMFOLA	follitropin alfa	Anovulation	G03GA05	Gedeon Richter Plc.	26/03/2014
GRASTOFIL	filgrastim	Neutropenia	L03AA02	Accord Healthcare, SLU	17/10/2013
OVALEAP	follitropin alfa	Anovulation	G03GA05	Theramex Ireland Limited	27/09/2013
INFLECTRA	infliximab	Arthritis, Psoriatic, Spondylitis, Ankylosing, Colitis, Ulcerative, Psoriasis, Crohn Disease, Arthritis, Rheumatoid	L04AB02	Pfizer Europe MA EEIG	10/09/2013
REMSIMA	infliximab	Arthritis, Psoriatic, Spondylitis, Ankylosing, Colitis, Ulcerative, Psoriasis, Crohn Disease, Arthritis, Rheumatoid	L04AB02	Celltrion Healthcare Hungary Kft.	10/09/2013
NIVESTIM	filgrastim	Neutropenia, Hematopoietic Stem Cell Transplantation, Cancer	L03AA02	Pfizer Europe MA EEIG	7/06/2010
FILGRASTIM HEXAL	filgrastim	Neutropenia, Hematopoietic Stem Cell Transplantation, Cancer	L03AA02	Hexal AG	6/02/2009
ZARZIO	filgrastim	Neutropenia, Hematopoietic Stem Cell Transplantation, Cancer	L03AA02	Sandoz GmbH	6/02/2009
TEVAGRASTIM	filgrastim	Neutropenia, Hematopoietic Stem Cell Transplantation, Cancer	L03AA02	Teva GmbH	15/09/2008
RATIOGRASTIM	filgrastim	Neutropenia, Hematopoietic Stem Cell Transplantation, Cancer	L03AA02	Ratiopharm GmbH	15/09/2008
BIOGRASTIM	filgrastim	Neutropenia, Hematopoietic Stem Cell Transplantation, Cancer	L03AA02	AbZ-Pharma GmbH	15/09/2008
FILGRASTIM RATIOPHARM	filgrastim	Neutropenia, Hematopoietic Stem Cell Transplantation, Cancer	L03AA02	Ratiopharm GmbH	15/09/2008
RETACRIT	epoetin zeta	Anemia, Blood Transfusion, Autologous, Kidney Failure, Chronic, Cancer	B03XA01	Pfizer Europe MA EEIG	18/12/2007
SILAPO	epoetin zeta	Anemia, Blood Transfusion, Autologous, Cancer, Kidney Failure, Chronic	B03XA01	Stada Arzneimittel AG	18/12/2007
BINOCRIT	epoetin alfa	Anemia, Kidney Failure, Chronic	B03XA01	Sandoz GmbH	28/08/2007
EPOETIN ALFA HEXAL	epoetin alfa	Anemia, Kidney Failure, Chronic, Cancer	B03XA01	Hexal AG	27/08/2007
ABSEAMED	epoetin alfa	Anemia, Kidney Failure, Chronic, Cancer	B03XA01	Medice Arzneimittel Pütter GmbH Co. KG	27/08/2007
VALTROPIN	somatropin	Turner Syndrome, Dwarfism, Pituitary	H01AC01	BioPartners GmbH	24/04/2006
OMNITROPE	somatropin	Turner Syndrome, Prader-Willi Syndrome, Dwarfism, Pituitary	H01AC01	Sandoz GmbH	12/04/2006

Appendix

Table 2: List of Biosimilars Under Review by EMA (July 2020)

COMMON NAME	THERAPEUTIC AREA	NUMBER OF APPLICATIONS	EMA APPROVED ORIGINATOR(S)	ORIGINATOR COMPANY(IES)
ADALIMUMAB	Immunosuppressant	1	Humira	AbbVie
BEVACIZUMAB	Antineoplastic medicine (anticancer)	6	Avastin	Roche
GLUCAGON	Pancreatic hormones	1	Baqsimi	Eli Lilly
INSULIN ASPART	Diabetes	1	NovoLog	Novo Nordisk
INSULIN HUMAN (RDNA)	Diabetes	1	A ctrapid Mixtard Protaphane Insulatard Actraphane Insuman	Novo Nordisk
PEGFILGRASTIM	Immunostimulant (neutropenia)	2	Neulasta	Amgen
TERIPARATIDE	Calcium homeostasis	3	Forteo/Forsteo	Eli Lilly
TRASTUZUMAB	Antineoplastic medicine (anticancer)	1	Herceptin	Roche
TOTAL		**16**		

Source: EMA, July 2020: report accessed July 2020
https://www.ema.europa.eu/en/documents/report/applications-new-human-medicines-under-evaluation-chmp-july-2020_en.pdf

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