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June 2016

The Impact of Biosimilar Competition

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 document consists of a set of indicators and guidance on how to interpret these indicators. It has been prepared as a set of indicators to monitor the impact of biosimilars in the European markets. It was prepared by IMS Health at the request of the European Commission services with initial contributions from EFPIA, EGA (now Medicines for Europe), and EuropaBio.

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 warning. We have when appropriate quoted their information and statements.

IMS Health published three documents in May 2015:

- The Impact of Biosimilar Competition
    - IMS has prepared as a set of indicators to monitor the impact of biosimilars in the European markets at the request of the European Commission services with initial contributions from EFPIA, EGA (now Medicines for Europe), and EuropaBio.
    - The report was set out to describe the effects on price, volume and market share following the arrival and presence of biosimilar competition in the EEA.
    - This first report was based on full year 2014 data; the objective thereafter was to annually publish the previous year's updated indicators.
- Five Observations by IMS Health

  In this document IMS Health suggested five key observations based on the data from the report
- Reading guide
    - IMS Health has developed a simplified guide to read the report that has a broad set of KPIs for multiple countries
    - EPO and Austria were used as the example

The new 2016 document provides the set of key performer indicators updated with 2015 data and combines all three documents in one.

Contents

Definitions

The report uses some basic terms definded 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 **Key Performance Indicators (KPI)** 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-mnf 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 in 2015 versus pre-EMA approval.

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 + reference product volume, (ii) accessible market volume and (iii) total market volume
- **Volume evolution:** number of treatment days measured in 2015 versus pre-EMA approval.
- **Volume per capita:** number of treatment days consumed in 2015 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 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 IMS Health 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 is based on IMS Health 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.

Five Observations by IMS Health

1. Competition drives down the price

The rationale behind the introduction of biosimilars is to increase price competition resulting in reduced prices. The fourestablished therapy areas (Epoetins, G-CSF, HGH and Anti-tnf) with biosimilar competition show a consistent picture of reduced average prices in European Economic Area (EEA) countries (see Exhibit 1).

The increased competition affects not just the price for the directly comparable product but also has an effect on the price of the whole product class. It can have a similar or even a larger impact on the total therapy area price as it has on the biosimilar/reference product price.

Exhibit 2 shows the 3 countries where the highest price reduction has been achieved.

Other countries might have a similarly high reduction, which is not included in the data, through non-published discounting. Highest reduction may not be the same as the lowest price. The present price is also impacted by the starting price and the mix.

The countries with the highest reduction show reduction of 50-70%. In order to achieve long-term savings, there should be a competition with multiple players; however, too high short term savings might preclude this.

Exhibit 1

	Price per TD 2015/ Year before Biosimilar entrance		
	Biosimilar and Reference product	Accessible market	Total market
EPO	-33%	-34%	-26%
G-CSF	-32%	-32%	-23%
GH	-19%	-13%	-13%
Anti-TNF	-8%	-8%	-4%

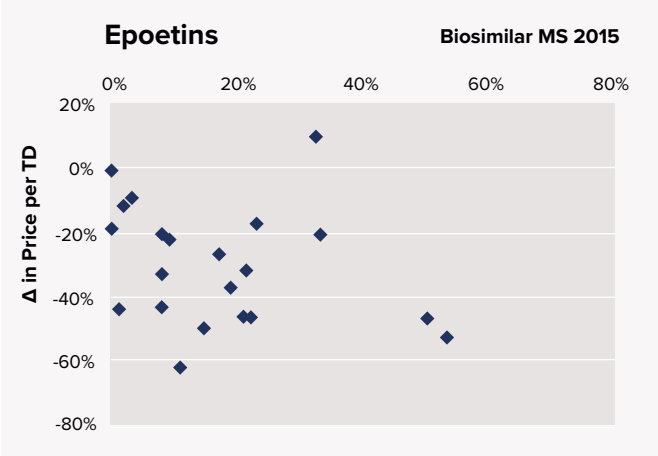
Exhibit 2

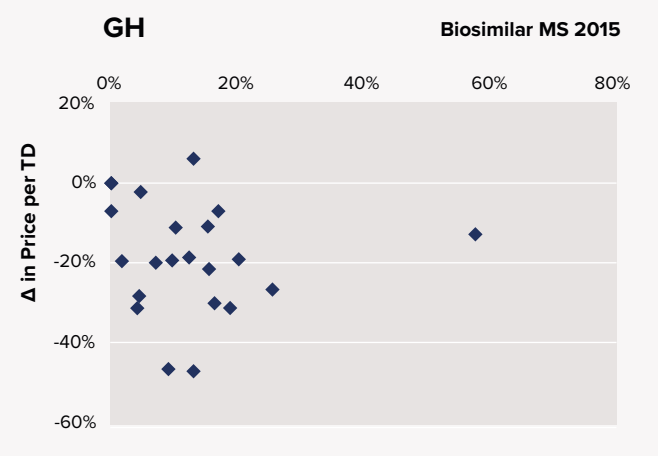
	Price per TD 2015 / Year before Biosimilar entrance
Epoetins	Total market
Portugal	-61%
Slovakia	-52%
Poland	-49%
G-CSF	
Slovakia	-59%
Bulgaria	-58%
Slovenia	-50%
HGH	
Finland	-47%
Poland	-47%
Slovakia	-31%
Anti-TNF	
Sweden	-21%
Bulgaria	-19%
Denmark	-15%

2. The correlation between biosimilars market share and price is weak

The correlation between biosimilar market share and price reduction is weak, as can be seen by the four (Epoetins, G-CSF, HGH and Anti-tnf) established biosimilar classes.

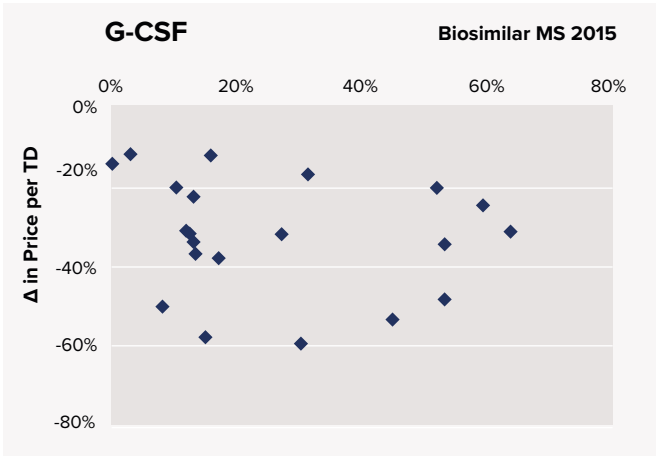
Exhibit 3: Biosimilar market share in 2015 vs change in price per treatment day 2015/year before biosimilar entrance by country

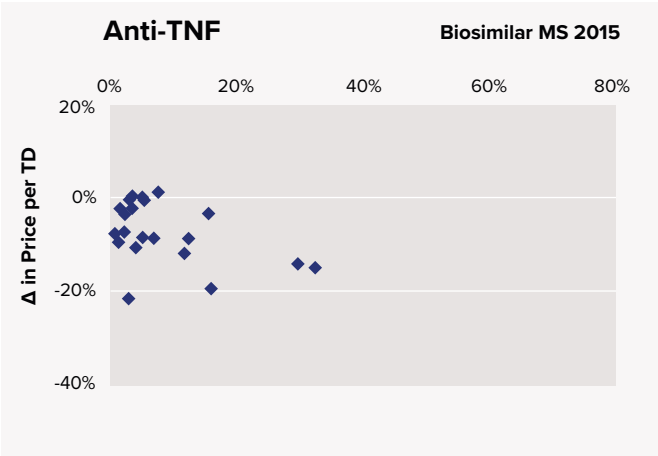




For the 4 classes we can see the same pattern; high savings can be achieved even if biosimilar uptake is low. Price reduction can be achieved through price regulation interventions and/or commercial decisions of manufacturers.

Even if the biosimilar product does not end to be the product sold it is likely an essential step to generate a more competitive environment, which leads to lower prices.



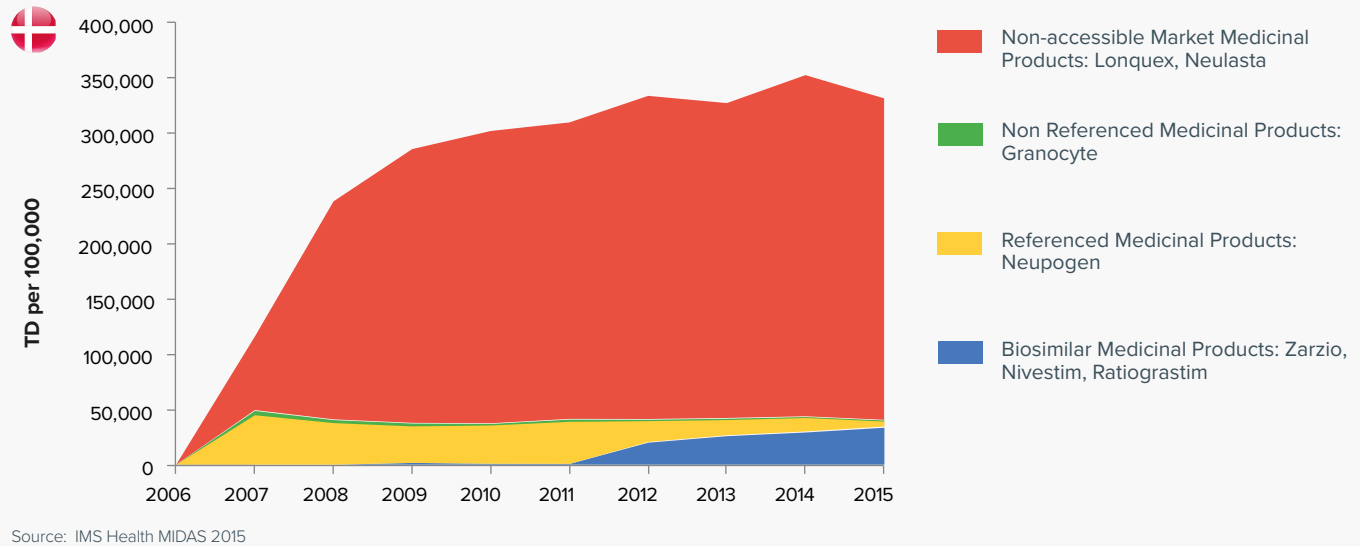


3. Competition can also influence the originator behaviours

The originators have acted differently in many cases than what we have experienced for small molecules. Traditionally, behaviour has been that the originator has either maintained price or reduced price based on mandatory price regulations. In the Biosimilar classes we have seen a multitude of different behaviours:

- Originators launching innovative long-acting/pegylated products without a price premium versus the short-acting, changing the treatment paradigm and therefore usage pattern. Example of such event can be observed in Denmark.

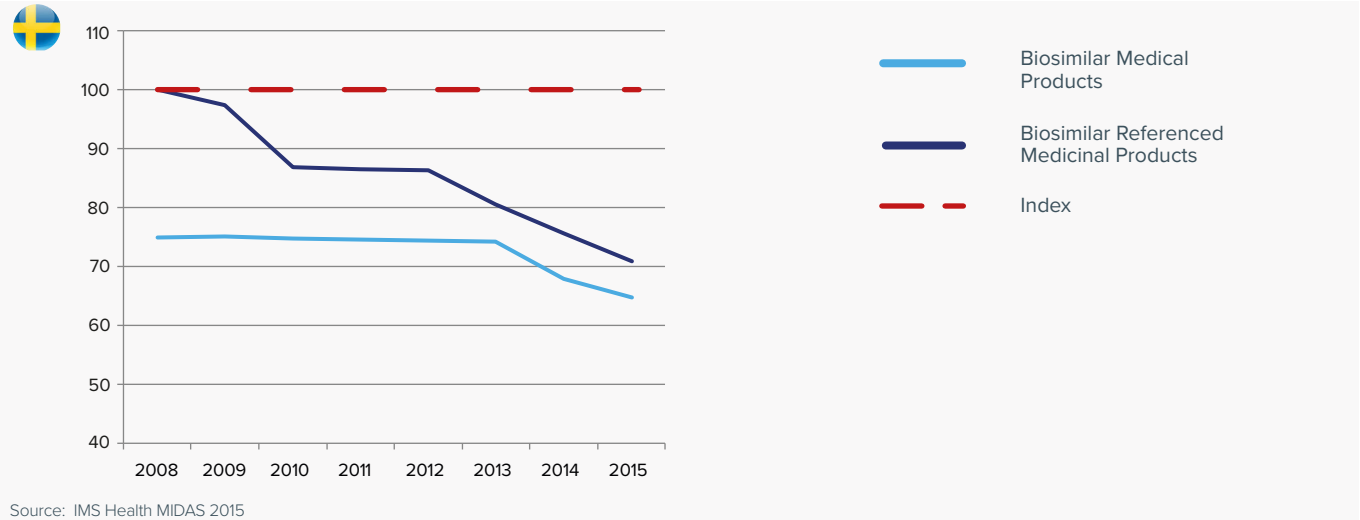
Exhibit 4: G-CSF volume development in Denmark



Source: IMS Health MIDAS 2015

- Originators effectively reducing the price levels

Exhibit 5: HGH price per treatment day in Sweden



Source: IMS Health MIDAS 2015

- There is also a trend when originator companies are manufacturing biosimilar products

A part of the explanation for the changed behaviour in many cases can be that the product classes are hospital products. The hospital market is characterised by a rather strong competition, including on price, between the manufacturers.

4. Lower prices increase patient access in countries with low initial usage

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 Epoetins, we can see significant increases in consumption for countries with low starting volumes at time of introduction of biosimilars and at the same time volume reductions in countries with a high use based on safety warnings.

Lowered prices impact usage but we also need to be aware of other factors:

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

In countries which used to have low usage/availability in the classes the price reductions seem to have a significant impact on the increased access.

Exhibit 6

		Price per TD 2015/ Year before Biosimilar entrance	TD per capita (Year before Biosimilar entrance)	Volume TD 2015/ Year before Biosimilar entrance
	Epoetins			
Low historical usage	Romania	-36%	0.036	460%
	Bulgaria	-46%	0.125	120%
	Poland	-49%	0.027	186%
High historical usage	Ireland	-18%	0.523	-32%
	Austria	-36%	0.942	-28%
	Germany	-45%	0.412	-25%
	HGH			
	Romamia	-27%	0.024	177%
	Czech Rep	-20%	0.060	54%
	Poland	-47%	0.043	78%
	G-CSF			
	Romania	-48%	0.004	498%
	Bulgaria	-58%	0.001	1016%
	Slovakia	-59%	0.004	371%
	Anti-TNF			
	Bulgaria	-19	0.099	131%
	Czech Rep	-12%	0.232	53%
	Slovakia	-8%	0.492	78%

5. The product profile differences in classes can explain differences in impact on the KPIs

The differences in approved indications are relatively small for HGH and G-CSF, somewhat larger for EPO and the largest for Anti-TNF. As a result, different products are used for different indications which impact the patients for which they compete in the class. This is most obvious in Anti-TNF.

Frequency of administration and mode of administration also impact the competition within a class:

- We can see the differences in frequency impacting both for EPO and G-CSF but mainly for selected patients (for example patients recovering at home after a chemotherapy cycle).
- The main differences are seen in Anti-TNF between a more frequent subcutaneous injection in home treatment and or a less frequent intravenous infusion in a hospital setting.
- User friendliness of device, simpler preparation or no need for refrigeration has mainly been a differentiator for Growth Hormones

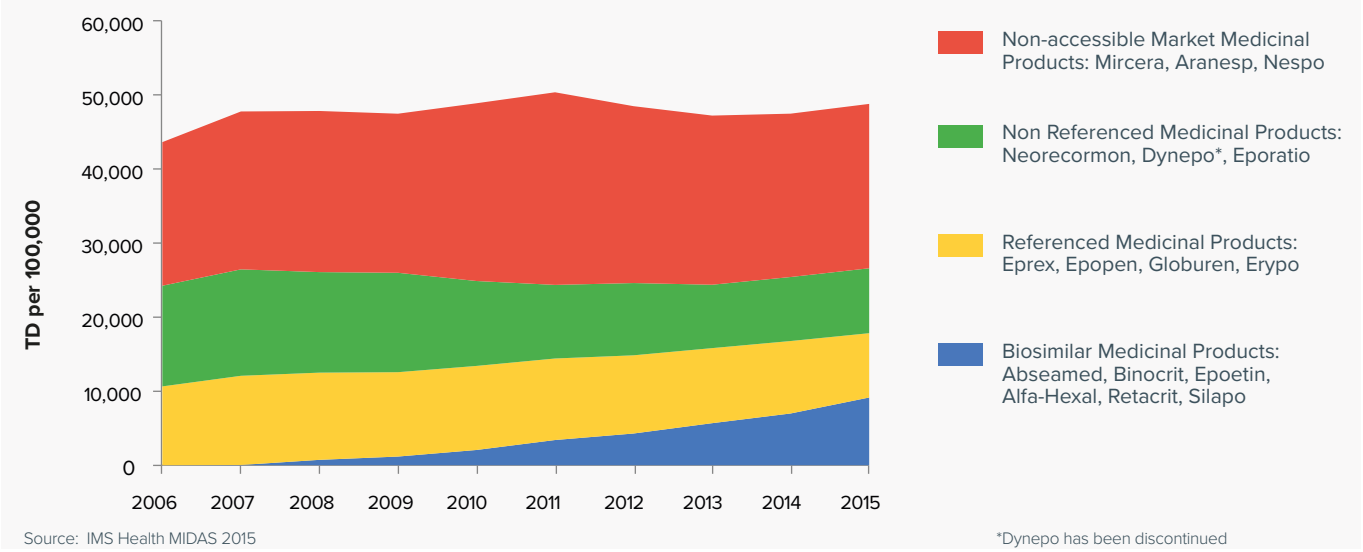
There are relevant product differentiations in all four classes which impact the product mix.

The country and therapy areas KPIs

EPO

Epoetin (Epo) is a form of human erythropoietin produced by recombinant technology and having 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 hemoglobin, the molecule within red blood cells that transports oxygen.

Epoetin volume development



Source: IMS Health MIDAS 2015

*Dynepo has been discontinued

The average for EEA is not representative for any individual country which is illustrated in the next section.

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	Eprex	●				●	●		●	●	●	●	3x a week	●	●
	Epopen	●				●	●		●	●	●	●	3x a week	●	●
	Erypo	●				●	●		●	●	●	●	3x a week	●	●
	Globuren	●				●	●		●	●	●	●	3x a week	●	●
	Abseamed		●			●	●		●	●	●	●	3x a week	●	●
	Epoetin Alfa Hexal		●			●	●		●	●	●	●	3x a week	●	●
	Binocrit		●			●	●		●	●	●	●	3x a week	●	●
Epoetin beta	NeoRecormon			●		●	●	●	●	●	●	●	3x a week	●	●
Epoetin zeta	Retacrit		●			●	●		●		●	●	3x a week	●	●
	Silapo		●			●	●		●		●	●		●	●
Epoetin theta	Eporatio			●		●	●				●		3x a week	●	●
Methoxy polyethlene glycol-epotein beta	Mircera				●	●					●		Every 2 weeks	●	●
Darbepoetin alfa	Aranesp				●	●	●				●		Weekly	●	●
	Nespo				●	●	●				●	●	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 **The European Medicines Agency** (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. It also advised that prescribers take into account patients' individual circumstances and preferences when making the decision to use Epoetins. The Committee for Medicinal Products for Human Use (CHMP) made clear that the new information does not apply to the use of Epoetins for patients with chronic renal failure. (EMA website)

Selected KPIs to illustrate volume share, price evolution, and volume evolution in the EEA countries:

	Market share TD (2015)			Price per TD (2015/the year before biosimilar entrance)			Volume TD (2015/the year before biosimilar entrance)			TD per capita 2015	First Recorded Sales of Biosimilar
	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		
AU	76%	27%	17%	-36%	-37%	-26%	-27%	-10%	-28%	0.69	2008
BE	0%	0%	0%	-1%	-1%	-1%	-13%	-9%	-4%	0.51	2014
BU	100%	83%	50%	-72%	-63%	-46%	482%	34%	120%	0.28	2011
CZ	97%	31%	21%	-47%	-35%	-31%	55%	31%	35%	0.13	2011
DK*	95%	39%	2%	-34%	-12%	-11%	-65%	-90%	-9%	0.45	2010
FI	100%	53%	9%	-42%	-34%	-21%	1033%	-48%	2%	0.35	2008
FR	35%	21%	8%	-33%	-32%	-32%	-2%	-25%	0%	0.91	2009
DE	69%	40%	22%	-53%	-56%	-45%	-12%	-27%	-20%	0.31	2007
GR (R)*	96%	92%	88%	-50%	-50%	-49%	415%	218%	119%	0.05	2008
HU	85%	49%	33%	-55%	-31%	-20%	8%	-2%	-31%	0.27	2009
IE	15%	0%	0%	-35%	-28%	-18%	-96%	-58%	-32%	0.35	2008
IT	52%	44%	33%	-11%	-10%	10%	127%	54%	13%	1.08	2008
NL*	39%	12%	3%	-27%	-16%	-8%	81%	71%	89%	0.28	2009
NO	90%	63%	8%	-48%	-41%	-20%	95%	-46%	5%	0.22	2008
PL	96%	18%	15%	-67%	-57%	-49%	3231%	266%	186%	0.08	2009
PT*	67%	16%	11%	-71%	-78%	-61%	105%	106%	-5%	0.42%	2010
RO	54%	31%	19%	-51%	-40%	-36%	8020%	268%	460%	0.21%	2009
SK	100%	70%	53%	-60%	-57%	-52%	334%	65%	13%	0.51	2010
SL	41%	19%	8%	-50%	-44%	-42%	-35%	-32%	10%	0.58	2009
ES	49%	37%	23%	-30%	-25%	-16%	32%	-7%	-8%	0.65	2008
SE	93%	57%	21%	-20%	-28%	-45%	48%	-19%	22%	0.59	2008
UK	5%	3%	1%	-7%	-12%	-8%	55%	-19%	20%	0.29	2009
EU	51%	34%	19%	-33%	-34%	-26%	71%	12%	14%	0.50	

* The following data history is used: NL (2009-2015), DK (2007-2015), PT (2010-2015), only retail panel is available for Greece.
**Caveats may apply - refer to page 2 for details

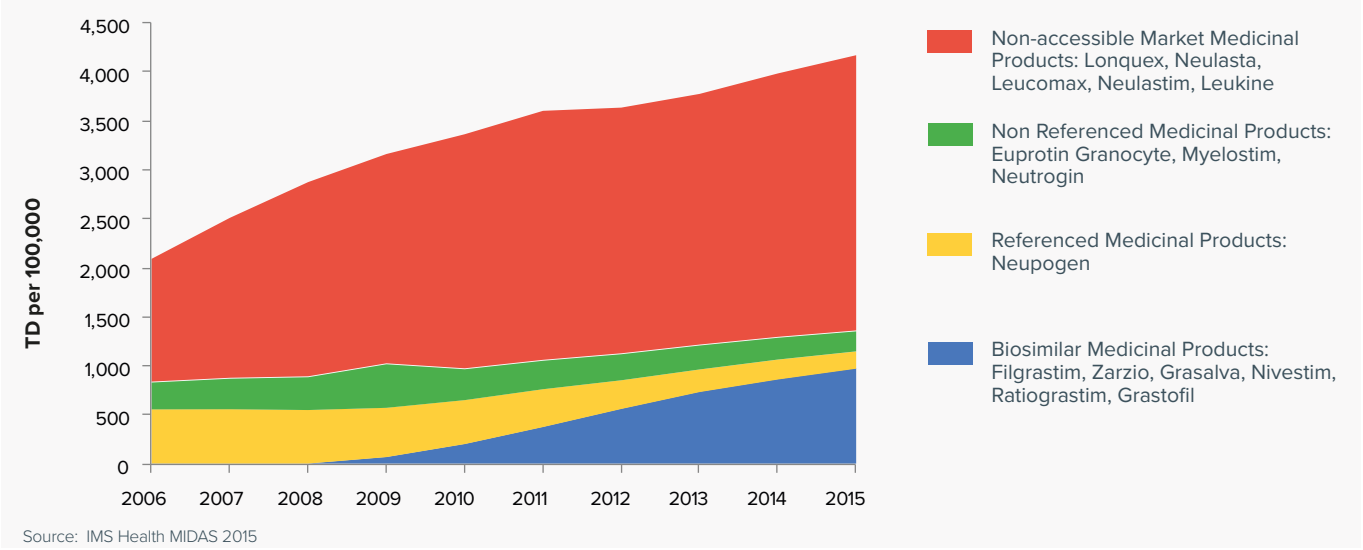
Prices per treatment days (total market) has been reduced in all markets but to a different degree ((-8%)-(-61%)) due to a combination of factors; the level of competition, to what extent Non Accessible Market products (largely differentiated by fewer injections) have been accepted, but also the price development of reference and biosimilar medicinal products.

The volume development shows that markets with already high usage were greatly reduced following the 2011 safety alert and countries with low usage increased partly based on lower prices.

G-CSF

Granulocyte-colony stimulating factor (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 following chemotherapy, to enable a high relative dose intensity, therefore allowing for the planned chemotherapy schedule.

G-CSF volume development



Source: IMS Health MIDAS 2015

The average for EEA is not representative for any individual country which is illustrated in the next section.

Summary of EMA information for approved indications of G-CSF

		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	●				●	●	●	●	●	●
	Zarzio		●			●	●	●	●	●	●
	Grasalva		●			●		●	●	●	●
	Nivestim		●			●		●	●	●	●
	Ratiograstim		●			●		●	●	●	●
	Grastofil		●			●		●	●	●	●
Lenograstim	Euprotin			●		●		●	●		
	Granocyte			●		●		●	●		
	Myelostim			●		●		●	●		
	Neutrogin			●		●		●	●		
Lipegfilgrastim	Lonquex				●	●					
Pegfilgrastim	Neulasta				●	●					
	Neulastim				●	●					
Molgramostim	Leucomax				●	●	●	●	●		
Sargramostim	Leukine				●	●	●	●	●		

Additional information about G-CSF

Subcutaneous injection is 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 the EEA countries:

	Market share TD (2015)			Price per TD (2015/the year before biosimilar entrance)			Volume TD (2015/the year before biosimilar entrance)			TD per capita 2015	First Recorded Sales of Biosimilar
	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		
AU	83%	83%	17%	-43%	-43%	-38%	77%	57%	87%	0.10	2008
BE	1%	1%	0%	-29%	-30%	-14%	14%	-1%	78%	0.06	2009
BU	95%	93%	15%	-75%	-77%	-58%	187%	80%	1016%	0.02	2009
CZ	99%	99%	52%	-28%	-28%	-20%	187%	187%	106%	0.01	2010
DK*	87%	85%	10%	-46%	-45%	-20%	4%	-1%	-39%	0.06	2009
FI	97%	97%	16%	-31%	-31%	-12%	61%	-58%	41%	0.08	2009
FR	84%	48%	13%	-28%	-24%	-22%	161%	38%	44%	0.08	2009
DE	78%	65%	13%	-30%	-29%	-32%	54%	22%	120%	0.06	2008
GR (R)*	99%	98%	83%	-60%	-60%	-34%	561%	283%	-89%	0.00	2009
HU	100%	100%	64%	-53%	-53%	-31%	162%	158%	-5%	0.03	2009
IE	28%	25%	3%	-24%	-22%	-11%	-1%	2%	-36%	0.08	2009
IT	88%	76%	31%	-24%	-24%	-17%	115%	17%	17%	0.04	2009
NL*	47%	46%	13%	-40%	-39%	-37%	26%	25%	17%	0.04	2009
NO	84%	84%	6%	-56%	-56%	-34%	36%	36%	115%	0.06	2009
PL	85%	85%	27%	-47%	-48%	-32%	101%	70%	161%	0.04	2009
PT*	85%	84%	45%	-87%	-86%	-53%	48%	37%	-39%	0.02	2010
RO	100%	100%	53%	-51%	-51%	-48%	237%	237%	498%	0.02	2009
SK	100%	100%	30%	-79%	-79%	-59%	351%	351%	371%	0.04	2009
SL	50%	50%	8%	-68%	-68%	-50%	62%	62%	200%	0.05	2009
ES	79%	78%	60%	-41%	-41%	-24%	54%	42%	-32%	0.02	2009
SE	93%	93%	53%	-52%	-52%	-34%	216%	187%	40%	0.03	2009
UK	98%	82%	46%	4%	-5%	0%	174%	116%	89%	0.03	2008
EU	85%	72%	23%	-32%	-32%	-23%	99%	50%	104%	0.04	

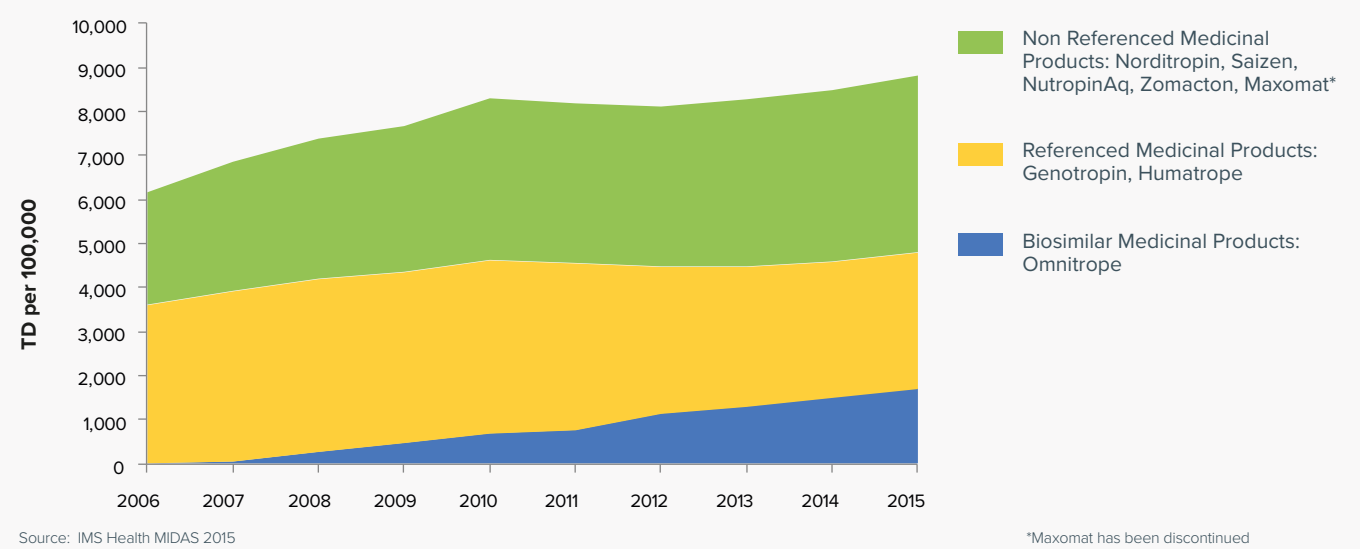
* The following data history is used: NL (2009-2015), DK (2007-2015), PT (2010-2015), only retail panel is available for Greece.
**Caveats may apply - refer to page 2 for details

Price changes per treatment days (total market) vary considerably across the different EEA countries, this ranges between (-59%) and 0%.

HGH

Human Growth Hormone (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.

GH volume development



Source: IMS Health MIDAS 2015

*Maxomat has been discontinued

The average for EEA is not representative for any individual country which is illustrated in the next section.

Summary of EMA information for approved indication and administration frequency details 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			●	●		●					

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 the EEA countries:

	Market share TD (2015)			Price per TD (2015/the year before biosimilar entrance)			Volume TD (2015/the year before biosimilar entrance)			TD per capita 2015	First Recorded Sales of Biosimilar
	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		
AU	34%	34%	17%	-13%	-13%	-7%	15%	15%	34%	0.05	2008
BE	23%	23%	12%	-21%	-21%	-19%	33%	33%	34%	0.11	2009
BU	16%	16%	16%	-20%	-20%	-22%	-16%	-16%	-23%	0.01	2012
CZ	17%	17%	7%	-16%	-16%	-20%	60%	60%	54%	0.12	2010
DK*	96%	96%	58%	-15%	-15%	-13%	78%	78%	-6%	0.14	2011
FI	33%	33%	9%	-28%	-28%	-47%	-6%	-6%	44%	0.09	2008
FR	32%	32%	15%	-13%	-13%	-11%	40%	40%	47%	0.14	2007
DE	26%	26%	13%	3%	3%	6%	0%	0%	22%	0.08	2007
GR (R)*	0%	0%	0%	-3&	-3%	3%	-15%	-15%	41%	0.00	2015
HU	9%	9%	5%	-2%	-2%	-2%	-10%	-10%	1%	0.05	2012
IE	0%	0%	0%	-11%	-11%	5%	32%	32%	35%	0.07	
IT	23%	23%	10%	-17%	-17%	-11%	48%	48%	47%	0.10	2007
NL*	32%	32%	16%	-39%	-39%	-30%	26%	26%	33%	0.12	2008
NO	25%	25%	10%	-23%	-23%	-19%	2%	2%	24%	0.17	2011
PL	99%	99%	99%	-47%	-47%	-47%	79%	79%	78%	0.07	2008
PT*	4%	4%	2%	-33%	-33%	-20%	-5%	-5%	-9%	0.04	2014
RO	56%	56%	26%	-12%	-12%	-27%	241%	241%	177%	0.06	2008
SK	0%	0%	0%	-10%	-10%	-7%	16%	16%	20%	0.08	2013
SL	9%	9%	4%	-24%	-24%	-31%	12%	12%	12%	0.06	2010
ES	29%	29%	20%	-19%	-19%	-19%	42%	42%	32%	0.13	2007
SE	30%	30%	19%	-31%	-31%	-31%	-11%	-11%	-5%	0.15	2007
UK	17%	17%	9%	-26%	-26%	-17%	45%	45%	72%	0.07	2007
EU	35%	35%	19%	-19%	-19%	-13%	38%	38%	44%	0.09	

* The following data history is used: NL (2009-2015), DK (2007-2015), PT (2010-2015), only retail panel is available for Greece.
**Caveats may apply - refer to page 2 for details

Price changes per treatment days (total market) vary considerably across the different EEA countries, this ranges between (-47%) and 6%.

Anti-TNF

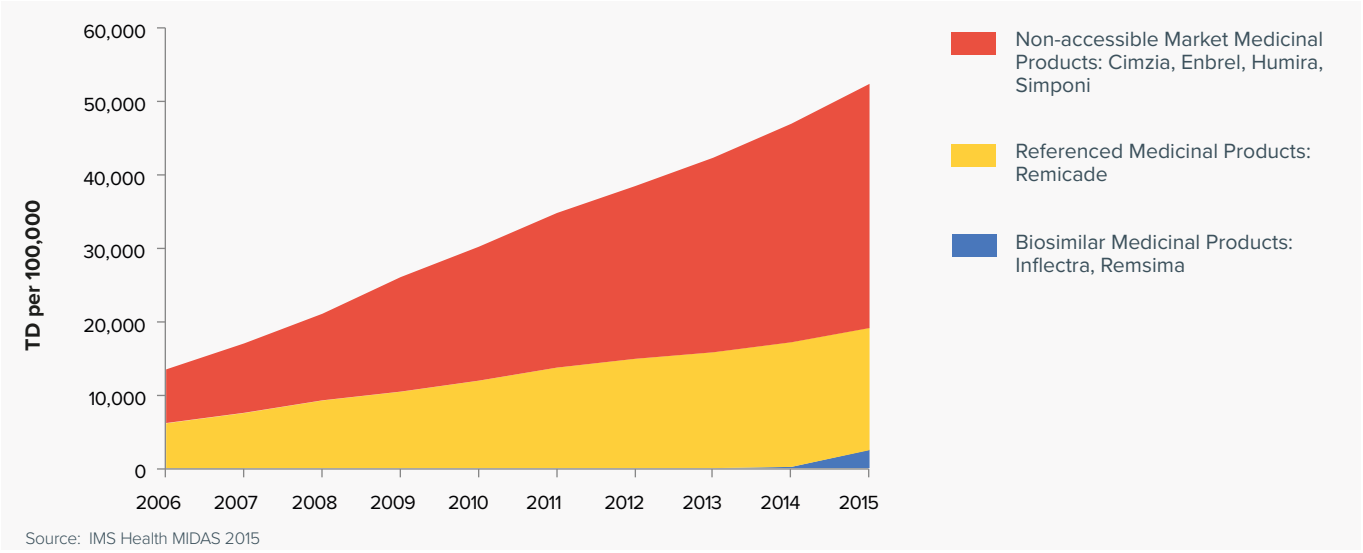
Anti-TNF (Anti-tumour necrosis factor) drugs are a class of drugs that are used to treat inflammatory conditions such as rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, juvenile arthritis, crohn's disease, ulcerative colitis, psoriasis and hidradinitis suppurativa. These drugs are 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, joints 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.

The European Medicines Agency's (EMA's) Committee for Medicinal Products for Human Use (CHMP) announced on 14 January 2016 that it had recommended granting of marketing authorization for a biosimilar etanercept product Benepali.

By the time this report is published, Benepali biosimilar will have been launched by Samsung Bioepis (joint venture between Samsung and Biogen) in Norway, Germany, UK and Sweden.

Anti-TNF volume development



Source: IMS Health MIDAS 2015

The average for EEA is not representative for any individual country which is illustrated in the next section.

Additional information about Anti-TNF

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

	Humira	Remicade	Remsima	Inflectra	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	●							

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	Indication	
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		●
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 the EEA countries: infliximab biosimilar only

	Market share TD (2015)			Price per TD (2015/the year before biosimilar entrance)			Volume TD (2015/the year before biosimilar entrance)			TD per capita 2015	First Recorded Sales of Biosimilar
	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		
AU	3%	3%	2%	-1%	-1%	-3%	43%	43%	41%	0.19	2015
BE	1%	1%	0%	-14%	-14%	-7%	23%	23%	21%	1.05	2015
BU	100%	100%	16%	-50%	-50%	-19%	96660%	96660%	131%	0.23	2014
CZ	21%	21%	11%	-16%	-16%	-12%	56%	56%	53%	0.35	2014
DK*	68%	68%	32%	-29%	-29%	-15%	23%	23%	12%	1.02	2015
FI	32%	32%	12%	-10%	-10%	-9%	33%	33%	38%	0.88	2013
FR	4%	4%	2%	-10%	-10%	-7%	20%	20%	24%	0.70	2015
DE	10%	10%	3%	-4%	-4%	-2%	23%	23%	25%	0.56	2015
GR (R)*										0.01	
HU	25%	25%	7%	-7%	-7%	1%	-5%	-5%	14%	0.36	2014
IE	4%	4%	1%	-1%	-1%	-2%	46%	46%	30%	1.31	2014
IT	11%	11%	3%	-1%	-1%	1%	6%	6%	13%	0.37	2015
NL*	13%	13%	5%	-3%	-3%	0%	4%	4%	3%	1.03	2015
NO	68%	68%	29%	-48%	-48%	-14%	51%	51%	28%	1.52	2013
PL	78%	78%	15%	-38%	-38%	-3%	-18%	-18%	16%	0.04	2014
PT*	15%	15%	6%	-20%	-20%	-8%	33%	33%	27%	0.37	2013
RO	11%	11%	4%	-12%	-12%	-10%	-15%	-15%	7%	0.21	2014
SK	9%	9%	5%	-6%	-6%	-8%	95%	95%	78%	0.88	2014
SL	3%	3%	1%	-18%	-18%	-9%	33%	33%	34%	0.57	2015
ES	13%	13%	5%	-2%	-2%	0%	9%	9%	18%	0.55	2015
SE	8%	8%	2%	-10%	-10%	-21%	14%	14%	48%	1.29	2015
UK	9%	9%	3%	0%	0%	0%	26%	26%	22%	0.69	2015
EU	13%	13%	5%	-8%	-8%	-4%	20%	20%	23%	0.56	

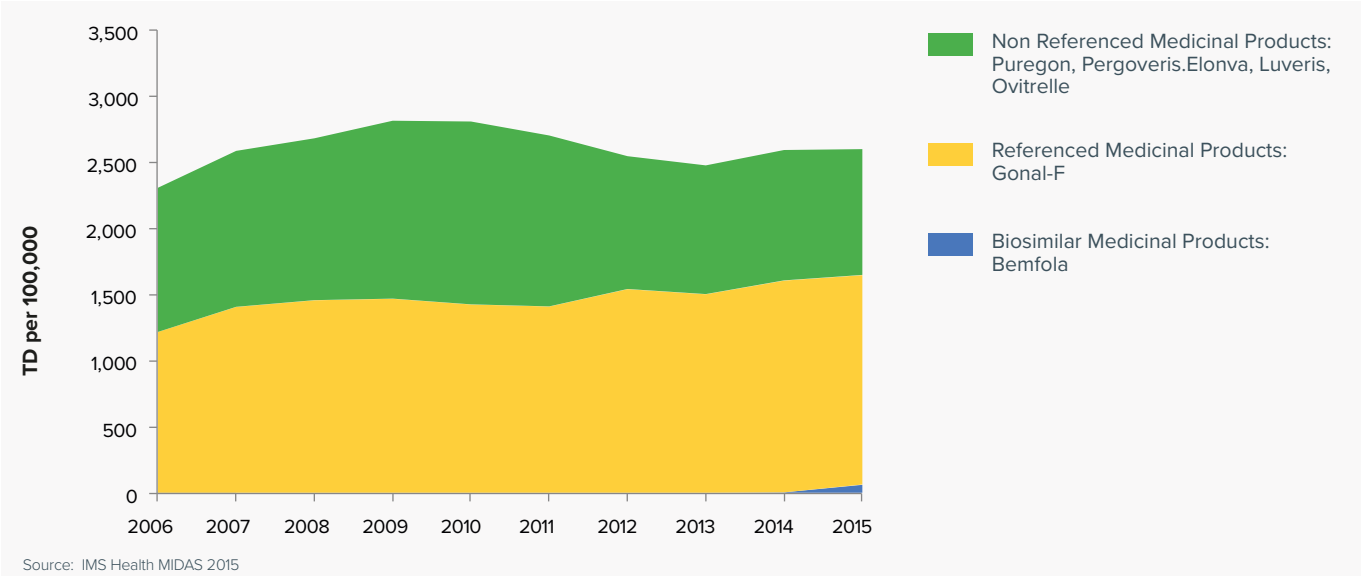
* The following data history is used: NL (2009-2015), DK (2007-2015), PT (2010-2015), only retail panel is available for Greece.
**Caveats may apply - refer to page 2 for details

Price changes per treatment days (total market) vary considerably across the different EEA countries, this ranges between (–21%) and 0%.

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 recombinant preparations were considered.

Fertility volume development



Source: IMS Health MIDAS 2015

The average for EEA is not representative for any individual country which is illustrated in the next section.

Additional information about fertility medicines:

Summary of information for approved indications for Fertility products

		Classification			Indications					Frequency	Route	
Molecule	Product	Reference product	Biosimilar	Non-reference	Infertility	Hypogonadism	Anovulation	Ovulation Induction	Reproductive Techniques, Assisted		Subcutaneous	Intravenous
Follitropin alfa	Gonal-F	●			●		●			Daily	●	●
	Bemfola		●		●	●	●		●	Daily	●	●
Follitropin alfa/lutropin alfa	Pergoveris			●	●					Daily	●	●
Follitropin beta	Puregon			●	●	●				Patient specific	●	
Corifollitropin alfa	Elonva			●	●					Patient specific	●	
Lutropin alfa	Luveris			●	●			●		Daily	●	●
Choriogonadotropin alfa	Ovitrelle			●	●		●	●	●	Patient specific	●	

Selected KPIs to illustrate volume share, price evolution, and volume evolution in the EEA countries:

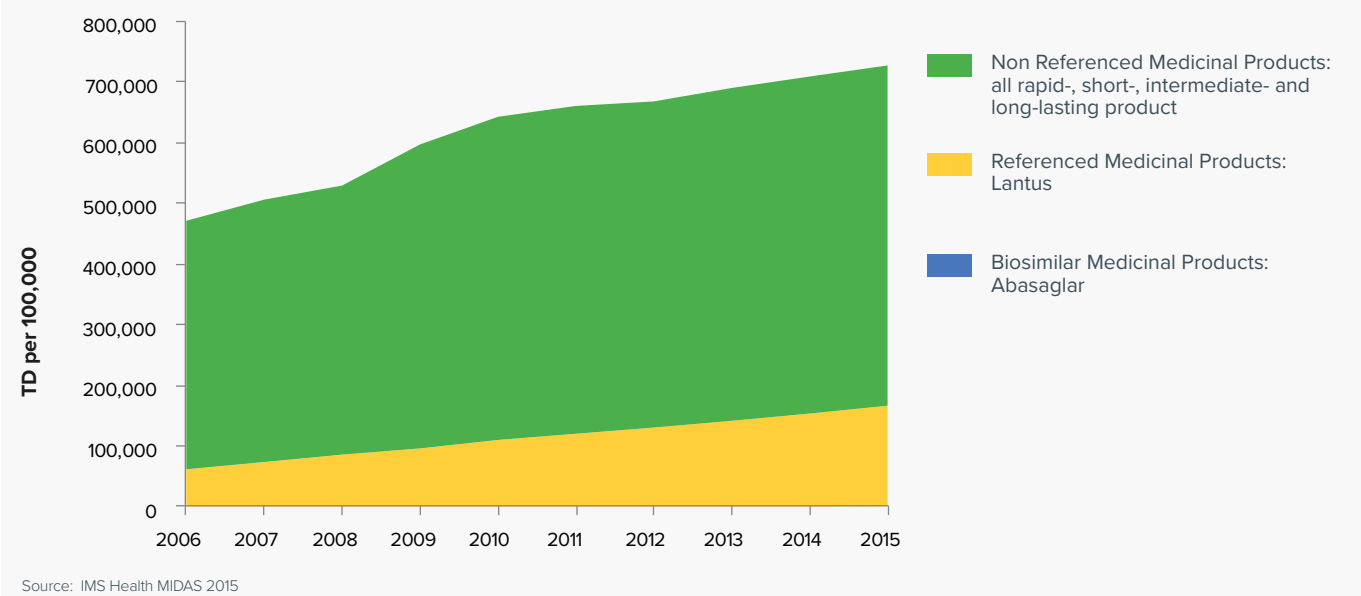
	Market share TD (2015)			Price per TD (2015/the year before biosimilar entrance)			Volume TD (2015/the year before biosimilar entrance)			TD per capita 2015	First Recorded Sales of Biosimilar
	Biosimilar vs Reference product	Biosimilar vs Accessible market	Biosimilar vs Total market	Biosimilar and Reference product	Biosimilar Accessible market	Total market	Biosimilar and Reference product	Biosimilar Accessible market	Total market		
AU	16%	16%	4%	2%	2%	-5%	60%	60%	52%	0.07	2014
BE	4%	4%	2%	0%	0%	2%	5%	5%	2%	0.16	2015
BU										0.09	
CZ										0.16	
DK*	9%	9%	5%	-12%	-12%	-12%	24%	24%	15%	0.15	2014
FI	18%	18%	10%	-10%	-10%	-5%	48%	48%	8%	0.12	2014
FR	4%	4%	2%	-1%	-1%	0%	7%	7%	1%	0.12	2015
DE	3%	3%	2%	-1%	-1%	-2%	27%	27%	21%	0.12	2014
GR										0.27	
HU	8%	8%	7%	-2%	-2%	-2%	24%	24%	21%	0.12	
IE										0.23	
IT										0.18	
NL*										0.06	
NO	22%	22%	13%	-4%	-4%	-3%	34%	34%	13%	0.10	2014
PL	3%	3%	1%	32%	32%	15%	-22%	-22%	56%	0.10	2015
PT*	2%	2%	1%	-1%	-1%	2%	13%	13%	7%	0.10	2015
RO										0.03	
SK										0.08	
SL	1%	1%	0%	0%	0%	-3%	11%	11%	7%	0.12	2015
ES	9%	9%	5%	-6%	-6%	-3%	7%	7%	-2%	0.08	2015
SE	9%	9%	8%	-18%	-18%	-15%	33%	33%	10%	0.12	2014
UK	3%	3%	3%	0%	0%	-1%	13%	13%	11%	0.04	2015
EU	4%	4%	2%	-1%	-1%	-1%	10%	10%	6%	0.11	

* The following data history is used: NL (2009-2015), DK (2007-2015), PT (2010-2015), only retail panel is available for Greece.
**Caveats may apply - refer to page 2 for details

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: IMS Health MIDAS 2015

The average for EEA is not representative for any individual country which is illustrated in the next section.

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.

Summary of information for approved indications for Insulin products

		Classification			Indications	Frequency*	Mode of action	Route	
Molecule	Product	Reference product	Biosimilar	Non-reference	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 Aspart	Novorapid			●	●	Twice / 5x a day	Short-acting	●	
	Novomix			●	●	Twice / 5x a day	Short-acting	●	
Insulin Degludec / Insulin Aspart	Ryzodeg			●	●	Daily	Short-acting / Long-acting	●	
Insulin Glulisine	Apidra			●	●	Twice / 5x a day	Short-acting	●	
Insulin Human	Actraphane			●	●	Once / twice a day	Short-acting / Long-acting	●	
	Actrapid			●	●	Twice / 5x a day	Short-acting	●	
	Insulatard			●	●	Once / twice a day	Long-acting	●	
	Insuman			●	●	Twice / 5x a day	Short-acting	●	●
	Mixtard			●	●	Once / twice a day	Short-acting / Long-acting	●	
	Monotard			●	●	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	●	●
Insulin Degludec / Liraglutide	Xultophy			●	●	Daily	Long-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 the EEA countries:

	Market share TD (2015)			Price per TD (2015/the year before biosimilar entrance)			Volume TD (2015/the year before biosimilar entrance)			TD per capita 2015	First Recorded Sales of Biosimilar
	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		
AU										5.47	
BE										6.48	
BU	0%	0%	0%	-4%	-4%	-1%	35%	35%	5%	5.99	2015
CZ	3%	3%	0%	-6%	-6%	4%	26%	26%	7%	8.02	2015
DK*	0%	0%	0%	-4%	-4%	-2%	30%	30%	4%	6.62	2015
FI	0%	0%	0%	0%	0%	0%	2%	2%	0%	11.41	2015
FR										5.94	
DE	0%	0%	0%	-4%	-4%	1%	17%	17%	2%	11.62	2015
GR (R)*										6.64	
HU	1%	1%	0%	0%	0%	1%	7%	7%	3%	9.34	2015
IE										4.45	
IT										5.28	
NL*	0%	0%	0%	-2%	-2%	1%	9%	9%	2%	9.25	2015
NO	0%	0%	0%	4%	4%	5%	12%	12%	2%	6.78	2015
PL	7%	7%	0%	-6%	-6%	1%	37%	37%	1%	6.73	2015
PT*										5.36	
RO										5.10	
SK	10%	10%	2%	-4%	-4%	1%	30%	30%	11%	7.02	2015
SL										8.54	
ES	0%	0%	0%	-1%	-1%	1%	9%	9%	2%	7.12	2015
SE	0%	0%	0%	0%	0%	0%	3%	3%	2%	9.33	2015
UK	0%	0%	0%	-1%	-1%	0%	1%	1%	3%	7.38	2015
EU	0%	0%	0%	-1%	-1%	1%	6%	6%	2%	7.43	

* The following data history is used: NL (2009-2015), DK (2007-2015), PT (2010-2015), only retail panel is available for Greece.
**Caveats may apply - refer to page 2 for details

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 and Austria are used as the example.

Volume development

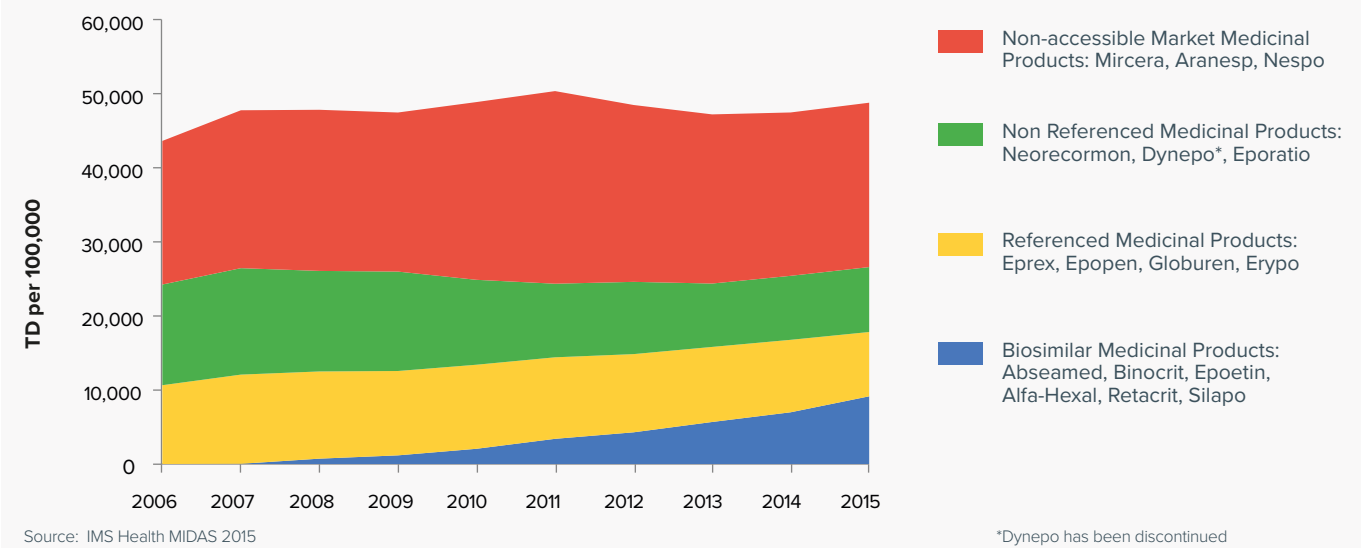
Chart *Epoetin Volume Development* shows volume development over time for the total European Economic Area (EEA). Volume is expressed in (WHO) DDDs as a proxy to be able to include different products.

The blue part of the chart shows the volume share of Biosimilar Medicinal Products (listed) which is currently at 19%. The yellow part shows volume share of Referenced Medicinal Products to the approved Biosimilar products which is currently at 18%.

After the introduction of Biosimilar Medicinal Products, the combined market of Referenced Products and Biosimilars has taken an increased share of 37% of the total market. The Non-Referenced 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 29% in 2007 to 18% in 2015. The Non-accessible market (red part of the chart) are the Pegylated (long acting) products, with 45% market share.

Overall the market grew until 2011. The slight volume drop in 2011 is largely explained by a safety warning from EMA that is described on page 4 of the report.

Epoetin volume development



Source: IMS Health MIDAS 2015

*Dynepo has been discontinued

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; 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	Paediatric		Subcutaneous	Intravenous
Epoetin alfa	Eprex	●				●	●		●	●	●	●	3x a week	●	●
	Epopen	●				●	●		●	●	●	●	3x a week	●	●
	Erypo	●				●	●		●	●	●	●	3x a week	●	●
	Globuren	●				●	●		●	●	●	●	3x a week	●	●
	Abseamed		●			●	●		●	●	●	●	3x a week	●	●
	Epoetin Alfa Hexal		●			●	●		●	●	●	●	3x a week	●	●
	Binocrit		●			●	●		●	●	●	●	3x a week	●	●

Selected KPIs

The first set of indicators is the Market share TD 2015 calculated in treatments days/ DDDs. In Austria, Biosimilars represent 76% of Biosimilar + Referenced Products. If the Non-Referenced Medicinal Product also is included (total accessible market), the share of Biosimilar Medicinal Product is 27%. If it is Biosimilar Medicinal Product versus total market, it is 17%.

Selected KPIs to illustrate volume share, price evolution, and volume evolution in the EEA 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 per capita 2015	First Recorded Sales of Biosimilar
AU	76%	27%	17%	-36%	-37%	-26%	-27%	-10%	-28%	0.69	2008

The second set of indicators, Price per TD (2015/Year before biosimilar entrance), shows price development per treatment day (DDD) comparing 2015 price with prices in the year before the first Epo Biosimilar Medicinal Product was launched (which is 2008 in the case of Austria). The volume weighted average price in 2015 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 price also on other products as competition intensifies.

Selected KPIs to illustrate volume share, price evolution, and volume evolution in the EEA 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 per capita 2015	First Recorded Sales of Biosimilar
AU	76%	27%	17%	-36%	-37%	-26%	-27%	-10%	-28%	0.69	2008

The third set of indicators, Volume TD (2015/Year before biosimilar entrance), shows the volume development in treatment days (DDDs) comparing 2015 versus the year before the first Epo Biosimilar Medicinal Product was launched (which is 2008 in the case of Austria).While the Biosimilar and the Referenced Product volume has decreased 27%; the full accessible market volume decreased 10% and the total market volume decreased 28%.

Selected KPIs to illustrate volume share, price evolution, and volume evolution in the EEA 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 per capita 2015	First Recorded Sales of Biosimilar
AU	76%	27%	17%	-36%	-37%	-26%	-27%	-10%	-28%	0.69	2008

The last set of indicators, TD per capita, shows the usage per capita of the total market in 2015 which is 0.69 in Austria. The year with the First recorded sales of Biosimilar in Austria is 2008.

Selected KPIs to illustrate volume share, price evolution, and volume evolution in the EEA 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 per capita 2015	First Recorded Sales of Biosimilar
AU	76%	27%	17%	-36%	-37%	-26%	-27%	-10%	-28%	0.69	2008

Appendices

1 EMA list of approved Biosimilars

Medicine Name	Active Substance	Atc code	Marketing Authorisation Holder	Authorisation date
Omnitrope	somatropin	H01AC01	Sandoz GmbH	12/04/2006
Abseamed	epoetin alfa	B03XA01	Medice Arzneimittel Pütter GmbH & Co. KG	28/08/2007
Binocrit	epoetin alfa	B03XA01	Sandoz GmbH	28/08/2007
Epoetin Alfa Hexal	epoetin alfa	B03XA01	Hexal AG	28/08/2007
Retacrit	epoetin zeta	B03XA01	Hospira UK Limited	18/12/2007
Silapo	epoetin zeta	B03XA01	Stada Arzneimittel AG	18/12/2007
Biograstim	filgrastim	L03AA02	AbZ-Pharma GmbH	15/09/2008
Ratiograstim	filgrastim	L03AA02	Ratiopharm GmbH	15/09/2008
Tevagrastim	filgrastim	L03AA02	Teva GmbH	15/09/2008
Filgrastim Hexal	filgrastim	L03AA02	Hexal AG	06/02/2009
Zarzio	filgrastim	L03AA02	Sandoz GmbH	06/02/2009
Nivestim	filgrastim	L03AA02	Hospira UK Ltd	08/06/2010
Ovaleap	follitropin alfa	G03GA05	Teva Pharma B.V.	27/09/2013
Grastofil	filgrastim	L03AA02	Apotex Europe BV	18/10/2013
Inflectra	infliximab	L04AB02	Hospira UK Limited	10/09/2013
Remsima	infliximab	L04AB02	Celltrion Healthcare Hungary Kft.	10/09/2013
Bemfola	follitropin alfa	G03GA05	Finox Biotech AG	27/03/2014
Accofil	filgrastim	L03AA02	Accord Healthcare Ltd	18/09/2014
Abasaglar (previously Abasria)	insulin glargine	A10AE04	Eli Lilly Regional Operations GmbH	09/09/2014
Benepali	etanercept	L04AB01	Samsung Bioepis UK Limited (SBUK)	14/01/2016

A list of Biosimilars under review by EMA

Common name	Therapeutic area	Number of applications	Originator product	Originator company
Adalimumab	Immunosuppressant	2	Humira	AbbVie
Enoxaparin sodium	Antithrombotic (blood-clot prevention)	2	Lovenox	Sanofi-Aventis
Etanercept	Immunosuppressant	1	Enbrel	Amgen
Insulin glargine	Diabetes	1	Lantus	Sanofi-Aventis
Pegfilgrastim	Immunostimulant	3	Neulasta	Amgen
Rituximab	Antineoplastic medicine (anticancer)	1	MabThera / Rituxan	Roche
Teriparatide	Calcium homeostasis	2	Forteo	Eli Lilly
Infliximab	Immunosuppressant	1	Remicade	Johnson and Johnson

* Data collected on May 2016
Source: EMA

2 Methodology

- The volumes have been converted by IMS Health 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 that 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 average.
- Price evolution is calculated as the present price for the relevant market versus the price for the same relevant market before EMA approval of biosimilars.
- Volume evolution is calculated as the present total volume versus the total volume before introduction of biosimilars.

		Methodology
Market share TD	Biosimilar vs Reference product	TD Biosimilars as % of TD Reference products in 2015
	Biosimilar vs Accessible market	TD Biosimilars as % of TD Accessible market in 2015
	Biosimilar vs Total market	TD Biosimilars as % of TD Total market in 2015
Price per TD	Biosimilar and Reference product	Δ in Price per TD for Biosimilar Reference products 2015/the year before biosimilar entrance
	Biosimilar Accessible market	Δ in Price per TD for Biosimilar Accessible market 2015/the year before biosimilar entrance
	Total market	Δ in Price per TD for Total market 2015/the year before biosimilar entrance
Volume TD	Biosimilar and Reference product	Δ in TD for Biosimilars and Reference products 2015/the year before biosimilar entrance
	Biosimilar Accessible market	Δ in TD for Biosimilar Accessible market 2015/the year before biosimilar entrance
	Total market	Δ in TD for Total market 2015/the year before biosimilar entrance
TD per capita		No. Of Treatment Days per capita in 2015
First recorded sales		The year first sales of biosimilar were recorded

3 IMS Health 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 manufacturer to dispensing locations. IMS Health 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 (R)*	HU	IE	IT	NL*	NO	PL	PT*	RO	SK	SL	ES	SE	UK
Retail	In	In	In	In	In	In	Out	Out	Out	In	In	In	In	In	In	In	Out	In		Out	Out	Out
Hospital	C	C	In	In	In	In	C	C		In	In	C	In	In	In	C	In	In		C	In	C
Combined																			In			

4 IMS Health source and treatment 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.

Table below to show the price source reference within each EU country:

EU Geography		
Country	**Sector (Data Type)**	**Price Source**
Austria	HOSPITAL (CONSUMPTION),RETAIL (SELL-IN)	Hospital & Retail - List price - Arzneimittelverzeichnis or Taxe (Apotheker-Verlag)
Belgium	HOSPITAL (CONSUMPTION),RETAIL (SELL-IN)	Hospital - List price - Association Général de l'Industrie du Médicament (AGIM), Retail - List price - Association Pharmaceutique Belge (APB)
Bulgaria	HOSPITAL (SELL-IN),RETAIL (SELL-IN)	Hospital & Retail - Average invoiced pack price
Czech Rep.	HOSPITAL (SELL-IN),RETAIL (SELL-IN)	Hospital & Retail - Average invoiced pack price
Denmark	RETAIL (SELL-IN),HOSPITAL (SELL-IN)	Hospital & Retail - Average invoiced pack price
Finland	RETAIL (SELL-IN),HOSPITAL (SELL-IN)	List price - Wholesalers, based on official published prices of Finnish Pharmacy Association
France	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	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	RETAIL (SELL-OUT)	Retail - List price - Ministry of Development
Hungary	HOSPITAL (SELL-IN),RETAIL (SELL-IN)	Hospital & Retail - List price - National Health Fund, National Institute of Pharmacy
Ireland	HOSPITAL (SELL-IN),RETAIL (SELL-IN)	Hospital & Retail - List price - Irish prescription drug
Italy	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	HOSPITAL (SELL-IN),RETAIL (SELL-IN)	Hospital & Retail - List price - Wholesaler price list
Norway	HOSPITAL (SELL-IN),RETAIL (SELL-IN)	Hospital & Retail - Average invoiced pack price
Poland	HOSPITAL (SELL-IN),RETAIL (SELL-IN)	Hospital & Retail - Average invoiced pack price
Portugal	HOSPITAL (CONSUMPTION),RETAIL (SELL-IN)	Hospital - Average invoiced pack price, Retail - List price - Manufacturer published price list
Romania	HOSPITAL (SELL-IN),RETAIL (SELL-OUT)	Hospital - Average invoiced pack price, Retail - Canamed, average transaction price if no Canamed Price
Slovakia	HOSPITAL (SELL-IN),RETAIL (SELL-IN)	Hospital & Retail - Average invoiced pack price
Slovenia	COMBINED (SELL-IN),HOSPITAL (CONSUMPTION)	Hospital & Retail - Average invoiced pack price
Spain	HOSPITAL (CONSUMPTION), RETAIL (SELL-OUT)	Hospital & Retail - List price - Manufacturer price list, Base de Datos del Medicamento (BOT)
Sweden	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	HOSPITAL (SELL-IN),RETAIL (SELL-IN)	Hospital & Retail - List price - Wholesalers, manufacturers
UK	HOSPITAL (CONSUMPTION),RETAIL (SELL-OUT)	Hospital & Retail - List price - Chemist and Druggist, Drug Tariff

United Kingdom

IMS Health
210 Pentonville Road
London N1 9JY
United Kingdom

Global Supplier Service and Association Relations

Per Troein, VP p.troein@uk.imshealth.com
Elena Klimova, Senior Consultant eklimova@uk.imshealth.com
Neelam Patel, Consultant npatel@uk.imshealth.com
Jyoti Patel, Senior Analyst jpatel@uk.imshealth.com

About IMS Health

IMS Health 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 One™ 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, IMS Health 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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