White paper

THE IMPACT OF BIOSIMILAR COMPETITION IN EUROPE

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INTRODUCTION

This document sets out to describe the effects on price, volume and market share following the arrival and presence of biosimilar competition in Europe, as defined by the countries listed in the Appendices. The report consists of a set of Key Performance Indicators (KPIs) to monitor the impact of biosimilars in European markets, using full year 2018 data.

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 5 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.

DEFINITIONS

THE REPORT USES SOME BASIC TERMS DEFINED AS FOLLOWS:

- **Accessible category:** products within the same ATC4 code including the following three product categories:

    1. 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.

    2. Non-Referenced Medicinal Product: Original product, granted market exclusivity at the start of its life, exclusivity has now expired, and the product has never been categorised as a Referenced Medicinal product, or may have been referenced but the referencing biosimilar has not been launched.

    3. 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 category:** products within the same ATC4 code as the accessible category products and 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.

- **Total market:** includes both the Accessible and the Non-accessible product markets.

The KPIs used in the report focus on price and volume trends

- **Launch date:** date of first recorded sales of Biosimilar Medicinal Product in the country.

- **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 taking into account rebates or discounts.

    - Price evolution: price per Treatment Day (TD) in 2018 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 2018 versus year before biosimilar entry.

    - Volume per capita 2018: number of Treatment Days consumed in 2018 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.

CAVEATS

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 payers there are a few key caveats that need to be made 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.

KEY OBSERVATIONS

BIOSIMILAR COMPETITION HAS A SIGNIFICANT POTENTIAL TO IMPACT OVERALL DRUG SPEND

Biological products are taking an increasing share of the total drug spend. In Europe over 30% of all drug spend is on biological medicines of which 1.5% are biosimilars. This figure has increased by 3.4% over the last 5-years for all biologic medicines, and by 1.2% since 2014 for biosimilars. However, by 2018, 16 molecules have biosimilar products available in Europe meaning that 21% of the total spend (€12 billion) is exposed to competition from biosimilars.

Figure 1: Proportion of European healthcare spending on biologic molecules 2014 – 2018 (LC EUR Bn)[i]

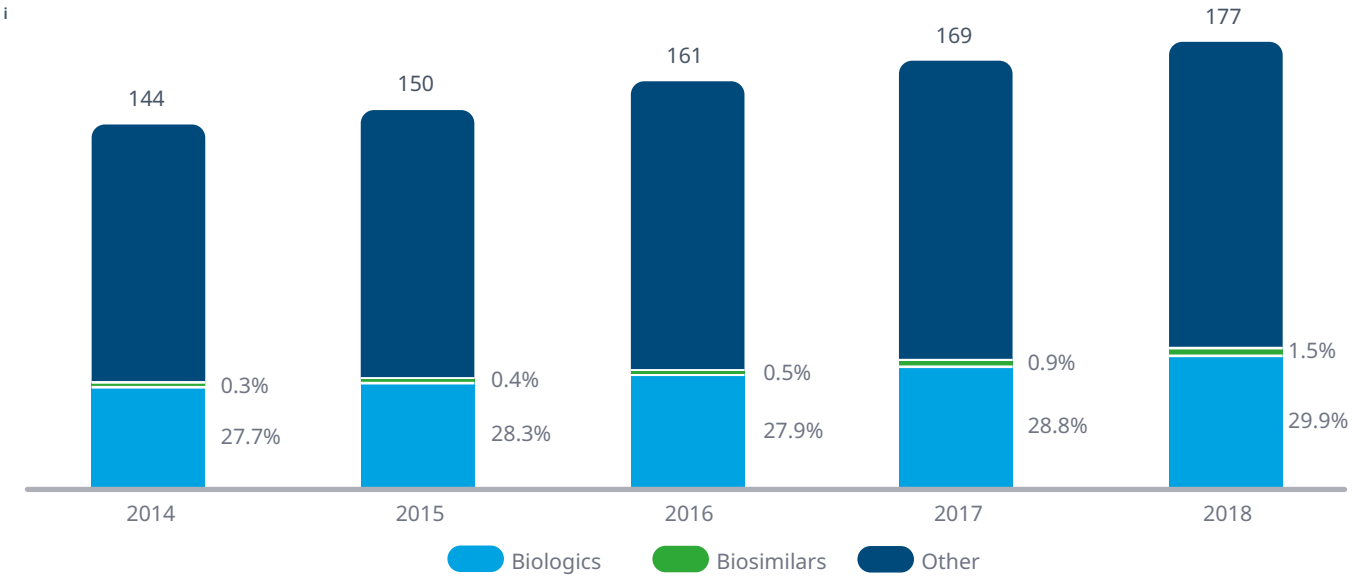
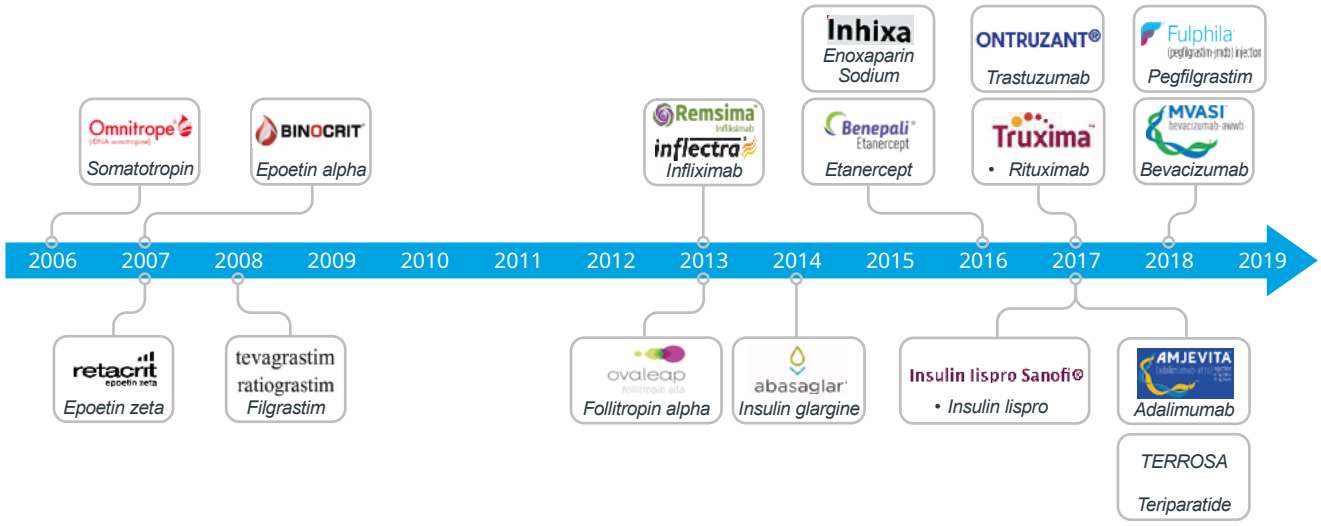


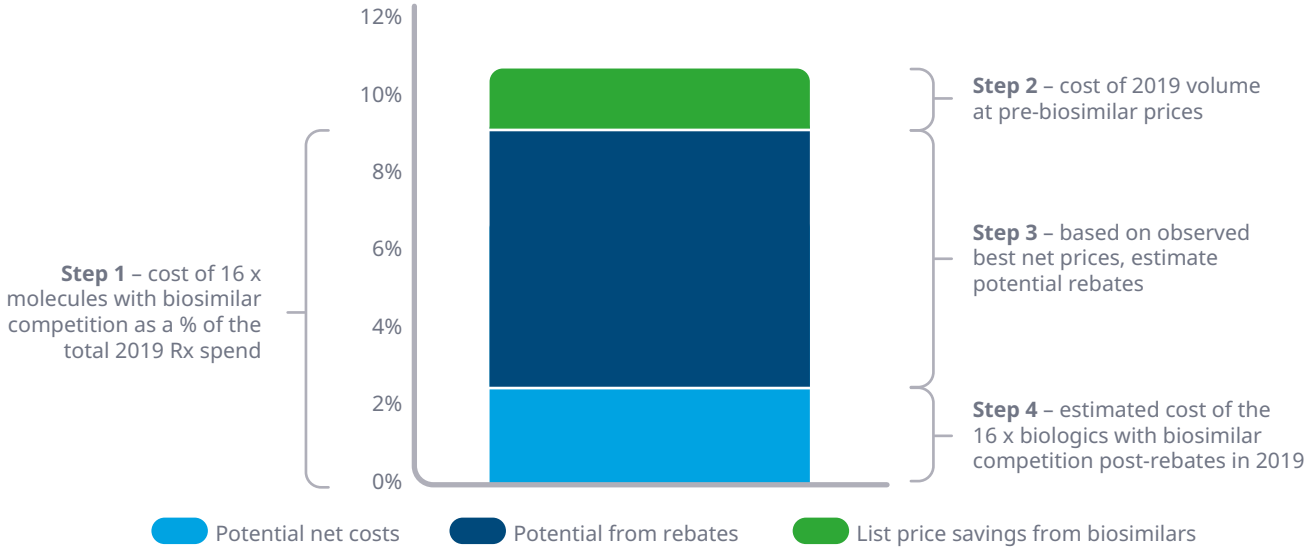
Figure 2: Date of first biosimilar launched per originator medicine[ii]



By 2018, 16 molecules have biosimilar products available in Europe meaning that 21% of the total spend (€12 billion) is exposed to competition from biosimilars.

The impact that biosimilar competition has on the total drugs bill can be modelled to highlight how successfully creating a competitive market can reduce total drug spend. The amount of savings per country will vary based on the volume and list price of each country prior to biosimilar entry. IQVIA has calculate the 2018 spend at list price, and the extent to which list prices have been reduced since the introduction of biosimilars across multiple markets through the method outlined below in figure 3.

Figure 3: Methodology for modeling biologic spending and savings as a proportion of total Rx-spend (2019, %)[iii]



Other discounts (confidential discounts, and rebates) are not as readily available. Based on the available data points, it is possible to model the size of potential total savings if the competition was fully leveraged and similar net prices were achieved at a country-level. In percentage terms, those reductions vary depending on starting price level and due to variations between the usage of molecules. The overall cost reduction is estimated to be significant (up to 8%) and outweighs the cost of new innovative therapies entering the market in 2019 and beyond. Countries are to different degree capturing these today.

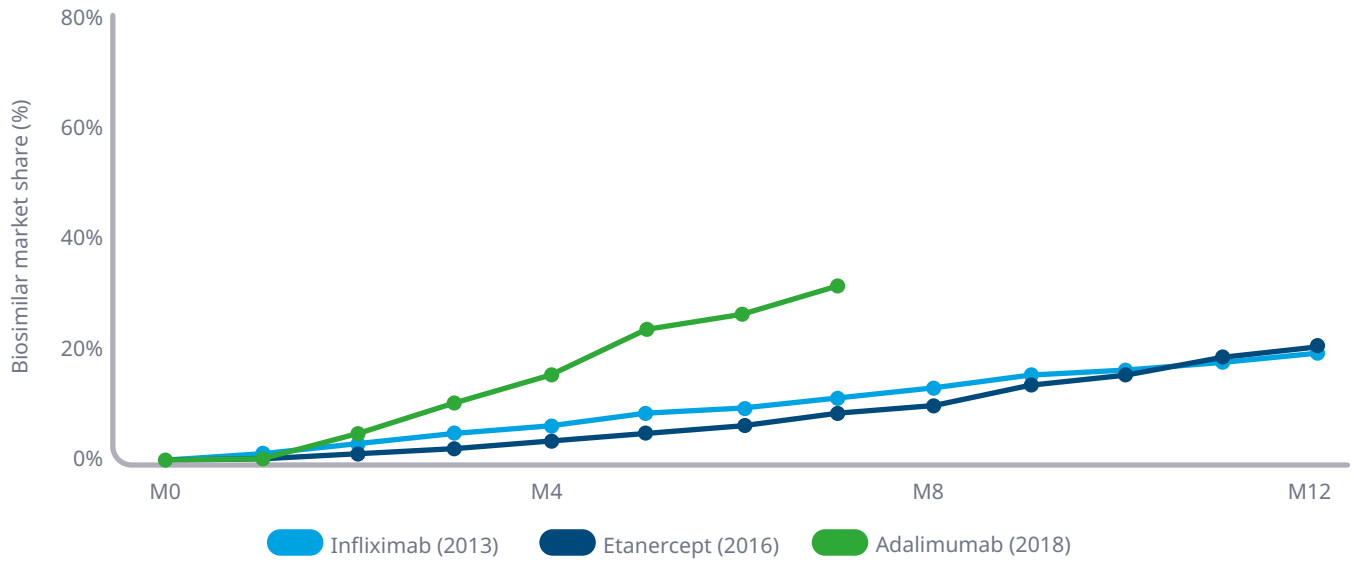
Figure 4: Biologic spending and savings as a proportion of total Rx-spend (2019, %)[iv]

MAJOR PRODUCTS SEE FAST UPTAKE AND LARGE PRICE REDUCTIONS

Humira, the number-one selling drug in Europe, showed a very fast immediate uptake and net price erosion. Several Biosimilars for adalimumab (Hymrioz, Imraldi) were available directly after October 16th, when Humira relinquished protection status. Due to the size of the spend (~2% of total drug spend in Europe), many countries had prepared in advance to tender to achieve savings. This is highlighted by the uptake curve for adalimumab biosimilars which within the first 7 months of launch has been very step despite some level of originator level product differentiation, and ~20% greater than previous major biosimilar launches such as infliximab in 2013, and etanercept in 2016.

Examples of public net price releases are present in nordic markets and in Holland, where substantial price reduction (up to 89% in some cases) has meant that patients were able to continue to be treated on the originator medicine.[iv]

Figure 5: Weighted biosimilar uptake rates in top-5 European markets[v]

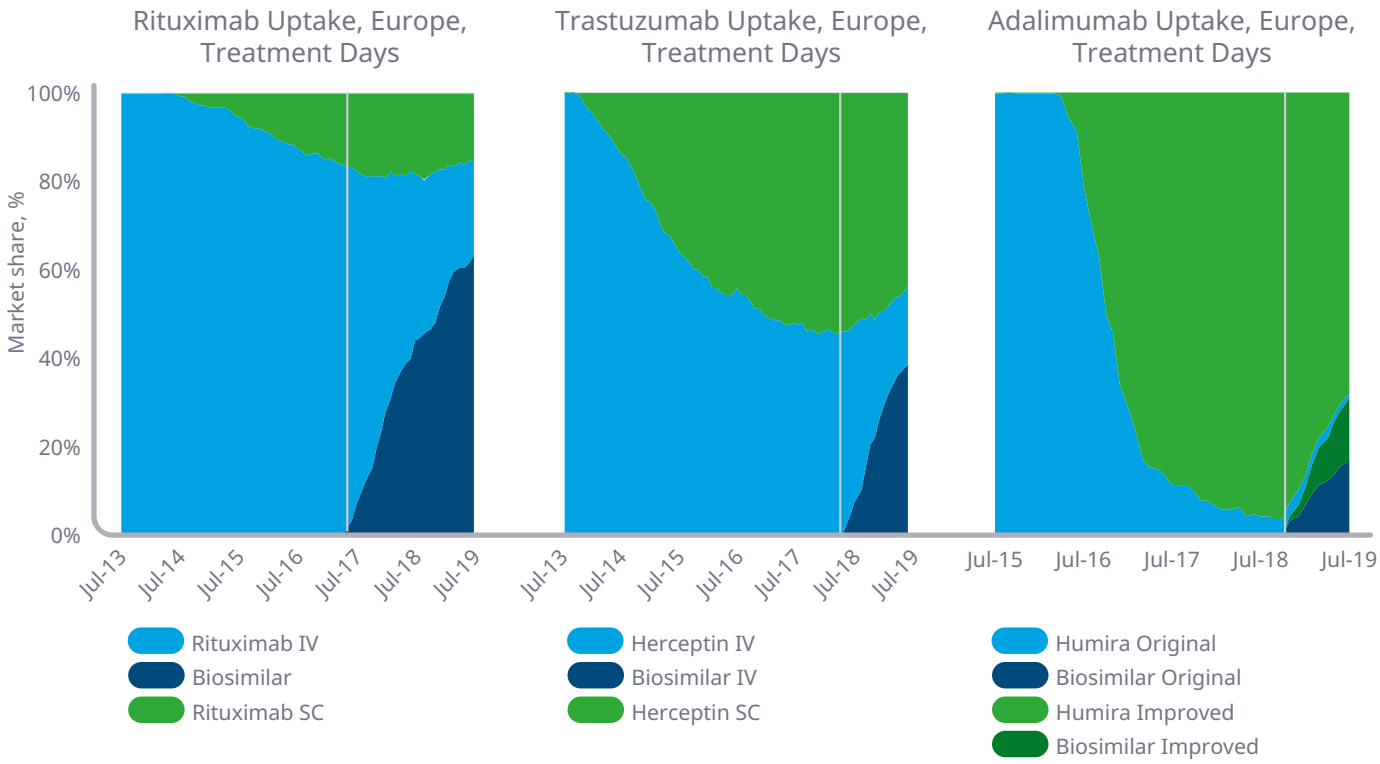


Net prices are confidential. The size of the rebate is also dependent on the original price. However, in the Scandinavian countries it was reported that rebates of 80% were provided during the first round of tenders in 2019.

ORIGINATOR MANUFACTURERS HAVE CHANGED STRATEGY TO STAY COMPETITIVE

Traditionally, we have seen manufacturers defending against loss of patent exclusivity with second generation, or reformulated products. For example, Humira launched a new formulation aimed for less pain at the injection site, Mabthera and Herceptin launched versions to be given subcutaneously rather than as an infusion. These modifications have been able to protect segments of the originators market share from biosimilar entry. The effectiveness of these reformulations varies from molecule to molecule.

Figure 6: Originator product enhancements prior to biosimilar entry[vii]



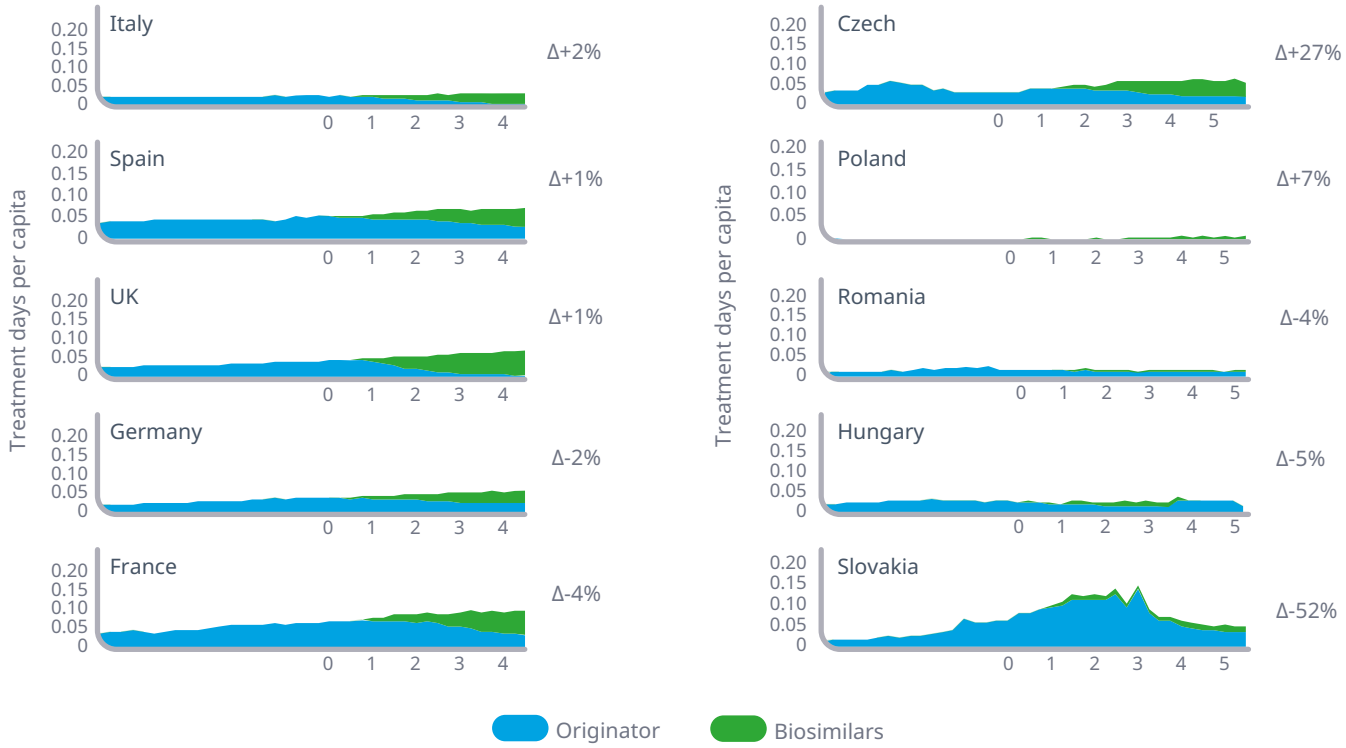
Increasingly, we observe that origionators win tenders with price as the major success factor. Several originators have adopted a price competition strategy previously unemployed by earlier original manufacturers. By being able to offer significant reductions, the lowest price, or at least a price that is able to make switching un-attractive, originator manufacturers are able to maintain their market share in key European markets. Examples include:

- **Infliximab** – Remicade (MSD) winner in Finland based on lowest price (Jan 2017)
- **Etanercept** – Enbrel (Pfizer) winner in Sweden based on lowest price (Oct 2017)
- **Adalimumab** – Humira (Abbvie) winner in Norway based on lowest price (Nov 2018)

ACCESS IS NOT YET INCREASING FOR ALL MOLECULES AND IN ALL COUNTRIES AFTER BIOSIMILAR INTRODUCTION

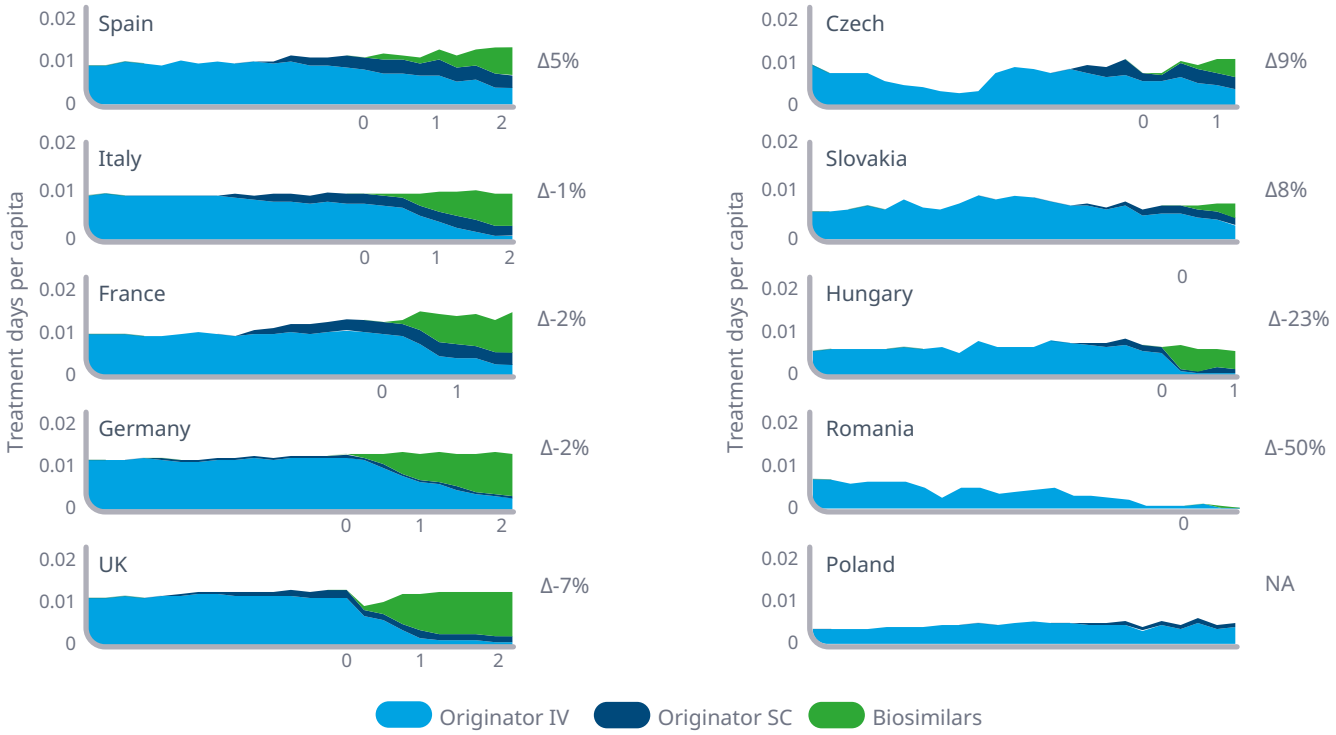
There has been a mixed change in uptake across markets since introduction of biosimilars. The observation for the 3 first classes of biosimilars (HGH, EPO, GCSF) was that lower prices in general increased access. With the entry of the biosimilar competition in anti-TNF and cancer the shorter-term trend is more mixed. Countries that already had a high usage of anti-TNF increased usage such as north-western Europe saw nominal increases in the usage of biologic medicines as a result of biosimilar introduction. In central and eastern European countries which had historically lower usage of biologic medicines, the large variations was noticed and can be attributed to increasing from a small base (specifically in the case of the Czech Republic).

Figure 7: Growth per Capita in treatment days for infliximab since biosimilar introduction[viii]



For cancer treatment, the similar phenomenon is observed. While we see a switching of patients, the second-generation products maintains or even increase its share over time. Countries with low access still have low access almost 1-2 years after the launch of a major biosimilar molecule.

Figure 8: Growth per Capita in treatment days for rituximab biologics since biosimilar introduction[ix]



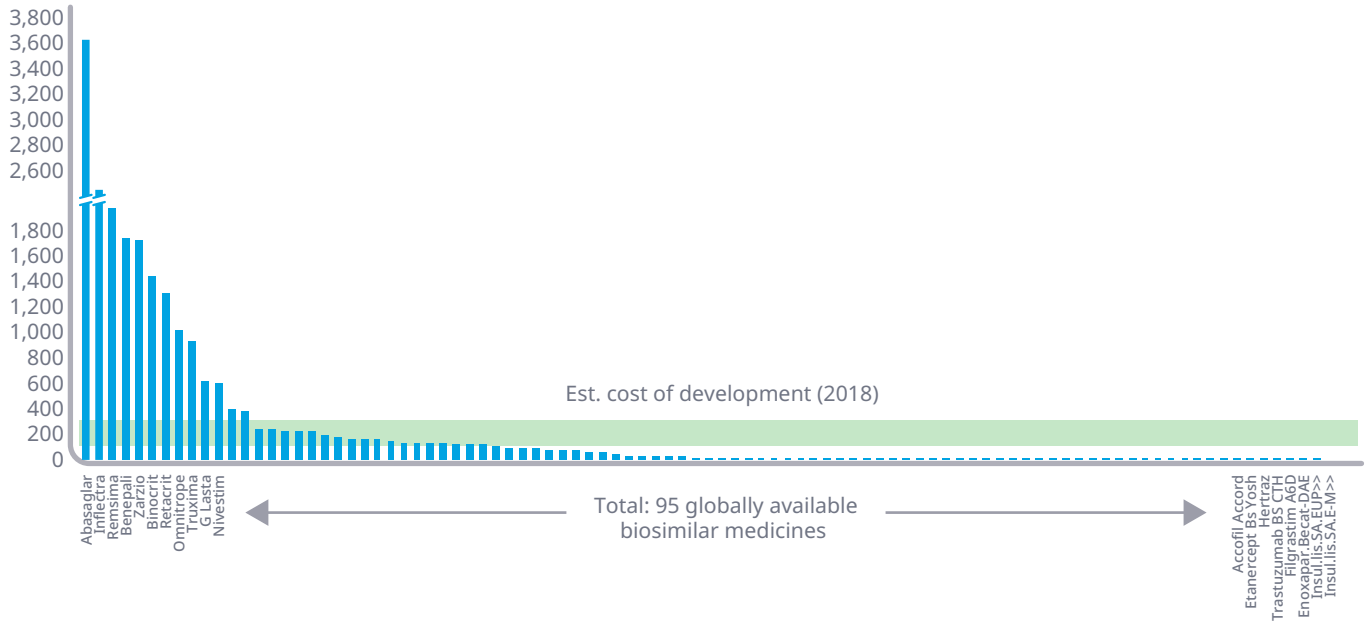
MORE IS NEEDED TO CREATE A SUSTAINABLE MARKET FOR BIOSIMILAR MANUFACTURERS

To support a long-term sustainable model through competition, developers need to be able to achieve sufficient sales to attain a return on investment with a profit. We can see that this has occurred for few products so far. While uptake in Europe has been strong for many products, there is a significant issue in the US and other major markets (e.g. Japan).

On April 21, 2018, the head of US FDA Scott Gottlieb stated: "The range of cost for [developing] a biosimilar is anywhere from $100m to $300m". While the precise number is not known for individual product, this can be used as an indication of cost. The cost for development can often be reduced by co-development, or by creating a US-specific version which results in more than one approved product.

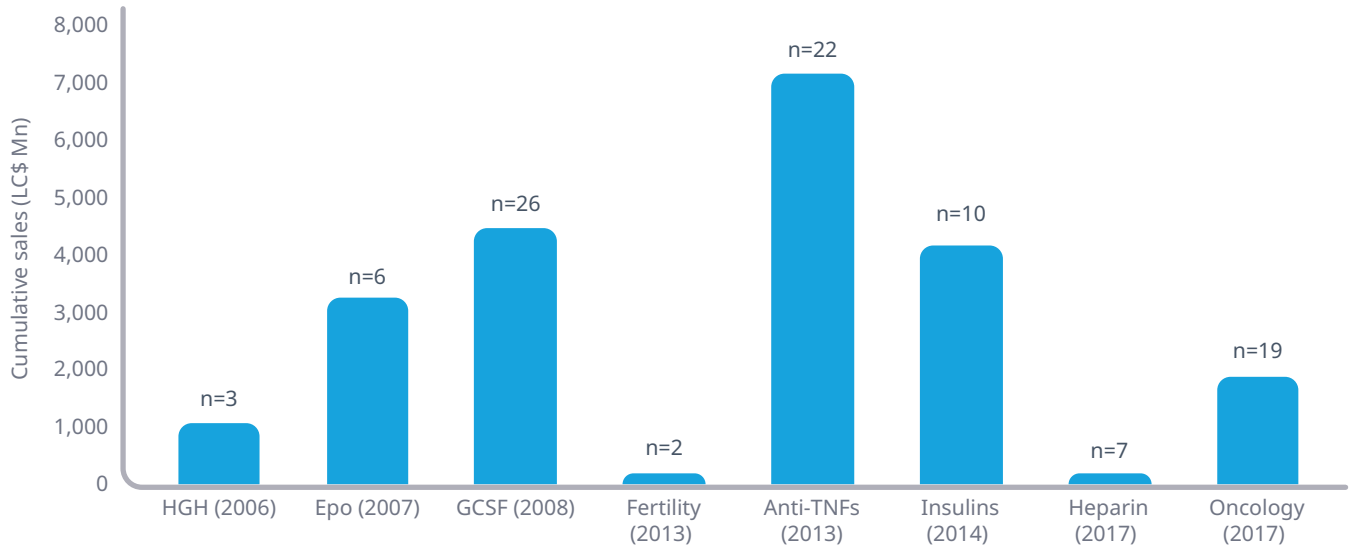
In 2019, there are 95 approved biosimilar products in use across the globe. By calculating the accumulated sales per product at list price (2008-2019, IQVIA MIDAS), it is possible to get an indication of the number of biosimilar molecules that have been able to earn back the development cost estimated by Gottlieb. Only approximately 1/3 have sales above the lower threshold of $100m.

Figure 9: Cumulative global sales for biosimilars launched since 2008 (LC$ Mn)[x]



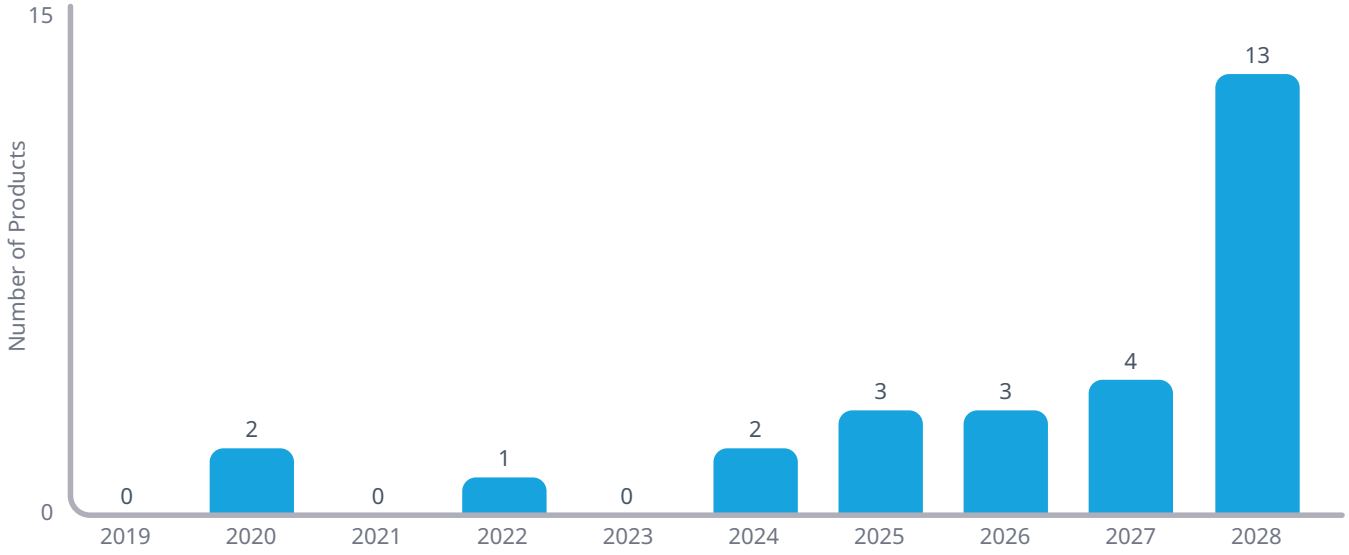
As other investments and rebates are taken into consideration, it is likely even less biosimilar research & development programmes will break even. The growth in the number of biosimilars competing for market share with an originator has increased significantly, making a more competitive market possible, but also having negative implications for future incentives. The average originator biologic in 2009 was competing with 2.5 biosimilar entrants, versus 2019 where the average molecule can expect to be competing with 3.5 biosimilar entrants. This figure rises significantly for the high value markets such as anti-TNFs.

Figure 10: Cumulative global biosimilar sales per class launched since 2008[xi]



The future development in both uptake and net price will be critical. The implication for European healthcare systems is that if less companies will invest in development and, without a fierce competition, the level of savings we see today will not come through to allow for spending to be reallocated to new products. This dilemma is clear when looking at the number of orphan medicines that are expected to lose market exclusivity in the next 5 years, many of which are biologic drugs. By 2028, a total of 28 biologic orphan medicines will be eligible for biosimilar competition. However, the majority of orphan medicines do not have a product in clinical development. Only 11% of orphan biologic molecules have a product in clinical developmenzt, versus 23% for total biologic medicines.

Figure 11: Orphan biologic medicines with expected loss of market exclusivity in Europe to 2028[xii]

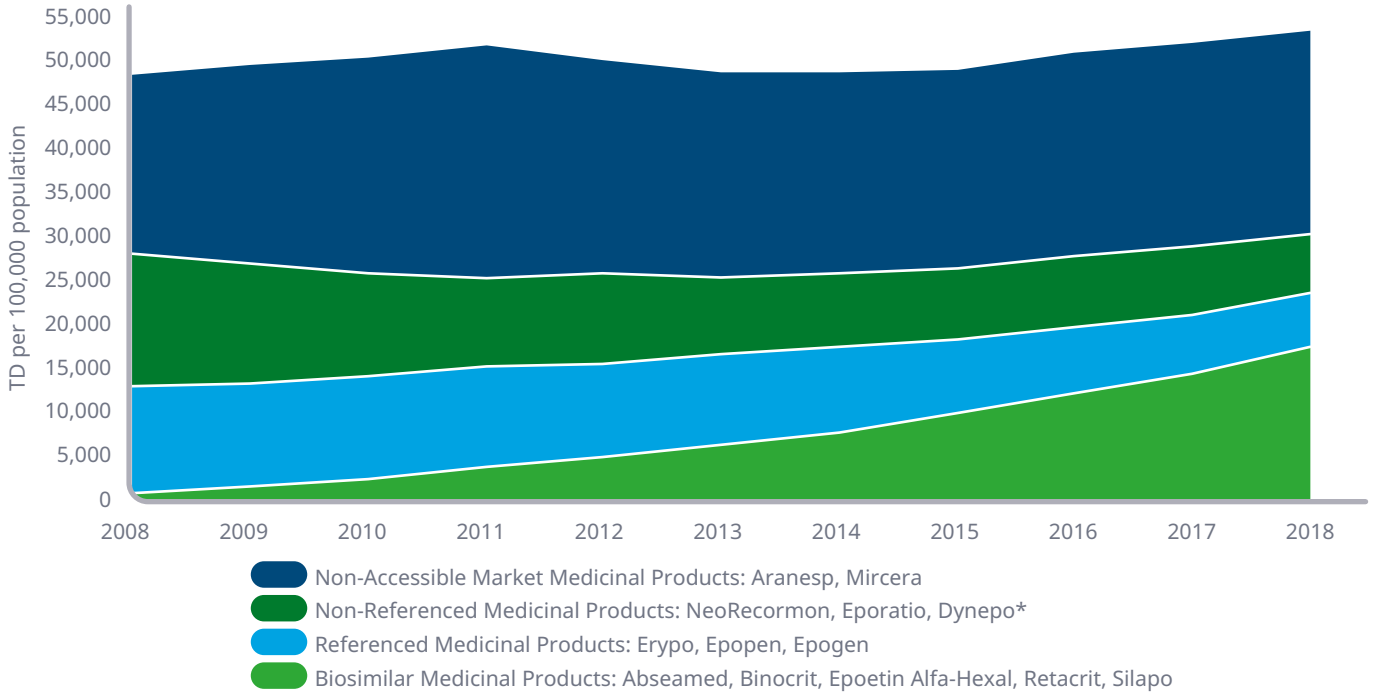


COUNTRY AND THERAPY AREA KPIs

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 volume development



ADDITIONAL INFORMATION ABOUT EPO MEDICINES

In June 2008 EMA recommended updating the product information for Epoetin-containing medicines with a new warning for their use in cancer patients stating that blood transfusion should be the preferred method of correcting anaemia.

The Agency's Committee for Medicinal Products for Human Use (CHMP) had reviewed data from studies that showed an increased risk of tumour progression, venous thrombo-embolism and shorter overall survival in cancer patients who received Epoetins compared to patients who did not receive them. It also advised that prescribers take into account patients' individual circumstances and preferences when making the decision to use Epoetins. The Committee agreed that there is no consequence of the new information on the use of Epoetin-containing medicines for the treatment of anaemia in patients with chronic renal failure.

EPO approved indications

		CLASSIFICATION				INDICATIONS								
MOLECULE	PRODUCT	REFERENCED	BIOSIMILAR PRODUCTS	NON-REFERENCED	NON-ACCESSIBLE	ANEMIA FOR CHEMOTHERAPY PATIENTS	ANEMIA FOR PATIENTS WITH CKD	PREVENTING ANEMIA IN PREMATURE BABIES	AUTOLOGUS BLOOD TRANSFUION	AMENIA IN ADULTS WITH MDS	REUDCTIOJN OF ALLOGENIC TRANSFUSION EXPOSURE IN ORTHAPEDICSURGERY	PATIENT TYPE (ADULT OR PEDIATRIC)	FREQUENCY	ROUTE (SUBQ/IV)
Epoetin alfa	Epogen Erypo Epogen Abseamed Epoetin alfa Hexal Binocrit	●	●			●	●		●	●	●	Both	3 x a week	Both
Epoetin beta	NeoRecormon			●		●	●	●	●		●	Both	3 x a week	Both
Epoetin zeta	Retacrit Silapo		●			●	●		●		●	Both	3 x a week	Both
Epoetin theta	Eporatio			●		●	●					Adult	3 x a week	Both
Methoxy polyethlene glycol-epoetin beta	Miracera				●		●					Adult	Fortnightly	Both
Darbepoetin alfa	Aranesp Darbepogen				●	●	●					Adult	Weekly	Both

*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.

Selected KPIs to illustrate volume share, price evolution, and volume evolution in selected European countries

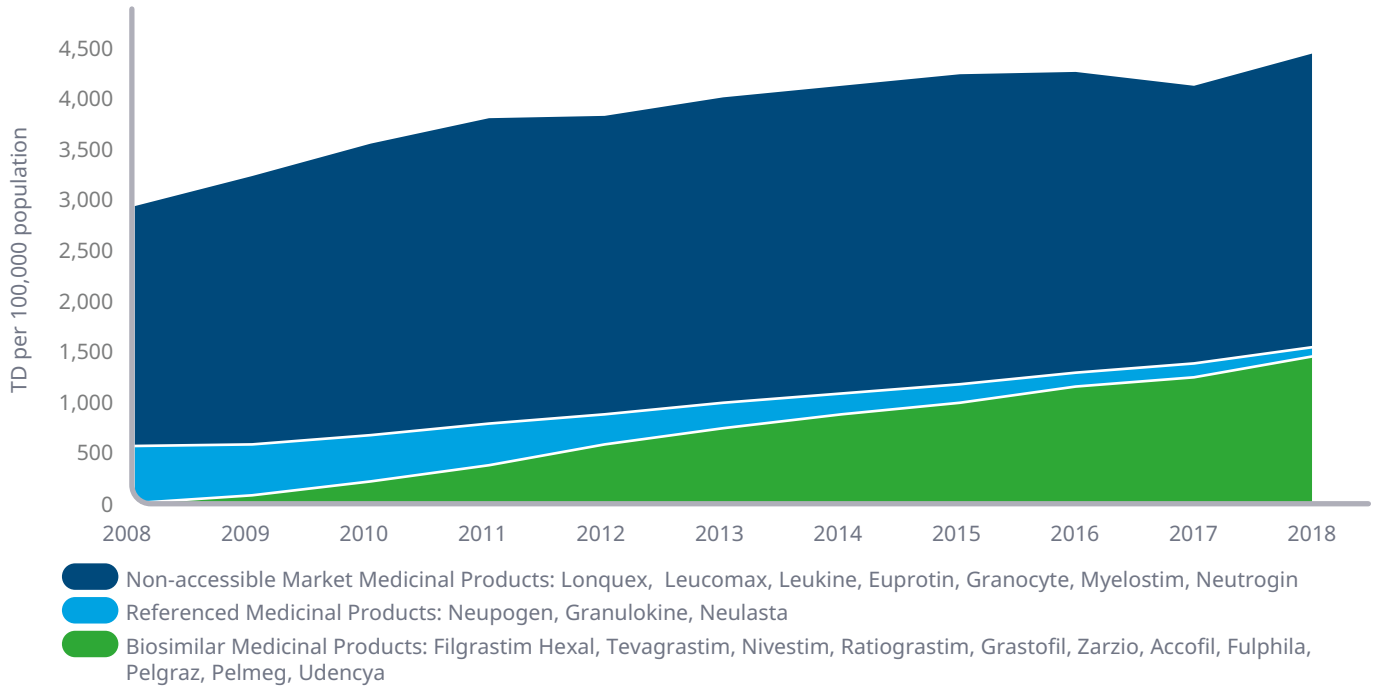
	MARKET SHARE TD (2018)			PRICE PER TD (2018/YR BEFORE BS ENTRY)			VOLUME TD (2018/YR BEFORE BS ENTRY)					
	BIOSIMILAR VS REFERENCED PRODUCT	BIOSIMILAR VS ACCESSIBLE MARKET	BIOSIMILAR VS TOTAL MARKET	BIOSIMILAR AND REFERENCED PRODUCT	BIOSIMILAR ACCESSIBLE MARKET	TOTAL MARKET	BIOSIMILAR AND REFERENCED PRODUCT	BIOSIMILAR ACCESSIBLE MARKET	TOTAL MARKET	TD PER CAPITA	TD/CAPITA (YR BEFORE BS ENTRANCE)	FIRST RECORDED SALES OF BIOSIMILARS
AU	80%	35%	23%	-40%	-42%	-30%	-2%	-3%	-25%	0.69	0.92	2008
BE	14%	9%	2%	-3%	-2%	2%	-31%	-23%	7%	0.56	0.52	2014
BU	100%	78%	50%	-1%	-33%	-20%	82%	19%	42%	0.34	0.24	2011
CZ	74%	38%	19%	-56%	-48%	-38%	299%	110%	204%	0.28	0.09	2011
DK	30%	8%	0%	-10%	-2%	-17%	-93%	-97%	-8%	0.44	0.48	2010
FI	100%	76%	12%	-47%	-43%	-27%	1541%	-47%	15%	0.38	0.33	2008
FR	62%	42%	16%	-35%	-34%	-33%	15%	-23%	5%	0.94	0.90	2009
DE	84%	73%	46%	-54%	-57%	-47%	75%	-3%	-5%	0.37	0.38	2007
GR*	88%	87%	81%	-51%	-52%	-50%	393%	195%	109%	0.04	0.02	2008
HU	100%	56%	34%	-78%	-48%	-30%	52%	19%	-13%	0.31	0.36	2009
IE	98%	19%	7%	-33%	-34%	-21%	61%	-52%	-19%	0.40	0.50	2008
IT	79%	74%	61%	-16%	-14%	-10%	212%	89%	46%	1.21	0.83	2008
NL	60%	15%	3%	-51%	-44%	-35%	-84%	-68%	-38%	0.33	0.52	2009
NO	57%	13%	1%	314%	54%	-2%	-72%	-76%	11%	0.23	0.20	2008
PL	100%	84%	20%	-63%	-58%	-27%	4758%	19%	217%	0.09	0.03	2009
PT	93%	30%	21%	-79%	-79%	-65%	224%	139%	11%	0.49	0.45	2010
RO	95%	74%	44%	-58%	-52%	-43%	87%	-72%	-60%	0.12	0.30	2009
SK	100%	74%	56%	-60%	-57%	-52%	345%	60%	12%	0.50	0.45	2010
SL	62%	32%	11%	-47%	-52%	-49%	-41%	-46%	9%	0.57	0.52	2009
ES	70%	57%	35%	-31%	-31%	-20%	55%	-8%	-11%	0.62	0.69	2009
SE	93%	40%	26%	-29%	-40%	-30%	45%	13%	-2%	0.45	0.46	2008
CH	25%	7%	1%	-51%	-45%	-41%	-45%	-52%	15%	0.38	0.33	2009
UK	5%	3%	1%	-13%	-21%	-13%	110%	9%	44%	0.34	0.24	2009
EU	74%	58%	33%	-31%	-33%	-27%	92%	10%	10%	0.53	0.49	

The following data history is used: Portugal Hospital (2010-2018), only retail panel is available for Greece. Prices per treatment day (total market) have been reduced in almost all markets but to a different degree from -65% to 2%, due to a combination of factors; the level of competition, to what extent non- accessible market products (largely differentiated by fewer injections) have been accepted, but also the price development of referenced and biosimilar medicinal products.

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 volume 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

		CLASSIFICATION				INDICATIONS					
MOLECULE	PRODUCT	REFERENCED PRODUCT	BIOSIMILAR PRODUCT	NON-REFERENCED PRODUCT	NON-ACCESSIBLE PRODUCT	CYTOTOXIC CHEMOTHERAPY 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 (PBCs)	SEVERE CHRONIC NEUTROPENIA (SCN) WITH DIAGNOIS OF CONGENITAL, CYCLIC, OR IDIOPATHIC NEUTROPENIA	NEUTROPENIA PREVENTION AND TREATMENT IN PATIENTS WITH HIV
Filgrastim	Neupogen Granulokine Filgrastim Hexal Tevagrastim Grastofil Accofil Nivestim Ratiograstim Zarzio	● ●	● ● ● ● ● ● ●			● ● ● ● ● ● ● ● ●	● ●	● ● ● ● ● ● ● ● ●	● ● ● ● ● ● ● ● ●	● ● ● ● ● ● ● ● ●	● ● ● ● ● ● ● ● ●
Lenograstim	Euprotin Granocyte Myelostim Neutrogin				● ● ● ●	● ● ● ●		● ● ● ●	● ● ● ●		
Lipegfilgrastim	Lonquex				●	●					
Pegfilgrastim	Neulasta Pelmeg Pelgraz Grasustek Fulphila Ziextenzo Udenyca	●	● ● ● ● ● ● ●			● ● ● ● ● ● ● ●					
Molgramostim	Leucomax				●	●	●	●	●		
Sargramostim	Leukine				●	●	●	●	●		

Selected KPIs to illustrate volume share, price evolution, and volume evolution in selected European countries

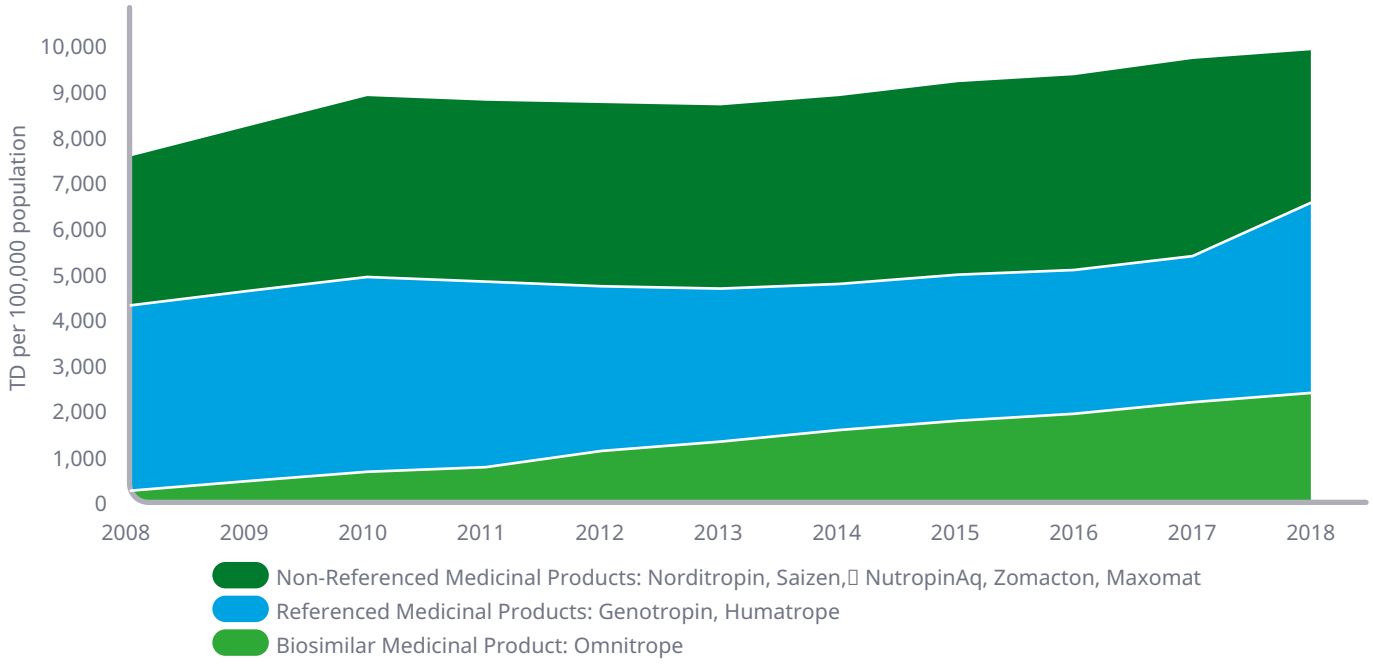
	MARKET SHARE TD (2018)			PRICE PER TD (2018/YR BEFORE BS ENTRY)			VOLUME TD (2018/YR BEFORE BS ENTRY)					
	BIOSIMILAR VS REFERENCED PRODUCT	BIOSIMILAR VS ACCESSIBLE MARKET	BIOSIMILAR VS TOTAL MARKET	BIOSIMILAR AND REFERENCED PRODUCT	BIOSIMILAR ACCESSIBLE MARKET	TOTAL MARKET	BIOSIMILAR AND REFERENCED PRODUCT	BIOSIMILAR ACCESSIBLE MARKET	TOTAL MARKET	TD PER CAPITA	TD/CAPITA (YR BEFORE BS ENTRANCE)	FIRST RECORDED SALES OF BIOSIMILARS
AU	99%	99%	26%	-61%	-61%	-44%	144%	144%	90%	0.10	0.05	2009
BE	29%	29%	3%	-34%	-34%	-30%	13%	13%	55%	0.07	0.04	2011
BU	100%	100%	12%	-78%	-78%	-63%	368%	368%	2255%	0.04	0.00	2009
CZ	100%	100%	26%	-58%	-58%	-48%	305%	305%	481%	0.03	0.00	2010
DK	97%	97%	12%	-52%	-52%	-22%	17%	17%	47%	0.06	0.04	2009
FI	98%	98%	14%	-50%	-50%	-28%	65%	65%	60%	0.09	0.05	2009
FR	93%	93%	22%	-39%	-39%	-26%	292%	292%	47%	0.08	0.05	2009
DE	81%	81%	14%	-34%	-34%	-35%	64%	64%	114%	0.05	0.02	2008
GR*	100%	100%	80%	-75%	-75%	-56%	1372%	1372%	-75%	0.00	0.02	2009
HU	100%	100%	82%	-74%	-74%	-58%	360%	360%	30%	0.05	0.04	2009
IE	27%	27%	3%	-29%	-29%	-19%	11%	11%	54%	0.08	0.05	2009
IT	96%	96%	44%	-27%	-27%	-16%	149%	149%	5%	0.03	0.03	2009
NL	62%	62%	10%	-42%	-42%	-28%	94%	94%	-5%	0.03	0.03	2009
NO	86%	86%	4%	-37%	-37%	-20%	23%	23%	163%	0.07	0.03	2009
PL	97%	97%	44%	-74%	-74%	-59%	184%	184%	162%	0.04	0.02	2009
PT	89%	89%	45%	-90%	-90%	-55%	66%	66%	-43%	0.02	0.04	2010
RO	100%	100%	69%	-72%	-72%	-64%	383%	383%	564%	0.02	0.00	2009
SK	100%	100%	34%	-84%	-84%	-65%	524%	524%	484%	0.05	0.01	2009
SL	63%	63%	9%	-71%	-71%	-58%	67%	67%	265%	0.07	0.02	2009
ES	93%	93%	76%	-41%	-41%	-25%	40%	40%	-42%	0.02	0.04	2009
SE	98%	98%	93%	-85%	-85%	-70%	1013%	1013%	199%	0.07	0.02	2009
CH	66%	66%	17%	-36%	-36%	-27%	46%	46%	63%	0.04	0.03	2009
UK	99%	99%	74%	5%	5%	15%	289%	289%	70%	0.02	0.01	2008
EU	93%	93%	33%	-44%	-44%	-30%	165%	165%	54%	0.04	0.03	

The following data history is used: Portugal Hospital (2010-2018), only retail panel is available for Greece. Price changes per treatment day (total market) vary considerably across the different European countries included in this study, ranging between -70% and 15%.

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 volume 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

		CLASSIFICATION				INDICATIONS								
MOLECULE	PRODUCT	REFERENCED PRODUCT	BIOSIMILAR PRODUCT	NON-REFERENCED PRODUCT	NON-ACCESSIBLE PRODUCT	PEDIATRIC GROWTH HORMONE DEFINCIENCY	ADULT GROWTH HORMONE DEFINICIENCY	TURNER SYNDROME	GROWTH FAILURE DUE TO CRI	SMALL FOR GESTATIONAL AGE (SGA)	PRADER-WILLI-SYNDROME	IDIOPATHIC SHORT STATURE	SHORT-STATURE HOMEBOX CONTAINING GENE DEFICIENCY (SHOX)	NOONAN SYNDROME
Mecasermin	Increlex													
Sermorelin	Geref													
Somatorelin	Somatorelin SNFI													
Somatropin	Omnitrope		●			●	●	●	●	●	●	●		
	Norditropin			●		●	●	●	●	●				●
	Saizen			●		●	●	●	●	●				
	Nutropinaq			●		●	●	●	●					
	Zomacton			●			●	●						
	Somatropin L.U.			●		●	●	●	●	●				
	Maxomat			●		●	●	●	●	●				
	Genotropin	●				●	●	●	●	●	●	●	●	
	Humatrope	●				●	●	●	●	●		●		

Selected KPIs to illustrate volume share, price evolution, and volume evolution in selected European countries

	MARKET SHARE TD (2018)			PRICE PER TD (2018/YR BEFORE BS ENTRY)			VOLUME TD (2018/YR BEFORE BS ENTRY)					
	BIOSIMILAR VS REFERENCED PRODUCT	BIOSIMILAR VS ACCESSIBLE MARKET	BIOSIMILAR VS TOTAL MARKET	BIOSIMILAR AND REFERENCED PRODUCT	BIOSIMILAR ACCESSIBLE MARKET	TOTAL MARKET	BIOSIMILAR AND REFERENCED PRODUCT	BIOSIMILAR ACCESSIBLE MARKET	TOTAL MARKET	TD PER CAPITA	TD/CAPITA (YR BEFORE BS ENTRANCE)	FIRST RECORDED SALES OF BIOSIMILARS
AU	38%	12%	12%	-17%	-7%	-7%	24%	127%	127%	0.08	0.03	2008
BE	32%	20%	20%	-20%	-20%	-20%	44%	36%	36%	0.13	0.09	2009
BU	52%	52%	52%	-26%	-26%	-26%	3%	1%	1%	0.02	0.02	2012
CZ	17%	6%	6%	-22%	-28%	-28%	77%	89%	89%	0.15	0.08	2010
DK	97%	70%	70%	17%	5%	5%	80%	-21%	-21%	0.12	0.15	2011
FI	50%	14%	14%	-31%	-43%	-43%	18%	80%	80%	0.11	0.06	2008
FR	39%	18%	18%	-14%	-11%	-11%	36%	49%	49%	0.14	0.1	2007
DE	42%	21%	21%	3%	6%	6%	17%	39%	39%	0.08	0.05	2006
GR*	0%	0%	0%	-16%	-16%	-16%	92%	92%	92%	0	0	2015
HU	12%	6%	6%	-7%	-7%	-7%	-1%	19%	19%	0.06	0.05	2012
IE	0%	0%	0%	-9%	-11%	-11%	60%	86%	86%	0.08	0.04	2006
IT	42%	24%	24%	-23%	-17%	-17%	97%	60%	60%	0.1	0.06	2007
NL	30%	16%	16%	-37%	-34%	-34%	29%	33%	33%	0.11	0.09	2008
NO	3%	3%	3%	-20%	-17%	-17%	168%	43%	43%	0.18	0.13	2011
PL	99%	99%	99%	-39%	-39%	-39%	128%	128%	128%	0.09	0.04	2008
PT	24%	11%	11%	-47%	-35%	-35%	19%	12%	12%	0.05	0.04	2014
RO	64%	38%	38%	-21%	-34%	-34%	298%	147%	147%	0.06	0.02	2008
SK	0%	0%	0%	-12%	-13%	-13%	32%	44%	44%	0.09	0.06	2013
SL	12%	6%	6%	-40%	-40%	-40%	36%	34%	34%	0.08	0.06	2010
ES	25%	18%	18%	-19%	-19%	-19%	92%	75%	75%	0.17	0.1	2007
SE	39%	27%	27%	-41%	-40%	-40%	-1%	-2%	-2%	0.14	0.15	2007
CH	26%	6%	6%	-36%	-15%	-15%	-17%	20%	20%	0.08	0.06	2010
UK	23%	11%	11%	-15%	-10%	-10%	22%	68%	68%	0.06	0.04	2007
EU	42%	24%	24%	-23%	-17%	-17%	56%	54%	54%	0.1	0.06	

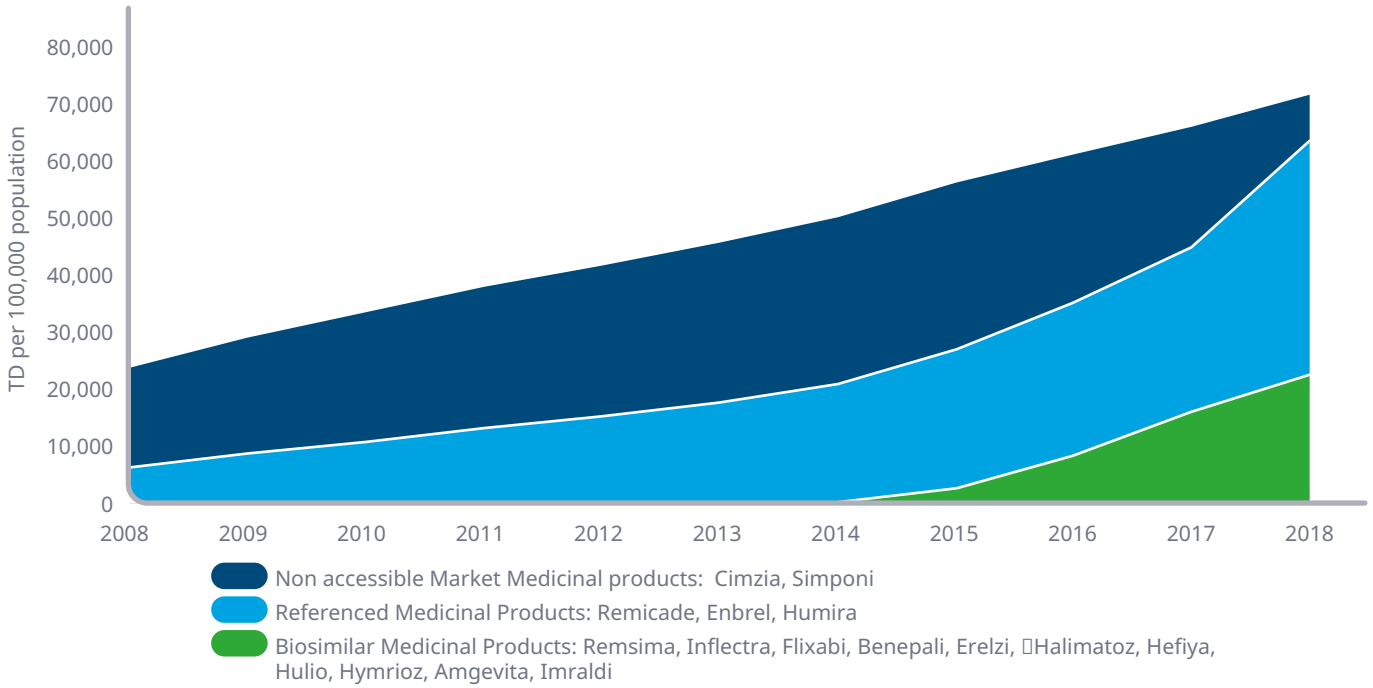
The following data history is used: Portugal Hospital (2010-2018), only retail panel is available for Greece. Prices per treatment day (total market) vary considerably across the different European countries studied, ranging between -43% to 6%.

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 volume 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

		CLASSIFICATION				INDICATIONS												
MOLECULE	PRODUCT	REFERENCED	BIOSIMILAR PRODUCTS	NON-REFERENCED	NON-ACCESSIBLE	RA	JIA	PsA	AS	AS WITHOUT RADIOGRAPHIC EVIDENCE	CD	CD (PEDIATRIC)	UC	UC (PEDIATRIC)	PPs	HS	Uv	FREQUENCY	ROUTE (SUBQ/ IV)
Infliximab	Remicade Remsima Inflectra Flixabi	●	●●●			●●●●		●●●●	●●●		●●●	●●●	●●●	●●●	●●●			Every 8 weeks	IV
Etanercept	Enbrel Benepali Erelzi	●●●	●●●			●●●	●●●	●●●	●●●	●●●					●●			Once or twice weekly	SC
Adalimumab	Humira Halimatoz Hefiya Hulio Hyrimoz Amgenvita Imraldi	●	●●●●●●			●●●●●●●●●	●●●●●●	●●●●●●●●●	●●●●●●●●●	●●●●●●●●●	●●●●●●	●●●●●●	●●●●●●	●●●●●●	●●●●●●	●●●●●	●●●●●	Every 2 weeks	Both
Certolizumab Pegol	Cimzia				●	●		●	●	●					●			Every 4 weeks	SC
Golimumab	Simponi				●	●		●	●	●								Monthly	SC

Selected KPIs to illustrate volume share, price evolution, and volume evolution in selected European countries

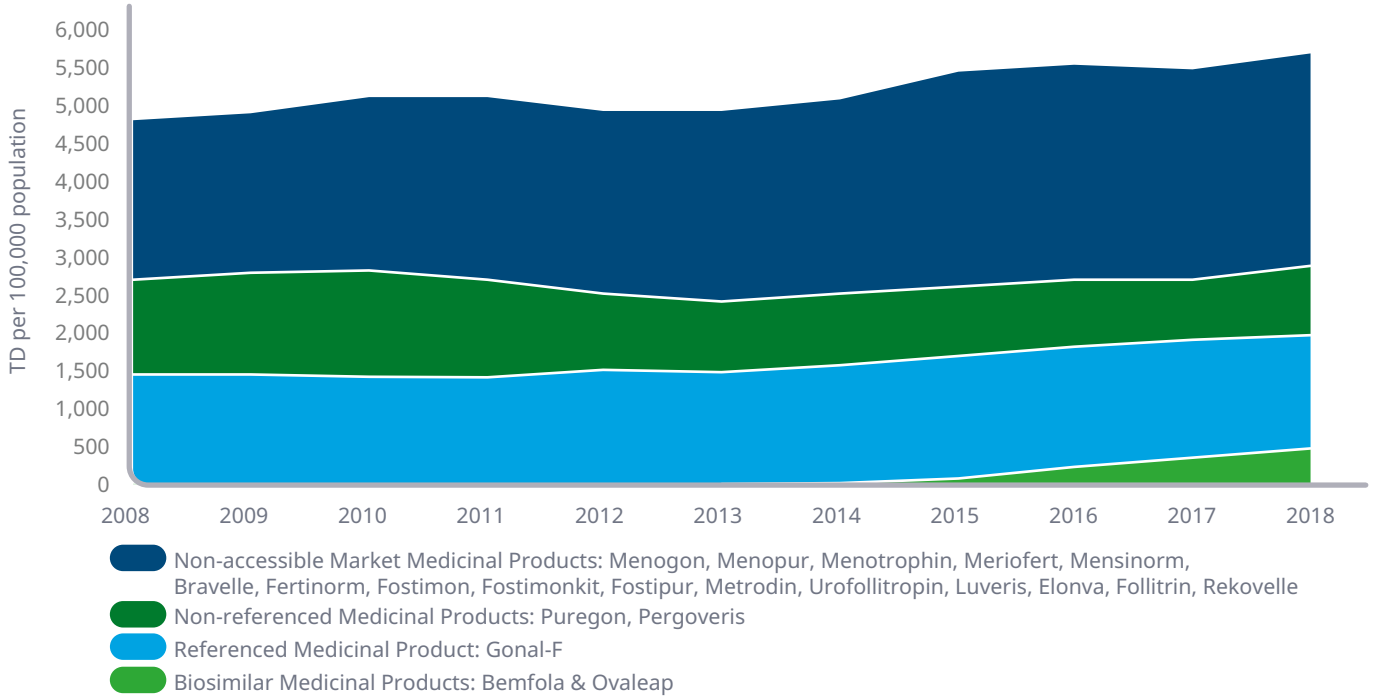
	MARKET SHARE TD (2018)			PRICE PER TD (2018/YR BEFORE BS ENTRY)			VOLUME TD (2018/YR BEFORE BS ENTRY)					
	BIOSIMILAR VS REFERENCED PRODUCT	BIOSIMILAR VS ACCESSIBLE MARKET	BIOSIMILAR VS TOTAL MARKET	BIOSIMILAR AND REFERENCED PRODUCT	BIOSIMILAR ACCESSIBLE MARKET	TOTAL MARKET	BIOSIMILAR AND REFERENCED PRODUCT	BIOSIMILAR ACCESSIBLE MARKET	TOTAL MARKET	TD PER CAPITA	TD/CAPITA (YR BEFORE BS ENTRANCE)	FIRST RECORDED SALES OF BIOSIMILARS
AU	29%	29%	22%	15%	15%	3%	492%	492%	471%	0.93	0.16	2015
BE	17%	17%	15%	3%	3%	-9%	102%	102%	38%	1.28	0.93	2015
BU	24%	24%	20%	-20%	-20%	-20%	736%	736%	293%	0.4	0.1	2014
CZ	36%	36%	32%	9%	9%	-4%	199%	199%	140%	0.57	0.24	2013
DK	96%	96%	88%	23%	23%	6%	95%	95%	26%	1.12	0.89	2015
FI	12%	12%	10%	3%	3%	-8%	166%	166%	96%	1.25	0.64	2013
FR	29%	29%	26%	-10%	-10%	-19%	104%	104%	44%	0.89	0.62	2015
DE	34%	34%	29%	19%	19%	1%	131%	131%	45%	0.72	0.5	2015
GR	0%	0%	0%	29%	29%	18%	116%	116%	-53%	0	0.01	
HU	0%	0%	0%	27%	27%	10%	78%	78%	14%	0.37	0.32	2014
IE	13%	13%	11%	14%	14%	0%	180%	180%	73%	1.65	0.96	2014
IT	35%	35%	30%	14%	14%	3%	88%	88%	29%	0.47	0.36	2015
NL	44%	44%	41%	3%	3%	-8%	90%	90%	26%	1.23	0.98	2015
NO	81%	81%	70%	2%	2%	-1%	138%	138%	86%	1.96	1.05	2013
PL	44%	44%	38%	-13%	-13%	-19%	191%	191%	115%	0.09	0.04	2014
PT	33%	33%	30%	-6%	-6%	-17%	172%	172%	100%	0.53	0.26	2013
RO	10%	10%	9%	15%	15%	1%	57%	57%	26%	0.26	0.2	2014
SK	9%	9%	8%	12%	12%	-5%	103%	103%	41%	0.69	0.49	2014
SL	28%	28%	25%	-12%	-12%	-20%	149%	149%	40%	0.66	0.47	2015
ES	28%	28%	25%	14%	14%	-1%	132%	132%	51%	0.74	0.49	2015
SE	46%	46%	42%	-9%	-9%	-18%	116%	116%	46%	1.32	0.91	2015
CH	11%	11%	9%	20%	20%	6%	73%	73%	24%	1.01	0.81	2016
UK	48%	48%	44%	21%	21%	9%	142%	142%	42%	0.86	0.6	2015
EU	35%	35%	31%	10%	10%	-4%	122%	122%	47%	0.72	0.49	

The following data history is used: Portugal Hospital (2010-2018), only retail panel is available for Greece. Prices per treatment day (total market) vary considerably across the different European countries studied, ranging between -20% to 9%.

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 volume development



Fertility approved indications

		CLASSIFICATION				INDICATIONS						
MOLECULE	PRODUCT	REFERENCED	BIOSIMILAR PRODUCTS	NON-REFERENCED	NON-ACCESSIBLE	INFERTILITY	HYPOGONADISM	ANOVULATION	OVULATION INDUCTION	REPRODUCTIVE TECHNICQUES (ASSISTED)	FREQUENCY	ROUTE (SUBQ / IV / IM)
Follitropin alfa	Gonal-F	●				●	●	●			Daily	All
	Bemfola		●			●	●	●		●	Daily	All
	Ovaleap		●			●				●	Daily	All
Follitropin alfa / Lutropin alfa	Pergoveris			●		●	●				Daily	All
Follitropin beta	Puregon			●		●					Patient specific	S/C
Follitropin delta	Rekevelle			●		●			●	●	Daily	S/C
	Follitrin			●		●			●	●	Daily	S/C
Corifollitrophin alfa	Elonva				●	●					Patient specific	S/C
												S/C
Lutropin alfa	Luertis				●	●			●		Daily	All
Follicle-stimulating hormone / Luteinising hormone	Menogon				●	●		●		●	Daily	SC/IM
	Menopur				●	●				●	Daily	SC
	Mentropin				●	●				●	Daily	SC/IM
	Merlofert				●	●			●		Daily	SC
Follicle-stimulating hormone / Luteinising alfa	Menisnorm				●	●			●		Patient specific	SC/IM
Urofollitropin	Bravelle				●	●		●	●	●	Daily	SC/IM
	Fertinorm				●	●			●	●	Daily	SC/IM
	Fostimon				●	●			●		Daily	IM
	Fostlimonkit				●	●			●		Daily	IM
	Fostipur				●	●			●		Daily	SC
	Metrodin				●	●			●	●	Daily	SC/IM

Selected KPIs to illustrate volume share, price evolution, and volume evolution in selected European countries

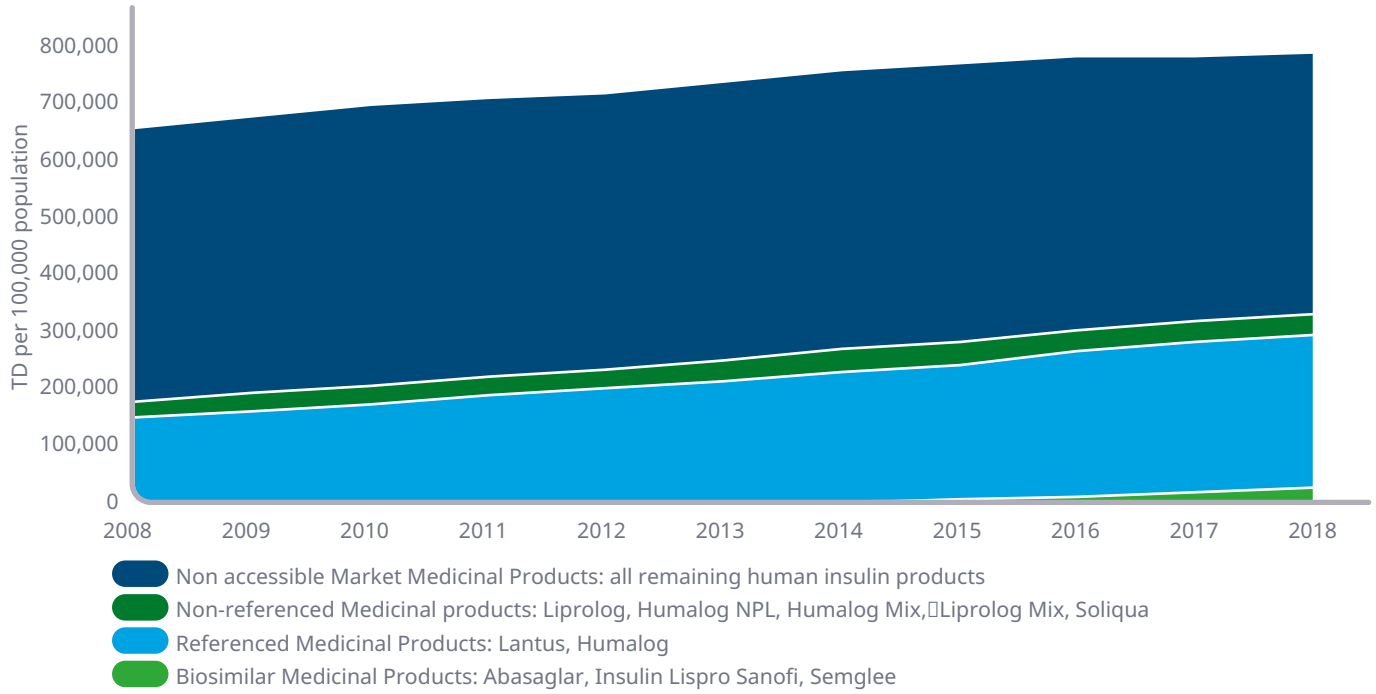
	MARKET SHARE TD (2018)			PRICE PER TD (2018/YR BEFORE BS ENTRY)			VOLUME TD (2018/YR BEFORE BS ENTRY)					
	BIOSIMILAR VS REFERENCED PRODUCT	BIOSIMILAR VS ACCESSIBLE MARKET	BIOSIMILAR VS TOTAL MARKET	BIOSIMILAR AND REFERENCED PRODUCT	BIOSIMILAR ACCESSIBLE MARKET	TOTAL MARKET	BIOSIMILAR AND REFERENCED PRODUCT	BIOSIMILAR ACCESSIBLE MARKET	TOTAL MARKET	TD PER CAPITA	TD/CAPITA (YR BEFORE BS ENTRANCE)	FIRST RECORDED SALES OF BIOSIMILARS
AU	0%	0%	0%	0%	5%	-52%	569%	145%	302%	0.02	0.00	2014
BE	41%	27%	9%	-6%	-1%	-25%	50%	33%	60%	0.06	0.04	2015
BU	79%	31%	28%	-16%	-10%	84%	283%	-12%	-64%	0.00	0.01	2016
CZ	15%	12%	7%	-16%	-14%	-10%	47%	47%	46%	0.08	0.05	2015
DK*	15%	10%	5%	-30%	-25%	-20%	65%	43%	20%	0.12	0.10	2014
FI	21%	15%	8%	-28%	-24%	-14%	93%	13%	3%	0.05	0.04	2014
FR	25%	18%	10%	-5%	-3%	-6%	31%	6%	12%	0.10	0.09	2015
DE	36%	16%	11%	-9%	-12%	2%	42%	57%	20%	0.04	0.04	2014
GR	13%	10%	4%	-15%	-11%	-3%	53%	41%		0.03	0.02	2016
HU	29%	19%	13%	-10%	-9%	-5%	7%	33%	24%	0.05	0.04	2015
IE	2%	1%	0%	-10%	-11%	-7%	34%	13%	14%	0.11	0.09	2016
IT	21%	15%	7%	-10%	-7%	-6%	-16%	-15%	-8%	0.07	0.07	2015
NL*	2%	2%	1%	-7%	-4%	9%	56%	58%	29%	0.09	0.07	2016
NO	30%	23%	10%	-5%	1%	0%	114%	36%	37%	0.09	0.06	2014
PL	29%	19%	6%	18%	27%	2%	37%	13%	25%	0.02	0.02	2015
PT*	27%	17%	8%	-15%	4%	11%	42%	17%	19%	0.04	0.03	2015
RO	5%	3%	1%	-5%	1%	19%	47%	96%	35%	0.02	0.02	2016
SK	26%	25%	6%	-13%	-11%	-11%	70%	43%	61%	0.04	0.03	2016
SL	6%	5%	3%	-1%	7%	13%	77%	40%	8%	0.07	0.06	2015
ES	34%	21%	10%	-26%	-16%	-11%	23%	3%	6%	0.08	0.08	2015
SE	22%	21%	9%	-25%	-25%	-14%	73%	26%	14%	0.09	0.08	2014
CH	2%	1%	1%	-7%	-5%	-2%	4%	2%	2%	0.05	0.00	2018
UK	37%	36%	11%	0%	1%	9%	27%	26%	27%	0.02	0.02	2015
EU	24%	16%	8%	-11%	-7%	-5%	28%	18%	14%	0.06	0.05	

The following data history is used: Portugal Hospital (2010-2018), only retail panel available for Greece. Prices per treatment day (total market) vary considerably across the European markets included in this study, ranging between -52% to 84%.

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 volume 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

MOLECULE	PRODUCT	CLASSIFICATION: REFERENCED	CLASSIFICATION: BIOSIMILAR PRODUCTS	CLASSIFICATION: NON-REFERENCED	CLASSIFICATION: NON-ACCESSIBLE	INDICATIONS: DIABETES MELLITUS	FREQUENCY	MODE OF ACTION	ROUTE (SUBQ/IV)
Insulin glargine	Abasaglar		●			●	Daily	Long-acting	SubQ
	Lantus	●				●	Daily	Long-acting	SubQ
Insulin Glargine / Lixisenatide	Soliqua			●		●	Daily	Long-acting	SubQ
Insulin Degludec	Tresiba					●	Daily	Long-acting	SubQ
Insulin Determir	Levemir				●	●	Twice daily	Long-acting	SubQ
Insulin Degludec / Liraglutide	Xultophy				●	●	Daily	Long-acting	SubQ
Insulin Degludec / Lliraglutide	Ryzedog				●	●	Daily	Fast-acting	SubQ
Insulin Gluisine	Apidra				●	●	Before every meal	Fast-acting	SubQ
Insulin Human	Actraphane				●	●	Once/twice daily	Intermediate-acting	SubQ
	Actrapid				●	●	Before every meal	Short-acting	SubQ
	Insuman				●	●	Determined by HCP	Fast-acting	Both
	Monotard				●	●	Once/twice daily	Intermediate-acting	SubQ
	Humalin				●	●	Once/twice daily	Short-acting	SubQ
	Protophane				●	●	Once/twice daily	Intermediate-acting	SubQ
	Ultratard				●	●	Once/twice daily	Intermediate-acting	SubQ
Insulin Lispro	Liprolog			●		●	Before every meal	Fast-acting	Both
	Humalog	●				●	Before every meal	Fast-acting	Both
	Insulin Lispro Sanofi		●			●	Determined by HCP	Fast-acting	Both
Insulin Lispro / Insulin Lispro Protamine	Humalog Mix			●		●	Determined by HCP	Fast-acting	SubQ
Insulin Aspart	Novorapid				●	●	Before every meal	Fast-acting	SubQ
Insulin Aspart/ Insulin Aspart Protamine	Novomix						Before every meal	Fast-acting	SubQ

Selected KPIs to illustrate volume share, price evolution, and volume evolution in selected European countries

	MARKET SHARE TD (2018)			PRICE PER TD (2018/YR BEFORE BS ENTRY)			VOLUME TD (2018/YR BEFORE BS ENTRY)					
	BIOSIMILAR VS REFERENCED PRODUCT	BIOSIMILAR VS ACCESSIBLE MARKET	BIOSIMILAR VS TOTAL MARKET	BIOSIMILAR AND REFERENCED PRODUCT	BIOSIMILAR ACCESSIBLE MARKET	TOTAL MARKET	BIOSIMILAR AND REFERENCED PRODUCT	BIOSIMILAR ACCESSIBLE MARKET	TOTAL MARKET	TD PER CAPITA	TD/CAPITA (YR BEFORE BS ENTRANCE)	FIRST RECORDED SALES OF BIOSIMILARS
AU	0%	0%	0%	14%	15%	14%	19%	12%	7%	5.79	5.43	2017
BE	2%	2%	1%	-3%	-1%	14%	42%	36%	5%	6.92	6.59	2016
BU	6%	4%	1%	-5%	3%	18%	59%	37%	15%	6.71	5.85	2015
CZ	7%	6%	2%	12%	19%	41%	108%	82%	28%	9.77	7.64	2015
DK	6%	6%	2%	4%	4%	20%	45%	44%	10%	7.15	6.52	2015
FI	6%	6%	3%	-5%	-5%	1%	13%	12%	2%	11.77	11.50	2015
FR	8%	7%	4%	-4%	-3%	10%	18%	14%	9%	6.78	6.21	2016
DE	7%	6%	3%	13%	13%	18%	48%	45%	0%	11.52	11.48	2015
GR	9%	8%	4%	1%	5%	30%	24%	10%	7%	7.45	6.95	2016
HU	6%	5%	1%	9%	16%	41%	26%	20%	6%	9.81	9.21	2015
IE	0%	0%	0%	-8%	-7%	4%	7%	8%	10%	5.10	4.64	2016
IT	10%	9%	5%	5%	7%	19%	12%	6%	2%	5.77	5.68	2016
NL	6%	6%	2%	-4%	-3%	15%	7%	6%	3%	9.27	8.97	2015
NO	2%	2%	1%	22%	22%	43%	21%	20%	13%	7.69	6.79	2015
PL	23%	19%	4%	-7%	0%	10%	131%	71%	3%	6.88	6.66	2015
PT	7%	6%	3%	2%	5%	13%	37%	29%	8%	6.11	5.67	2016
RO	5%	5%	2%	7%	12%	18%	55%	42%	15%	5.96	5.20	2016
SK	24%	20%	8%	4%	7%	21%	56%	44%	8%	7.00	6.48	2015
SL	5%	4%	1%	-7%	0%	21%	19%	9%	3%	8.75	8.54	2016
ES	8%	7%	4%	-14%	-10%	5%	33%	21%	5%	7.35	7.03	2015
SE	14%	12%	4%	-1%	1%	12%	26%	21%	6%	10.13	9.59	2015
CH	1%	1%	0%	4%	5%	37%	-7%	-6%	1%	4.54	4.50	2015
UK	5%	4%	1%	5%	7%	13%	3%	1%	3%	7.58	7.33	2015
EU	8%	7%	3%	2%	5%	15%	29%	23%	5%	7.83	7.49	

The following data history is used: Portugal Hospital (2010-2018), only retail panel is available for Greece. Prices per treatment day (total market) vary over the European markets. Prices per treatment day (total market) vary over the European markets included in this study, ranging between 1% to 43%.

ONCOLOGY (RITUXIMAB)

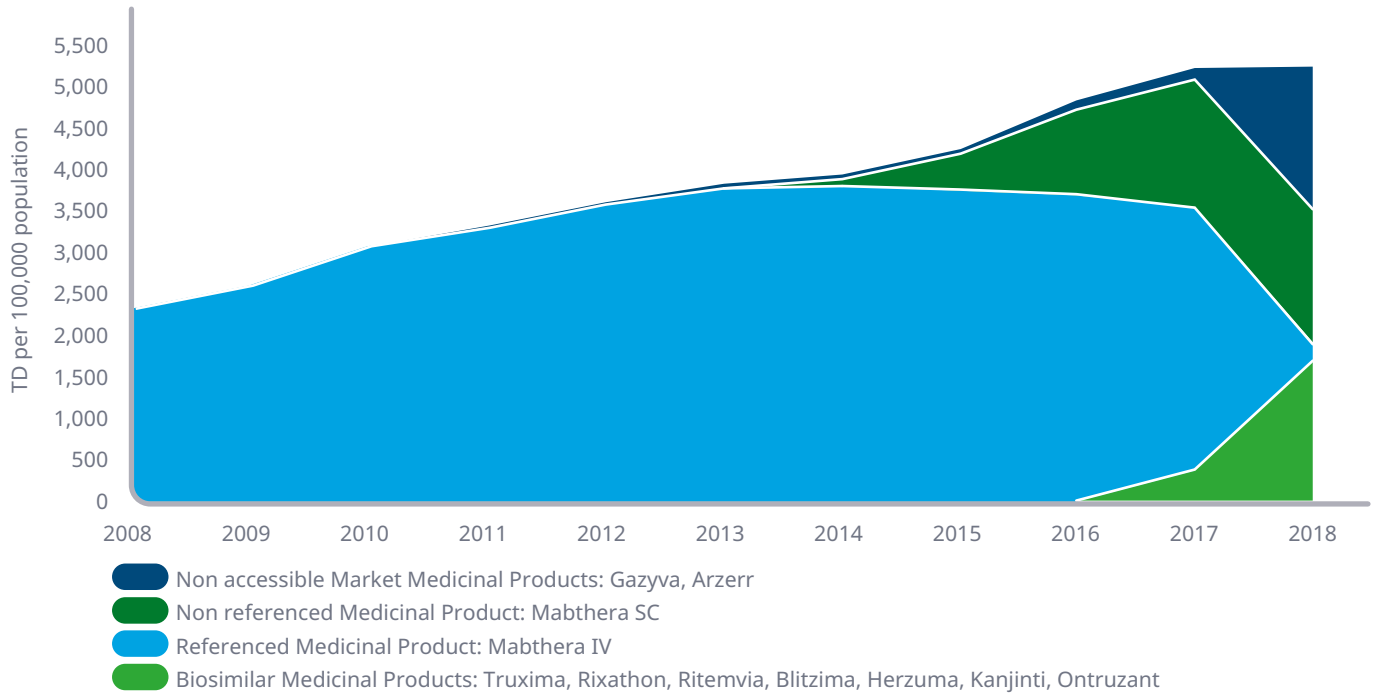
Monoclonal Antibody Antineoplastic agents use monoclonal antibodies (mAb) to bind monospecifically to certain cells or proteins to treat cancer. The objective is that this treatment will stimulate the patient's immune system to attack those cells.

Mabthera is a medicine used to treat several blood cancers and inflammatory conditions, including follicular lymphoma and diffuse large B cell non-Hodgkin's lymphoma (two types of non-Hodgkin's lymphoma) and chronic lymphocytic leukaemia (CLL). It is also used to treat severe RA and other inflammatory conditions. 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.

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 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 volume development



Oncology approved indications

MOLECULE	PRODUCT	CLASSIFICATION: REFERENCED	CLASSIFICATION: BIOSIMILAR PRODUCTS	CLASSIFICATION: NON-REFERENCED	CLASSIFICATION: NON-ACCESSIBLE	INDICATIONS: CLL	INDICATIONS: FL	INDICATIONS: NHL	INDICATIONS: RA	INDICATIONS: Granulmastosis with polyanglitis	ROUTE (SUBQ/IV)
Rituxumab	Mabthera (IV) Mabthera (SC) Truxima Ritxathon Ritemvia	●	● ● ●	●		● ● ● ●	● ● ● ●	● ● ● ● ●	● ● ● ●	● ● ●	IV SubQ IVV IV IV
Obintuzumab	Gazyva				●	●	●		●		IV
Ofatumumab	Arzerra				●	●					IV

Selected KPIs to illustrate volume share, price evolution, and volume evolution in selected European countries

	MARKET SHARE TD (2018): BIOSIMILAR VS REFERENCED PRODUCT	MARKET SHARE TD (2018): BIOSIMILAR VS ACCESSIBLE MARKET	MARKET SHARE TD (2018): BIOSIMILAR VS TOTAL MARKET	PRICE PER TD (2018/YR BEFORE BS ENTRY): BIOSIMILAR AND REFERENCED PRODUCT	PRICE PER TD (2018/YR BEFORE BS ENTRY): BIOSIMILAR ACCESSIBLE MARKET	PRICE PER TD (2018/YR BEFORE BS ENTRY): TOTAL MARKET	VOLUME TD (2018/YR BEFORE BS ENTRY): BIOSIMILAR AND REFERENCED PRODUCT	VOLUME TD (2018/YR BEFORE BS ENTRY): BIOSIMILAR ACCESSIBLE MARKET	VOLUME TD (2018/YR BEFORE BS ENTRY): TOTAL MARKET	TD PER CAPITA	TD/CAPITA (YR BEFORE BS ENTRANCE)	FIRST RECORDED SALES OF BIOSIMILARS
AU	75%	53%	47%	109%	88%	87%	-30%	-34%	-29%	0.06	0.08	2017
BE	0%	0%	0%	14%	0%	2%	-10%	27%	28%	0.06	0.05	2018
BU	6%	4%	4%	-12%	-13%	-12%	-16%	3%	3%	0.03	0.03	2018
CZ	8%	4%	4%	3%	-17%	-15%	194%	440%	450%	0.05	0.01	2018
DK	57%	29%	27%	34%	21%	19%	2%	12%	12%	0.09	0.08	2017
FI	16%	8%	8%	-3%	4%	5%	16%	9%	9%	0.10	0.09	2018
FR	55%	34%	33%	-24%	-24%	-22%	10%	28%	29%	0.08	0.06	2017
DE	60%	54%	50%	7%	7%	9%	1%	-1%	2%	0.06	0.06	2017
GR*	0%	0%	0%	12%	12%	12%	0%	0%	0%	0.00	0.00	
HU	49%	36%	31%	-8%	-9%	-1%	-18%	-9%	-3%	0.04	0.04	2018
IE	14%	13%	13%	0%	-2%	-1%	1%	6%	7%	0.06	0.06	2017
IT	58%	36%	35%	4%	1%	2%	0%	11%	12%	0.05	0.05	2017
NL	89%	83%	82%	30%	35%	35%	11%	4%	5%	0.05	0.05	2017
NO	14%	7%	7%	23%	21%	23%	-1%	8%	9%	0.09	0.08	2017
PL	0%	0%	0%	28%	18%	19%	0%	0%	0%	0.02	0.02	
PT	53%	23%	23%	-2%	4%	5%	15%	7%	7%	0.05	0.04	2017
RO	1%	1%	1%	10%	10%	19%	-68%	-68%	-63%	0.00	0.01	2018
SK	4%	3%	3%	9%	-4%	-3%	0%	0%	0%	0.03	0.03	2018
SL	11%	9%	8%	7%	10%	13%	0%	0%	0%	0.06	0.06	2018
ES	29%	17%	16%	10%	-1%	2%	7%	44%	47%	0.07	0.04	2017
SE	12%	7%	7%	4%	4%	4%	0%	0%	0%	0.09	0.08	2018
CH	2%	2%	2%	1%	0%	-1%	0%	0%	0%	0.07	0.06	2018
UK	89%	58%	55%	114%	81%	82%	-46%	-34%	-31%	0.04	0.06	2017
EU	50%	34%	32%	14%	8%	10%	-6%	6%	8%	0.05	0.05	

The following data history is used: Portugal Hospital (2010-2018), only retail panel is available for Greece. Prices per treatment day (total market) vary over the European markets. Prices per treatment day (total market) vary over the European markets included in this study, ranging between -24% to 87%.

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), therefore, the KPI tables and charts are not included for this section.

REFERENCES

i IQVIA MIDAS analysis 2019 Q2 MAT (Rx only); LCEUR Bn

ii EMA list of approved biosimilars (June 2019); IQVIA Institute analysis

iii Global Supplier & Association Relations model 2019; MIDAS Q2 2019

iv Global Supplier & Association Relations model 2019; MIDAS Q2 2019

v IQVIA European Thought Leadership; IQVIA MIDAS MTH May 2019

vi RAPS, GROENE outlets https://www.raps.org/news-and-articles/news-articles/2018/11/abbvie-sees-80-discounts-in-nordic-market-with-ne; https://www.groene.nl/artikel/het-patent-gaat-voor-de-patient

vii IQVIA European Thought Leadership; IQVIA MIDAS MTH May 2019

viii IQVIA MIDAS INTDDD Jun 2019; Notes: Graphs display data from Q3 2009 – Q2 2019. Compound annual growth is calculated from the quarter before date of first sales within MIDAS (denoting biosimilar entry), to Q2 2019. Deltas have subtracted the organic growth of the biologic prior to biosimilar entry (3-year CAGR) to determine change in usage post-biosimilar entry.

ix IQVIA MIDAS INTDDD Jun 2019, Notes: Graphs display data from Q3 2013 – Q2 2019. Compound annual growth is calculated from the quarter before date of first sales within MIDAS (denoting biosimilar entry), to Q2 2019. Deltas subtract the organic growth of the biologic (3-year CAGR prior to biosimilar entry) to determine change in usage post-biosimilar entry.

x MIDAS MAT 2019 Q2 data (2008 – 2019); LCUSD

xi IQVIA Global Supplier & Association Relation analysis 2019, MIDAS global sales (2008 – 2019)

xii ARK Patent Intelligence insights, Q2 2019

READING GUIDE

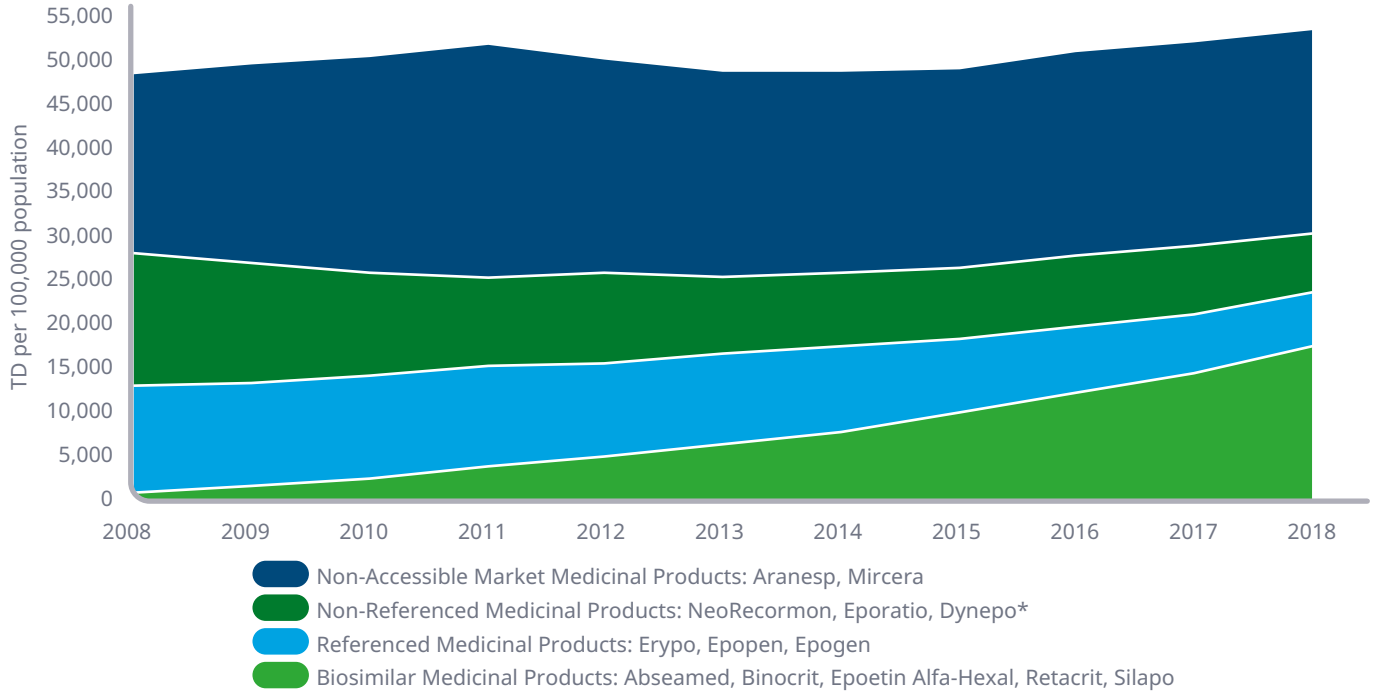
This example has been developed as a simplified guide to read the report that has a broad set of Key Performance Indicators for multiple countries. EPO in Austria is used as the example

VOLUME DEVELOPMENT

The chart Epoetin Volume Development shows volume development over time across all the European countries included in the study. Volume is expressed in (WHO) DDDs as a proxy to be able to compare different products. The **light-green** part of the chart shows the volume share of Biosimilar Medicinal Products (listed) which is currently at 33% in the chosen example. The **light-blue** part shows volume share of Referenced Medicinal Products to the approved Biosimilar products which is currently at 12%.

The Non-Referenced Competing Medicinal Products (**dark-green** part of the chart) are other products with a largely similar profile to the Referenced Products, but have not been referenced. This category was affected by biosimilar entrance, which resulted in a loss of market share from 31% in 2008 to 12% in 2018.
The Non–Accessible market (**dark-blue** part of the chart) are the Pegylated (long-acting) products, with 43% market share.

Epoetin volume development



APPROVED INDICATIONS

The table Summary of EMA information for approved indications for Epoetin products shows that the Biosimilar Medicinal Products receive the same indications as the Referenced Medicinal Products. It also shows that not all products are approved for all indications.

		CLASSIFICATION				INDICATIONS								
MOLECULE	PRODUCT	REFERENCED	BIOSIMILAR PRODUCTS	NON-REFERENCED	NON-ACCESSIBLE	ANEMIA FOR CHEMOTHERAPY PATIENTS	ANEMIA FOR PATIENTS WITH CKD	PREVENTING ANEMIA IN PREMATURE BABIES	AUTOLOGUS BLOOD TRANSFUION	AMENIA IN ADULTS WITH MDS	REUDCTIOJN OF ALLOGENIC TRANSFUSION EXPOSURE IN ORTHAPEDIC SURGERY	PATIENT TYPE (ADULT OR PEDIATRIC)	FREQUENCY	ROUTE (SUBQ/IV)
Epoetin alfa	Epogen Erypo Epogen Abseamed Epoetin Alfa Hexal Binocrit	●	●			●	●		●	●	●	Both	3 x a week	Both
Epoetin beta	NeoRecormon			●		●	●	●	●		●	Both	3 x a week	Both
Epoetin zeta	Retacrit Silapo		●			●	●		●		●	Both	3 x a week	Both
Epoetin theta	Eporatio			●		●	●					Adult	3 x a week	Both
Methoxy polyethlene glycol-epoetin beta	Miracera				●		●					Adult	Fortnightly	Both
Darbepoetin alfa	Aranesp Darbepogen				●	●	●					Adult	Weekly	Both

SELECTED KPIS

The first set of indicators is the Market share TD 2018 calculated in treatments days. In Austria, Biosimilars represent 80% of Biosimilar + Referenced Products (which includes all the biosimilars and all the referenced products on the market for a therapy area). If the Non-Referenced Medicinal Product is also included (total accessible market), the share of Biosimilar Medicinal Product is 35%. Looking at the Biosimilar Medicinal Product versus total market, the market share is 23%.

	MARKET SHARE TD (2018)			PRICE PER TD (2018/YR BEFORE BS ENTRY)			VOLUME TD (2018/YR BEFORE BS ENTRY)					
	BIOSIMILAR VS REFERENCED PRODUCT	BIOSIMILAR VS ACCESSIBLE MARKET	BIOSIMILAR VS TOTAL MARKET	BIOSIMILAR AND REFERENCED PRODUCT	BIOSIMILAR ACCESSIBLE MARKET	TOTAL MARKET	BIOSIMILAR AND REFERENCED PRODUCT	BIOSIMILAR ACCESSIBLE MARKET	TOTAL MARKET	TD PER CAPITA	TD/CAPITA (YR BEFORE BS ENTRANCE)	FIRST RECORDED SALES OF BIOSIMILARS
AU	80%	35%	23%	-40%	-42%	-30%	-2%	-3%	-25%	0.69	0.92	2008

The second set of indicators, Price per TD (2018/Year before biosimilar entrance), shows price development per treatment day (DDD) comparing 2018 price with prices in the year before the first Epoetin Biosimilar Medicinal Product was launched (which is 2008 in the case of Austria). The volume-weighted average price in 2018 v 2007 has fallen 40% for the Biosimilar Medicinal Product and Referenced Product, 42%for Biosimilar Accessible Market and 30 for the total market. This data illustrates that the competitive response, or the price regulators response is to lower prices on other products in the market, as competition intensifies.

	MARKET SHARE TD (2018)			PRICE PER TD (2018/YR BEFORE BS ENTRY)			VOLUME TD (2018/YR BEFORE BS ENTRY)					
	BIOSIMILAR VS REFERENCED PRODUCT	BIOSIMILAR VS ACCESSIBLE MARKET	BIOSIMILAR VS TOTAL MARKET	BIOSIMILAR AND REFERENCED PRODUCT	BIOSIMILAR ACCESSIBLE MARKET	TOTAL MARKET	BIOSIMILAR AND REFERENCED PRODUCT	BIOSIMILAR ACCESSIBLE MARKET	TOTAL MARKET	TD PER CAPITA	TD/CAPITA (YR BEFORE BS ENTRANCE)	FIRST RECORDED SALES OF BIOSIMILARS
AU	80%	35%	23%	-40%	-42%	-30%	-2%	-3%	-25%	0.69	0.92	2008

The third set of indicators, Volume TD (2018/Year before biosimilar entrance), shows the volume development in treatment days (DDDs) comparing 2018 versus the year before the first Epoetin Biosimilar Medicinal Product was launched (which is 2008 in the case of Austria). While the Biosimilar and the Referenced Product volume has decreased 2%%; the full accessible market volume decreased 3% and the total market volume decreased 25%.

	MARKET SHARE TD (2018)			PRICE PER TD (2018/YR BEFORE BS ENTRY)			VOLUME TD (2018/YR BEFORE BS ENTRY)					
	BIOSIMILAR VS REFERENCED PRODUCT	BIOSIMILAR VS ACCESSIBLE MARKET	BIOSIMILAR VS TOTAL MARKET	BIOSIMILAR AND REFERENCED PRODUCT	BIOSIMILAR ACCESSIBLE MARKET	TOTAL MARKET	BIOSIMILAR AND REFERENCED PRODUCT	BIOSIMILAR ACCESSIBLE MARKET	TOTAL MARKET	TD PER CAPITA	TD/CAPITA (YR BEFORE BS ENTRANCE)	FIRST RECORDED SALES OF BIOSIMILARS
AU	80%	35%	23%	-40%	-42%	-30%	-2%	-3%	-25%	0.69	0.92	2008

The last set of indicators, TD per capita (Year before biosimilar entrance) and TD per capita 2018, show the usage per capita before the entrance of biosimilars (which is 0.92 in Austria), and the usage per capita of the total market in 2018 (which is 0.69 in Austria). The year with the First recorded sales of Biosimilar in Austria is 2008. In classes where there are multiple biosimilars, this will reflect the first recorded sales of the first biosimilar which entered the market.

	MARKET SHARE TD (2018)			PRICE PER TD (2018/YR BEFORE BS ENTRY)			VOLUME TD (2018/YR BEFORE BS ENTRY)					
	BIOSIMILAR VS REFERENCED PRODUCT	BIOSIMILAR VS ACCESSIBLE MARKET	BIOSIMILAR VS TOTAL MARKET	BIOSIMILAR AND REFERENCED PRODUCT	BIOSIMILAR ACCESSIBLE MARKET	TOTAL MARKET	BIOSIMILAR AND REFERENCED PRODUCT	BIOSIMILAR ACCESSIBLE MARKET	TOTAL MARKET	TD PER CAPITA	TD/CAPITA (YR BEFORE BS ENTRANCE)	FIRST RECORDED SALES OF BIOSIMILARS
AU	80%	35%	23%	-40%	-42%	-30%	-2%	-3%	-25%	0.69	0.92	2008

APPENDICES

EMA LIST OF APPROVED BIOSIMILARS (MAY 2018)

Some of the biosimilars which have been authorised for use in Europe by the EMA are not yet captured in IQVIA MIDAS, either because they are not launched yet, or because there were no sales reported as of MAT Dec 2018. These products have not been included in the study.

Table 1: EMA list of approved biosimilars (July 2019)

MEDICINE NAME	ACTIVE SUBSTANCE	ATC CODE	MARKETING AUTHORISATION HOLDER	AUTHORISATION DATE
ABASAGLAR (PREVIOUSLY ABASRIA)	insulin glargine	A10AE04	Eli Lilly Nederland B.V.	8/09/2014
ABSEAMED	epoetin alfa	B03XA01	Medice Arzneimittel Pütter GmbH Co. KG	26/08/2007
ACCOFIL	filgrastim	L03AA02	Accord Healthcare S.L.U.	16/09/2014
AMGEVITA	adalimumab	L04AB04	Amgen Europe B.V.	20/03/2017
BEMFOLA	follitropin alfa	G03GA05	Gedeon Richter Plc.	25/03/2014
BENEPALI	etanercept	L04AB01	Samsung Bioepis NL B.V.	12/01/2016
BINOCRIT	epoetin alfa	B03XA01	Sandoz GmbH	27/08/2007
BLITZIMA	rituximab	L01XC02	Celltrion Healthcare Hungary Kft.	12/07/2017
EPOETIN ALFA HEXAL	epoetin alfa	B03XA01	Hexal AG	26/08/2007
ERELZI	etanercept	L04AB01	Sandoz GmbH	22/06/2017
FILGRASTIM HEXAL	filgrastim	L03AA02	Hexal AG	5/02/2009
FLIXABI	infliximab	L04AB02	Samsung Bioepis NL B.V.	25/05/2016
FULPHILA	pegfilgrastim	L03AA13	Mylan S.A.S	19/11/2018
GRASTOFIL	filgrastim	L03AA02	Apotex Europe BV	16/10/2013
GRASUSTEK	pegfilgrastim	L03AA13	Juta Pharma GmbH	25/04/2019
HALIMATOZ	adalimumab	L04AB04	Sandoz GmbH	25/07/2018
HEFIYA	adalimumab	L04AB04	Sandoz GmbH	25/07/2018
HERZUMA	trastuzumab	L01XC03	Celltrion Healthcare Hungary Kft.	7/02/2018
HULIO	adalimumab	L04AB04	Mylan S.A.S.	15/09/2018
HYRIMOZ	adalimumab	L04AB04	Sandoz GmbH	25/07/2018
IDACIO	adalimumab	L04AB04	Fresenius Kabi Deutschland GmbH	1/04/2019
IMRALDI	adalimumab	L04AB04	Samsung Bioepis NL B.V.	23/08/2017
INFLECTRA	infliximab	L04AB02	Pfizer Europe MA EEIG	8/09/2013
INHIXA	enoxaparin sodium	B01AB05	Techdow Europe AB	14/09/2016
INSULIN LISPRO SANOFI	insulin lispro	A10AB04	sanofi-aventis groupe	17/07/2017
KANJINTI	trastuzumab	L01XC03	Amgen Europe B.V., Breda	15/05/2018
KROMEYA	adalimumab	L04AB04	Fresenius Kabi Deutschland GmbH	1/04/2019
MOVYMIA	teriparatide	H05AA02	STADA Arzneimittel AG	10/01/2017
MVASI	bevacizumab	L01XC07	Amgen Europe B.V.	14/01/2018
NIVESTIM	filgrastim	L03AA02	Pfizer Europe MA EEIG	6/06/2010
OGIVRI	trastuzumab	L01XC03	Mylan S.A.S	11/12/2018
OMNITROPE	somatropin	H01AC01	Sandoz GmbH	11/04/2006
ONTRUZANT	trastuzumab	L01XC03	Samsung Bioepis NL B.V.	14/11/2017
OVALEAP	follitropin alfa	G03GA05	Theramex Ireland Limited	26/09/2013
PELGRAZ	pegfilgrastim	L03AA13	Accord Healthcare S.L.U.	20/09/2018

MEDICINE NAME	ACTIVE SUBSTANCE	ATC CODE	MARKETING AUTHORISATION HOLDER	AUTHORISATION DATE
PELMEG	pegfilgrastim	L03AA13	Mundipharma Biologics S.L.	19/11/2018
RATIOGRASTIM	filgrastim	L03AA02	Ratiopharm GmbH	14/09/2008
REMSIMA	infliximab	L04AB02	Celltrion Healthcare Hungary Kft.	9/09/2013
RETACRIT	epoetin zeta	B03XA01	Pfizer Europe MA EEIG	17/12/2007
RITEMVIA	rituximab	L01XC02	Celltrion Healthcare Hungary Kft.	12/07/2017
RIXATHON	rituximab	L01XC02	Sandoz GmbH	14/06/2017
RIXIMYO	rituximab	L01XC02	Sandoz GmbH	14/06/2017
SEMGLEE	insulin glargine	A10AE04	Mylan S.A.S	22/03/2018
SILAPO	epoetin zeta	B03XA01	Stada Arzneimittel AG	17/12/2007
TERROSA	teriparatide	H05AA02	Gedeon Richter Plc.	3/01/2017
TEVAGRASTIM	filgrastim	L03AA02	Teva GmbH	14/09/2008
THORINANE	enoxaparin sodium	B01AB05	Pharmathen S.A.	13/09/2016
TRAZIMERA	trastuzumab	L01XC03	Pfizer Europe MA EEIG	25/07/2018
TRUXIMA	rituximab	L01XC02	Celltrion Healthcare Hungary Kft.	16/02/2017
UDENYCA	pegfilgrastim	L03AA13	ERA Consulting GmbH	20/09/2018
ZARZIO	filgrastim	L03AA02	Sandoz GmbH	5/02/2009
ZESSLY	infliximab	L04AB02	Sandoz GmbH	17/05/2018
ZIEXTENZO	pegfilgrastim	L03AA13	Sandoz GmbH	21/11/2018
ZIRABEV	bevacizumab	L01XC07	Pfizer Europe MA EEIG	13/02/2019

Source: EMA website, data accessed 23 Oct 2019
https://www.ema.europa.eu/en/medicines/download-medicine-data

List of Biosimilars under review by EMA (July 2019)

COMMON NAME	THERAPEUTIC AREA	NUMBER OF APPLICATIONS	EMA-APPROVED ORIGINATOR(S)	ORIGINATOR COMPANY(IES)
ADALIMUMAB	Immunosuppressant	1	Humira	AbbVie
ETANERCEPT	Immunosuppressant	1	Enbrel	Amgen/Pfizer
INSULIN ASPART	Diabetes	1	NovoLog	Novo Nordisk
RITUXIMAB	Antineoplastic medicine (anticancer)	3	MabThera/Rituxan	Roche
TERIPARATIDE	Calcium homeostasis	3	Forteo/Forsteo	Eli Lilly
TRASTUZUMAB	Antineoplastic medicines	2	Herceptin	Roche

Source: EMA, July 2019: report accessed 23 Oct 2019
https://www.ema.europa.eu/en/documents/report/applications-new-human-medicines-under-evaluation-chmp-july-2019_en.pdf

METHODOLOGY

- The volumes have been converted by IQVIA into daily doses using WHO DDDs. Consumption measures are therefore not adjusted for clinical practice guidelines, patient characteristics, indications for which the molecule is used, or other factors which may result in different volumes utilised on a per patient treatment day basis.
- Volume share is calculated as the volume in DDD versus the relevant market (reference market, accessible market, total market).
- Prices are calculated as a volume weighted ex-manufacturing price.
- Price evolution is calculated as the present price for the relevant market versus the price for the same relevant market before the introduction of biosimilars in the country.
- Volume evolution is calculated as the present total volume versus the total volume before the introduction of biosimilars in the country.

		METHODOLOGY
Market share TD	Biosimilar vs Reference Product	TD Biosimilars as a % of TD reference products in 2018
	Biosimilar vs Accessible Market	TD Biosimilars as a % of Accessible market in 2018
	Biosimilar vs Total Market	TD Biosimilars as a % of TD Total market in 2018
Price TD	Biosimilar Reference Product	△ in Price per TD for Biosimilar Reference products 2018/the year before biosimilar entrance
	Biosimilar Accessible Market	△ in Price per TD for Biosimilar Accessible products 2018/the year before biosimilar entrance
	Total Market	△ in Price per TD for Total market 2018/the year before biosimilar entrance
Volumn TD	Biosimilar Reference Product	△ in TD for Biosimilar and Reference products 2018/the year before biosimilar entrance
	Biosimilar Accessible Market	△ in TD for Biosimilar Accessible market products 2018/the year before biosimilar entrance
	Total Market	△ in TD for Total market 2018/the year before biosimilar entrance
TD per Capita 2018		No. of Treatment Days per Capita in 2018
TD per capita year before biosimilar entrance		No. if Treatment Days per Capita the year before biosimilars entered the market
First recorded sales		The year first sales of biosimilars were recorded

IQVIA SOURCE OF VOLUME DATA

Volume information is based on channel audits for retail and non-retail channels, covering the majority of volume consumed in a country market, though may exclude some direct sales made from the manufacturer to dispensing locations. IQVIA source of volume data collection route and sample varies by country; data can be collected at various points within the pharmaceutical supply chain.

Note: Points of collection

- Sell-in data represents the supply of products from wholesalers to pharmacies.
- Sell-out data represents the demand for products from the pharmacies to patients.
- Hospital consumption data measures dispensing of products by hospital pharmacies within the hospital wards.

The table below is a matrix to identify these points of collection by country.

	AU	BE	BU	CZ	DK	FI	FR	DE	GR	HU	IE	IT	NL	NO	PL	PT	RO	SK	SL	ES	SE	CH	UK
Retail	In	In	In	In	In	In	Out	Out	Out	In	In	In	In	In	In	In	In	In		In	Out	In	Out
Hospital	C	In	In	In	In	In	C	C		In	In	C	In	In	In	C	In	In		C	In	In	C
Retail																			In				

IQVIA SOURCE OF PRICE DATA

Sales data is collected in terms of the number of Pack Units sold and are then multiplied by the Pack Price to produce the sales values. Pricing information is based on a variety of sources including list price, wholesaler transactions, government price list and industry publications, but does not reflect rebates and discounts which in some countries and channels may be significant. Country volumes may also be impacted by unknown parallel exports or imports which cannot be identified or adjusted for. Inclusion of VAT and taxes varies per country. The table below shows the price source reference within each country included in the study:

EU GEOGRAPHY			
COUNTRY		**SECTOR (DATA TYPE)**	**PRICE SOURCE**
Austria	AU	HOSPITAL (CONSUMPTION) RETAIL (SELL-IN)	Hospital & Retail - List price - Arzneimittelverzeichnis or Taxe (Apotheker-Verlag)
Belgium	BE	HOSPITAL (CONSUMPTION) RETAIL (SELL-IN)	Hospital - List price - Association Général de l'Industrie due Médicament (AGIM), Retail - List price - Association Pharmaceutique Beige (APB)
Bulgaria	BU	HOSPITAL (CONSUMPTION) RETAIL (SELL-IN)	Hospital & Retail - Average invoiced pack price
Czech Rep.	CZ	HOSPITAL (SELL-IN) RETAIL (SELL-IN)	Hospital & Retail - Average invoiced pack price
Denmark	DK	HOSPITAL (SELL-IN) RETAIL (SELL-IN)	Hospital & Retail - Average invoiced pack price
Finland	FI	HOSPITAL (SELL-IN) RETAIL (SELL-IN)	Hospital & Retail - List Price - Wholesalers, based on official published prices of Finnish Pharmacy Association
France	FR	HOSPITAL (CONSUMPTION) RETAIL (SELL-OUT)	Hospital - List price - Journal Officiel, manufacturer hospital price lists, Retail - List price, Jounal Officiel, wholesaler catalogues, average transaction prices
Germany	DE	HOSPITAL (CONSUMPTION) RETAIL (SELL-OUT)	Hospital - Estimated transaction price reflecting the average level of rebates and discounts, Pharmascope - List price - ABDATA (Pharmacist Associated), sourced from IFA (German Health Institute)
Greece	GR	RETAIL (SELL-OUT)	Retail - List price - Ministry of Development
Hungary	HU	HOSPITAL (SELL-IN) RETAIL (SELL-IN)	Hospital & Retail - List price - National Health Fund, National Institute of Pharmacy
Ireland	IE	HOSPITAL (SELL-IN) RETAIL (SELL-IN)	Hospital & Retail - List price - Irish prescription drug databases
Italy	IT	DPC (CONSUMTION), HOSPIAL (CONSUMPTION), RETAIL (SELL-IN)	DPC & Retail - List price - CFO - Farmadati, Gazzetta Ufficiale della Repubblica Italiana, Hospital - List price - 45% public level retail list price
Netherlands	NL	HOSPITAL (SELL-IN) RETAIL (SELL-IN)	Hospital & Retail - List price - Wholesaler price list
Norway	NO	HOSPITAL (SELL-IN) RETAIL (SELL-IN)	Hospital & Retail - Average invoiced pack price
Poland	PL	HOSPITAL (SELL-IN) RETAIL (SELL-IN)	Hospital & Retail - Average invoiced pack price
Portugal	PT	HOSPITAL (CONSUMPTION) RETAIL (SELL-IN)	Hospital - Average invoiced pack price, Retail - List price - Manufacturer published price list
Romania	RO	HOSPITAL (SELL-IN) RETAIL (SELL-IN)	Hospital & Retail - Average invoiced pack price
Slovakia	SK	HOSPITAL (SELL-IN) RETAIL (SELL-IN)	Hospital & Retail - Average invoiced pack price
Slovenia	SL	COMBINED (SELL-IN)	Hospital & Retail - Average invoiced pack price
Spain	ES	HOSPITAL (CONSUMPTION), RETAIL (SELL-IN)	Hospital & Retail - List Price - Manufacturer price list, Base de Datos del Medicamento (BOT)
Sweden	SE	RETAIL (SELL-OUT), HOSPITAL (SELL-IN)	Hospital & Retail - List price - Apoteket AB, The Dental and Pharmaceutical Benefits Agency, The Drug Benefit Board, The LFN
Switzerland	CH	HOSPITAL (SELL-IN), RETAIL (SELL-IN)	Hospital & Retail - List price - Wholesalers, manufacturers
UK	UK	HOSPITAL (CONSUMPTION), RETAIL (SELL-IN)	Hospital & Retail - List price - Chemist and Druggist, Drug Tariff

CONTACT US

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