QuintilesIMS™

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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 the European Economic Area (EEA). The report consists of a set of Key Performance Indicators (KPI's) to monitor the impact of biosimilars in European markets, using full year 2016 data.

This report has been prepared by QuintilesIMS at the request of the European Commission services with initial contributions from EFPIA, Medicines for Europe, and EuropaBio.

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 issue 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:
  - **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.
  - **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.
  - **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 **KPI's** 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, 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 2016 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 2016 versus year before biosimilar entry.
  - **Volume per capita 2016:** number of Treatment Days consumed in 2016 normalised by population size.
  - **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 publically 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 QuintilesIMS 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 reference products and are inferred to have similar efficacy.
- **Volume estimates:** the pack volumes reported are based on QuintilesIMS 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.

Four Observations by QuintilesIMS

1. The entrance of biosimilars increases price competition

1a. Competition drives down price

The rationale behind the introduction of biosimilars is to increase price competition, an effect of which is often reduced prices. The six established therapy areas with biosimilar competition show a consistent picture of reduced average list prices in European Economic Area (EEA) countries (see Exhibit 1).

The increased competition resulting from biosimilars entering the market affects not just the price of the respective biosimilars reference product, but also the price of the whole product class. It can have almost as large an impact on the total market price as it has on the biosimilar/reference product price.

Exhibit 2 shows the three countries where the highest price reduction of the total market has been achieved. In the case of EPO's in Portugal, the price decease can be as much as -66%.

Exhibit 1: Total change in price per TD since the entrance of biosimilars for each therapy area

	Price per TD 2016/ Year before Biosimilar entrance		
	Biosimilar and Reference product	Biosimilar Accessible market	Total market
EPO	-31%	-33%	-27%
G-CSF	-37%	-36%	-27%
HGH	-21%	-15%	-15%
Anti-TNF	-13%	-13%	-10%
Fertility	-6%	-5%	-4%
Insulins	-7%	-3%	1%

Other countries may also have high price reductions, through non-published discounting. However, such reductions are not visible in the data in this report. In addition, the highest reduction may not equal the lowest price.

Exhibit 2: Countries with the highest price reduction of the total market since the entrance of biosimilars

EPO	Price per TD 2016 / Year before Biosimilar entrance Total market
Portugal	-66%
Slovakia	-53%
Norway	-51%

G-CSF	Price per TD 2016 / Year before Biosimilar entrance Total market
Romania	-62%
Slovakia	-61%
Slovenia	-57%

HGH	
Finland	-52%
Poland	-42%
Norway	-37%

Anti-TNF	
Sweden	-39%
Norway	-32%
Denmark	-24%

Fertility	
Denmark	-24%
Spain	-14%
Sweden	-10%

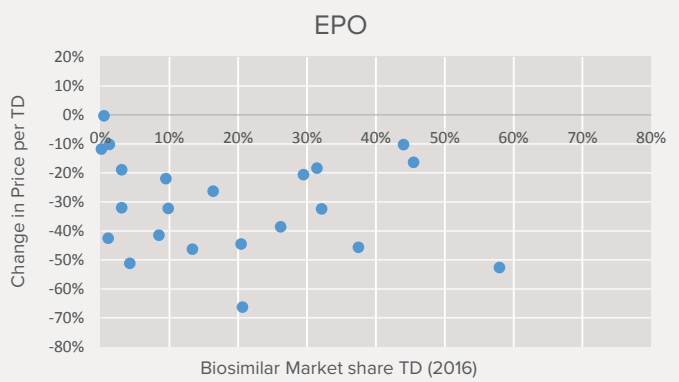
Insulins	
Finland	-18%
France	-5%
Ireland	-3%

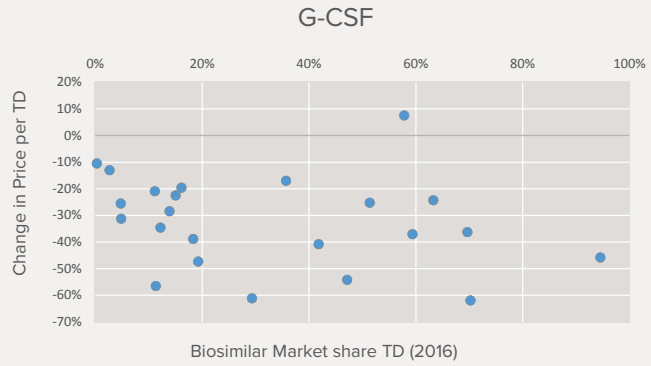
1b. The correlation between biosimilar market share and price is weak

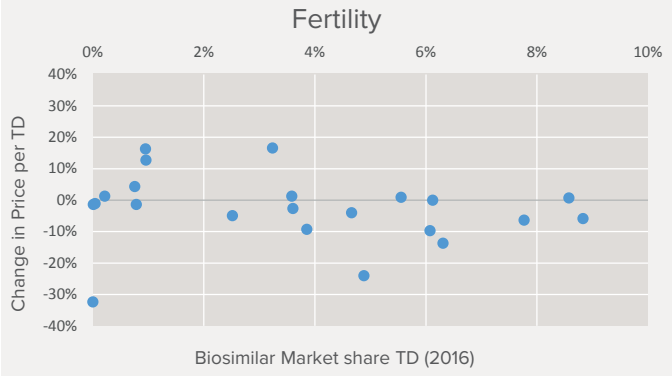
The correlation between biosimilar volume market share of the total market and price reduction of the total market is weak, as can be seen by the six established biosimilar classes.

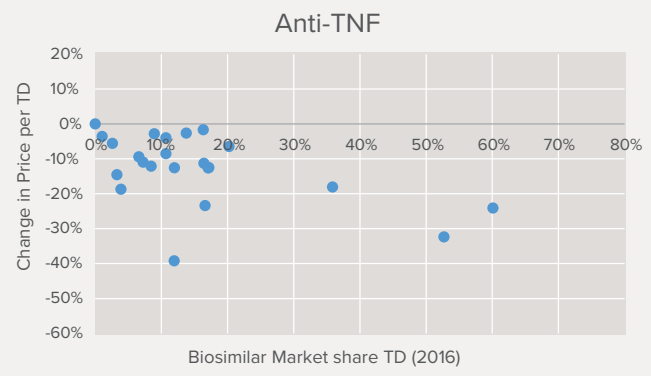
For the six classes we can see the same pattern; high savings can be achieved even if the biosimilar market share is low. Price reduction can be achieved through price regulation interventions and/or commercial decisions of manufacturers. Even if the biosimilar product does not end up to be the product sold, it is likely an essential step to generate a more competitive environment, which leads to lower prices. However, in the long term, low biosimilar uptake could lead to fewer new biosimilars being developed, reducing the overall competitive pressure.

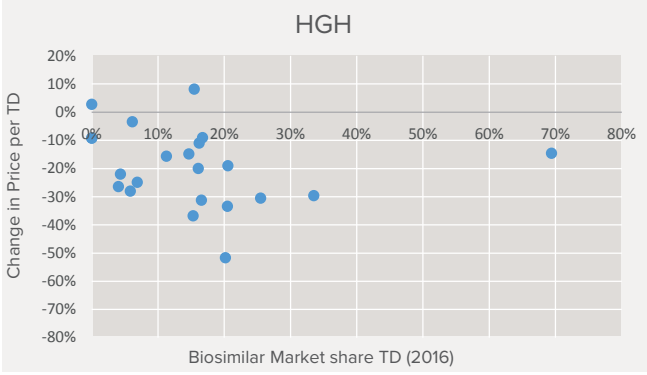
Exhibit 3: Biosimilar market share in 2016 vs change in price per TD (2016/year before biosimilar entrance) by country

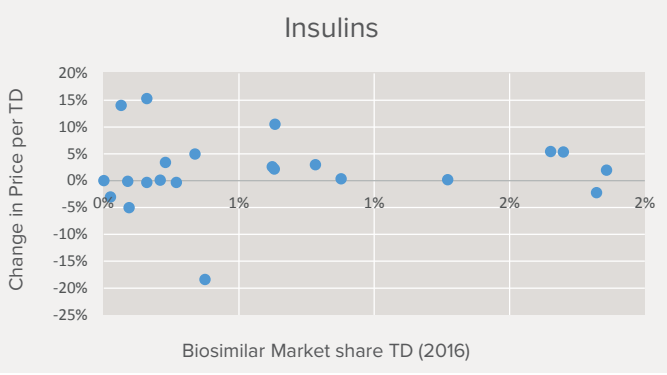








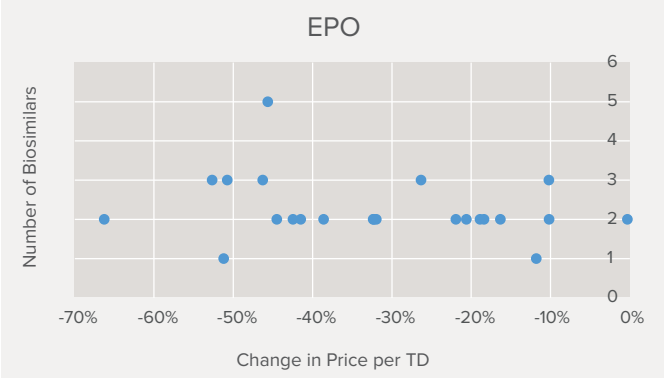




1c. The entrance of just one biosimilar in the market can be sufficient to lower the price

In classes with more than one biosimilar, there is a weak correlation between the number of biosimilar competitors and the change in price of the total market.

In order to achieve savings, there does not have to be competition with multiple biosimilars. However, in the long term, it may be necessary to have multiple biosimilars in order to achieve the full effect of competition. This dynamic is very different to small molecule generics, but may differ by class, and may evolve as we see more competition in newer classes.



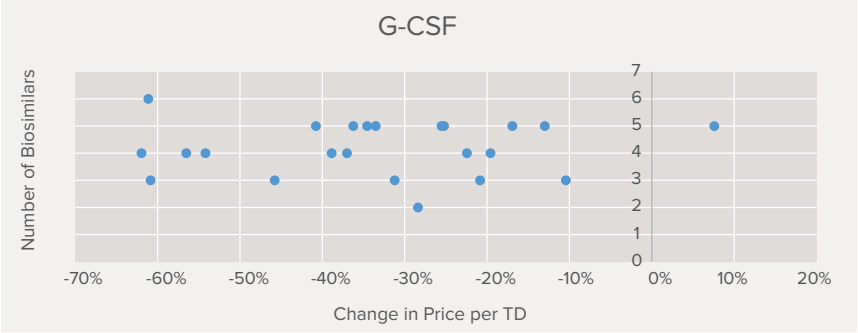


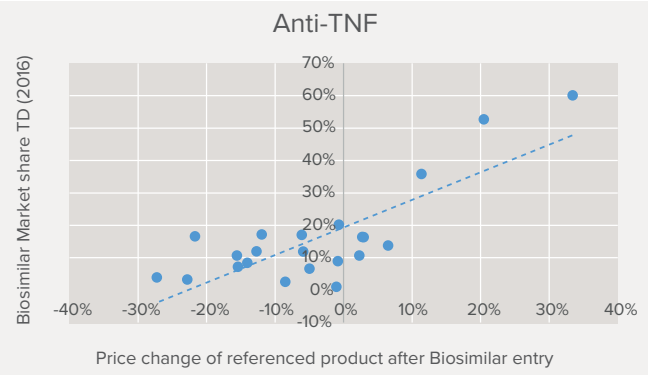
Exhibit 4: Change in price per TD (2016/year before biosimilar entrance) vs total number of biosimilars on the market in a country

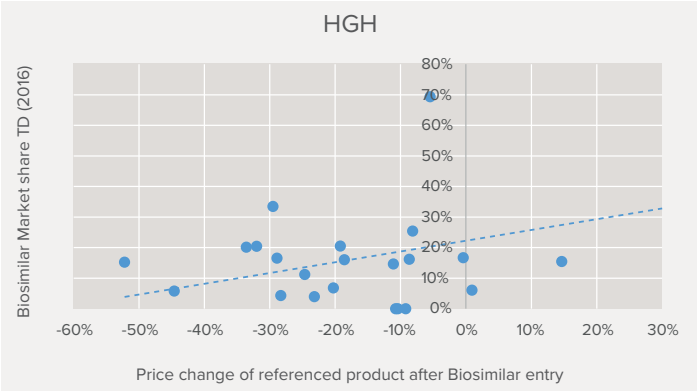
2. In some therapeutic classes, lowering the price of the referenced product can limit the market penetration of the biosimilar

For two of the therapeutic classes, anti-TNF and HGH, the same observation can be seen: there is a correlation between the price reduction of referenced products (after biosimilar entry), and the biosimilar market share. Therefore the larger the originator's price cut on the referenced product, the less impact of biosimilars is seen.

This illustrates that originator competitive pricing strategies can influence the uptake of biosimilars in some areas. However, reducing originator prices (either because of regulations applied in a country or competitive originator pricing strategies), could result in biosimilars not entering the market at all, restricting competition in the market.

Exhibit 5: Change in price of the referenced product(s) (2016/year before biosimilar entrance) vs biosimilar market share in 2016





3. There is a first to market advantage in biosimilar markets

In those therapy classes where more than one biosimilar has been launched, assessing all biosimilars in each class, the first biosimilar to market usually takes the highest biosimilar market share. Therefore time to market for biosimilars can impact uptake in the class.

Where multiple launches occurred in the same month in a country, market shares for these products were assigned to the same rank. For Anti-TNF's, biosimilars for both etanercept and infliximab were considered in a country.

Exhibit 6: Average biosimilar market share in 2016 across all countries for each biosimilar, according to their time to market in a country

Anti-TNF

Biosimilar time to Market	Biosimilar 2016 Volume (TD) market share% (average across all countries)
1st	72%
2nd	30%
3rd	5%
4th	0%

EPO

Biosimilar time to Market	Biosimilar 2016 Volume (TD) market share% (average across all countries)
1st	73%
2nd	40%
3rd	22%

4. Biosimilars have the potential to improve patient access of the total market

4a. Lower prices increase patient access

Some level of price-elasticity is expected to be observed for these products. The report however shows different levels of impact to lowered prices for different countries and different classes.

For most classes, there is a significant increase in consumption since biosimilar entry in countries which had low starting volumes. There are also some countries which already had high usage of classes before biosimilar entry, such as Sweden with Anti-TNF's, which show a significant increase in consumption.

Therefore lowered prices can impact usage, however there are other factors to consider:

- New indications or restriction of indications (for example the EPO safety warnings)
- General economic conditions imposing use restrictions
- Changes in diagnosis and prevalence of diseases

Exhibit 7: Countries with highest change in volume TD (2016/year before biosimilar entrance)

Anti-TNF	Price per TD 2016/ Year before Biosimilar entrance	Volume TD 2016/ Year before Biosimilar entrance	TD/capita (Year before Biosimilar entrance)
Bulgaria	-23%	190%	0.10
Slovakia	-19%	93%	0.49
Sweden	-39%	74%	0.94
Portugal	-13%	63%	0.26
Czech	-13%	59%	0.24

G-CSF	Price per TD 2016/ Year before Biosimilar entrance	Volume TD 2016/ Year before Biosimilar entrance	TD/capita (Year before Biosimilar entrance)
Romania	-62%	2542%	0.02
Bulgaria	-47%	581%	0.02
Slovakia	-61%	509%	0.05
Slovenia	-57%	178%	0.05
Norway	-31%	164%	0.07

EPO			
Poland	-46%	237%	0.03
Greece	-51%	196%	0.02
Italy	-10%	39%	0.82
Czech	-32%	36%	0.09
Bulgaria	-16%	36%	0.23

HGH			
Romania	-31%	152%	0.02
Poland	-42%	82%	0.04
UK	-16%	79%	0.04
Finland	-52%	70%	0.06
Czech	-25%	68%	0.08

4b. Overall, Biosimilar competition contributes to the increased patient access of the whole market

Increased competition (an effect of which is often reduced prices) in the market is one of several drivers of volume growth. Our analysis reports that the increased competition of biosimilars entering the market has an impact on not just the volume of the directly comparable referenced product, but also the volume of the whole product class. The total market volume uptake varies significantly by class in Europe. It must be noted that all products in these therapy areas, including biosimilars, are contributing to this increased patient access (TD), to varying degrees in each country.

Exhibit 8: Total change in volume per TD since the entrance of biosimilars for each therapy area

	Volume per TD (2016/Yr before BS entrance)			
	Referenced product only	Biosimilar and Referenced product	Biosimilar Accessible market	Total markets
G-CSF	-74%	122%	63%	58%
HGH	-14%	41%	45%	45%
Anti-TNF	-10%	19%	19%	26%
Fertility	2%	16%	8%	10%
EPO	-37%	66%	4%	7%
Insulins	14%	19%	15%	4%

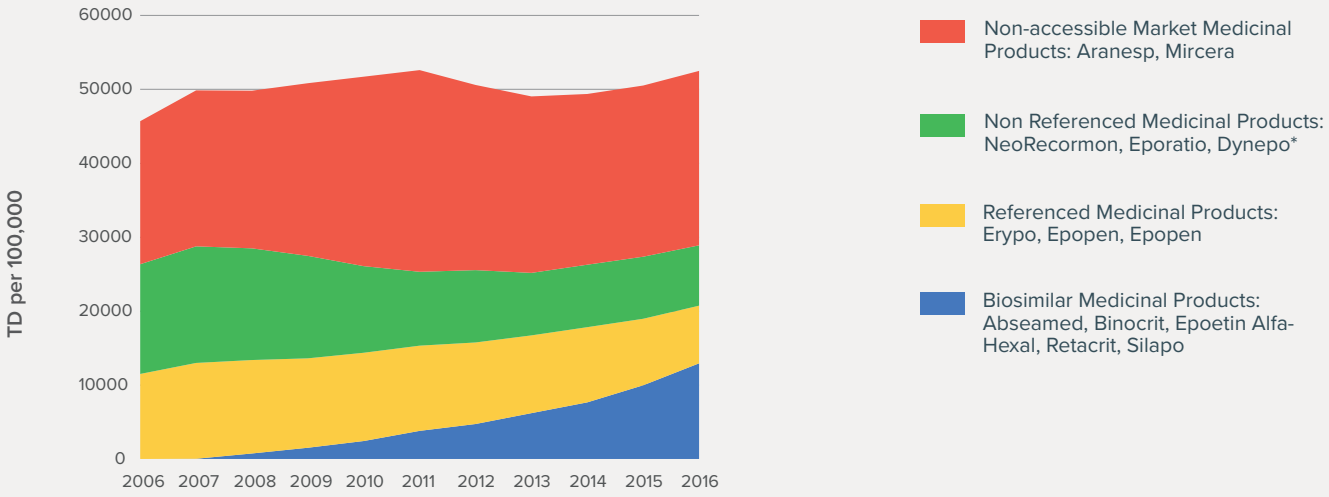
The experience so far with Biosimilars in Europe illustrates the heterogeneity between biosimilar products, therapy areas, and countries. There is not just one formula that will work to achieve the savings potential, but learnings can be taken from all areas.

The country and therapy areas 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.

Epoetin volume development



Source: QuintilesIMS MIDAS December 2016; Total volume development across all European countries included in the study

*Dynepo has been withdrawn by the EMA.

Summary of EMA information for approved indications for Epoetin products

Molecule	Product	Reference product	Biosimilar	Non-reference	Non-accessible	Anaemia for Chemotherapy patients	Anaemia for patients with Chronic Kidney Disease	Preventing Anaemia in premature babies	Autologuos Blood Transfusion	Reduction of allogenic transfusion exposure in Orthopedic surgery	Patient type: Adult	Patient type: Paediatric	Frequency*	Route**: Subcutaneous	Route**: Intravenous
Epoetin alfa	Epopen	●				●	●		●	●	●	●	3x a week	●	●
	Erypo	●				●	●		●	●	●	●	3x a week	●	●
	Epogen	●				●	●		●	●	●	●	3x a week	●	●
	Abseamed		●			●	●		●	●	●	●	3x a week	●	●
	Epoetin Alfa Hexal		●			●	●		●	●	●	●	3x a week	●	●
	Binocrit		●			●	●		●	●	●	●	3x a week	●	●
Epoetin zeta	Retacrit		●			●	●		●		●	●	3x a week	●	●
	Silapo		●			●	●		●		●	●		●	●
Epoetin beta	NeoRecormon			●		●	●	●	●	●	●	●	3x a week	●	●
Epoetin theta	Eporatio			●		●	●				●		3x a week	●	●
Methoxy polyethlene glycol-epotein beta	Mircera				●		●				●		Every 2 weeks	●	●
Darbepoetin alfa	Aranesp				●	●	●				●		Weekly	●	●

*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.

Additional information about Epoetin

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.

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

	Market share TD (2015)			Price per TD (2015/the year before biosimilar entrance)			Volume TD (2015/the year before biosimilar entrance)					
	Biosimilar vs Reference product	Biosimilar vs Accessible market	Biosimilar vs Total market	Biosimilar and Reference product	Biosimilar Accessible market	Total market	Biosimilar and Reference product	Biosimilar Accessible market	Total market	TD/capita (Yr before BS entrance)	TD per capita 2015	First Recorded Sales of Biosimilar
AU	76%	25%	16%	-36%	-37%	-26%	-29%	-8%	-26%	0.95	0.70	2008
BE	2%	1%	1%	-1%	-1%	0%	-14%	-10%	-5%	0.53	0.50	2014
BU	100%	79%	45%	-5%	-35%	-16%	59%	2%	36%	0.23	0.32	2011
CZ	99%	50%	32%	-47%	-38%	-32%	129%	21%	36%	0.09	0.13	2011
DK	70%	5%	0%	-41%	-1%	-12%	-96%	-94%	-7%	0.49	0.46	2010
FI	100%	60%	10%	-42%	-36%	-22%	1137%	-49%	8%	0.34	0.36	2008
FR	45%	26%	10%	-33%	-33%	-32%	-3%	-24%	4%	0.90	0.93	2009
DE	81%	67%	37%	-53%	-56%	-46%	33%	-22%	-16%	0.39	0.33	2007
GR*	98%	97%	95%	-51%	-52%	-51%	630%	337%	196%	0.02	0.06	2008
HU	100%	52%	31%	-67%	-33%	-18%	-9%	-9%	-27%	0.38	0.28	2009
IE	91%	8%	3%	-32%	-30%	-19%	-32%	-56%	-30%	0.52	0.36	2008
IT	65%	57%	44%	-17%	-15%	10%	160%	68%	39%	0.82	1.15	2008
NL	30%	12%	3%	-47%	-42%	-32%	-63%	-53%	-25%	0.58	0.43	2009
NO	87%	44%	4%	-55%	-51%	-51%	16%	-55%	11%	0.21	0.23	2008
PL	100%	16%	13%	-63%	-54%	-46%	3327%	338%	237%	0.03	0.09	2009
PT	87%	28%	21%	-79%	-80%	-66%	232%	139%	6%	0.44	0.47	2010
RO	70%	50%	26%	-54%	-48%	-39%	130%	-63%	-38%	0.29	0.18	2009
SK	100%	73%	58%	-60%	-58%	-53%	361%	67%	11%	0.45	0.50	2010
SL	46%	22%	8%	-50%	-44%	-42%	-40%	-41%	7%	0.52	0.56	2009
ES	60%	46%	29%	-31%	-31%	-21%	64%	1%	-4%	0.70	0.67	2009
SE	94%	51%	20%	-20%	-31%	-45%	44%	-12%	23%	0.48	0.58	2008
CH	22%	6%	1%	-46%	-45%	-42%	-43%	-50%	13%	0.34	0.39	2009
UK	6%	3%	1%	-7%	-13%	-10%	70%	-10%	27%	0.24	0.31	2009
EU	62%	45%	25%	-31%	-33%	-27%	66%	4%	7%	0.49	0.53	

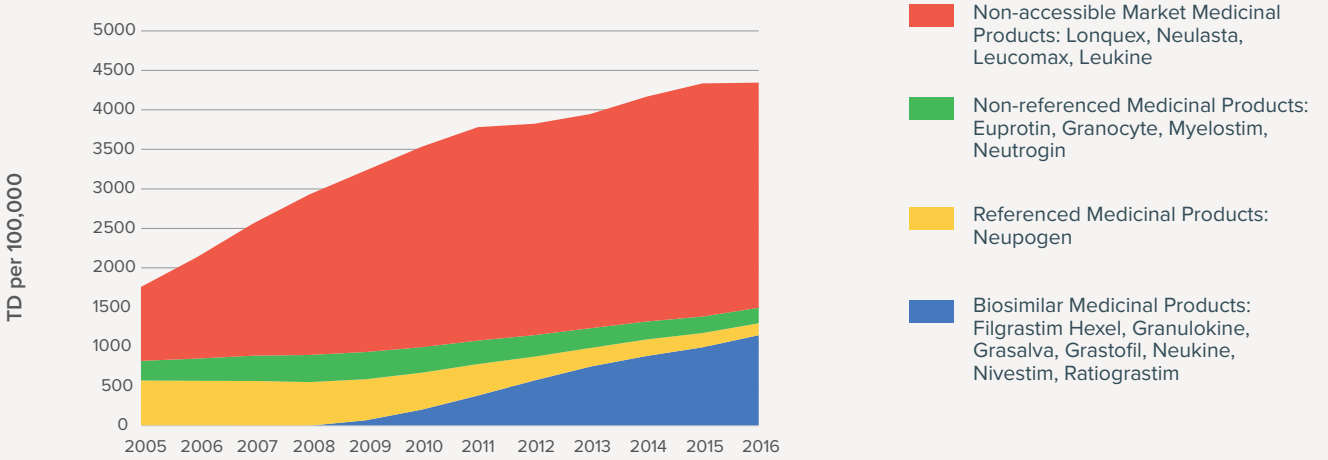
The following data history is used: PT Hospital (2010-2016), DK (2007-2016), IE Hospital (2006-2016), *Only retail panel is available for Greece.

Prices per TD (total market) have been reduced in almost all markets but to a different degree (0) to (-66%) 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. The volume development shows that in several of the markets, the usage is greatly reduced following the 2008 safety warning.

Granulocyte-colony stimulating factor (G-CSF)

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 to accelerate recovery from neutropenia after chemotherapy, allowing higher-intensity treatment regimens.

G-CSF volume development



Source: QuintilesIMS MIDAS December 2016; Total volume development across all European countries included in the study

Summary of EMA information for approved indications for G-CSF products

		Classification				Indication					
Molecule	Product	Reference product	Biosimilar Product	Non-reference Product	Non-accessible Product	Cytotoxic Chemoterapy associated with Febrile induced Neutropenia	Neutropenia induced by Acute Myeloid Leukemia	Bone Marrow Transplantation 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	Neupogen	●				●	●	●	●	●	●
	Filgrastim		●			●	●	●	●	●	●
	Hexal		●			●		●	●	●	●
	Granulokine		●			●	●	●	●	●	●
	Grasalva		●			●		●	●	●	●
	Grastofil		●			●		●	●	●	●
	Neukine		●			●	●	●	●	●	●
	Nivestim		●			●		●	●	●	●
	Ratiograstim		●			●		●	●	●	●
Lenograstim	Euprotin			●		●		●	●		
	Granocyte			●		●		●	●		
	Myelostim			●		●		●	●		
	Neutrogin			●		●		●	●		
Lipegfilgrastim	Lonquex				●	●					
Pegfilgrastim	Neulasta				●	●					
Molgramostim	Leucomax				●	●	●	●	●		
Sargramostim	Leukine				●	●	●	●	●		

Additional information about G-CSF

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).

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

	Market share TD (2016)			Price per TD (2016/the year before biosimilar entrance)			Volume TD (2016/the year before biosimilar entrance)					
	Biosimilar vs Reference product	Biosimilar vs Accessible market	Biosimilar vs Total market	Biosimilar and Reference product	Biosimilar Accessible market	Total market	Biosimilar and Reference product	Biosimilar Accessible market	Total market	TD/capita (Yr before BS entrance)	TD per capita 2016	First Recorded Sales of Biosimilar
AU	88%	87%	18%	-48%	-48%	-39%	84%	66%	79%	0.05	0.10	2009
BE	3%	3%	0%	-28%	-27%	-10%	3%	4%	27%	0.04	0.06	2011
BU	100%	100%	19%	-81%	-83%	-47%	272%	105%	581%	0.00	0.02	2010
CZ	100%	100%	51%	-33%	-33%	-25%	195%	195%	117%	0.00	0.01	2010
DK	93%	91%	11%	-48%	-48%	-21%	-3%	-8%	30%	0.04	0.05	2009
FI	98%	97%	16%	-32%	-32%	-20%	75%	72%	52%	0.05	0.08	2009
FR	86%	52%	15%	-31%	-26%	-22%	193%	46%	46%	0.05	0.08	2009
DE	78%	65%	12%	-29%	-29%	-35%	54%	22%	127%	0.03	0.06	2008
GR	100	100%	95%	-66%	-67%	-46%	1323%	714%	-79%	0.02	0.00	2009
HU	100%	100%	70%	-58%	-58%	-36%	209%	205%	3%	0.03	0.04	2009
IE	23%	21%	3%	-26%	-24%	-13%	2%	6%	36%	0.06	0.08	2009
IT	92%	83%	36%	-26%	-26%	-17%	123%	16%	12%	0.03	0.04	2009
NL	45%	45%	5%	-31%	-31%	-26%	26%	24%	-5%	0.03	0.03	2009
NO	86%	86%	5%	-56%	-56%	-31%	38%	38%	164%	0.03	0.07	2009
PL	96%	96%	42%	-55%	-56%	-41%	163%	122%	146%	0.02	0.04	2009
PT	88%	87%	47%	-87%	-86%	-54%	42%	33%	-42%	0.04	0.02	2009
RO	100%	100%	70%	-66%	-66%	-62%	1755%	1755%	2542%	0.00	0.02	2009
SK	100%	100%	29%	-82%	-82%	-61%	464%	464%	509%	0.01	0.05	2009
SL	56%	56%	11%	-70%	-70%	-57%	87%	87%	178%	0.02	0.05	2009
ES	83%	82%	63%	-40%	-40%	-24%	59%	47%	-30%	0.04	0.03	2009
SE	94%	94%	56%	-54%	-54%	-37%	242%	212%	38%	0.02	0.03	2009
CH	52%	51%	14%	-37%	-37%	-28%	39%	32%	53%	0.03	0.04	2009
UK	98%	86%	58%	-4%	-5%	-8%	228%	150%	80%	0.01	0.03	2008
EU	88%	77%	26%	-37%	-36%	-27%	122%	63%	58%	0.03	0.04	

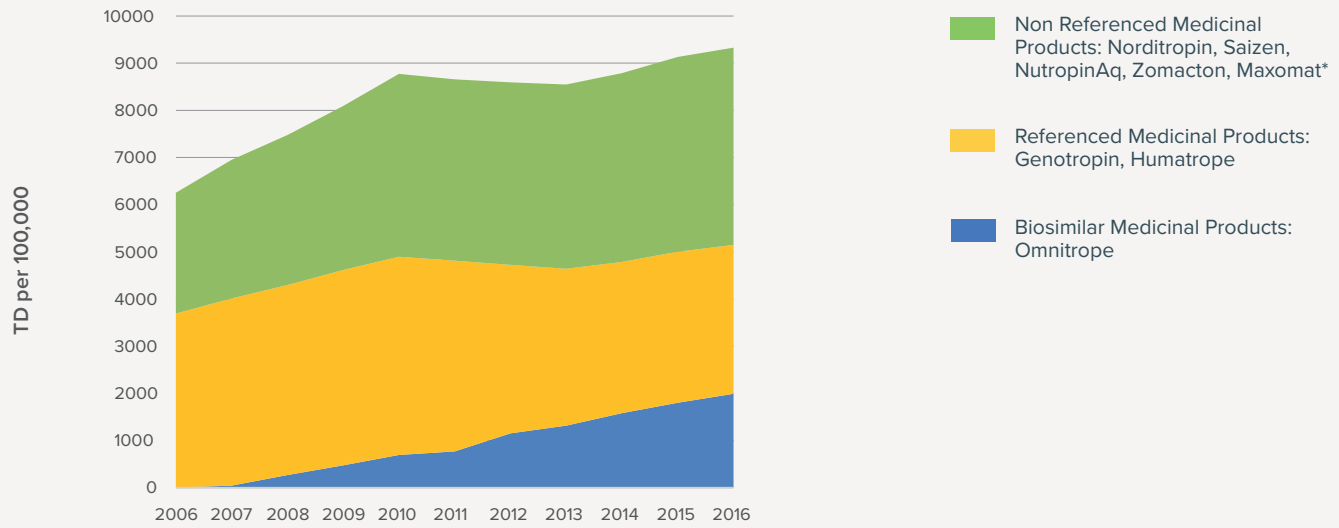
The following data history is used: PT Hospital (2010-2016), DK (2007-2016), IE Hospital (2006-2016), *Only retail panel is available for Greece.

Price changes per TD (total market) vary considerably across the different European countries included in this study, ranging between (-62%) and 8%.

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



Source: QuintilesIMS MIDAS December 2016; Total volume development across all European countries included in the study

*Maxomat has been discontinued

Summary of EMA information for approved indications for HGH products:

		Classification			Indication							
Molecule	Product	Reference product	Biosimilar Product	Non-reference Product	Pediatric Growth Hormone Deficiency	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
Somatropin	Genotropin	●			●	●	●	●	●	●	●	
	Humatrope	●			●	●	●	●	●		●	
	Omnitrope		●		●	●	●	●	●	●		
	Norditropin			●	●	●	●	●	●			●
	Saizen			●	●	●	●	●	●			
	NutropinAq			●	●	●	●	●				
	Zomacton			●	●		●					

Additional information about HGH

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.

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

	Market share TD (2016)			Price per TD (2016/the year before biosimilar entrance)			Volume TD (2016/the year before biosimilar entrance)					
	Biosimilar vs Reference product	Biosimilar vs Accessible market	Biosimilar vs Total market	Biosimilar and Reference product	Biosimilar Accessible market	Total market	Biosimilar and Reference product	Biosimilar Accessible market	Total market	TD/capita (Yr before BS entrance)	TD per capita 2016	First Recorded Sales of Biosimilar
AU	37%	17%	17%	-17%	-9%	-9%	22%	54%	54%	0.04	0.05	2008
BE	28%	16%	16%	-24%	-20%	-20%	48%	39%	39%	0.08	0.11	2009
BU	34%	34%	34%	-30%	-30%	-30%	-31%	-32%	-32%	0.02	0.02	2012
CZ	17%	7%	7%	-23%	-25%	-25%	69%	68%	68%	0.08	0.13	2010
DK	97%	69%	69%	-14%	-15%	-15%	109%	-7%	-7%	0.15	0.14	2011
FI	57%	20%	20%	-48%	-52%	-52%	42%	70%	70%	0.06	0.10	2008
FR	34%	16%	16%	-14%	-11%	-11%	42%	51%	51%	0.10	0.15	2007
DE	32%	15%	15%	7%	8%	8%	10%	36%	36%	0.06	0.08	2006
GR*	0%	0%	0%	-9%	-9%	-9%	-8%	-8%	-8%	0.00	0.00	2015
HU	13%	6%	6%	-4%	-3%	-3%	-9%	8%	8%	0.05	0.05	2012
IE	0%	0%	0%	-11%	3%	3%	51%	54%	54%	0.05	0.07	2006
IT	29%	15%	15%	-19%	-15%	-15%	62%	51%	51%	0.06	0.09	2007
NL	31%	17%	17%	-38%	-31%	-31%	35%	46%	46%	0.08	0.12	2008
NO	29%	15%	15%	-54%	-37%	-37%	57%	35%	35%	0.13	0.18	2011
PL	99%	99%	99%	-41%	-42%	-42%	83%	82%	82%	0.04	0.08	2008
PT	13%	6%	6%	-46%	-28%	-28%	-1%	-9%	-9%	0.04	0.04	2014
RO	56%	25%	25%	-17%	-31%	-31%	211%	152%	152%	0.02	0.06	2008
SK	0%	0%	0%	-10%	-9%	-9%	15%	25%	25%	0.06	0.08	2013
SL	8%	4%	4%	-24%	-26%	-26%	22%	17%	17%	0.06	0.07	2010
ES	30%	21%	21%	-19%	-19%	-19%	46%	38%	38%	0.10	0.13	2007
SE	33%	20%	20%	-34%	-33%	-33%	-15%	-7%	-7%	0.15	0.14	2007
CH	19%	4%	4%	-30%	-22%	-22%	-8%	45%	45%	0.07	0.10	2010
UK	22%	11%	11%	-25%	-16%	-16%	46%	79%	79%	0.04	0.07	2007
EU	39%	21%	21%	-21%	-15%	-15%	41%	45%	45%	0.06	0.09	

The following data history is used: PT Hospital (2010-2016), DK (2007-2016), IE Hospital (2006-2016), *Only retail panel is available for Greece.

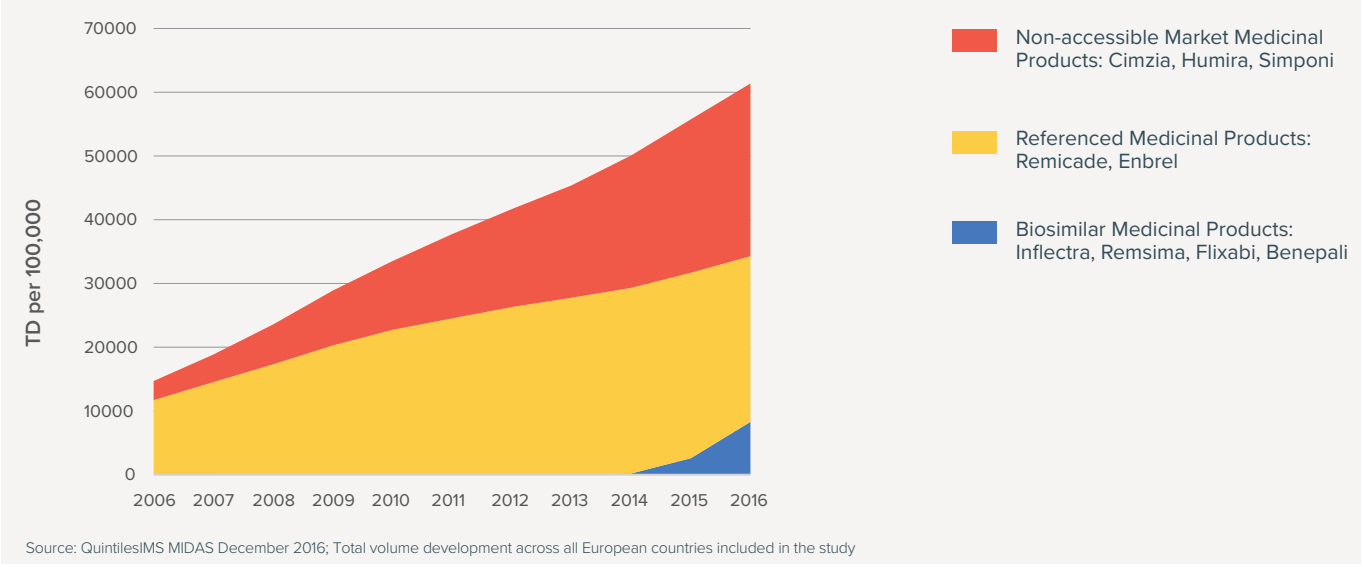
Prices per TD (total market) vary considerably across the different European countries studied, ranging between (-52%) to 8%.

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



Source: QuintilesIMS MIDAS December 2016; Total volume development across all European countries included in the study

Additional information about Anti-TNF's

There are currently biosimilars on the market for two Anti-TNF molecules in Europe, infliximab and etanercept. The EMA approved the first infliximab biosimilars in September 2013, and the first etanercept biosimilar in January 2016. The biosimilar share of molecule treatment days in the EU5 is reported below:

	Biosimilar treatment day share vs Referenced product (December 2016)	
Country	**infliximab**	**etanercept**
UK	64.1% (22)	31.6% (10)
France	24.6% (22)	1.0% (3)
Germany	27.2% (23)	19.0% (10)
Italy	46.6% (22)	1.0% (3)
Spain	34.8% (23)	0.4% (3)

Source: QuintilesIMS MIDAS December 2016

Summary of EMA information for approved indications for Anti-TNF products:

	Humira	Remicade	Remsima	Inflectra	Flixabi	Enbrel	Benepali	Simponi	Cimzia
Rheumatoid Arthritis	●	●	●	●	●	●	●	●	●
Juvenile Idiopathic Arthritis	●					●	●		
Psoriatic Arthritis	●	●	●	●	●	●	●	●	●
Axial Spondyloarthritis, comprising: Ankylosing Spondylitis (AS)	●	●	●	●	●	●	●	●	●
Axial Spondyloarthritis without radiographic evidence of AS	●					●	●	●	●
Crohn's Disease	●	●	●	●	●				
Paediatric Crohn's Disease	●	●	●	●	●				
Ulcerative Colitis	●	●	●	●	●			●	
Paediatric Ulcerative Colitis		●	●	●	●				
Psoriasis	●	●	●	●	●	●	●		
Paediatric Plaque Psoriasis	●					●	●		
Hidradenitis Suppurativa*	●								
Uveitis	●								

*Hidradenitis Suppurativa includes both adults and adolescents from the age of 12 years. Adolescents do not have a separate pediatric indication.

Indications have been added over time expanding the potential patient population.

Summary of EMA information for administration frequency details for Anti-TNF products:

		Classification				Frequency of administration	Route of administartion	
Molecule	Product	Reference product	Biosimilar Product	Non- reference Product	Non-accessible Product		Subcutaneous	Intravenous
INFLIXIMAB	Remsima		●			every 8 weeks		●
	Inflectra		●			every 8 weeks		●
	Remicade	●				every 8 weeks		●
	Flixabi		●			every 8 weeks		●
ETANERCEPT	Enbrel	●				once or twice weekly	●	
	Benepali		●			once weekly	●	
ADALIMUMAB	Humira				●	every 2 weeks	●	
CERTOLIZUMAB PEGOL	Cimzia				●	every 4 weeks	●	
GOLIMUMAB	Simponi				●	monthly	●	

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

	Market share TD (2016)			Price per TD (2016/the year before biosimilar entrance)			Volume TD (2016/the year before biosimilar entrance)					
	Biosimilar vs Reference product	Biosimilar vs Accessible market	Biosimilar vs Total market	Biosimilar and Reference product	Biosimilar Accessible market	Total market	Biosimilar and Reference product	Biosimilar Accessible market	Total market	TD/capita (Yr before BS entrance)	TD per capita 2016	First Recorded Sales of Biosimilar
AU	23%	23%	17%	-17%	-17%	-12%	29%	29%	33%	0.17	0.22	2015
BE	5%	5%	3%	-24%	-24%	-15%	19%	19%	17%	0.94	1.10	2015
BU	48%	48%	17%	-41%	-41%	-23%	163%	163%	190%	0.10	0.29	2014
CZ	25%	25%	17%	-14%	-14%	-13%	51%	51%	59%	0.24	0.38	2013
DK	90%	90%	60%	-35%	-35%	-24%	45%	45%	28%	0.91	1.17	2015
FI	61%	61%	36%	-24%	-24%	-18%	47%	47%	54%	0.64	0.99	2013
FR	14%	14%	8%	-16%	-16%	-12%	22%	22%	27%	0.62	0.78	2015
DE	17%	17%	9%	-6%	-6%	-3%	18%	18%	22%	0.51	0.62	2015
GR*										0.00	0.01	
HU	26%	26%	14%	-6%	-6%	-3%	-6%	-6%	-5%	0.32	0.30	2014
IE	5%	5%	3%	-10%	-10%	-6%	43%	43%	48%	1.00	1.48	2014
IT	20%	20%	11%	-6%	-6%	-4%	4%	4%	14%	0.36	0.41	2015
NL	32%	32%	20%	-8%	-8%	-6%	11%	11%	8%	1.00	1.08	2015
NO	82%	82%	53%	-48%	-48%	-32%	48%	48%	56%	1.08	1.68	2013
PL	24%	24%	16%	-13%	-13%	-11%	-14%	-14%	7%	0.03	0.03	2014
PT	18%	18%	12%	-20%	-20%	-13%	56%	56%	63%	0.26	0.43	2013
RO	11%	11%	7%	-10%	-10%	-9%	-9%	-9%	12%	0.20	0.22	2014
SK	6%	6%	4%	-28%	-28%	-19%	92%	92%	93%	0.49	0.95	2014
SL	14%	14%	7%	-19%	-19%	-11%	26%	26%	24%	0.47	0.58	2015
ES	19%	19%	11%	-20%	-20%	-9%	16%	16%	21%	0.49	0.60	2015
SE	29%	29%	12%	-16%	-16%	-39%	18%	18%	74%	0.94	1.64	2015
CH	2%	2%	1%	-2%	-2%	-4%	9%	9%	10%	0.84	0.92	2016
UK	33%	33%	16%	-6%	-6%	-2%	12%	12%	20%	0.62	0.74	2015
EU	24%	24%	13%	-13%	-13%	-10%	19%	19%	26%	0.49	0.61	

The following data history is used: PT Hospital (2010-2016), DK (2007-2016), IE Hospital (2006-2016), *Only retail panel is available for Greece.

Prices per TD (total market) have been reduced in all markets but to a different degree (-2) to (-39).

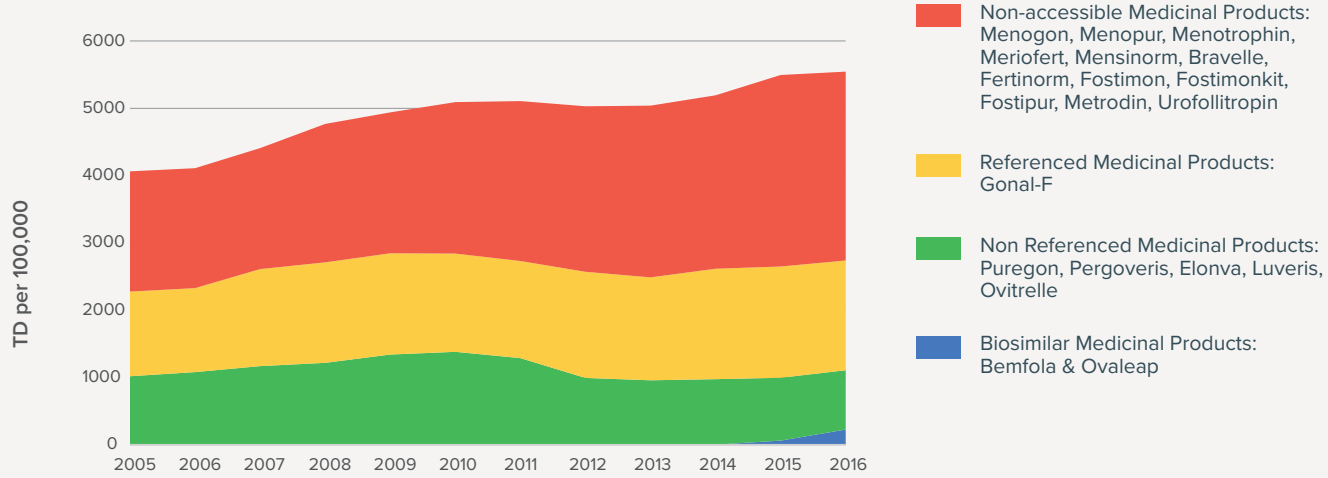
The Anti-TNF market is unique as it has two referenced products with different biosimilar molecules. The market shares and price/volume evolution figures refer to the total Anti-TNF market, therefore include all products within each category. This means, for example, in markets where only infliximab has launched, the "biosimilar vs referenced product" market share will still represent the biosimilar market share of all the biosimilars and referenced products on the market (including Enbrel).

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



Source: QuintilesIMS MIDAS December 2016; Total volume development across all European countries included in the study

Summary of EMA information for approved indications for Fertility products

		Classification				Indications					Frequency	Route		
Molecule	Product	Reference product	Biosimilar	Non-reference	Non-accessible	Infertility	Hypogonadism	Anovulation	Ovulation Induction	Reproductive Techniques, Assisted		Subcutaneous	Intravenous	Iintramuscular
Follitropin alfa	Gonal-F	●				●		●			Daily	●	●	●
	Bemfola		●			●	●	●		●	Daily	●	●	●
	Ovaleap		●			●	●			●	Daily	●	●	
Follitropin alfa/lutropin alfa	Pergoveris			●		●					Daily	●	●	●
Follitropin beta	Puregon			●		●	●				Patient specific	●		
Corifollitropin alfa	Elonva				●	●					Patient specific	●		
Lutropin alfa	Luveris				●	●			●		Daily	●	●	●
FOLLICLE-STIMULATING HORMONE/LUTEINISING HORMONE	Menogon				●	●		●		●	Daily	●		●
	Menopur				●	●				●	Daily	●		
	Menotrophin				●	●				●	Daily	●		●
	Meriofert				●	●			●		Daily	●		
	Mensinorm				●	●	●	●			Daily	●		
UROFOLLITROPIN	Bravelle				●	●		●	●	●	Daily	●		●
	Fertinorm				●	●			●	●	Daily	●		●
	Fostimon				●	●			●		Daily			●
	Fostimonkit				●	●			●		Daily			●
	Fostipur				●	●			●		Daily	●		
	Metrodin				●	●			●	●	Daily	●		●

Additional information about fertility medicines:

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

	Market share TD (2016)			Price per TD (2016/the year before biosimilar entrance)			Volume TD (2016/the year before biosimilar entrance)					
	Biosimilar vs Reference product	Biosimilar vs Accessible market	Biosimilar vs Total market	Biosimilar and Reference product	Biosimilar Accessible market	Total market	Biosimilar and Reference product	Biosimilar Accessible market	Total market	TD/capita (Yr before BS entrance)	TD per capita 2016	First Recorded Sales of Biosimilar
AU	3%	1%	1%	1%	-1%	16%	614%	170%	69%	0.01	0.02	2014
BE	17%	11%	4%	-1%	-1%	-9%	12%	8%	22%	0.04	0.05	2015
BU	32%	7%	3%	-6%	-3%	17%	131%	-10%	-27%	0.01	0.01	2016
CZ	6%	4%	2%	-16%	-15%	-5%	1%	10%	-5%	0.05	0.05	2015
DK	16%	11%	5%	-21%	-20%	-24%	43%	20%	19%	0.10	0.12	2014
FI	24%	16%	8%	-12%	-10%	-6%	76%	8%	6%	0.04	0.05	2014
FR	13%	9%	5%	-2%	-2%	-4%	18%	3%	9%	0.09	0.10	2015
DE	19%	11%	6%	-4%	-3%	0%	48%	28%	21%	0.04	0.05	2014
GR*	14%	11%	4%	-5%	-3%	-3%	29%	16%	23%	0.02	0.03	2016
HU	15%	13%	9%	-3%	-3%	1%	46%	44%	35%	0.04	0.06	2015
IE	0%	0%	0%	-3%	-3%	-1%	14%	7%	6%	0.10	0.10	2016
IT	2%	2%	1%	0%	0%	-1%	-6%	-7%	-1%	0.07	0.07	2015
NL	0%	0%	0%	0%	0%	1%	5%	4%	3%	0.07	0.07	2016
NO	35%	21%	9%	-4%	-3%	-6%	43%	18%	23%	0.06	0.08	2014
PL	7%	2%	1%	27%	6%	4%	-12%	65%	45%	0.02	0.03	2015
PT	14%	7%	4%	-13%	-8%	1%	14%	10%	9%	0.03	0.04	2015
RO										0.00	0.02	
SK	3%	3%	1%	-4%	-3%	13%	30%	17%	-4%	0.02	0.02	2016
SL	0%	0%	0%	0%	1%	-1%	7%	3%	2%	0.06	0.06	2015
ES	21%	13%	6%	-26%	-17%	-14%	-1%	-10%	-7%	0.09	0.09	2015
SE	18%	15%	6%	-18%	-18%	-10%	42%	14%	11%	0.09	0.09	2014
CH										0.01	0.04	
UK	18%	17%	6%	0%	0%	1%	21%	20%	15%	0.02	0.02	2015
EU	12%	8%	4%	-6%	-5%	-4%	16%	8%	10%	0.05	0.06	

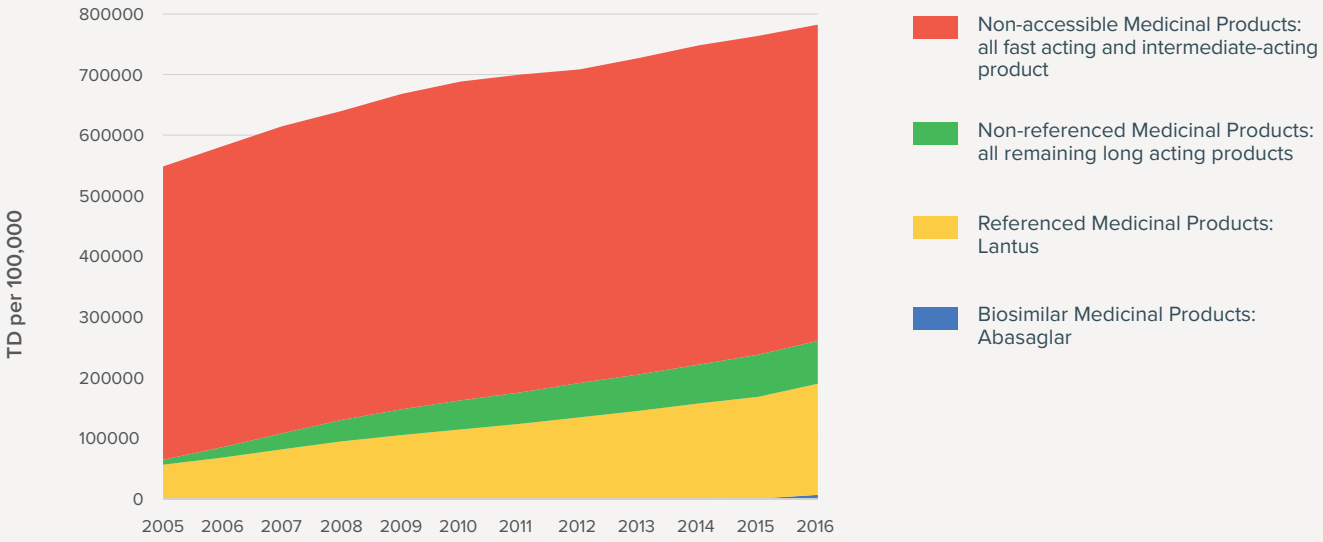
The following data history is used: PT Hospital (2010-2016), DK (2007-2016), IE Hospital (2006-2016), *Only retail panel is available for Greece.

Prices per TD (total market) have been reduced in all markets but to a different degree (–24%) to 17%.

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.

Insulins volume development



Source: QuintilesIMS MIDAS December 2016; Total volume development across all European countries included in the study

Additional information about Insulins

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- (e.g. human isophane insulin = NPH insulin), and long-acting preparations (insulins with action profiles significantly longer than NPH insulin), and are used alone or as free mixtures or premixed preparations of rapid/short-acting insulin and intermediate/long-acting (biphasic) insulin in various proportions.

The EMA authorised Lusduna, the second insulin glargine biosimilar to be authorised in Europe, in January 2017. This product was not included in the study.

Summary of EMA information for approved indications for Insulin products

		Classification				Indications	Frequency*	Mode of action	Route	
Molecule	Product	Reference product	Biosimilar	Non-reference	Non-accessible	Diabetes Mellitus			Subcutaneous	Intravenous
Insulin Glargine	Abasaglar (previously Abasria)		●			●	Daily	Long-acting	●	
	Lantus	●				●	Daily	Long-acting	●	
Insulin Degludec	Tresiba			●		●	Daily	Long-acting	●	
Insulin Detemir	Levemir			●		●	Twice a day	Long-acting	●	
Insulin Degludec / Liraglutide	Xultophy			●		●	Daily	Long-acting	●	
Insulin Aspart	Novorapid				●	●	Twice / 5x a day	Short-acting	●	
	Novomix				●	●	Twice / 5x a day	Short-acting	●	
Insulin Degludec / Insulin Aspart	Ryzodeg				●	●	Daily	Short-acting	●	
Insulin Glulisine	Apidra				●	●	Twice / 5x a day	Short-acting	●	
Insulin Human	Actraphane				●	●	Once / twice a day	Short-acting	●	
	Actrapid				●	●	Twice / 5x a day	Short-acting	●	
	Insulatard				●	●	Once / twice a day	Long-acting	●	
	Insuman				●	●	Once / twice a day	Short-acting	●	●
	Mixtard				●	●	Once / twice a day	Short-acting	●	
	Monotard				●	●	Once / twice a day	Intermediate-acting	●	
	Humalin				●	●	Once / twice a day	Intermediate-acting	●	●
	Protaphane				●	●	Once / twice a day	Long-acting	●	
	Ultratard				●	●	Once / twice a day	Long-acting	●	
Insulin Lispro	Liprolog				●	●	Twice / 5x a day	Short-acting	●	●
	Humalog				●	●	Twice daily	Short-acting	●	●

Regular insulin is a short-acting insulin and is generally injected subcutaneously 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.

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

	Market share TD (2016)			Price per TD (2016/the year before biosimilar entrance)			Volume TD (2016/the year before biosimilar entrance)					
	Biosimilar vs Reference product	Biosimilar vs Accessible market	Biosimilar vs Total market	Biosimilar and Reference product	Biosimilar Accessible market	Total market	Biosimilar and Reference product	Biosimilar Accessible market	Total market	TD/capita (Yr before BS entrance)	TD per capita 2016	First Recorded Sales of Biosimilar
AU	0%	0%	0%	0%	0%	0%	0%	0%	0%	5.65	5.65	
BE	0%	0%	0%	-6%	-5%	0%	19%	15%	5%	6.54	6.87	2016
BU	2%	1%	0%	-7%	-3%	3%	49%	47%	9%	5.73	6.24	2015
CZ	10%	6%	2%	-5%	-4%	5%	48%	40%	13%	7.70	8.72	2015
DK	3%	2%	1%	-0%	2%	3%	43%	32%	6%	6.66	7.05	2015
FI	1%	1%	0%	-36%	-26%	-18%	74%	39%	23%	11.58	14.28	2015
FR	0%	0%	0%	-12%	-9%	-5%	7%	5%	3%	6.22	6.43	2016
DE	4%	3%	1%	-1%	0%	3%	38%	22%	2%	11.69	11.88	2015
GR*	5%	4%	2%	-2%	4%	5%	13%	15%	3%	6.89	7.09	2016
HU	5%	3%	1%	-1%	16%	11%	29%	27%	7%	9.14	9.74	2015
IE	0%	0%	0%	-9%	-5%	-3%	5%	5%	3%	4.86	5.02	2016
IT	7%	5%	2%	-5%	2%	2%	1%	4%	0%	5.64	5.65	2016
NL	1%	1%	0%	-3%	3%	5%	7%	9%	0%	9.12	9.06	2015
NO	1%	1%	0%	15%	18%	15%	24%	17%	5%	6.95	7.26	2015
PL	23%	19%	1%	-21%	-18%	0%	95%	76%	2%	6.69	6.82	2015
PT	1%	0%	0%	-6%	-4%	0%	14%	13%	7%	5.63	6.02	2016
RO	3%	2%	1%	0%	-2%	0%	21%	19%	6%	4.98	5.30	2016
SK	26%	22%	6%	-10%	-8%	3%	94%	67%	18%	651	7.65	2015
SL	3%	2%	0%	-8%	-2%	0%	4%	5%	2%	8.55	8.72	2016
ES	5%	4%	2%	-12%	-7%	-2%	18%	17%	6%	6.97	7.42	2015
SE	4%	2%	1%	-1%	4%	2%	9%	13%	4%	9.97	10.35	2015
CH	0%	0%	0%	-10%	18%	14%	-4%	10%	3%	4.63	4.76	2015
UK	1%	1%	0%	-1%	1%	0%	3%	5%	6%	7.48	7.90	2015
EU	4%	3%	1%	-7%	-3%	1%	19%	15%	4%	7.53	7.82	

The following data history is used: PT Hospital (2010-2016), DK (2007-2016), IE Hospital (2006-2016), *Only retail panel is available for Greece.

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.

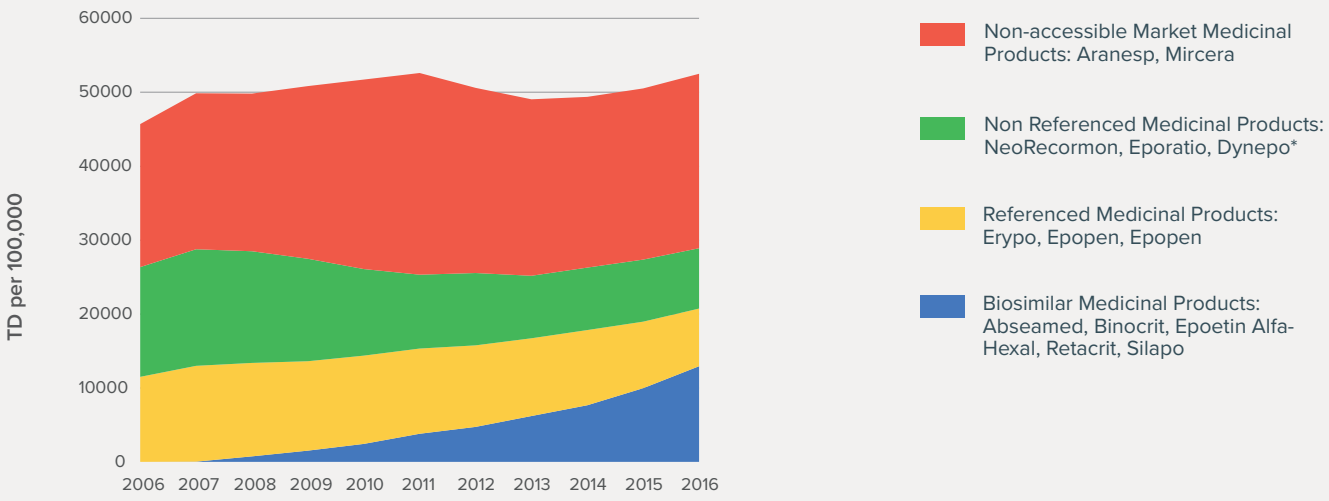
Volume development

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 blue part of the chart shows the volume share of Biosimilar Medicinal Products (listed) which is currently at 25%. The yellow part shows volume share of Referenced Medicinal Products to the approved Biosimilar products which is currently at 15%.

The Non-Referenced Competing Medicinal Products (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 32% in 2007 to 16% in 2016. The Non-accessible market (red part of the chart) are the Pegylated (long-acting) products, with 45% market share.

Epoetin volume development



Source: QuintilesIMS MIDAS December 2016; Total volume development across all European countries included in the study

*Dynepo has been withdrawn by the EMA.

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. However, indications are very different in patient populations; this difference can be effective in limiting patient potential. Frequency of injecting can also vary and the implication of this might vary with patient type.

Summary of EMA information for approved indications for Epoetin products:

											Patient type		Frequency*	Route**	
Molecule	Product	Reference product	Biosimilar	Non-reference	Non-accessible	Anaemia for Chemotherapy patients	Anaemia for patients with Chronic Kidney Disease	Preventing Anaemia in premature babies	Autologuos Blood Transfusion	Reduction of allogenic transfusion exposure in Orthopedic surgery	Adult	Paediatic		Subcutaneous	Intravenous
Epoetin alfa	Epopen	●				●	●		●	●	●	●	3x a week	●	●
	Erypo	●				●	●		●	●	●	●	3x a week	●	●
	Epogen	●				●	●		●	●	●	●	3x a week	●	●
	Abseamed		●			●	●		●	●	●	●	3x a week	●	●
	Epoetin Alfa Hexal		●			●	●		●	●	●	●	3x a week	●	●
	Binocrit		●			●	●		●	●	●	●	3x a week	●	●
Epoetin zeta	Retacrit		●			●	●		●		●	●	3x a week	●	●
	Silapo		●			●	●		●		●	●		●	●
Epoetin beta	NeoRecormon			●		●	●	●	●	●	●	●	3x a week	●	●
Epoetin theta	Eporatio			●		●	●				●		3x a week	●	●
Methoxy polyethlene glycol-epotein beta	Mircera				●		●				●		Every 2 weeks	●	●
Darbepoetin alfa	Aranesp				●	●	●				●		Weekly	●	●

*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

The first set of indicators is the *Market share TD 2016* calculated in treatments days. In Austria, Biosimilars represent 76% 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 25%. Looking at the Biosimilar Medicinal Product versus total market, the market share is 16%.

	Market share TD (2015)			Price per TD (2015/the year before biosimilar entrance)			Volume TD (2015/the year before biosimilar entrance)					
	Biosimilar vs Reference product	Biosimilar vs Accessible market	Biosimilar vs Total market	Biosimilar and Reference product	Biosimilar Accessible market	Total market	Biosimilar and Reference product	Biosimilar Accessible market	Total market	TD/capita (Yr before BS entrance)	TD per capita 2015	First Recorded Sales of Biosimilar
AU	76%	25%	16%	-36%	-37%	-26%	-29%	-8%	-26%	0.95	0.70	2008

The second set of indicators, Price per TD (2016/Year before biosimilar entrance), shows price development per treatment day (DDD) comparing 2016 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 2016 vs. 2007 has fallen 36% for the Biosimilar Medicinal Product and Referenced Product, 37% for Biosimilar Accessible Market and 26% 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 (2015)			Price per TD (2015/the year before biosimilar entrance)			Volume TD (2015/the year before biosimilar entrance)					
	Biosimilar vs Reference product	Biosimilar vs Accessible market	Biosimilar vs Total market	Biosimilar and Reference product	Biosimilar Accessible market	Total market	Biosimilar and Reference product	Biosimilar Accessible market	Total market	TD/capita (Yr before BS entrance)	TD per capita 2015	First Recorded Sales of Biosimilar
AU	76%	25%	16%	-36%	-37%	-26%	-29%	-8%	-26%	0.95	0.70	2008

The third set of indicators, Volume TD (2016/Year before biosimilar entrance), shows the volume development in treatment days (DDDs) comparing 2016 versus the year before the first Epoeitin Biosimilar Medicinal Product was launched (which is 2008 in the case of Austria).While the Biosimilar and the Referenced Product volume has decreased 29%; the full accessible market volume decreased 8% and the total market volume decreased 26%.

	Market share TD (2015)			Price per TD (2015/the year before biosimilar entrance)			Volume TD (2015/the year before biosimilar entrance)					
	Biosimilar vs Reference product	Biosimilar vs Accessible market	Biosimilar vs Total market	Biosimilar and Reference product	Biosimilar Accessible market	Total market	Biosimilar and Reference product	Biosimilar Accessible market	Total market	TD/capita (Yr before BS entrance)	TD per capita 2015	First Recorded Sales of Biosimilar
AU	76%	25%	16%	-36%	-37%	-26%	-29%	-8%	-26%	0.95	0.70	2008

The last set of indicators, TD per capita (Year before biosimilar entrance) and TD per capita 2016, show the usage per capita before the entrance of biosimilars (which is 0.95 in Austria), and the usage per capita of the total market in 2016 (which is 0.7 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 (2015)			Price per TD (2015/the year before biosimilar entrance)			Volume TD (2015/the year before biosimilar entrance)					
	Biosimilar vs Reference product	Biosimilar vs Accessible market	Biosimilar vs Total market	Biosimilar and Reference product	Biosimilar Accessible market	Total market	Biosimilar and Reference product	Biosimilar Accessible market	Total market	TD/capita (Yr before BS entrance)	TD per capita 2015	First Recorded Sales of Biosimilar
AU	76%	25%	16%	-36%	-37%	-26%	-29%	-8%	-26%	0.95	0.70	2008

Appendices

1 EMA list of approved Biosimilars (April 2017)

Medicine Name	Active Substance	Atc code	Marketing Authorisation Holder	Authorisation date
Abasaglar (previously Abasria)	insulin glargine	A10AE04	Eli Lilly Regional Operations GmbH	09/09/2014
Abseamed	epoetin alfa	B03XA01	Medice Arzneimittel Pütter GmbH & Co. KG	28/08/2007
Accofil	filgrastim	L03AA02	Accord Healthcare Ltd	18/09/2014
Amgevita	adalimumab	L04AB04	Amgen Europe B.V.	22/03/2017
Bemfola	follitropin alfa	G03GA05	Gedeon Richter Plc.	27/03/2014
Benepali	etanercept	L04AB01	Samsung Bioepis UK Limited (SBUK)	14/01/2016
Binocrit	epoetin alfa	B03XA01	Sandoz GmbH	28/08/2007
Epoetin Alfa Hexal	epoetin alfa	B03XA01	Hexal AG	28/08/2007
Filgrastim Hexal	filgrastim	L03AA02	Hexal AG	06/02/2009
Flixabi	infliximab	L04AB02	Samsung Bioepis UK Limited (SBUK)	26/05/2016
Grastofil	filgrastim	L03AA02	Apotex Europe BV	18/10/2013
Inflectra	infliximab	L04AB02	Hospira UK Limited	10/09/2013
Inhixa	enoxaparin sodium	B01AB05	Techdow Europe AB	15/09/2016
Lusduna	insulin glargine	A10AE04	Merck Sharp & Dohme Limited	04/01/2017
Movymia	teriparatide	H05AA02	STADA Arzneimittel AG	11/01/2017
Nivestim	filgrastim	L03AA02	Hospira UK Ltd	08/06/2010
Omnitrope	somatropin	H01AC01	Sandoz GmbH	12/04/2006
Ovaleap	follitropin alfa	G03GA05	Teva Pharma B.V.	27/09/2013
Ratiograstim	filgrastim	L03AA02	Ratiopharm GmbH	15/09/2008
Remsima	infliximab	L04AB02	Celltrion Healthcare Hungary Kft.	10/09/2013
Retacrit	epoetin zeta	B03XA01	Hospira UK Limited	18/12/2007
Silapo	epoetin zeta	B03XA01	Stada Arzneimittel AG	18/12/2007
Solymbic	adalimumab	L04AB04	Amgen Europe B.V.	22/03/2017
Terrosa	teriparatide	H05AA02	Gedeon Richter Plc.	04/01/2017
Tevagrastim	filgrastim	L03AA02	Teva GmbH	15/09/2008
Thorinane	enoxaparin sodium	B01AB05	Pharmathen S.A.	15/09/2016
Truxima	rituximab	L01XC02	Celltrion Healthcare Hungary Kft.	17/02/2017
Zarzio	filgrastim	L03AA02	Sandoz GmbH	06/02/2009

A list of Biosimilars under review by EMA (April 2017)

Common name	Therapeutic area	Number of applications	Originator product	Originator company
Adalimumab	Immunosuppressant	2	Humira	AbbVie Ltd
Bevacizumab	Antineoplastic medicines	2	Avastin	Roche
Etanercept	Immunosuppressant	1	Enbrel	Amgen
Insulin glargine	Diabetes	1	Lantus	Sanofi-Aventis
Insulin lispro	Medicines used in diabetes	1	Humalog	Eli Lilly
Pegfilgrastim	Immunostimulants	2	Neulasta	Amgen
Rituximab	Antineoplastic medicines	5	MabThera	Roche
Trastuzumab	Antineoplastic medicines	4	Herceptin	Roche

2 Methodology

- The volumes have been converted by QuintilesIMS 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 % of TD Reference products in 2016
	Biosimilar vs Accessible market	TD Biosimilars as % of TD Accessible market in 2016
	Biosimilar vs Total market	TD Biosimilars as % of TD Total market in 2016
Price per TD	Biosimilar and Reference product	Δ in Price per TD for Biosimilar Reference products 2016/the year before biosimilar entrance
	Biosimilar Accessible market	Δ in Price per TD for Biosimilar Accessible market 2016/the year before biosimilar entrance
	Total market	Δ in Price per TD for Total market 2016/the year before biosimilar entrance
Volume TD	Biosimilar and Reference product	Δ in TD for Biosimilars and Reference products 2016/the year before biosimilar entrance
	Biosimilar Accessible market	Δ in TD for Biosimilar Accessible market 2016/the year before biosimilar entrance
	Total market	Δ in TD for Total market 2016/the year before biosimilar entrance
TD per capita		No. Of Treatment Days per capita in 2016
TD per capita year before biosimilar entrance		No. Of Treatment Days per capita the year before biosimilars entered the market
First recorded sales		The year first sales of biosimilar were recorded

3 QuintilesIMS 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. QuintilesIMS 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	Out	In		Out	Out	In	Out
Hospital	C	C	In	In	In	In	C	C		In	In	C	In	In	In	C	In	In		C	In	In	C
Combined																			In				

4 QuintilesIMS 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 du Médicament (AGIM), Retail - List price - Association Pharmaceutique Belge (APB)
Bulgaria	**BU**	HOSPITAL (SELL-IN),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**	RETAIL (SELL-IN),HOSPITAL (SELL-IN)	Hospital & Retail - Average invoiced pack price
Finland	**FI**	HOSPITAL (SELL-IN),RETAIL (SELL-IN)	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 - Journal 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 Association), 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
Italy	**IT**	DPC (CONSUMPTION),HOSPITAL (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-OUT)	Hospital - Average invoiced pack price, Retail - Canamed, average transaction price if no Canamed 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-OUT)	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-OUT)	Hospital & Retail - List price - Chemist and Druggist, Drug Tariff

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About QuintilesIMS

QunitilesIMS is a leading global information and technology services company providing clients in the healthcare industry with comprehensive solutions to measure and improve their performance. End-to-end proprietary applications and configurable solutions connect 10+ petabytes of complex healthcare data through the IMS OneTM cloud-based master data management platform, providing comprehensive insights into diseases, treatments, costs and outcomes. The company's 15,000 employees blend global consistency and local market knowledge across 100 countries to help clients run their operations more efficiently. Customers include pharmaceutical, consumer health and medical device manufacturers and distributors, providers, payers, government agencies, policymakers, researchers and the financial community.

As a global leader in protecting individual patient privacy, QunitilesIMS uses anonymous healthcare data to deliver critical, real-world disease and treatment insights. These insights help biotech and pharmaceutical companies, medical researchers, government agencies, payers and other healthcare stakeholders to identify unmet treatment needs and understand the effectiveness and value of pharmaceutical products in improving overall health outcomes. Additional information is available at www.imshealth.com.

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