White Paper

The Impact of Biosimilar Competition in Europe

December 2022

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Introduction

The 8th iteration of the 'Impact of Biosimilar Competition in Europe' report describes the effects on price, volume, and market share following the arrival of biosimilar competition in Europe. The report consists of observations on competitive markets, and a set of Key Performance Indicators (KPIs) to monitor the impact of biosimilars in 23 European markets. The report has been a long-standing source of information on the status of the biosimilars market.

Biosimilars are a critical part of the European healthcare system, and are able to balance spending by generating savings for payers, create headroom for innovation, and expand access to biologic therapy for patients. Since the first biosimilar was launched in 2006, biosimilar medicines have become a core component of an effective healthcare system, but headwinds are increasing with the challenges of orphan biosimilar development, and the disparity in access across Europe becoming more acute.

As the report adds new therapy areas, and as new classes emerge, we have new challenges that we must adapt to for this report to continue its relevance. This means that we continue to refine previous definitions to make them representative of the current environment, building on the 2020 (6th report) which permitted the classification historic dynamics in the market, and allows policymakers, national competent authorities, patient groups, and industry to view the market with greater granularity.

This report has been prepared by IQVIA at the request of the European Commission services with initial contributions on defining the KPIs from EFPIA, Medicines for Europe, and EuropaBio. The observations have been developed solely by IQVIA based on the data and analyses performed. The information and views set out in this report are those of its authors and are not to be attributed to, nor necessarily reflect the views of the European Commission or any of its services. The European Medicines Agency (EMA) has a central role in setting the rules for biosimilar submissions, approving applications, establishing approved indications, and monitoring adverse events, and if necessary, issuing safety warnings. We have, when appropriate, quoted their information and statements.

IQVIA gratefully acknowledges the contributions of those who have supported the development of this series over the years, notably: Aurelio Arias, Vibhu Tewary, Michael Kleinrock, Urvashi Porwal, Marco Travaglio, Kirstie Scott, and many others.

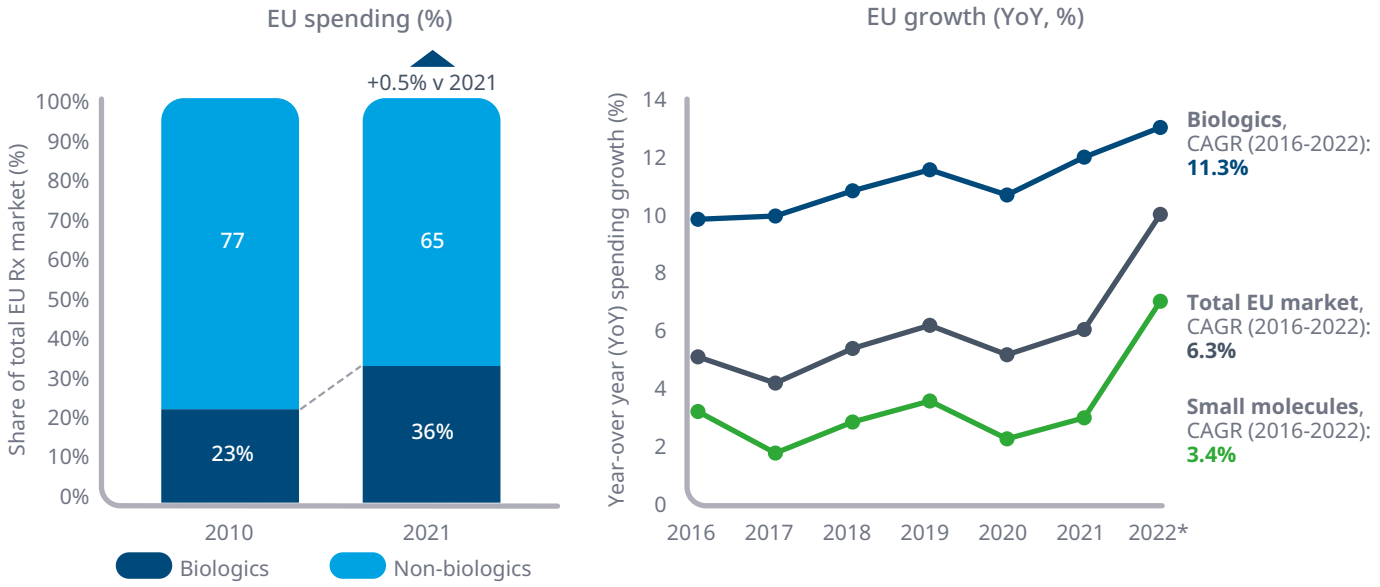
IQVIA observations
Impact of Biosimilar Competition (2022)

BACKGROUND

Biologic medicines are an increasingly important component of pharmaceutical expenditure, due to their efficacy as treatments for complex conditions. Biologics represent 35% of medicine spending in Europe at list prices and are growing at a 11.3% compound annual growth rate (CAGR) over the past five years. This compares to a 6.3% CAGR for the total market. Biologics are increasingly important and have continued to grow faster than non-biologic medicines for over a decade.

The importance of biologic medicines and the sustainability of biosimilar competition is an increasingly critical success factor for healthcare systems pre-, and post-COVID-19. Biosimilars represent €9 billion annually across Europe, but the competition they provide has far reaching benefits for patients, payers, and the healthcare system.

Exhibit 1: The importance of biologics within the European pharmaceutical market



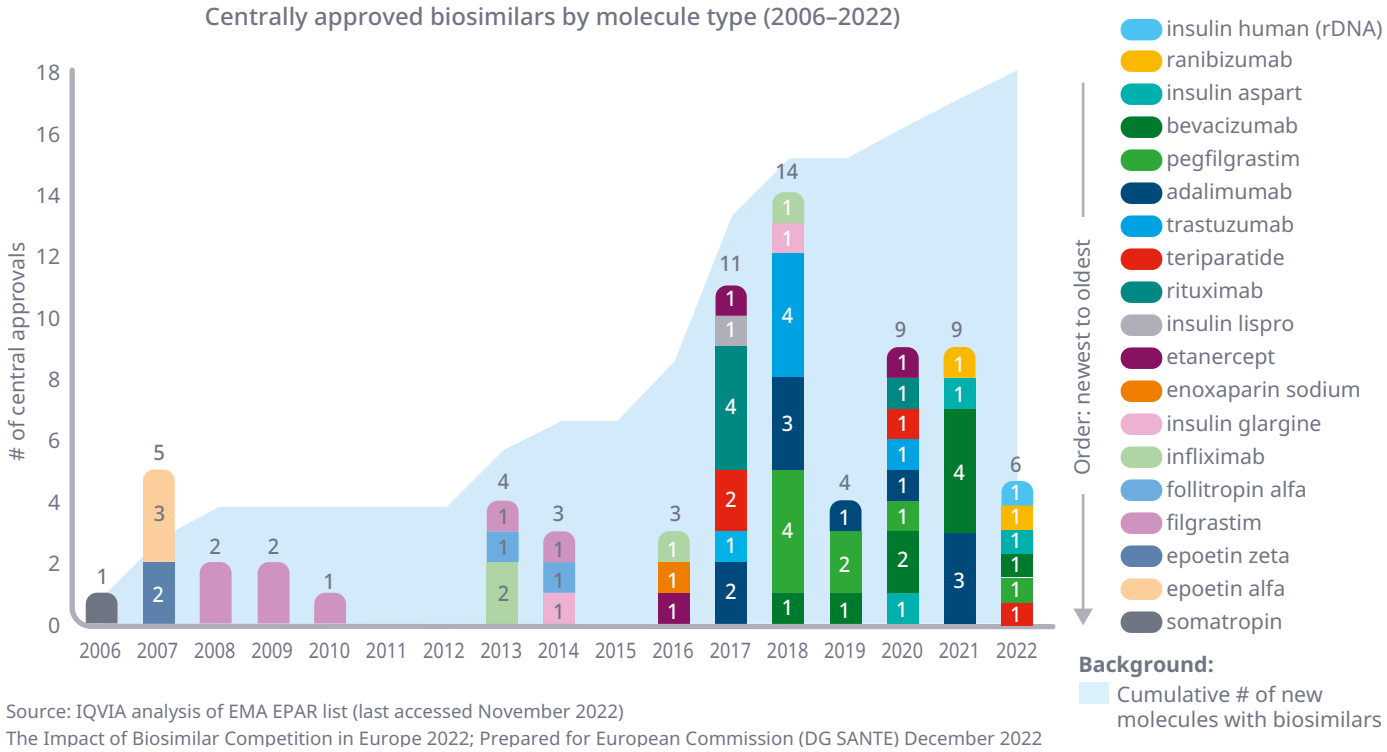
*H2 MAT 2022

Notes: Biologic market includes originator biologics and biosimilars; and EU country scope (excludes UK, Switzerland)

Source: IQVIA MIDAS (Q2 2022), Rx only; Biologic molecules exclude ATC-V (vaccines, and various)

The past 5 years have been a sign of the maturation of the biosimilars market. The number of new biologic molecules with a biosimilar doubled in the past 5 year period compared to the 10 years prior, and the number of competitors within each market has increased significantly. By 2022 a total of 18 molecules now have direct biosimilar competition and have an average of 3.8 competitors authorised, led by adalimumab which alone has 10 marketed biosimilar medicines authorised in Europe.

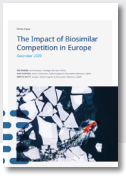
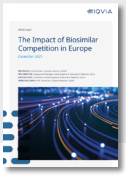
Exhibit 2: Centrally approved biosimilars and new molecules open to competition



Source: IQVIA analysis of EMA EPAR list (last accessed November 2022)
The Impact of Biosimilar Competition in Europe 2022; Prepared for European Commission (DG SANTE) December 2022

Since the creation of this series of reports, IQVIA has provided 5 observations on the market. The themes of these observations have been on savings, prices, access, strategy, and competition, which are the central tenants of biosimilar competition. Each year the aim is to provide novel insights on the market. Previous years' insights remain valid and are now referenced for posterity such as changing originator strategies (2019), the estimates of the net savings as a proportion of healthcare expenditure (2020), and the location of emerging biosimilar manufacturers (2021).

Exhibit 3: IQVIA's historic 5 observations on the biosimilar market (2015 – 2021)

2015	2016	2017	2018	2019	2020	2021
						
Competition drives down price	Competition drives down price	The entrance of biosimilars increases price competition	The entrance of biosimilars increases price competition	Biosimilar competition has a significant potential impact on overall drug spend	Biosimilar competition continues to offer opportunities to make healthcare savings	The pandemic has impacted certain segments of the biologic market
The correlation between biosimilars market share and price reduction is weak	The correlation between biosimilars market share and price reduction is weak	In some therapeutic classes, lowering the price of the referenced product can limit the market penetration of the biosimilar	Biosimilars have the potential to improve patient access of the total market	Major products see fast uptake and large price reductions	Some countries are not increasing usage despite price reductions	The savings from biosimilar competition reach an all-time high
Competition can also influence the originator's behaviours	Competition can also influence the originator's behaviours	There is a first to market advantage in biosimilar markets	In some countries, biosimilars have completely taken over	Originator manufacturers have changed strategy to stay competitive	The variation of originator response to protection expiry	Development of access to biologic medicines remains challenging
Lower prices has the most impact on usage (patient access) in countries with low initial usage	Lower prices increase patient access in countries with low initial usage	Biosimilars have the potential to improve patient access of the total market	In some therapeutic classes, lowering the price of the referenced product can limit the market penetration of the biosimilar	Access is not yet increasing for all molecules and in all countries after biosimilar introduction	Several models can work to support competitive markets	The competition environment in Europe is changing
The product profile differences in classes can explain differences in impact on the KPIs	The product profile differences in classes can explain differences in impact on the KPIs		The speed of uptake has increased for some of the more recent biosimilar launches	More is needed to create a sustainable market for biosimilar manufacturers	The real impact of biosimilar competition is just beginning	Ensuring preparedness for the future of biosimilar opportunity

Source: IQVIA/IMS Health, The Impact of Biosimilar competition in Europe (2015-2021)
The Impact of Biosimilar Competition in Europe 2022; Prepared for European Commission (DG SANTE) December 2022

In 2022 these observations focus on the European Commission's priority areas and have an increased focus on the areas of access, affordability, and competitor entry. The report continues to track the impact of COVID-19 on biologic (and biosimilar) prescribing trends and considers the challenges for all stakeholders to be ensuring the continued success of the market for future biologic loss of exclusivity (LOE) events.

The observations are as follows:

1. **COVID-19:** Biologic prescribing has rebounded, but macroeconomic challenges loom
2. **Savings:** The savings from biosimilar competition reach an all-time high
3. **Access:** Access is improving but a growing disparity is occurring across countries
4. **Competition:** Not all originators will see competition
5. **Future:** LOE will triple in the next 5 years versus the previous 5

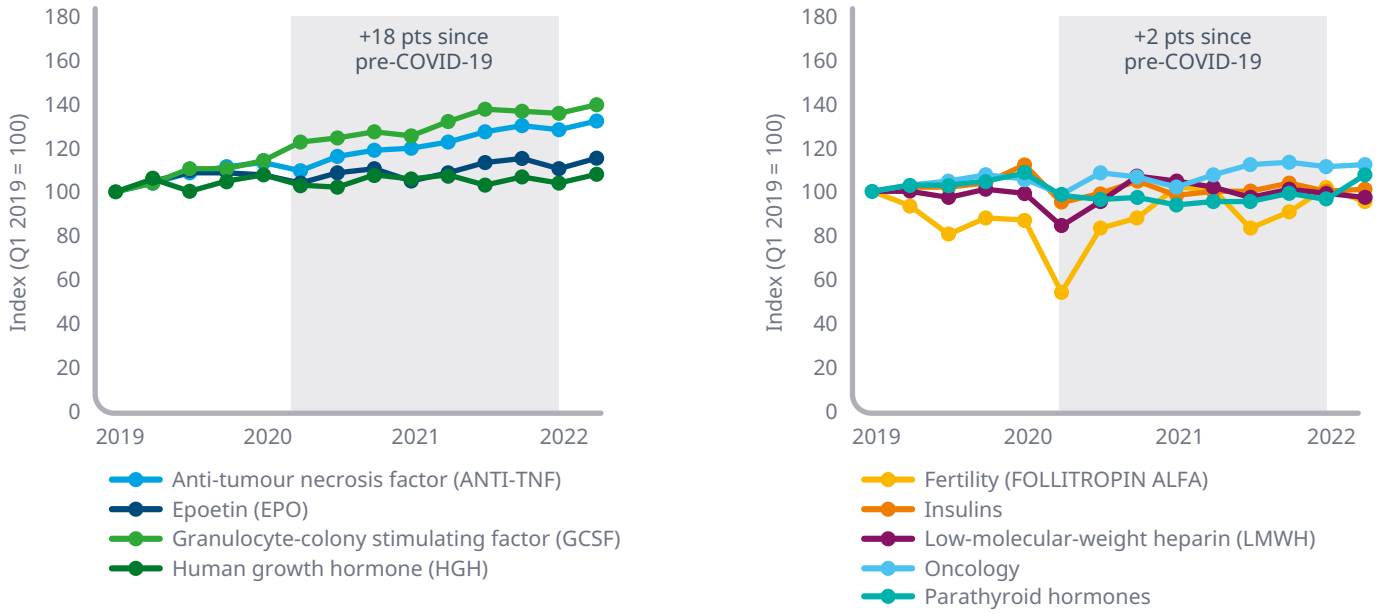
OBSERVATION 1: COVID-19

1.1 Biologic prescribing has rebounded since the pandemic

COVID-19 had a market effect on patients, populations, and healthcare systems. Access to healthcare professionals was restricted, and prescribing habits changed to as the priority of hospital care changed to support those affected by COVID-19. There was debate in the academic literature of the potential risks of biologic treatment during the pandemic, with new guidelines being provided at the beginning of the pandemic, and unexpected beneficial effects of anti-TNF agents for COVID-19 protection and treatment[i].

Initiation of new patients onto biologic therapy has been challenged in many countries. For example, in France biologic initiations were greatly reduced during the lockdown for anti-TNFs[ii], and were observed where the pandemic was more pronounced. Psoriasis patients in Italy being prescribed biologic therapies for immunomodulation faced variable advice to stop treatment or faced difficulties in obtaining supplies of their medicines due to the lockdown[iii].

Exhibit 4: Impact of COVID-19 pandemic on therapy classes open to biosimilar competition



Source: IQVIA MIDAS June 2022 MAT
Notes: Ophthalmology therapy area excluded due to the impact of new product entries within the class skewing the index

Assessing the total European market by therapy class, the analysis shows that the majority of treatment classes within this report have rebounded to above their pre-COVID-19 prescribing levels (anti-TNFs, EPO, GCSF, and HGH). This has not occurred equally, with noticeable drops in most therapy classes at the start of the pandemic, and noticeable increases as secondary uses for biologic therapies were tested. Fertility treatments faced a significant decline as the ability to access non-urgent care decline and risk of COVID-19 and pregnancy was considered.

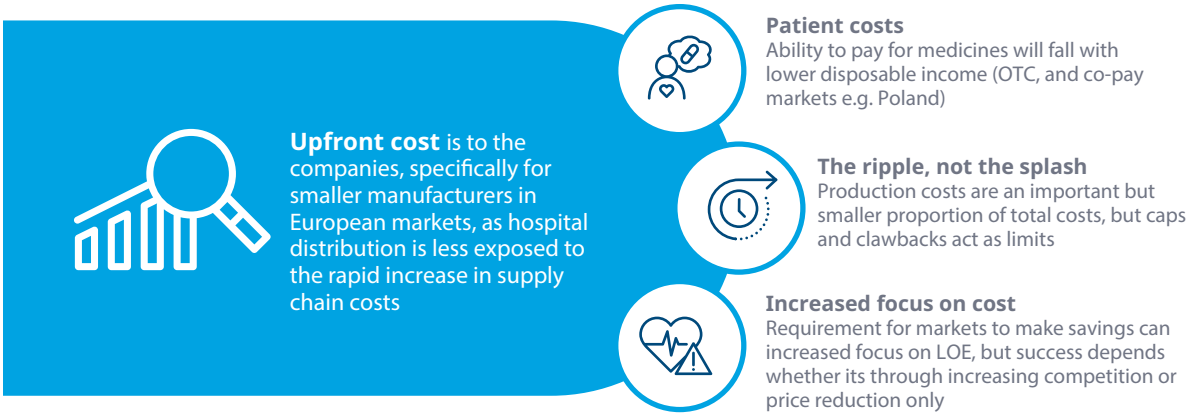
1.2. COVID-19 led to macroeconomic pressures that impact healthcare systems

It remains to be seen how the population and healthcare systems can combat COVID-19 pandemic during the 2022–2023 winter, but the pandemic has had a broader impact on patients, payers, and industry.

On top of this, inflation in the Eurozone reached 10% in November 2022[iv] (down from 10.6% in October) primarily driven by energy prices, as a result of the war in Ukraine. The secondary driver of this was the fragility of global supply chains, which caused an impact on consumer goods. While economists suggest this energy crisis will not be a long-term, the impact of inflation affects all stakeholders as prices remain high.

From a patient's perspective, countries where patients pay for their biologic treatments out of pocket or with co-pay (e.g. Poland) will find it increasingly difficult to afford their medications, smaller manufacturers of biosimilars record increases in the cost of packaging and distribution of medicines[v], and payers will have an increased need to make the savings to reduce the long-term impact that the COVID-19 pandemic had on healthcare systems. In markets with visible net prices (e.g. Sweden), the expectation does not always meet the reality; prices for medicines continue to fall, although the full effect remains to be seen.

Exhibit 5: Broader impact on healthcare systems, and the impact of inflation on biologic Rx



Source: IQVIA perspectives, [1] Medicines for Europe Open letter: https://www.medicinesforeurope.com/wp-content/uploads/2022/06/EPSCO-Council-_-Medicines-for-Europe-Executive-Committee-OPEN-letter-on-inflation-impacting-the-supply-of-essential-medicines.pdf

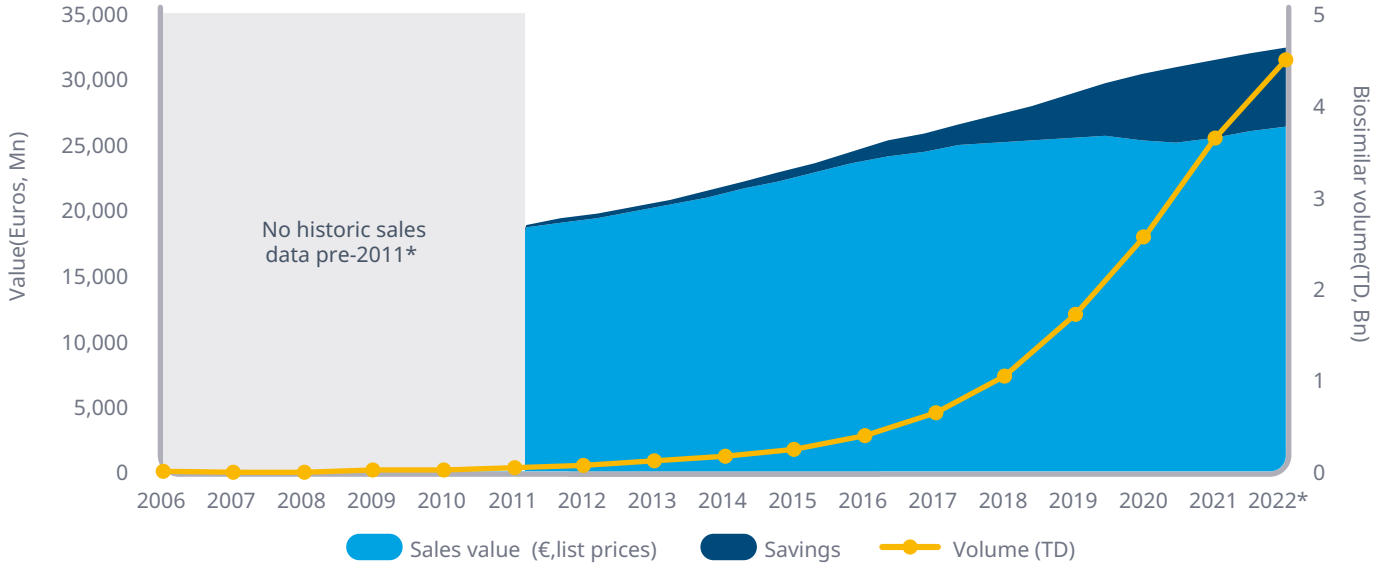
OBSERVATION 2: SAVINGS

2.1 Savings from the impact of biosimilar competition continues to grow

Using the 'pre-biosimilar' prices, it is possible to calculate the list price savings that are generated on 'post-biosimilar' volume. Biosimilars provided nearly 4.5 billion patient treatment days to European patients and continue to grow year-on-year. In the past year, 850 million patient treatment days were attributed to biosimilar therapies, up from 750 million in 2021. However, the true cost of biologic therapy (originator or biosimilar) is commercially sensitive, but list prices across Europe act as a base-case to estimate savings generated in European markets. In 2012, estimates suggested savings could be in the range of €12–€34 billion by 2020[vi]. As of 2022, the cumulative savings at list prices from the impact of biosimilar competition in Europe reached over €30 billion.

A number of different mechanisms can be used to stimulate savings. Savings from a reduction in list prices occurs automatically in many markets, others regulate price reductions, and market forces create price differentials, and a mix of biosimilar policies and levers. The model suggests that Germany saved €3.6 billion in savings since 2015 on anti-TNFs[vii].

Exhibit 6: Savings from the impact of biosimilar competition at list prices



Caveats: This figure is not equivalent to all savings. And is therefore an under-estimate. The data does not include the impact of rebates or discounts, which may have been present prior to the introduction of biosimilars in small quantities, and are highly significant post-biosimilar entry as it is based on publicly available list prices.. Source: IQVIA MIDAS™ data from 2006 – 2022, using Euros at constant exchange rates; value includes all originator products with approved biosimilars from 2006 – 2022, covering the full European Economic Area (33 CTYs), calculated volume is in treatment days determined by WHO-DDD, and where values are unavailable via Oncology Dynamics Physician Survey (2017) DDD estimates. Volume is solely biosimilar treatment days

Source: IQVIA MIDAS June 2022 MAT

2.2 Savings are a function of multiple components: rebates, usage, uptake, policies, and progress

Biosimilar uptake has increased markedly with new newer biologics that have lost exclusivity. In Europe, the average uptake rate in the first-year post-biosimilar entry has increased from between 5–40% for up to nearly 75% for bevacizumab biosimilars. This reflects an increasing comfort with biosimilar prescribing amongst physicians, and improvements in biosimilar policies.

However, not all areas see equivalent biosimilar uptake, and therefore are not equivalent contributors to the total savings calculations. The retail market for biologics sees significantly lower penetration of biosimilar medicines, lower list prices change, and a greater challenge to generating savings through the retail channel. Ireland and some Nordic markets employ a methodology to permit retail dispensing of hospital funded medicines (via High-Tech Drug Scheme and equivalents) to navigate this. Competition between manufacturers before biosimilar entry (in classes like Insulins, LMWHs, and HGH) mean that biosimilar uptake is lower due to the already competitive nature of the market and the lower opportunity for biosimilar manufacturers.

From a payer's perspective, savings are one, if not the, greatest benefit of biosimilar competition. To improve upon this, healthcare systems must consider: 1. the usage of the originator molecule which acts as a cap for the savings that can be achieved without increased treatment, 2. biosimilar competition which is a precursor for uptake, and 3. creating a robust set of policies that support a competitive, and sustainable market for biosimilar competition. Each country is Europe has a unique profile of policies related to biosimilars which can be improved upon to support savings, access, and create headroom for innovation.

[3] IQVIA, The Impact of Biosimilar Competition in Europe reports (2019, page 5; 2020, page 3)

Exhibit 7: Selected KPIs to illustrate volume share, price evolution, and volume evolution in selected European countries

	HOSPITAL									MIXED	INSULINS	
	infliximab	etanercept	rituximab	rituximab IV	trastuzumab	trastuzumab IV	pegfilgrastim	bevacizumab	teriparatide	adalimumab	Insulin Glargine	Insulin Lispro
Germany	83%	80%	86%	93%	83%	94%	56%	93%	45%	74%	16%	6%
France	84%	50%	75%	97%	45%	98%	79%	99%	53%	41%	28%	0%
Italy	95%	78%	88%	99%	79%	99%	85%	92%	71%	80%	15%	11%
Spain	82%	53%	73%	96%	69%	95%	87%	78%	60%	63%	18%	0%
Netherlands	90%	44%	97%	99%	84%	100%	95%	94%	68%	66%	34%	16%
Denmark	99%	93%	86%	100%	95%	99%	100%	99%	17%	97%	29%	0%
Finland	98%	50%	93%	100%	54%	100%	66%	90%	16%	58%	4%	44%
Norway	99%	94%	94%	199%	92%	100%	98%	91%	75%	92%	22%	5%
Poland	100%	68%	99%	99%	38%	100%	100%	96%	0%	99%	28%	27%

High uptake — Low uptake

Source: IQVIA MIDAS MTH June 2022

Net prices are confidential for competative reasons. The rebates can be published (or leaked) in certain cases, and these offer a further a large component of the savings available from biosimilar manufacturers, and increasingly from origionator manufacturers too beyond the list price reductions seen upon competitor entry. Previous estimates from IQVIA suggest that the overall cost reduction impact of rebates from biologics with biosimilar competition can be between 2%–8% of the total drug budget. Rebates vary and can be up to 90% of the list price, although this varies by class, product, original price level, and country.

OBSERVATION 3: ACCESS

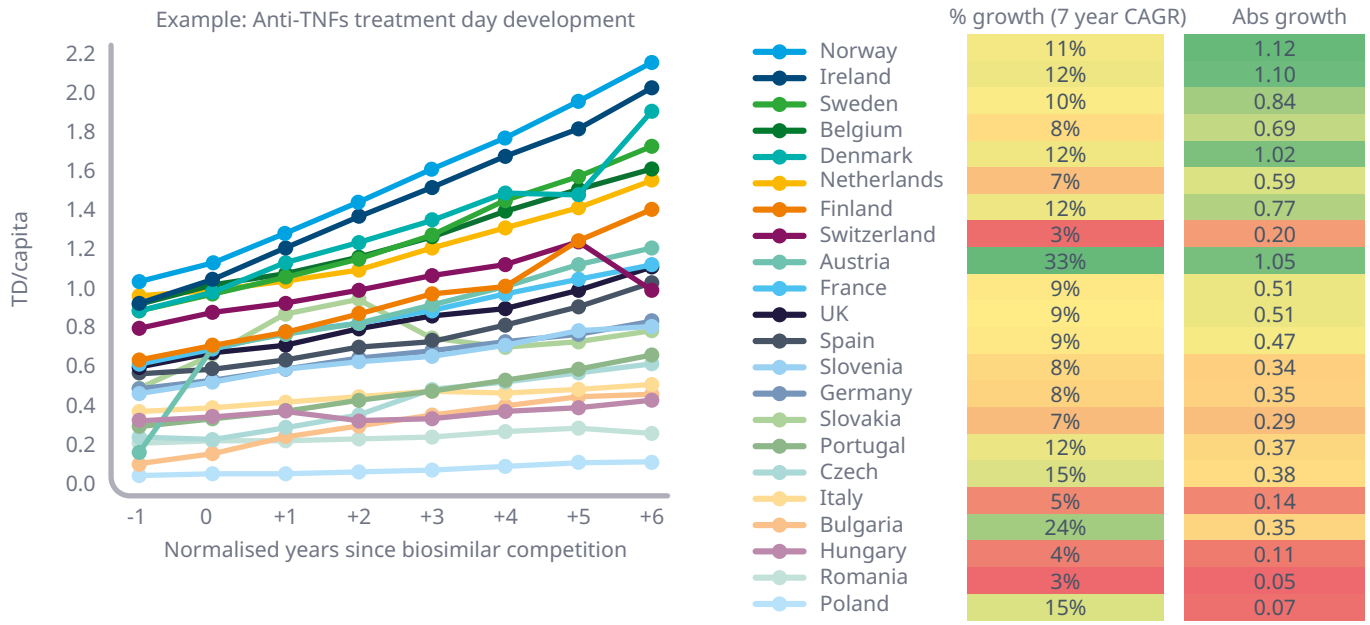
3.1 Access is increasing in all countries signalling progress

Biosimilar uptake remains a useful, but overall, limited performance metric to access the full benefits to payers and patients of biosimilar competition. With changing approaches from originator manufacturers who now compete directly on price and can provide lower prices than biosimilar manufacturers in some tenders, focussing on uptake remains one part of a country's toolkit to generate savings.

Using anti-TNF class as an example, prescribing of anti-TNF molecules has increased an average of 11% across Europe (~0.5 treatment days per capita) since the entry of biosimilars. Higher growth rates (7-year CAGR) are seen in countries that start from a lower base level of prescribing, but noticeably the absolute growth is significantly lower than those in the high usage countries pre-biosimilar competition often with only a nominal difference in the treatment days per capita prescribed (e.g., Poland +0.07).

[4] IQVIA Institute, Spotlight on biosimilars: Optimising the Sustainability of Healthcare Systems, published June 2021

Exhibit 8: Development of Anti-TNF class usage across European markets



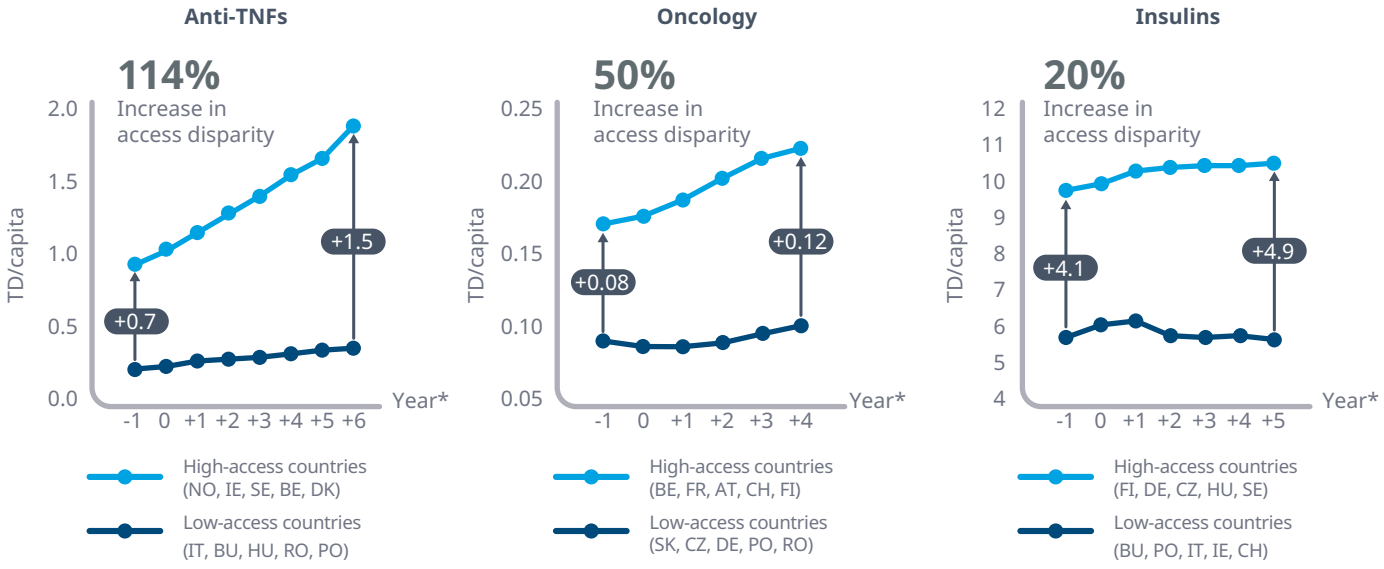
Notes: Calculation is based on the normalized year before biosimilar entry for each molecule in the anti-TNF class, and the treatment days before and since the LOE date in Europe

Source: IQVIA MIDAS June 2022 MAT

3.2 The disparity in access across Europe is expanding

Access to medicines is a critical priority for all stakeholders. However, the ability for countries to capitalise of the promise of biosimilar competition has not occurred evenly, and not all have had an equivalent starting point. In addition, the different approaches have been documented routinely, but the delta between the highest and lowest prescribing countries has grown, highlighted by the anti-TNF, oncology, and insulin classes.

Exhibit 9: A growing delta between high access and low access markets in Europe



*Normalised to the year of first recorded biosimilar sales in each country, to account for markets that are delayed in using biosimilars after loss of patent protection

Chart notes: Includes TD for all market segments (Non-accessible, Non-referenced, Referenced, Biosimilars); All countries are ranked based on TD/Capita at +6 years and the top-5 and bottom-5 countries includes in this analysis.

Source: IQVIA MIDAS June 2022 MAT.

OBSERVATION 4: COMPETITOR ENTRY

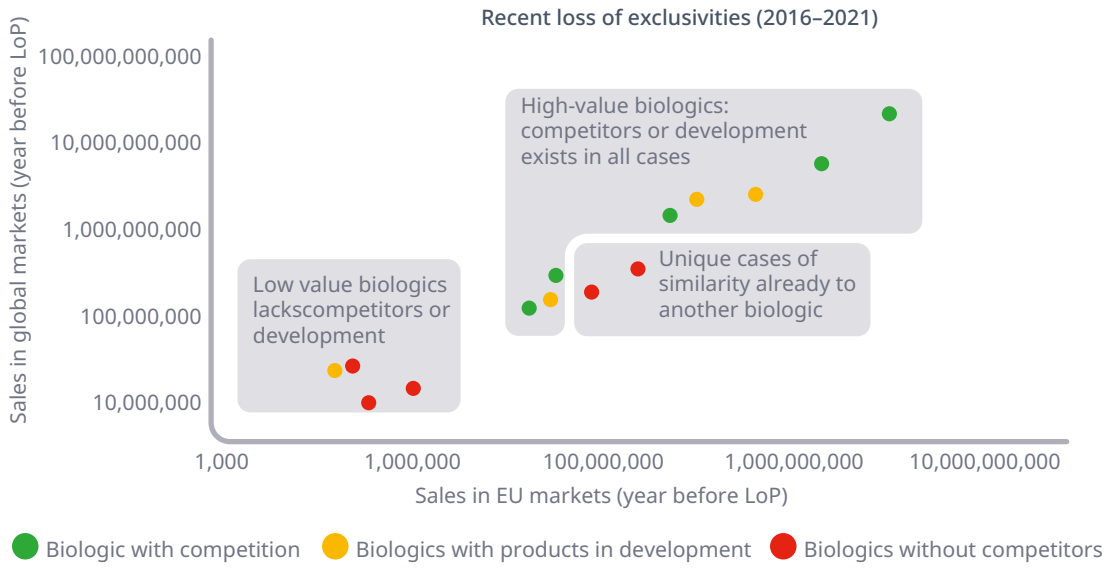
4.1 Recent biologics have received biosimilar competition

Biologic molecules are unlike traditional generics in the requirement for clinical equivalence studies, the cost of development, and the cost for comparators during trials. The increased cost of development means that not all molecules are currently suitable targets for the development the multiple biosimilars that are required to create a competitive market.

This analysis includes all biologic medicines that have lost exclusivity in the past 5 years, their global sales (as an indicator of overall attractiveness), and their European sales for context. All high value biologics which were valued at above €100 million in their year before loss of exclusivity either have biosimilars or have biosimilars in development.

There are lower value medicines, often those that treat rare conditions, that have limited sales value and would not support multiple competitors effectively in the current framework. These medicines are mostly recombinant hormones or recombinant enzymes that have very limited revenue or are highly complex to manufacture, especially in the U.S. which has significant weight in investment decisions globally. In addition, some biologics in this analysis are defined as 'very similar' or 'very slightly different'[viii] by the EMA to other biologics and are therefore unlikely to warrant their own unique biosimilar.

Exhibit 10: Status of competitor entry for recent biologic LOEs (2016 – 2021)

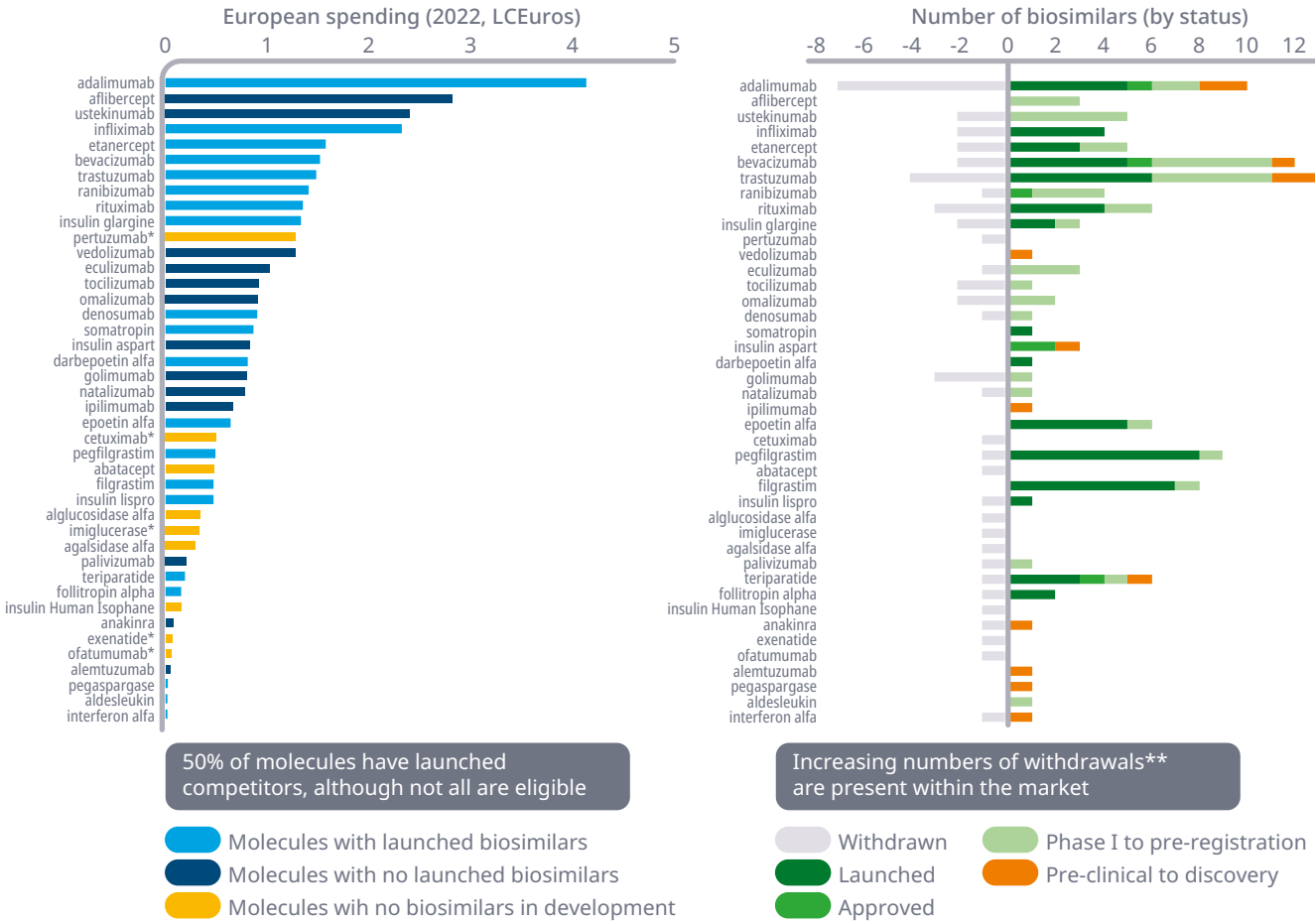


Source: IQVIA Institute, Protection Expiry and Journey into the Market: Pharmaceutical products in Europe (September 2022)
https://www.iqvia.com/insights/the-iqvia-institute/reports/protection-expiry-and-journey-into-the-market

4.2 High numbers of biosimilars are withdrawn or have development discontinued

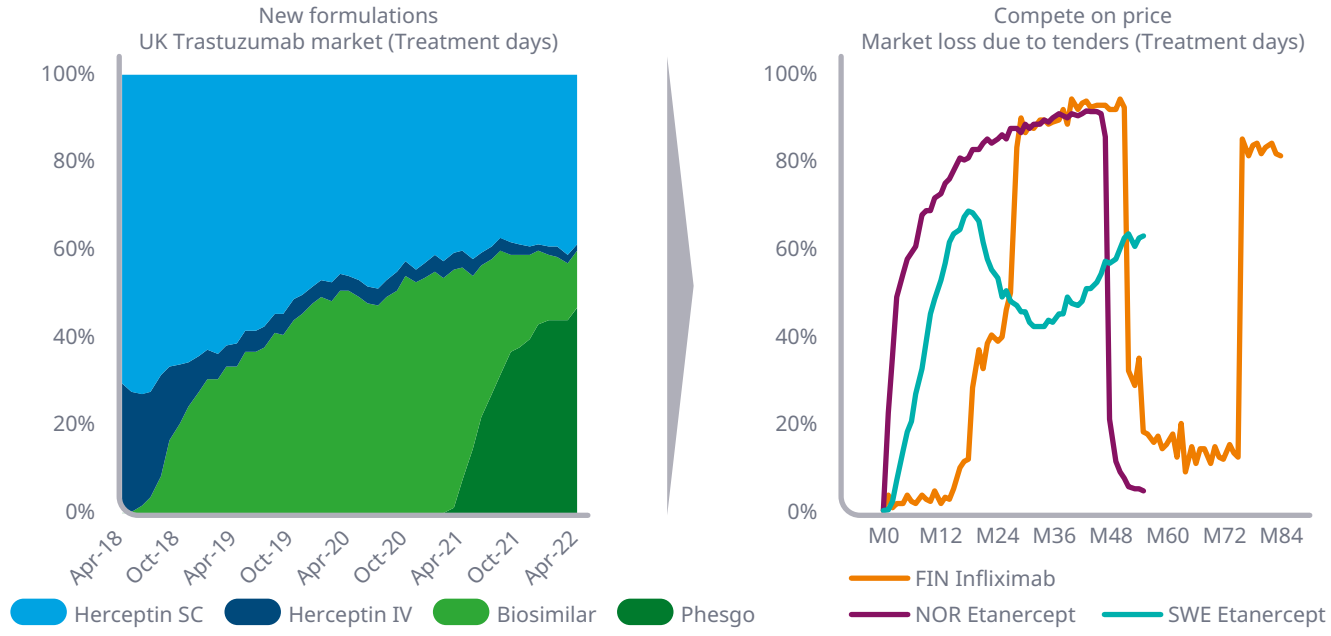
The top biologics by spend in Europe already have biosimilars or a development pipeline. The largest biologic molecules by spend are valued at ~€36 billion in 2022 alone. A number of these biologics are not yet eligible for competition due to their protection status, and others have had competition for many years. Competition within the biosimilar market is increasingly fierce, with multiple competitors entering for the larger molecules. Adalimumab alone has had 17 potential competitors, while a significant number were either withdrawn from the market or discontinued by their developers. The number of withdrawals / discontinuations signals an emerging saturation for some molecules.

Exhibit 11: Competitor status for top biologic molecules and pipeline



Source: June MAT 2022 data, IQVIA analysis (November 2022), source: IQVIA Institute, The Global Use of Medicines 2022, Outlook to 2026.
Notes: * Molecules for which no biosimilar development has been reported in last 3 years; **Withdrawals = pipeline withdrawals or discontinuations

Exhibit 12: Examples of strategies for biosimilar defence



Source: IQVIA EMEA Thought Leadership analysis (March 2022)

4.3 Biosimilar market share is not a given

Biosimilars share the market with originators in an approach that creates strong savings for the healthcare system. Novel routes of administration provide an additional layer of protection from biosimilar entry as well as providing healthcare systems with different approaches to patient care often at the end of the originator life cycle. Biosimilar manufacturers are therefore entering into an increasingly competitive and uncertain market, where in rare cases the market share is not guaranteed or requires resilience until tenders are relaunched. Considering the sub-optimal procurement processes[ix] in some European markets where multiple winners are not supported, the commercial incentive is considered by many to be increasingly unattractive.

OBSERVATION 5: FUTURE FORECAST

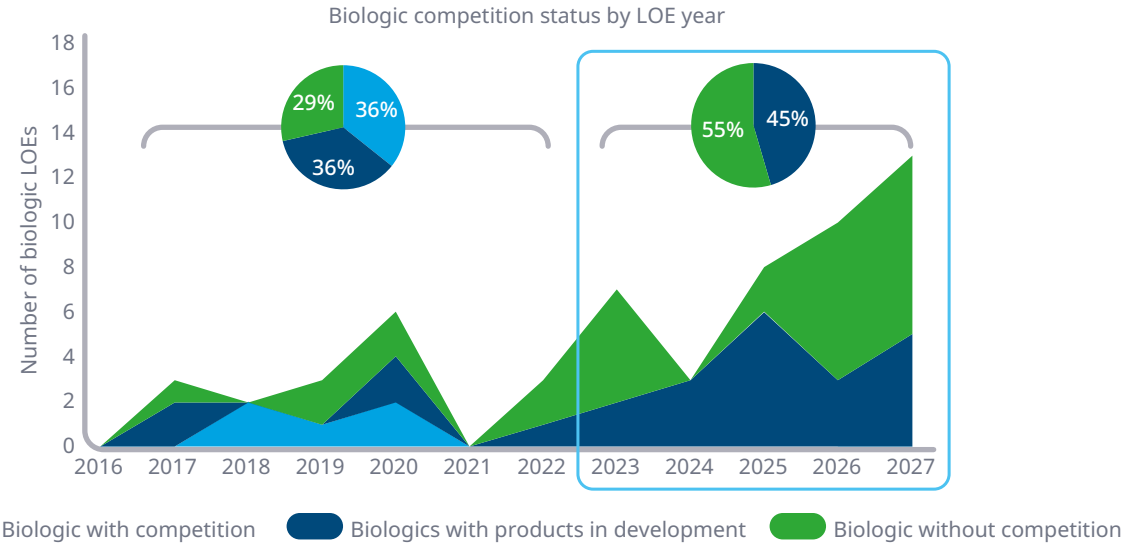
5.1 The future opportunity for biosimilars remains high

The major molecules (by value) have been impacted by biosimilar competition, with the historic assessment showing two out of 3 historic biologics received biosimilar competition. In the next 5 years, a greater number of biologics will be losing protection than historically (+30), and a greater number of biologics molecules have a competitor in development than in the previous 5 year period (+14). However, not all future biologics will have the capacity of biosimilar competition.

Previous analyses have shown that an increasing proportion of biologics losing exclusivity will be orphan medicines[x], although for healthcare systems there are still multiple high value biologics losing exclusivity 2025 which constitute a significant proportion of spending, and biologics with competitors' development are already present for products losing exclusivity in 2027.

Highly specific forecasts have importance, but countries looking to prepare for future biologic exclusivities can learn from the approach used in Denmark by AMGROS to horizon scan for future opportunities[xi]. This involves focussing on biosimilar medicines currently under review by the EMA as a proxy for upcoming launches (see appendix, table 2).

Exhibit 13: Forecast number molecules losing exclusivity in Europe and respective pipeline



Source: IQVIA Patent Intelligence, Pipeline Intelligence, and IQVIA Forecast Link analysis (November 2022); Historic analysis sourced from IQVIA Institute report, Protection expiry and Journey into the Market (2022)

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

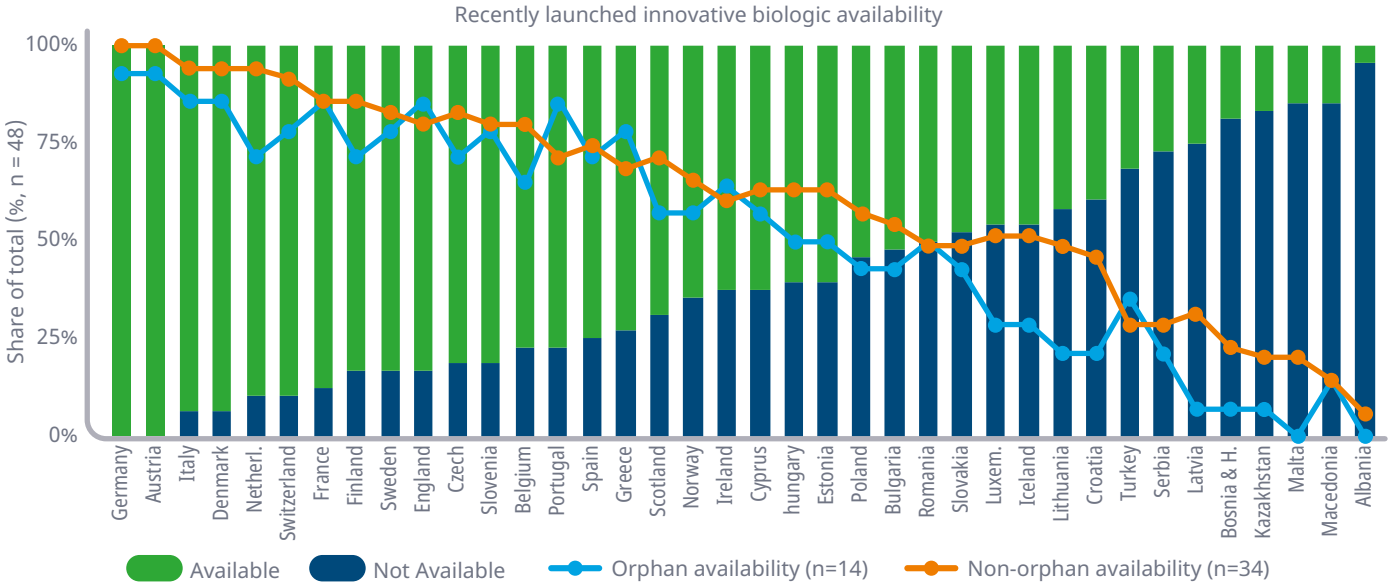
5.2 Access to novel biologic therapies provide the furthest forecast for the market

The current cohort of novel biologic medicines indicates the challenges faced by biosimilars and healthcare systems beyond the forecast dates for loss of exclusivity. This analysis is based on the public reimbursement status for new active substances authorised in Europe between 2014 – 2020, which therefore can be expected to maintain protection to beyond 2027.

The availability of these medicines on the public reimbursement list of European countries highlights the low proportion of these medicines that are currently available to patients. Biosimilar success requires the originator to be present in a market, to be reimbursed, and to have gathered clinical experience, and additional data. Countries that ether cannot afford the originator appear to be missing out or at risk from not benefitting from the biosimilar.

The sustainability of the market is a delicate balance of supporting competition, accumulating long-term savings, and preparing for the next wave.

Exhibit 14: Beyond the forecast using recently approved innovative biologics



Source: Based on IQVIA W.A.I.T dataset and IQVIA HTA-Accelerator datasets covering novel active substances (NAS) molecules launched within 2014 – 2020 (November 2022 analysis), including all current EU members, EEA members, and countries considering ascension. Reimbursement defined by availability on a public reimbursement list in a country. Orphan medicines defined by EMA EPAR list (last accessed 2022)

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Methodology

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

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

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

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

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

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

Other definitions found within the report include:

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

- **Price indicators**
  Price: the price level used is gross ex-manufacturer price (list price), which values the product at the level that the manufacturer sells out, without considering rebates or discounts. Price evolution: price per Treatment Day (TD) in 2022 (June MAT) versus year before biosimilar entry.

- **Volume indicators**

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

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

  Volume evolution: number of Treatment Days in 2022 (June MAT) versus year before biosimilar entry.

  Volume per capita 2022 (June MAT): number of Treatment Days consumed in 2022 (June MAT) normalised by population size (World Bank data).

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

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

TOTAL MARKET Products within the same ATC code	**ACCESSIBLE MARKET**	**Referenced Medicinal Product:** Original product, granted market exclusivity at the start of its life, exclusivity has now expired, and the product has been categorised as referenced by having a biosimilar with an EMA-approved marketing authorisation available on a European market.	
		Non-Referenced Medicinal Product: Original, or second generation 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 by a biosimilar receiving centrally-approved marketing authorisation.	
		Biosimilar Medicinal Product: Product, granted regulatory approval, demonstrating similarity to the Reference Medicinal Product in terms of quality characteristics, biological activity, safety and efficacy.	
	NON-ACCESSIBLE MARKET	**Non-accessible category:** Products within the same ATC4 code as the accessible category products. These are typically second-generation products; this category may include products with different dosing schedules and / or route of administration to those in the accessible category, and have valid protection status.	

Country and therapy area KPIs

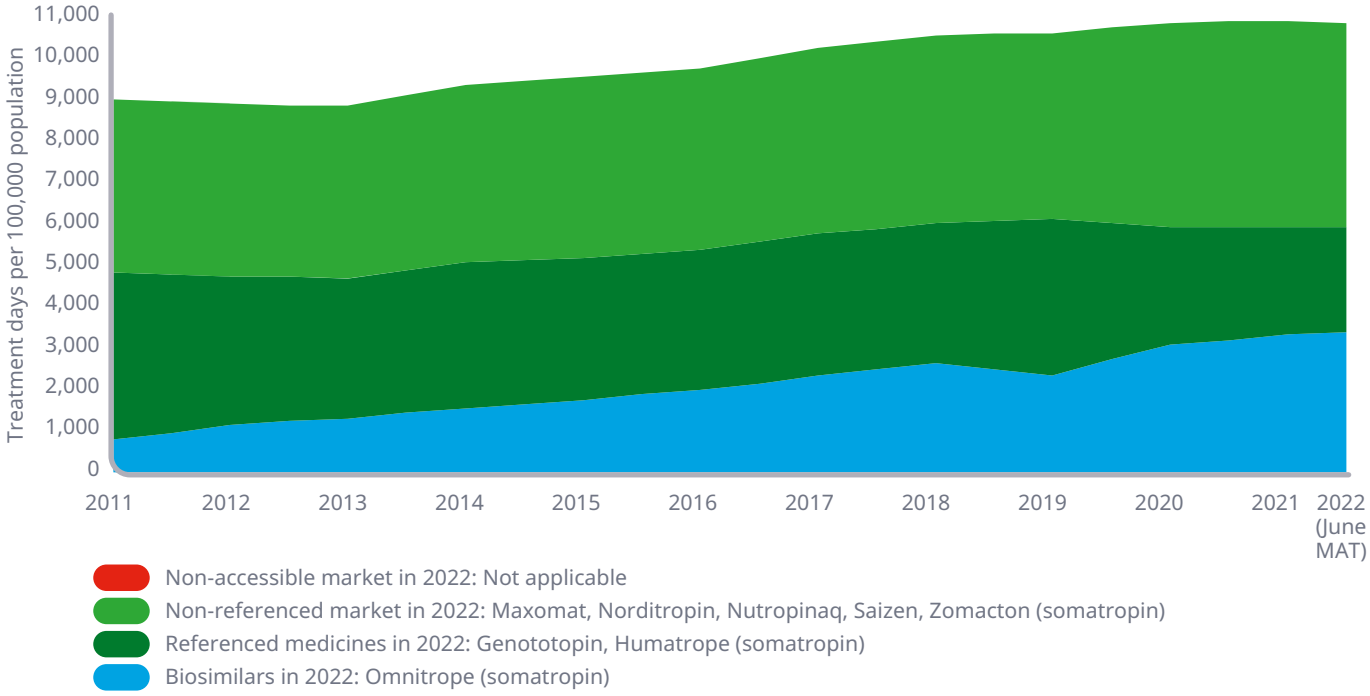
Human growth hormone (HGH)

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

HGH MARKET DEVELOPMENT

According to IQVIA MIDAS and ARK Patent Intelligence insights protection has expired for Humatrope (somatropin). The figure below reflects the existence of 2nd-generation products that are not classified as biosimilars, nor have protection status, and as such are not able to be classified within the 'referenced medicines' category. Products for mescasermin (another molecule within the same ATC4 class, [H4C0]) have been excluded from the analysis because despite being a competing product in the growth hormone area, this molecule works further down the response pathway from somatropin. Therefore, from a medical practice setting, they are different.

HGH market development



ADDITIONAL INFORMATION ABOUT HGH MEDICINES

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

HGH approved indications

NAMING		CLASSIFICATION												INDICATIONS								
MOLECULE	PRODUCT	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022 (JUNE MAT)	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	NOONAN SYNDROME
SOMATROPIN	GENOTROPIN HUMATROPE* OMNITROPE NORDITROPIN NUTROPINAQ SAIZEN ZOMACTON	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●

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

* Note: The biosimilar for Humatrope (Valtropin) has been withdrawn from the market, however Humatrope is still categorized as a referenced medicine.

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

		AT	BE	BU	CZ	DK	FI	FR	DE	GR*	HU	IE	IT	NL	NO	PL	PT	RO	SK	SL	ES	SE	CH	UK	EU
MARKET SHARE TD (2022, JUNE MAT)	Biosimilar vs Referenced product	36%	35%	52%	21%	99%	63%	48%	53%	0%	31%	0%	0.47	0.61	0.08	0.99	0.55	0.69	0.00	0.19	0.44	0.59	0.39	0.66	0.56
	Biosimilar vs Accessible market	11%	23%	52%	8%	61%	14%	18%	26%	0%	13%	0%	0.25	0.46	0.00	0.99	0.33	0.50	0.00	0.10	0.28	0.41	0.07	0.34	0.32
	Biosimilar vs Total market	11%	23%	52%	8%	61%	14%	18%	26%	0%	13%	0%	0.25	0.46	0.00	0.99	0.33	0.50	0.00	0.10	0.28	0.41	0.07	0.34	0.32
PRICE PER TD (2022 JUNE MAT/YR BEFORE BS ENTRY)	Biosimilar and Referenced product	-22%	-37%	-22%	-30%	-21%	-42%	-31%	-10%	-9%	-10%	-22%	-0.33	-0.62	-0.28	-0.54	-0.53	-0.33	-0.30	-0.38	-0.28	-0.49	-0.44	-0.47	-0.37
	Biosimilar accessible market	-17%	-38%	-22%	-35%	-23%	-47%	-29%	-5%	-9%	-6%	-22%	-0.32	-0.61	-0.22	-0.55	-0.44	-0.46	-0.20	-0.40	-0.28	-0.48	-0.39	-0.28	-0.32
	Total market	-17%	-38%	-22%	-35%	-23%	-47%	-29%	-5%	-9%	-6%	-22%	-0.32	-0.61	-0.22	-0.55	-0.44	-0.46	-0.20	-0.40	-0.28	-0.48	-0.39	-0.28	-0.32
VOLUME TD (2022, JUNE MAT/YR BEFORE BS ENTRY)	Biosimilar and Referenced product	21%	51%	71%	112%	95%	10%	17%	11%	-62%	-15%	66%	92%	109%	-85%	169%	61%	293%	30%	78%	90%	-17%	-22%	80%	61%
	Biosimilar accessible market	121%	33%	68%	110%	1%	104%	63%	35%	-62%	20%	94%	67%	51%	32%	168%	11%	100%	26%	64%	94%	-19%	50%	126%	63%
	Total market	121%	33%	68%	110%	1%	104%	63%	35%	-62%	20%	94%	67%	51%	32%	168%	11%	100%	26%	64%	94%	-19%	50%	126%	63%
	TD per capita	0.08	0.12	0.04	0.16	0.15	0.12	0.16	0.07	0.00	0.06	0.08	0.11	0.13	0.17	0.11	0.05	0.05	0.08	0.09	0.18	0.12	0.09	0.08	0.11
	TD/capita (Yr before BS entrance)	0.03	0.09	0.02	0.08	0.14	0.06	0.10	0.05	0.00	0.05	0.04	0.06	0.08	0.13	0.04	0.04	0.02	0.06	0.06	0.09	0.14	0.06	0.04	0.07
	First recorded sales of biosimilars	2008	2009	2012	2010	2011	2008	2007	2006	2015	2012	2006	2007	2008	2011	2008	2014	2008	2013	2010	2007	2007	2010	2007	2006

* Only retail panel data is available for Greece

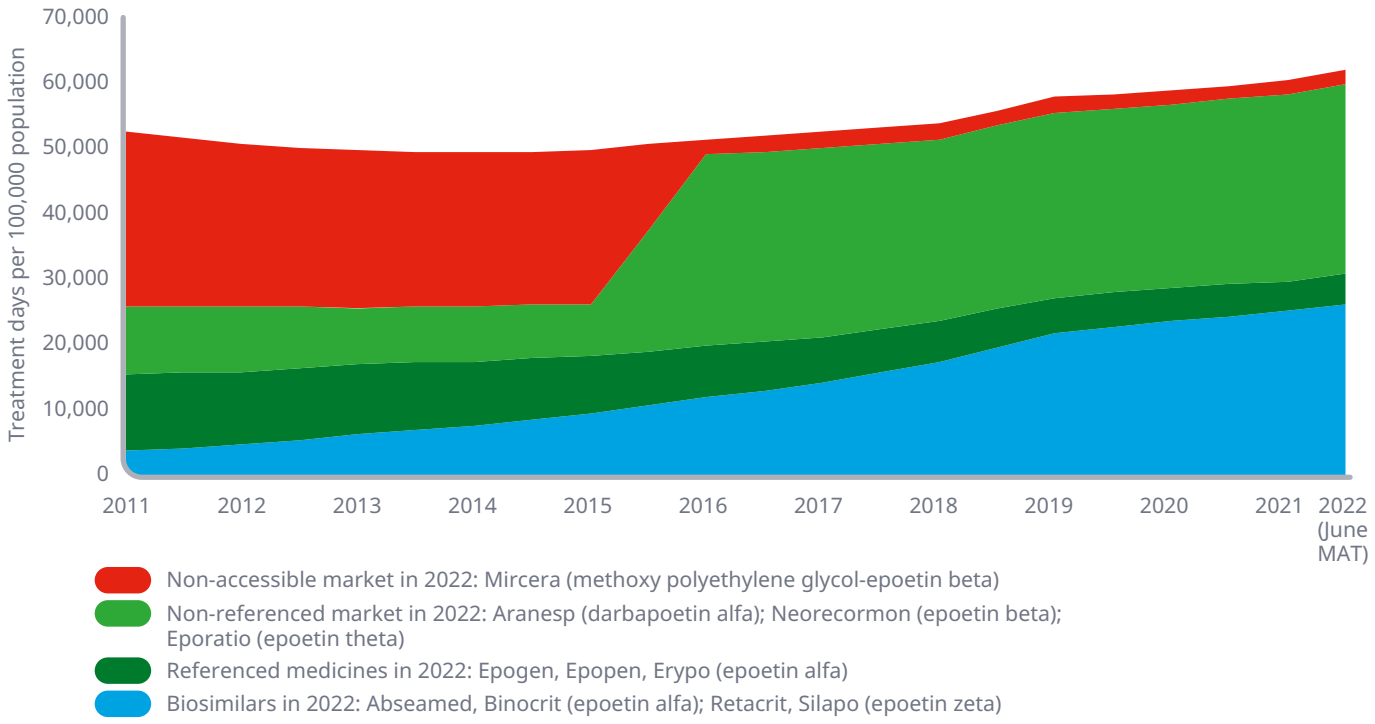
Epoetin (EPO)

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

EPO MARKET DEVELOPMENT

According to IQVIA MIDAS and ARK Patent Intelligence insights protection expired for a significant molecule in this class, Aranesp (darbepoetin alfa). The figure below reflects this shift from the molecule from a non-accessible product, to one that is now open to biosimilar competition but is yet to be referenced.

EPO market development



EPO approved indications

NAMING		CLASSIFICATION												INDICATIONS					DOSING/ADMINISTRATION	
MOLECULE	PRODUCT	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022 (JUNE MAT)	ANEMIA FOR CHEMOTHERAPY PATIENTS	ANEMIA FOR PATIENTS WITH CKD*	PREVENTING ANEMIA IN PREMATURE BABIES	ANEMIA IN ADULTS WITH MDS	REDUCTION OF ALLOGENIC TRANSFUSION EXPOSURE IN ORTHAPEDIC SURGERY	PATIENT TYPE** (ADULT OR PEDIATRIC)	FREQUENCY
DARBEPOETIN ALFA	ARANESP	●	●	●	●	●	●	●	●	●	●	●	●	●	●			●	Both	Weekly
EPOETIN ALFA	ABSEAMED BINOCRIT EPOGEN EPOPEN ERYPO	● ● ● ● ●	● ● ● ● ●	● ● ● ● ●	● ● ● ● ●	● ● ● ● ●	● ● ● ● ●	● ● ● ● ●	● ● ● ● ●	● ● ● ● ●	● ● ● ● ●	● ● ● ● ●	● ● ● ● ●	● ● ● ● ●	● ● ● ● ●		● ● ● ● ●	● ● ● ● ●	Both	3 x per week
EPOETIN BETA	NEORECORMON	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	Both	3 x per week
EPOETIN DELTA	DYNEPO***	●	●	●	●									●	●	●			Both	3 x per week
EPOETIN THETA	EPORATIO	●	●	●	●	●	●	●	●	●	●	●	●	●	●				Adult	3 x per week
EPOETIN ZETA	RETACRIT SILAPO	● ●	● ●	● ●	● ●	● ●	● ●	● ●	● ●	● ●	● ●	● ●	● ●	● ●	● ●				Both	3 x per week
METHOXY POLYETHYLENE GLYCOL-EPOETIN BETA	MIRCERA	●	●	●	●	●	●	●	●	●	●	●	●		●				Adult	Every 2 weeks

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

* Anaemia for patients with Chronic kidney disease.

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

*** Dynepo has been discontinued.

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

		AT	BE	BU	CZ	DK	FI	FR	DE	GR*	HU	IE	IT	NL	NO	PL	PT	RO	SK	SL	ES	SE	CH	UK	EU
MARKET SHARE TD (2022, JUNE MAT)	Biosimilar vs Referenced product	80%	12%	100%	96%	6%	100%	78%	91%	95%	100%	100%	91%	22%	100%	100%	98%	99%	100%	77%	90%	99%	33%	12%	88%
	Biosimilar vs Accessible market	23%	2%	59%	40%	0%	19%	28%	62%	88%	37%	1%	79%	1%	6%	19%	25%	53%	52%	20%	53%	20%	1%	3%	48%
	Biosimilar vs Total market	23%	2%	53%	29%	0%	17%	27%	58%	88%	36%	1%	79%	1%	4%	19%	25%	50%	51%	18%	53%	20%	1%	3%	46%
PRICE PER TD (2022 JUNE MAT/YR BEFORE BS ENTRY)	Biosimilar and Referenced product	-47%	-7%	-16%	-66%	-2%	-57%	-39%	-58%	-59%	-86%	-40%	-25%	-55%	6%	-70%	-83%	-66%	-65%	-53%	-78%	-35%	-52%	-16%	-44%
	Biosimilar accessible market	-51%	2%	-27%	-58%	-27%	-45%	-45%	-57%	-58%	-59%	-38%	-23%	-47%	-21%	-44%	-75%	-55%	-62%	-54%	-58%	-40%	-47%	-19%	-43%
	Total market	-48%	-11%	-32%	-52%	-20%	-42%	-43%	-55%	-58%	-52%	-34%	-20%	-48%	-17%	-39%	-72%	-53%	-60%	-53%	-56%	-40%	-45%	-17%	-41%
VOLUME TD (2022, JUNE MAT/YR BEFORE BS ENTRY)	Biosimilar and Referenced product	11%	21%	84%	427%	-48%	2747%	75%	158%	613%	91%	-82%	265%	-77%	22%	5738%	254%	118%	358%	-13%	122%	21%	-52%	145%	149%
	Biosimilar accessible market	69%	343%	59%	243%	326%	264%	125%	81%	353%	128%	43%	137%	87%	277%	538%	227%	-53%	132%	61%	79%	103%	166%	174%	112%
	Total market	-13%	75%	35%	238%	0%	42%	20%	19%	200%	3%	-16%	53%	-10%	37%	308%	7%	-57%	25%	22%	10%	12%	24%	65%	24%
	TD per capita	0.79	0.90	0.33	0.31	0.47	0.47	1.07	0.46	0.06	0.37	0.40	1.29	0.46	0.27	0.11	0.48	0.13	0.56	0.63	0.75	0.50	0.40	0.38	0.66
	TD/capita (Yr before BS entrance)	0.91	0.51	0.24	0.09	0.47	0.33	0.89	0.38	0.02	0.36	0.48	0.85	0.51	0.20	0.03	0.44	0.30	0.45	0.51	0.68	0.45	0.32	0.23	0.53
	First recorded sales of biosimilars	2008	2014	2011	2011	2012	2008	2009	2007	2008	2009	2008	2008	2009	2008	2009	2010	2009	2010	2009	2009	2008	2009	2009	2007

* Only retail panel data is available for Greece

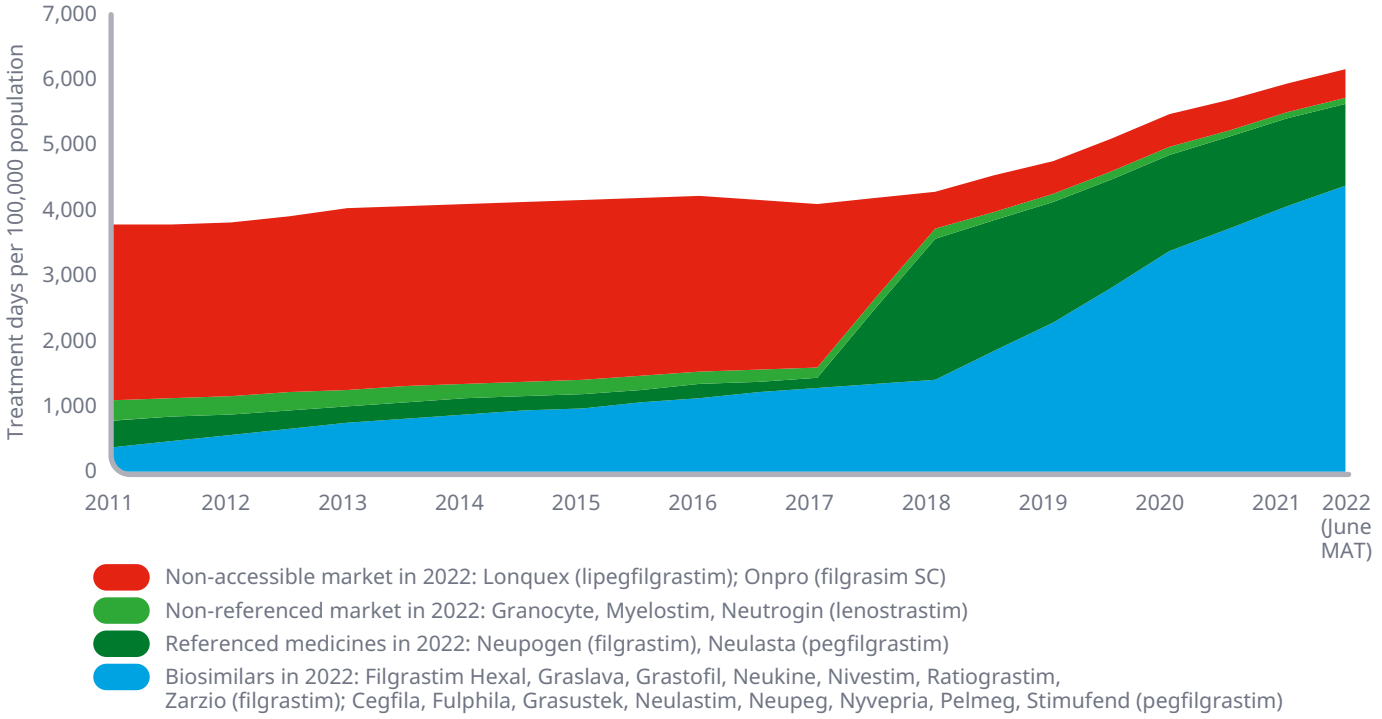
Granulocyte-colony stimulating factor (GCSF)

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

GCSF MARKET DEVELOPMENT

According to IQVIA MIDAS and ARK Patent Intelligence insights protection expired for a significant molecule in this class, Neulasta (pegfilgrastim). The figure below reflects this shift from the molecule as a non-accessible product with protection, to one that is now open to biosimilar competition and has been referenced within the same year by a significant number of biosimilars. Lenograstim products (Granocyte, Myelostim, Neutrogin) are not protected according to IQVIA MIDAS and ARK Patent Intelligence, meaning they are classified as 'non-referenced' products in 2021, according to the definition outlined on page 15.

GCSF market development



ADDITIONAL INFORMATION ABOUT GCSF MEDICINES

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

GSCF approved indications

NAMING		CLASSIFICATION												INDICATIONS					
MOLECULE	PRODUCT	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2222 (JUNE MAT)	CYTOTOXIC CHEMOTERAPY ASSOCIATED WITH FEBRILE INDUCED NEUTROPENIA	NEUTROPENIA INDUCED BY ACUTE MYELOID LEUKEMIA	BONE MARROW TRANSPLANTATION FOR NON MYELOID MALIGNANCY INDUCED NEUTROPENIA	MOBILISATION OF PERIPHERAL BLOOD PROGENITOR CELLS (PBPCS)	SEVERE CHRONIC NEUTROPENIA (SCN) WITH DIAGNOIS OF CONGENITAL, CYCLIC, OR IDIOPATHIC NEUTROPENIA	NEUTROPENIA PREVENTION AND TREATMENT IN PATIENTS WITH HIV
FILGRASTIM	GRANULOKINE GRASALVA GRASTOFIL NEUKINE NEUPOGEN NIVESTIM RATIOGRASTIM ZARZIO FILGRASTIM HEXAL	● ● ● ● ● ● ● ● ●	● ● ● ● ● ● ● ● ●	● ● ● ● ● ● ● ● ●	● ● ● ● ● ● ● ● ●	● ● ● ● ● ● ● ● ●	● ● ● ● ● ● ● ● ●	● ● ● ● ● ● ● ● ●	● ● ● ● ● ● ● ● ●	● ● ● ● ● ● ● ● ●	● ● ● ● ● ● ● ● ●	● ● ● ● ● ● ● ● ●	● ● ● ● ● ● ● ● ●	● ● ● ● ● ● ● ● ●	● ● ● ● ● ● ● ● ●	● ● ●	● ● ● ● ● ● ● ● ●	● ● ● ● ● ● ● ● ●	● ● ● ● ● ● ● ● ●
LENOGRASTIM	GRANOCYTE MYELOSTIM NEUTROGIN	● ● ●	● ● ●	● ● ●	● ● ●	● ● ●	● ● ●	● ● ●	● ● ●	● ● ●	● ● ●	● ● ●	● ● ●	● ● ●		● ● ●	● ● ●		
LIPEGFILGRASTIM	LONQUEX				●	●	●	●	●	●	●	●	●	●					
PEGFILGRASTIM	NEULASTA ONPRO NEULASTIM NEUPEG PELMEG FULPHILA CEGFILA GRASUSTEK NYVEPRIA STIMUFEND	●	●	●	●	●	●	●	● ●	● ●	● ●	● ●	● ●	●					

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

Notes: Tevagrastim = Grasalva in IQVIA MIDAS; Accofil = Neukine in IQVIA MIDAS; Ziextenzo = Neulastim in IQVIA MIDAS; Pelgraz is Neupeg in MIDAS.

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

		AT	BE	BU	CZ	DK	FI	FR	DE	GR*	HU	IE	IT	NL	NO	PL	PT	RO	SK	SL	ES	SE	CH	UK	EU
MARKET SHARE TD (2022, JUNE MAT)	Biosimilar vs Referenced product	61%	25%	54%	99%	100%	63%	81%	53%	97%	100%	16%	91%	83%	98%	100%	97%	95%	89%	42%	94%	98%	51%	86%	77%
	Biosimilar vs Accessible market	61%	25%	54%	99%	100%	63%	77%	52%	97%	100%	16%	90%	83%	98%	100%	96%	95%	89%	42%	93%	98%	51%	84%	76%
	Biosimilar vs Total market	53%	16%	39%	84%	100%	52%	76%	47%	96%	100%	14%	83%	72%	98%	100%	96%	95%	78%	38%	93%	97%	51%	82%	70%
PRICE PER TD (2022 JUNE MAT/YR BEFORE BS ENTRY)	Biosimilar and Referenced product	-79%	-68%	-89%	-83%	-64%	-81%	-75%	-71%	-73%	-88%	-67%	-56%	-73%	-56%	-94%	-97%	-72%	-88%	-87%	-52%	-72%	-56%	-24%	-72%
	Biosimilar accessible market	-79%	-68%	-89%	-83%	-64%	-81%	-73%	-70%	-73%	-88%	-67%	-56%	-73%	-56%	-94%	-97%	-72%	-88%	-87%	-51%	-72%	-56%	-23%	-71%
	Total market	-66%	-54%	-85%	-75%	-38%	-68%	-56%	-57%	-57%	-85%	-38%	-36%	-55%	-27%	-92%	-91%	-72%	-81%	-80%	-41%	-60%	-29%	-10%	-59%
VOLUME TD (2022, JUNE MAT/YR BEFORE BS ENTRY)	Biosimilar and Referenced product	832%	1548%	4151%	2259%	1168%	1119%	2273%	804%	4580%	685%	1072%	457%	1132%	3028%	1042%	359%	1770%	3025%	1506%	117%	783%	449%	617%	887%
	Biosimilar accessible market	832%	1551%	4151%	2259%	1170%	1119%	2373%	825%	4580%	685%	1085%	463%	1132%	3028%	1042%	360%	1770%	3025%	1506%	118%	783%	449%	636%	904%
	Total market	120%	226%	3513%	946%	104%	114%	118%	136%	-34%	82%	96%	19%	13%	239%	374%	-19%	1669%	1023%	431%	-27%	128%	61%	149%	110%
	TD per capita	0.12	0.14	0.07	0.05	0.08	0.11	0.11	0.06	0.01	0.06	0.10	0.04	0.04	0.09	0.08	0.03	0.06	0.10	0.09	0.03	0.05	0.04	0.03	0.07
	TD/capita (Yr before BS entrance)	0.05	0.04	0.00	0.00	0.04	0.05	0.05	0.02	0.02	0.04	0.05	0.03	0.03	0.03	0.02	0.04	0.00	0.01	0.02	0.04	0.02	0.03	0.01	0.03
	First recorded sales of biosimilars	2009	2011	2009	2010	2009	2009	2009	2008	2009	2009	2009	2009	2009	2009	2009	2010	2009	2009	2009	2009	2009	2009	2008	2008

* Only retail panel data is available for Greece

Anti-tumour necrosis factor (Anti-TNF)

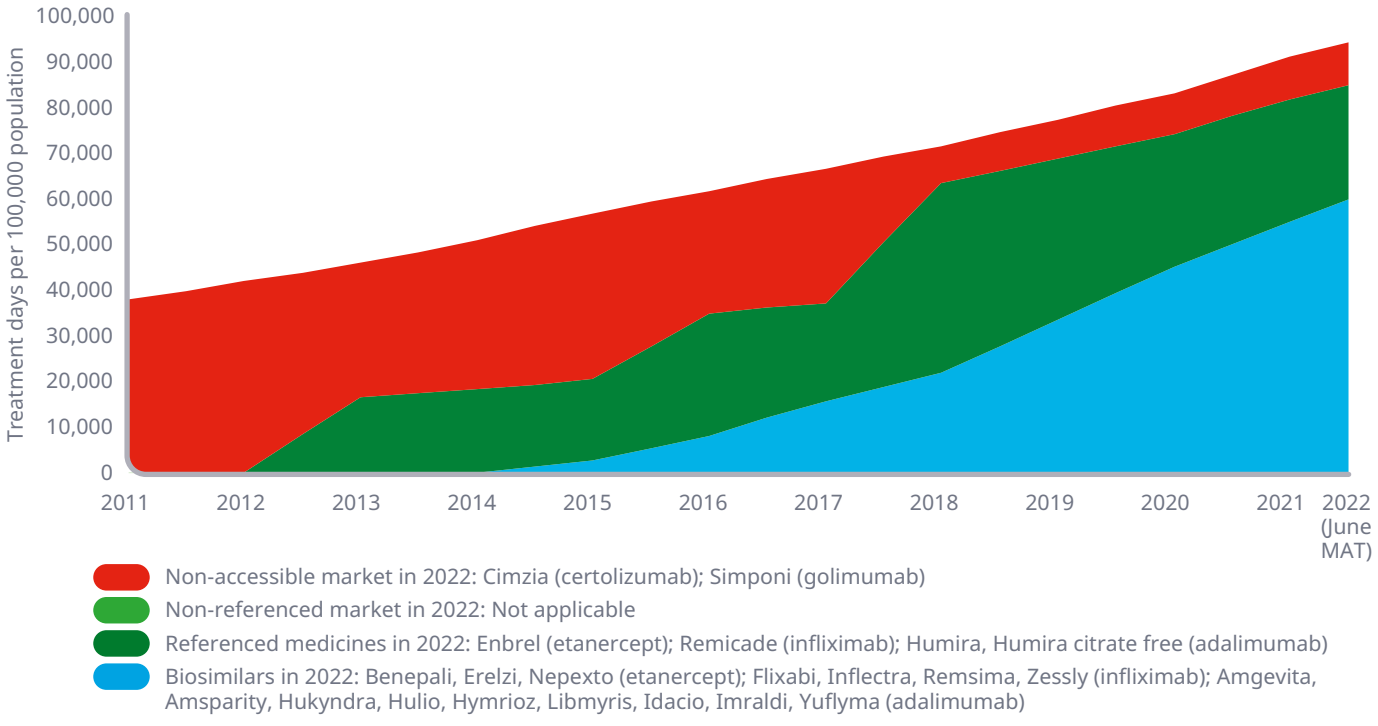
Anti-TNF drugs are a class of drugs that are used to treat inflammatory conditions such as Rheumatoid Arthritis, Ankylosing Spondylitis, Psoriatic Arthritis, Juvenile Arthritis, Crohn's Disease, Ulcerative Colitis, Psoriasis and Hidradinitis Suppurativa. These drugs are able to reduce inflammation and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

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

ANTI-TNF MARKET DEVELOPMENT

In 2016, Humira Citrate free was launched as an improved formulation to the original adalimumab molecule. This product has been categorised as non-accessible up until biosimilar entry in 2018.

Anti-TNF market development



ADDITIONAL INFORMATION ABOUT ANTI-TNF MEDICINES

In this section we report insights from biosimilars on the market in Europe for three anti-TNF molecules: infliximab, etanercept and adalimumab. The EU approved the first infliximab biosimilars in September 2013, the first etanercept biosimilar in January 2016 and the first adalimumab biosimilar in March 2017. The EMA has also approved several rituximab biosimilars, however these have been considered separately in the Oncology section of the report. The market shares and price/volume evolution figures refer to the total Anti-TNF market, therefore, include all products within each category. This means, for example, in markets where only infliximab biosimilars have launched, the "biosimilar versus referenced product" market share will still represent the biosimilar market share of all the biosimilars and referenced products on the market.

Anti-TNF approved indications

NAMING		CLASSIFICATION												INDICATIONS											DOSING	
MOLECULE	PRODUCT	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022 (JUNE MAT)	RA	JIA	PSA	AS	AS WITHOUT RADIOGRAPHIC EVIDENCE	CD (ADULT / PEDIATRIC)	UC (ADULT / PEDIATRIC)	PSO (ADULT/ PEDIATRIC)	HS	UV (ADULT/PAEDIATRIC)	FREQUENCY	ROUTE (SUBQ / IV)	CITRATE FREE (Y/N)
ADALIMUMAB	HUMIRA	🔴	🔴	🔴	🔴	🔴	🔴	🔴	🟢	🟢	🟢	🟢	🟢	●	●	●	●	●	●	●	●	●	●	Every 2 weeks	SC	N
	HUMIRA (citrate free)						🔴	🔴	🟢	🟢	🟢	🟢	🟢	●	●	●	●	●	●	●	●	●	●		SC	Y
	AMGEVITA							🔵	🔵	🔵	🔵	🔵	🔵	●	●	●	●	●	●	●	●	●	●		SC	Y
	HULIO								🔵	🔵	🔵	🔵	🔵	●	●	●	●	●	●	●	●	●	●		SC	Y
	HYRIMOZ								🔵	🔵	🔵	🔵	🔵	●	●	●	●	●	●	●	●	●	●		SC	N
	IMRALDI								🔵	🔵	🔵	🔵	🔵	●	●	●	●	●	●	●	●	●	●		SC	N
	IDACIO									🔵	🔵	🔵	🔵	●	●	●	●	●	●	●	●	●	●		SC	N
	AMSPARITY										🔵	🔵	🔵	●	●	●	●	●	●	●	●	●	●		SC	Y
	YUFLYMA											🔵	🔵	●	●	●	●	●	●	●	●	●	●		SC	Y
	LIBMYRIS											🔵	🔵	●	●	●	●	●	●	●	●	●	●		SC	Y
	HUKYNDRA											🔵	🔵	●	●	●	●	●	●	●	●	●	●		SC	Y
CERTOLIZUMAB PEGOL	CIMZIA	🔴	🔴	🔴	🔴	🔴	🔴	🔴	🔴	🔴	🔴	🔴	🔴	●		●	●				●			Monthly	SC	n/a
ETANERCEPT	ENBREL	🔴	🔴	🔴	🔴	🔴	🟢	🟢	🟢	🟢	🟢	🟢	🟢	●	●	●	●				●			Once or twice weekly	SC	n/a
	BENEPALI						🔵	🔵	🔵	🔵	🔵	🔵	🔵	●	●	●	●				●				SC	n/a
	ERELZI							🔵	🔵	🔵	🔵	🔵	🔵	●	●	●	●				●				SC	n/a
	NEPEXTO										🔵	🔵	🔵	●	●	●	●				●				SC	n/a
GOLIMUMAB	SIMPONI	🔴	🔴	🔴	🔴	🔴	🔴	🔴	🔴	🔴	🔴	🔴	🔴	●		●	●			●				Monthly	SC	n/a
INFLIXIMAB	REMICADE*	🔴	🔴	🟢	🟢	🟢	🟢	🟢	🟢	🟢	🟢	🟢	🟢	●		●	●		●	●	●			Every 8 weeks	IV	n/a
	REMSIMA			🔵	🔵	🔵	🔵	🔵	🔵	🔵	🔵	🔵	🔵	●		●	●		●	●	●				BOTH	n/a
	INFLECTRA				🔵	🔵	🔵	🔵	🔵	🔵	🔵	🔵	🔵	●		●	●		●	●	●				IV	n/a
	FLIXABI						🔵	🔵	🔵	🔵	🔵	🔵	🔵	●		●	●		●	●	●				IV	n/a
	ZESSLY								🔵	🔵	🔵	🔵	🔵	●		●	●		●	●	●				IV	n/a

🔴 Non-accessible market ● Non-referenced market 🟢 Referenced medicines 🔵 Biosimilars

* Adult only

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

		AT	BE	BU*	CZ	DK	FI	FR	DE	GR**	HU	IE	IT	NL	NO	PL	PT	RO	SK	SL	ES	SE	CH	UK	EU
MARKET SHARE TD (2022, JUNE MAT)	Biosimilar vs Referenced product	40%	40%	14%	55%	97%	76%	59%	74%	51%	85%	73%	81%	70%	87%	93%	72%	33%	21%	53%	66%	86%	32%	88%	67%
	Biosimilar vs Accessible market	40%	40%	14%	55%	97%	76%	59%	74%	51%	85%	73%	81%	70%	87%	93%	72%	33%	21%	53%	66%	86%	32%	88%	67%
	Biosimilar vs Total market	33%	37%	12%	49%	90%	64%	52%	65%	38%	74%	67%	69%	67%	83%	76%	67%	30%	19%	48%	59%	81%	25%	83%	60%
PRICE PER TD (2022 JUNE MAT/YR BEFORE BS ENTRY)	Biosimilar and Referenced product	-42%	-26%	-16%		8%		-30%	-5%	-34%	7%	-6%	36%	-20%		-71%	-54%	-6%	-40%	-52%	-8%	-49%	8%	30%	-15%
	Biosimilar accessible market	-42%	-26%	-16%		8%		-30%	-5%	-34%	7%	-6%	36%	-20%		-71%	-54%	-6%	-40%	-52%	-8%	-49%	8%	30%	-15%
	Total market	-45%	-44%	-33%	-40%	-26%	-47%	-47%	-44%	-29%	-22%	-33%	-17%	-43%	-14%	-74%	-68%	-37%	-52%	-60%	-33%	-62%	-22%	-8%	-42%
VOLUME TD (2022, JUNE MAT/YR BEFORE BS ENTRY)	Biosimilar and Referenced product	853%	285%	>1Mn%		353%		287%	403%	86%	244%	843%	308%	311%		1244%	487%	186%	211%	377%	363%	416%	192%	513%	376%
	Biosimilar accessible market	853%	285%	>1Mn%		353%		287%	403%	86%	244%	843%	308%	311%		1244%	487%	186%	211%	377%	363%	416%	192%	513%	376%
	Total market	676%	85%	360%	228%	105%	177%	88%	75%	56%	39%	164%	43%	67%	155%	240%	158%	29%	71%	85%	94%	104%	62%	91%	91%
	TD per capita	1.25	1.70	0.48	0.77	1.82	1.75	1.15	0.85	0.01	0.45	2.43	0.53	1.61	2.64	0.14	0.76	0.27	0.84	0.85	1.09	1.81	1.29	1.14	0.88
	TD/capita (Yr before BS entrance)	0.16	0.92	0.10	0.23	0.89	0.63	0.61	0.49	0.01	0.32	0.92	0.37	0.96	1.03	0.04	0.29	0.21	0.49	0.46	0.56	0.89	0.80	0.60	0.46
	First recorded sales of biosimilars	2015	2015	2014	2013	2015	2013	2015	2015	2019	2014	2014	2015	2015	2013	2014	2014	2014	2014	2015	2015	2015	2016	2015	2013

* The significant volume increase in Bulgaria is due to no sales of Remicade prior to biosimilar entry in 2014
** Only retail panel data is available for Greece
Note: Gaps in price and volume per TD are due to there being no 'Non-referenced' or 'Referenced' products in the year before biosimilar entry

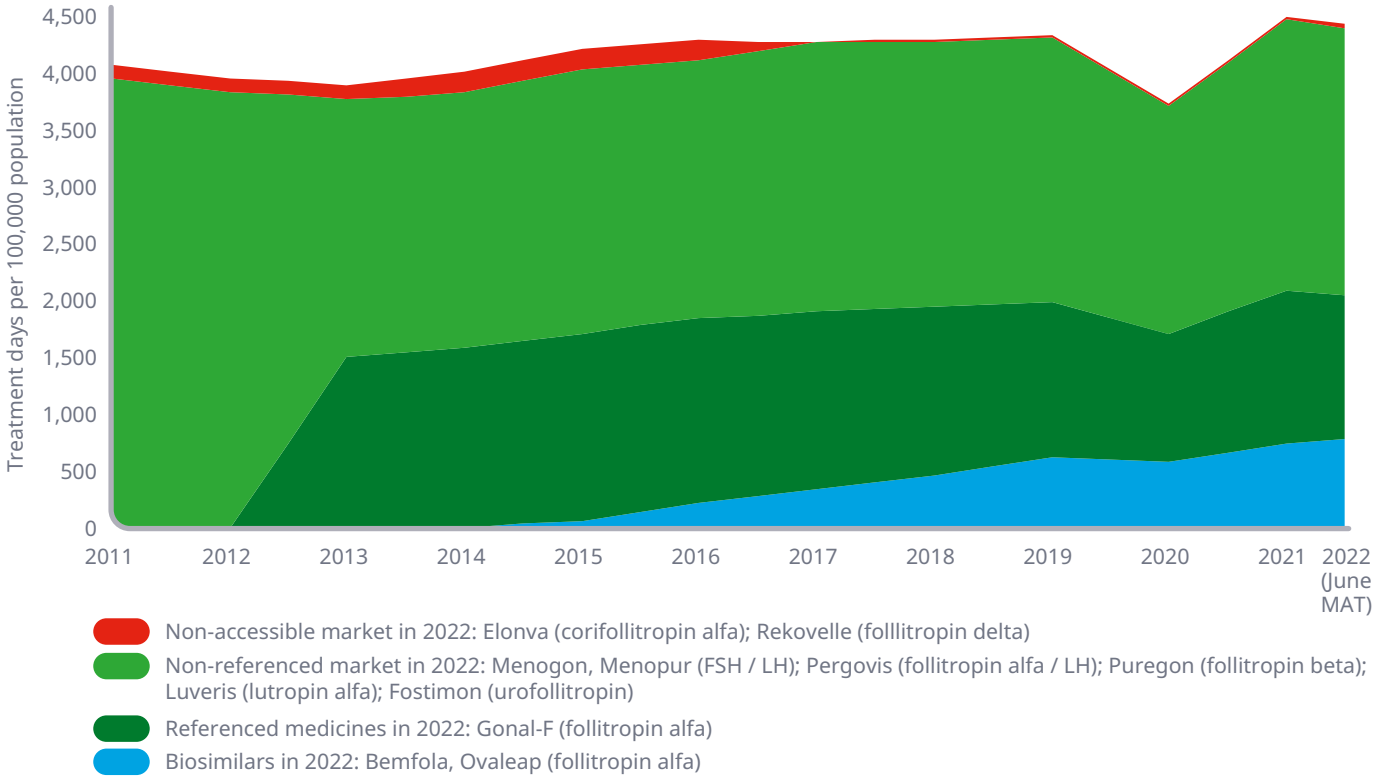
Fertility (follitropin alfa)

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

FERTILITY MARKET DEVELOPMENT

The total market is nominally smaller than 2021 report, due to an improved calculation methodology. Puregon, Fostimon, Menogon, Menopur are classified as 'non-referenced' products in 2021, according to the definition outlined on page 15 to reflect that they are not protected according to IQVIA MIDAS and ARK Patent intelligence and despite being a second-generation product have now been on the market for a significant number of years and are part of the accessible market for biosimilar competition. Such products may be unlikely to have a biosimilar directly manufactured for them given their age, current price erosion, chemical similarity, previous regulatory schemes, and total opportunity size. A significant decline in treatment volume in 2020 is not a trend break in reporting, but the impact of the COVID-19 pandemic on prescriptions in this area and is therefore an accurate assessment of the market dynamics.

Fertility market development



Fertility approved indications

NAMING		CLASSIFICATION												INDICATIONS					DOSING/ADMINISTRATION	
MOLECULE	PRODUCT	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022 (JUNE MAT)	INFERTILITY	HYPOGONADISM	ANOVULATION	OVULATION INDUCTION	REPRODUCTIVE TECHNIQUES, ASSISTED	ROUTE (SUBQ/IV/IM)	FREQUENCY
CORIFOLLITROPIN ALFA	ELONVA	●	●	●	●	●	●	●	●	●	●	●	●	●					SC	Patient specific
FOLLICLE-STIMULATING HORMONE / LUTEINISING HORMONE	MENOGON MENOPUR	● ●	● ●	● ●	● ●	● ●	● ●	● ●	● ●	● ●	● ●	● ●	● ●	● ●		●		● ●	SC/IM SC	Daily Daily
FOLLITROPIN ALFA	GONAL-F BEMFOLA OVALEAP	●	●	● ● ●	● ● ●	● ● ●	● ● ●	● ● ●	● ● ●	● ● ●	● ● ●	● ● ●	● ● ●	● ● ●	● ●	● ●		● ●	All All All	Daily Daily Daily
FOLLITROPIN ALFA / LUTEINISING HORMONE	PERGOVERIS	●	●	●	●	●	●	●	●	●	●	●	●	●					All	Daily
FOLLITROPIN BETA	PUREGON	●	●	●	●	●	●	●	●	●	●	●	●	●	●				SC	Patient specific
FOLLITROPIN DELTA	REKOVELLE	●	●	●	●	●	●	●	●	●	●	●	●	●			●	●	SC	Daily
LUTROPIN ALFA	LUVERIS	●	●	●	●	●	●	●	●	●	●	●	●	●			●		All	Daily
UROFOLLITROPIN	FOSTIMON	●	●	●	●	●	●	●	●	●	●	●	●	●			●		IM	Daily

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

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

		AT	BE	BU	CZ	DK	FI	FR	DE	GR*	HU	IE	IT	NL	NO	PL	PT	RO	SK	SL	ES	SE	CH	UK	EU
MARKET SHARE TD (2022, JUNE MAT)	Biosimilar vs Referenced product	16%	57%	1%	25%	35%	21%	41%	49%	40%	95%	1%	36%	0%	31%	56%	42%	8%	65%	22%	53%	26%	25%	32%	39%
	Biosimilar vs Accessible market	3%	21%	0%	14%	15%	10%	22%	21%	16%	59%	0%	13%	0%	15%	22%	16%	4%	32%	15%	21%	15%	8%	14%	18%
	Biosimilar vs Total market	3%	21%	0%	14%	15%	10%	22%	20%	16%	57%	0%	13%	0%	15%	21%	16%	3%	31%	15%	21%	15%	8%	14%	18%
PRICE PER TD (2022 JUNE MAT/YR BEFORE BS ENTRY)	Biosimilar and Referenced product	-30%	-5%	-20%	-20%	-23%	-33%	-28%	-11%	-25%	-25%	-13%	-9%	-17%	1%	-1%	-25%	-14%	-19%	-22%	-26%	-19%	-22%	16%	-21%
	Biosimilar accessible market	-7%	7%	-3%	-1%	-7%	-20%	-15%	0%	5%	8%	-1%	-3%	-7%	11%	-10%	-8%	9%	30%	-1%	-9%	-14%	-11%	10%	-7%
	Total market	-6%	6%	4%	-1%	-11%	-22%	-16%	0%	3%	10%	-1%	-4%	-1%	9%	-2%	-2%	11%	30%	-5%	-12%	-14%	-10%	11%	-7%
VOLUME TD (2022 JUNE MAT/YR BEFORE BS ENTRY)	Biosimilar and Referenced product	167%	89%	194%	137%	64%	117%	45%	31%	90%	66%	119%	-33%	2%	151%	102%	86%	111%	92%	93%	22%	91%	26%	-7%	31%
	Biosimilar accessible market	42%	33%	-61%	97%	41%	23%	18%	20%	46%	30%	82%	-10%	-7%	50%	53%	65%	87%	-4%	6%	12%	25%	6%	-13%	18%
	Total market	43%	33%	-61%	98%	35%	18%	14%	13%	45%	25%	83%	-12%	-5%	51%	53%	63%	87%	-2%	6%	1%	26%	6%	-13%	14%
	TD per capita	0.01	0.05	0.00	0.09	0.10	0.04	0.08	0.03	0.03	0.06	0.12	0.05	0.05	0.07	0.02	0.04	0.02	0.02	0.05	0.06	0.07	0.05	0.01	0.05
	TD/capita (Yr before BS entrance)	0.01	0.04	0.01	0.04	0.07	0.03	0.07	0.03	0.02	0.05	0.06	0.06	0.05	0.05	0.01	0.02	0.01	0.02	0.05	0.06	0.06	0.05	0.01	0.04
	First recorded sales of biosimilars	2014	2015	2016	2015	2014	2014	2015	2014	2016	2015	2016	2015	2016	2014	2015	2015	2017	2016	2015	2015	2014	2018	2015	2014

* Only retail panel data is available for Greece

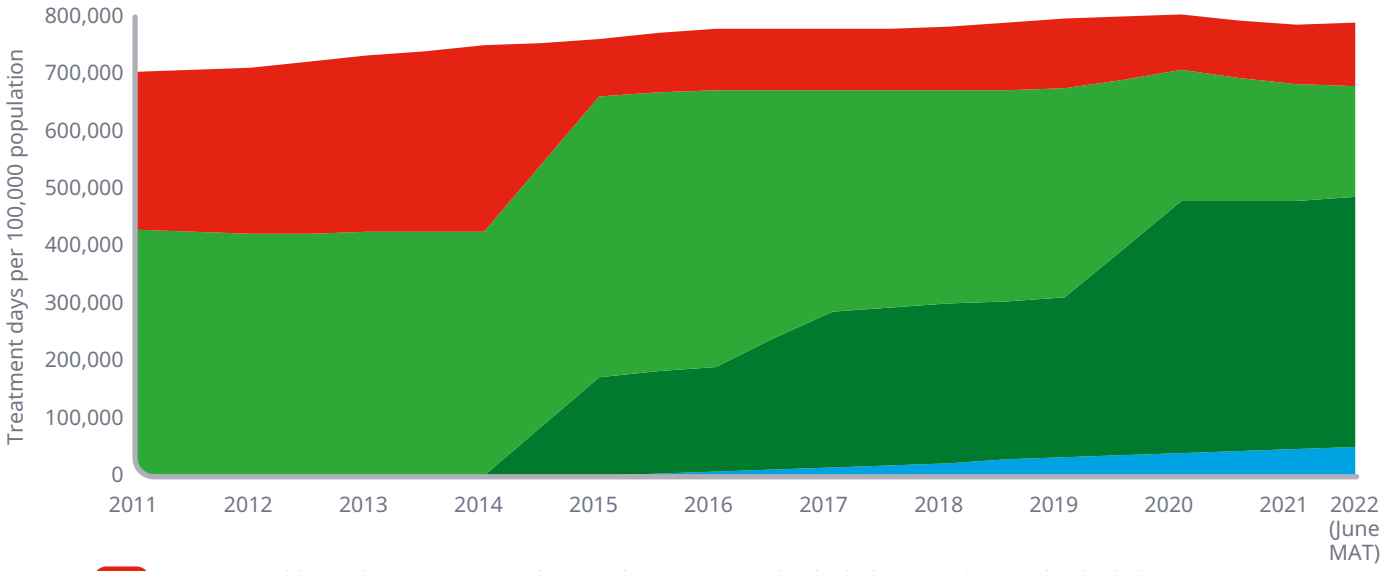
Insulins

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

INSULIN MARKET DEVELOPMENT

The total market is nominally smaller than 2021 report, due to an improved calculation methodology. Products for human insulin are classified as 'non-referenced' products from 2021 report onwards, according to the definition outlined on page 15 to reflect that they are not protected according to IQVIA MIDAS and ARK Patent intelligence.

Insulin market development



- Non-accessible market in 2022: Ryzodeg (insulin aspart / insulin degludec); Tresiba (insulin degludec); Xultophy (insulin degludec / liraglutide); Toujeo (insulin glargine); Soliqua (insulin glargine / lixisenatide); Apidra (insulin glusine)
- Non-referenced market in 2022: Novomix (insulin aspart / proatmine); Levemir (insulin detemir); Actrapid, Humulin, Protaphane (insulin human); Humalog/Liprolog Mix (insulin lispro / insulin lispro protamine)
- Referenced medicines in 2022: Novorapid (insulin aspart), Lantus (insulin glargine); Humalog / Liprolog (insulin lispro)
- Biosimilars in 2022: Insulin aspart SNFI, Kirsty (insulin aspart); Truvelog Mix 30 (insulin aspart / protamine); Abasaglar, Semglee (insulin glargine); Ademlog / insulin lispro SNFI (insulin lispro)

ADDITIONAL INFORMATION ABOUT INSULIN MEDICINES

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

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

Insulin approved indications

NAMING		CLASSIFICATION												INDICATIONS	DOSING/ADMINISTRATION	
MOLECULE	PRODUCT	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022 (JUNE MAT)	DIABETES MELLITUS	FREQUENCY	MODE OF ACTION
INSULIN ASPART	NOVORAPID INSULIN ASPART SANOFI KIRSTY	●	●	●	●	●	●	●	●	●	● ●	● ●	● ●	● ● ●	before every meal	Fast-acting
INSULIN ASPART#INSULIN ASPART PROTAMINE	NOVOMIX TRUVELOG MIX 30	●	●	●	●	●	●	●	●	●	●	●	● ●	● ●	before every meal	Fast-acting
INSULIN ASPART#INSULIN DEGLUDEC	RYZODEG			●	●	●	●	●	●	●	●	●	●	●	daily	Fast-acting
INSULIN DEGLUDEC	TRESIBA			●	●	●	●	●	●	●	●	●	●	●	daily	Long-acting
INSULIN DEGLUDEC / LIRAGLUTIDE	XULTOPHY				●	●	●	●	●	●	●	●	●	●	daily	Long-acting
INSULIN DETEMIR	LEVEMIR	●	●	●	●	●	●	●	●	●	●	●	●	●	twice a day	Long-acting
INSULIN GLARGINE	LANTUS TOUJEO ABASAGLAR SEMGLEE	●	●	●	●	● ● ●	● ● ●	● ● ●	● ● ● ●	● ● ● ●	● ● ● ●	● ● ● ●	● ● ● ●	● ● ● ●	daily daily daily daily	Long-acting Long-acting Long-acting Long-acting
INSULIN GLARGINE / LIXISENATIDE	SOLIQUA							●	●	●	●	●	●	●	daily	Long-acting
INSULIN GLULISINE	APIDRA	●	●	●	●	●	●	●	●	●	●	●	●	●	before every meal	Fast-acting
INSULIN HUMAN*	ACTRAPID HUMULIN PROTAPHANE	● ● ●	● ● ●	● ● ●	● ● ●	● ● ●	● ● ●	● ● ●	● ● ●	● ● ●	● ● ●	● ● ●	● ● ●	● ● ●	before every meal once/twice a day once/twice a day	Short-acting Short-acting Intermediate-acting
INSULIN LISPRO	HUMALOG/LIPROLOG ADEMLOG/ INSULIN LISPRO SANOFI	●	●	●	●	●	●	● ●	● ●	● ●	● ●	● ●	● ●	● ●	before every meal before every meal	Fast-acting Fast-acting
INSULIN LISPRO#INSULIN LISPRO PROTAMINE	HUMALOG /LIPROLOG MIX	●	●	●	●	●	●	●	●	●	●	●	●	●	determined by physician	Fast-acting

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

* Only the top 3 products by sales are shown in the table

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

		AT	BE	BU	CZ	DK	FI	FR	DE	GR*	HU	IE	IT	NL	NO	PL	PT	RO	SK	SL	ES	SE	CH	UK	EU
MARKET SHARE TD (2022, JUNE MAT)	Biosimilar vs Referenced product	2%	1%	4%	3%	14%	5%	13%	8%	10%	3%	0%	10%	34%	3%	21%	13%	4%	18%	4%	11%	23%	0%	5%	11%
	Biosimilar vs Accessible market	1%	1%	1%	2%	11%	5%	11%	6%	8%	1%	0%	10%	27%	2%	9%	8%	3%	10%	2%	9%	17%	0%	3%	8%
	Biosimilar vs Total market	1%	1%	1%	2%	8%	4%	10%	5%	6%	1%	0%	8%	23%	2%	8%	7%	2%	8%	2%	8%	16%	0%	3%	7%
PRICE PER TD (2022 JUNE MAT/YR BEFORE BS ENTRY)	Biosimilar and Referenced product	-30%	-36%					-36%		-22%		-35%	-27%				-26%	-15%		-42%					-24%
	Biosimilar accessible market	3%	-15%	25%	28%	-14%	7%	-17%	22%	-1%	29%	-11%	-3%	2%	37%	7%	4%	16%	25%	-11%	20%	18%	2%	13%	6%
	Total market	5%	-9%	23%	31%	-13%	-20%	-6%	8%	26%	56%	-7%	20%	-11%	53%	1%	1%	22%	26%	15%	-7%	5%	6%	-1%	5%
VOLUME TD (2022, JUNE MAT/YR BEFORE BS ENTRY)	Biosimilar and Referenced product	391%	220%					150%		113%		252%	175%				145%	163%		358%					540%
	Biosimilar accessible market	-9%	15%	22%	44%	66%	160%	19%	19%	-6%	4%	27%	-5%	89%	31%	18%	15%	26%	43%	-6%	150%	62%	74%	106%	27%
	Total market	-5%	20%	-28%	33%	7%	-3%	20%	-4%	10%	0%	21%	-3%	0%	16%	3%	13%	34%	9%	-1%	6%	3%	7%	18%	4%
	TD per capita	5.12	7.83	5.97	10.06	6.92	11.10	7.38	10.66	7.72	9.23	5.42	5.64	8.76	7.71	6.91	6.18	7.08	7.06	8.25	7.36	9.65	4.72	8.19	7.87
	TD/capita (Yr before BS entrance)	5.36	6.51	8.35	7.59	6.45	11.46	6.16	11.13	6.99	9.27	4.48	5.81	8.79	6.67	6.70	5.49	5.30	6.48	8.38	6.98	9.38	4.41	6.94	7.55
	First recorded sales of biosimilars	2017	2016	2015	2015	2015	2015	2016	2015	2016	2015	2016	2016	2015	2015	2015	2016	2016	2015	2016	2015	2015	2015	2015	2015

* Only retail panel data is available for Greece

Note: Gaps in price and volume per TD are due to there being no 'Non-referenced' or 'Referenced' products in the year before biosimilar entry

Oncology

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

Mabthera is a medicine used to treat several blood cancers and inflammatory conditions, including follicular lymphoma and diffuse large B cell non-Hodgkin's lymphoma (two types of non-Hodgkin's lymphoma) and chronic lymphocytic leukaemia (CLL). It is also used to treat severe RA and other inflammatory conditions. Considering that the primary indications used for Mabthera and rituximab biosimilars are in Oncology, and since IQVIA sales and treatment day volume cannot be split by indication, rituximab market dynamics are only considered in this separate Oncology section, within the Monoclonal Antibody Antineoplastic class.

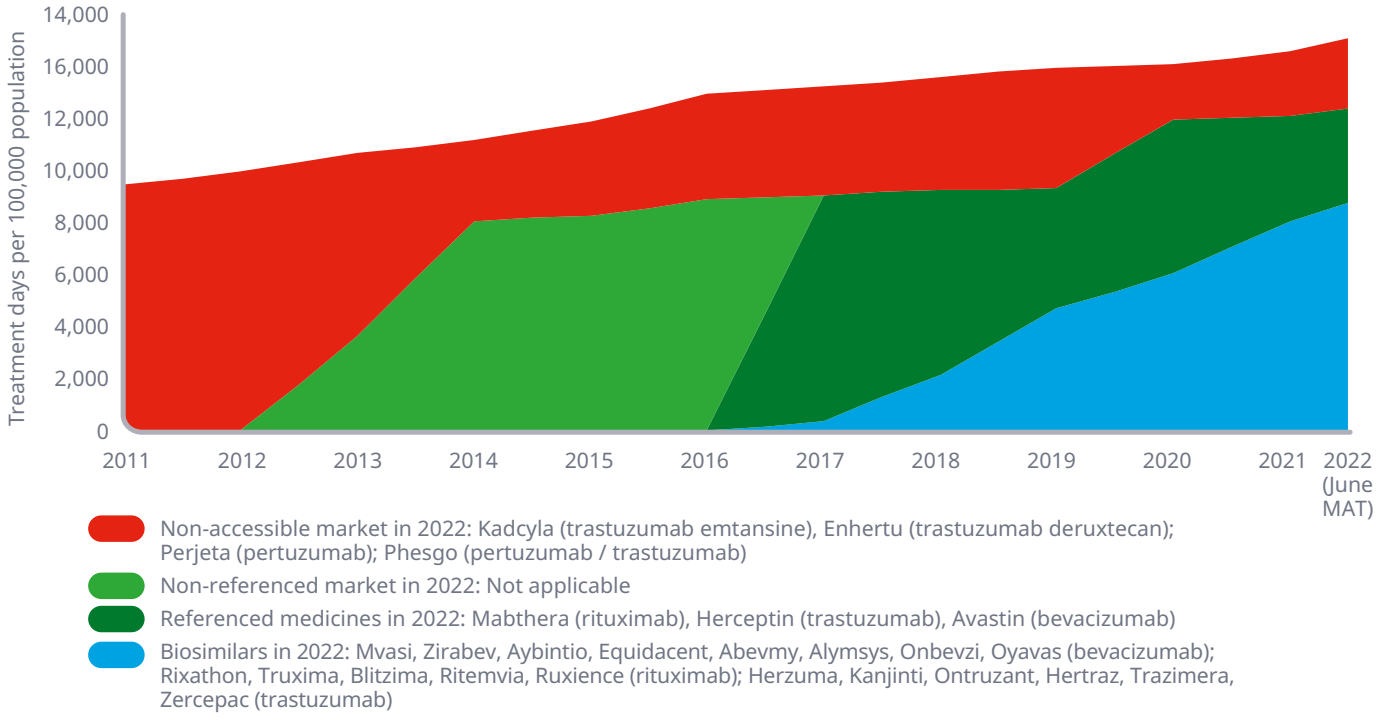
In this market the non-accessible products are classified by identifying products which have a similar mechanism of action, and are used for similar indications to rituximab. There are both IV and SC forms of Mabthera available, but because the biosimilar is only available in IV form, Mabthera IV is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

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

ONCOLOGY MARKET DEVELOPMENT

Perjeta (pertuzumab) and Phesgo (pertuzumab / trastuzumab) have been included in the 2022 report and classified within the 'non-accessible' market. This means that the total market is ~10–15% bigger than in the 2021 report, therefore caution should be taken when comparing between reports for this therapy area.

Oncology market development



Oncology approved indications

NAMING		CLASSIFICATION												INDICATIONS									DOSING	
MOLECULE	PRODUCT	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022 (JUNE MAT)	FL, DLBC (NON-GL)	CLL	MC	BC	METASTATIC GC	RCC	NSCLC	EOC	PPC	ROUTE (SUBQ / IV)	FREQUENCY
BEVACIZUMAB	AVASTIN MVASI ZIRABEV AYBINTIO EQUIDACENT ABEVMY ALYMSYS ONBEVZI OYAVAS	●	●	●	●	●	●	●	●	●	●	●	●			●	●		●	●	●	●	IV IV IV IV IV IV IV IV IV	2 - 3 week cycles (indication/ combination dependant)
RITUXIMAB*	MABTHERA RIXATHON TRUXIMA BLITZIMA RITEMVIA RUXIENCE	●	●	●	●	●	●	●	●	●	●	●	●	●	●								SC/IV IV IV IV IV IV	3 week cycles
TRASTUZUMAB**	HERCEPTIN HERZUMA KANJINTI ONTRUZANT HERTRAZ TRAZIMERA ZERCEPAC	●	●	●	●	●	●	●	●	●	●	●	●				●	●					SC/IV IV IV IV IV IV IV	3 week cycles
TRASTUZUMAB EMTANSINE	KADCYLA			●	●	●	●	●	●	●	●	●	●				●						IV	3 week cycles
TRASTUZUMAB DERUXTECAN	ENHERTU										●	●	●				●						IV	3 week cycles
PERTUZUMAB	PERJETA			●	●	●	●	●	●	●	●	●	●				●						IV	3 week cycles
ERTUZUMAB-#TRASTUZUMAB	PHESGO										●	●	●				●						SC	3 week cycles

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

* Indicated for non-onology indications such as rheumatoid arthritis, Granulomatosis with polyangiitis and microscopic polyangiitis, Pemphigus vulgaris;
** Eleftha has been excluded as it is not approved via EMA biosimilars pathway; Equidacent was withdrawn on 2021/10; Ritemvia was withdrawn on 2021/06
FL = follicular lymphoma, DLBC = Diffuse large B-cell lymphoma, MC = metastatic carcinoma, GC = gastic cancer, RCC = renal cell carcinoma, NSCLC = non-small cell lung cancer, EOC = epithelial ovarian cancer, PPC = Primary peritoneal cancer

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

		AT	BE	BU	CZ	DK	FI	FR	DE	GR*	HU	IE	IT	NL	NO	PL	PT	RO	SK	SL	ES	SE	CH	UK
MARKET SHARE TD (2022, JUNE MAT)	Biosimilar vs Referenced product	92%	21%	25%	39%	95%	74%	76%	79%		71%	52%	81%	91%	92%	58%	55%	75%	69%	51%	74%	87%	28%	62%
	Biosimilar vs Accessible market	92%	21%	25%	39%	95%	74%	76%	79%		71%	52%	81%	91%	92%	58%	55%	75%	69%	51%	74%	87%	28%	62%
	Biosimilar vs Total market	76%	18%	21%	34%	83%	65%	65%	65%		62%	45%	65%	76%	79%	46%	45%	52%	63%	39%	62%	75%	23%	46%
PRICE PER TD (2022 JUNE MAT/YR BEFORE BS ENTRY)	Biosimilar and Referenced product	-1%	-27%	-29%	-30%		-10%			0%	-20%					-66%		-6%	-34%	-40%		-6%	-18%	
	Biosimilar accessible market	-1%	-27%	-29%	-30%		-10%			0%	-20%					-66%		-6%	-34%	-40%		-6%	-18%	
	Total market	7%	-27%	-20%	-21%	-22%	-3%	-27%	-47%	0%	-16%	-37%	-26%	-41%	-11%	-38%	-40%	20%	-27%	-18%	-35%	11%	-14%	-30%
VOLUME TD (2022, JUNE MAT/YR BEFORE BS ENTRY)	Biosimilar and Referenced product	65%	150%	120%	37%		47%			0%	95%					21%		72%	83%	17%		15%	29%	
	Biosimilar accessible market	65%	150%	120%	37%		47%			0%	95%					21%		72%	83%	17%		15%	29%	
	Total market	11%	90%	44%	12%	233%	19%	241%	170%	0%	24%	326%	187%	303%	563%	26%	507%	29%	15%	20%	410%	3%	8%	673%
	TD per capita	0.20	0.31	0.16	0.12	0.18	0.19	0.24	0.12	0.00	0.15	0.18	0.14	0.16	0.20	0.08	0.14	0.07	0.12	0.15	0.19	0.15	0.19	0.12
	TD/capita (Yr before BS entrance)	0.18	0.16	0.11	0.11	0.05	0.16	0.07	0.04	0.00	0.12	0.04	0.05	0.04	0.03	0.07	0.02	0.05	0.11	0.12	0.04	0.14	0.18	0.02
	First recorded sales of biosimilars	2018	2018	2018	2018	2017	2018	2017	2017		2018	2017	2017	2017	2017	2018	2017	2018	2018	2018	2017	2018	2018	2017

* Only retail panel data is available for Greece

Note: Gaps in price and volume per TD are due to there being no 'Non-referenced' or 'Referenced' products in the year before biosimilar entry

Low-molecular-weight heparin (LMWH)

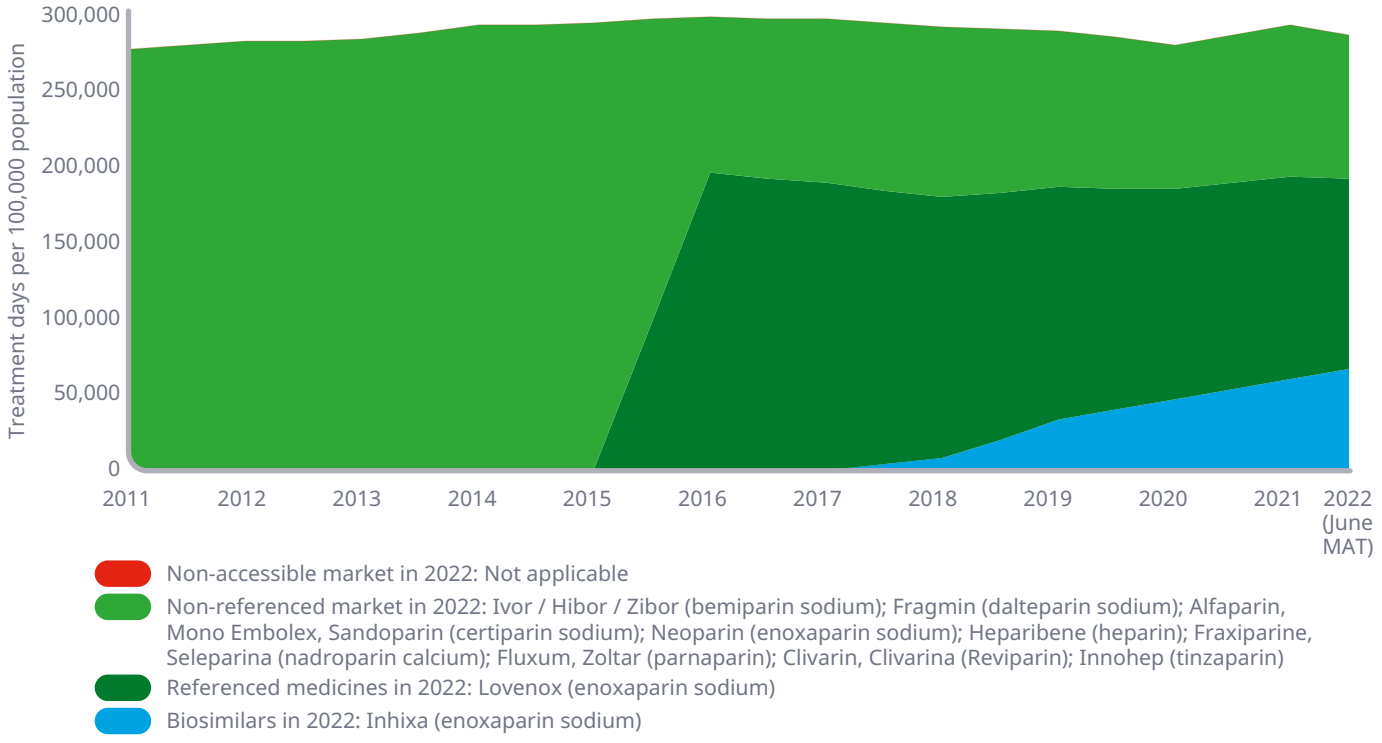
Low-Molecular-Weight Heparin (LMWH) is a class of anticoagulant medications. They are used in the prevention of blood clots, treatment of venous thromboembolism (deep vein thrombosis and pulmonary embolism) and in the treatment of myocardial infarction. LMWH is obtained by fractionation of polymeric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

Two enoxaparin sodium biosimilars (Inhixa and Thorinane) were authorised by the EMA in 09/2016, however Thorinane is now withdrawn meaning that Inhixa is the only remaining biosimilar in 2021.

LMWH MARKET DEVELOPMENT

Products for molecules in this class (bemiparin sodium, certoparin sodium, dalteparin sodium, heparin, nadroparin calcium, parnaparin, reviparin and tinzaparin) are classified as 'non-referenced' products in 2021, according to the definition outlined on page 15 to reflect that they are not protected according to IQVIA MIDAS and ARK Patent intelligence.

LMWH market development



LMWH approved indications

NAMING		CLASSIFICATION												INDICATIONS			
MOLECULE	PRODUCT	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022 (JUNE MAT)	DEEP VEIN THROMBOSIS TREATMENT AND PROPHYLAXIS	PULMONARY EMBOLISM	ATRIAL THROMBUS	BRIDGING THERAPY PRIOR TO STARTING WARFARIN
BEMIPARIN SODIUM	IVOR/HIBOR/ZIBOR	●	●	●	●	●	●	●	●	●	●	●	●	●	●		
CERTOPARIN SODIUM	ALFAPARIN MONO EMBOLEX SANDOPARIN	● ● ●	● ● ●	● ● ●	● ● ●	● ● ●	● ● ●	● ● ●	● ● ●	● ● ●	● ● ●	● ● ●	● ● ●	● ● ●	● ● ●		
DALTEPARIN SODIUM	FRAGMIN	●	●	●	●	●	●	●	●	●	●	●	●	●			
ENOXAPARIN SODIUM	LOVENOX NEOPARIN INHIXA	●	●	●	●	●	● ● ●	● ● ●	● ● ●	● ● ●	● ● ●	● ● ●	● ● ●	● ● ●			● ● ●
HEPARIN	HEPARIBENE	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	
NADROPARIN CALCIUM	FRAXIPARINE SELEPARINA	● ●	● ●	● ●	● ●	● ●	● ●	● ●	● ●	● ●	● ●	● ●	● ●	● ●	● ●		
PARNAPARIN	FLUXUM ZOLTAR	● ●	● ●	● ●	● ●	● ●	● ●	● ●	● ●	● ●	● ●	● ●	● ●	● ●	● ●		
REVIPARIN	CLIVARIN CLIVARINA	● ●	● ●	● ●	● ●	● ●	● ●	● ●	● ●	● ●	● ●	● ●	● ●	● ●	● ●		
TINZAPARIN	INNOHEP	●	●	●	●	●	●	●	●	●	●	●	●	●	●		●

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

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

		AT	BE	BU	CZ	DK	FI	FR	DE	GR*	HU	IE	IT	NL	NO	PL	PT	RO	SK	SL	ES	SE	CH	UK
MARKET SHARE TD (2022, JUNE MAT)	Biosimilar vs Referenced product	57%	4%		7%	88%	95%	6%	29%	0%	0%	0%	71%	0%	0%	0%	59%	0%	0%	0%	48%	0%	2%	64%
	Biosimilar vs Accessible market	46%	3%	0%	4%	1%	57%	4%	19%	0%	0%	0%	65%	0%	0%	0%	56%	0%	0%	0%	38%	0%	1%	36%
	Biosimilar vs Total market	46%	3%	0%	4%	1%	57%	4%	19%	0%	0%	0%	65%	0%	0%	0%	56%	0%	0%	0%	38%	0%	1%	36%
PRICE PER TD (2022 JUNE MAT/YR BEFORE BS ENTRY)	Biosimilar and Referenced product	-24%	-4%		-1%	30%	-29%	-11%	5%				-2%			14%	-16%				-20%	-1%	-10%	-2%
	Biosimilar accessible market	-21%	-3%		2%	-1%	-16%	-8%	5%				-3%			10%	-15%				-14%	-1%	-7%	-3%
	Total market	-21%	-3%		2%	-1%	-16%	-8%	5%				-3%			10%	-15%				-14%	-1%	-7%	-3%
VOLUME TD (2022, JUNE MAT/YR BEFORE BS ENTRY)	Biosimilar and Referenced product	-23%	3%		31%	-60%	-21%	11%	-32%				3%			49%	-4%				21%	-2%	10%	22%
	Biosimilar accessible market	-20%	4%		2%	-4%	0%	2%	-24%				-11%			2%	-5%				14%	-5%	3%	3%
	Total market	-20%	4%		2%	-4%	0%	2%	-24%				-11%			2%	-5%				14%	-5%	3%	3%
	TD per capita	3.99	3.26	0.60	3.78	1.30	2.48	2.73	3.14	2.77	5.42	1.79	3.25	1.00	1.79	3.58	1.78	1.73	5.72	2.79	3.85	1.79	2.12	2.07
	TD/capita (Yr before BS entrance)	4.99	3.12	0.00	3.70	1.36	2.49	2.67	4.13	0.00	0.00	0.00	3.64	0.00	0.00	3.52	1.88	0.00	0.00	0.00	3.38	1.87	2.06	2.02
	First recorded sales of biosimilars	2018	2021		2020	2019	2020	2018	2017				2017			2019	2019				2018	2020	2020	2017

* Only retail panel data is available for Greece

Note: Gaps in price and volume per TD are due to there being no 'Non-referenced' or 'Referenced' products in the year before biosimilar entry

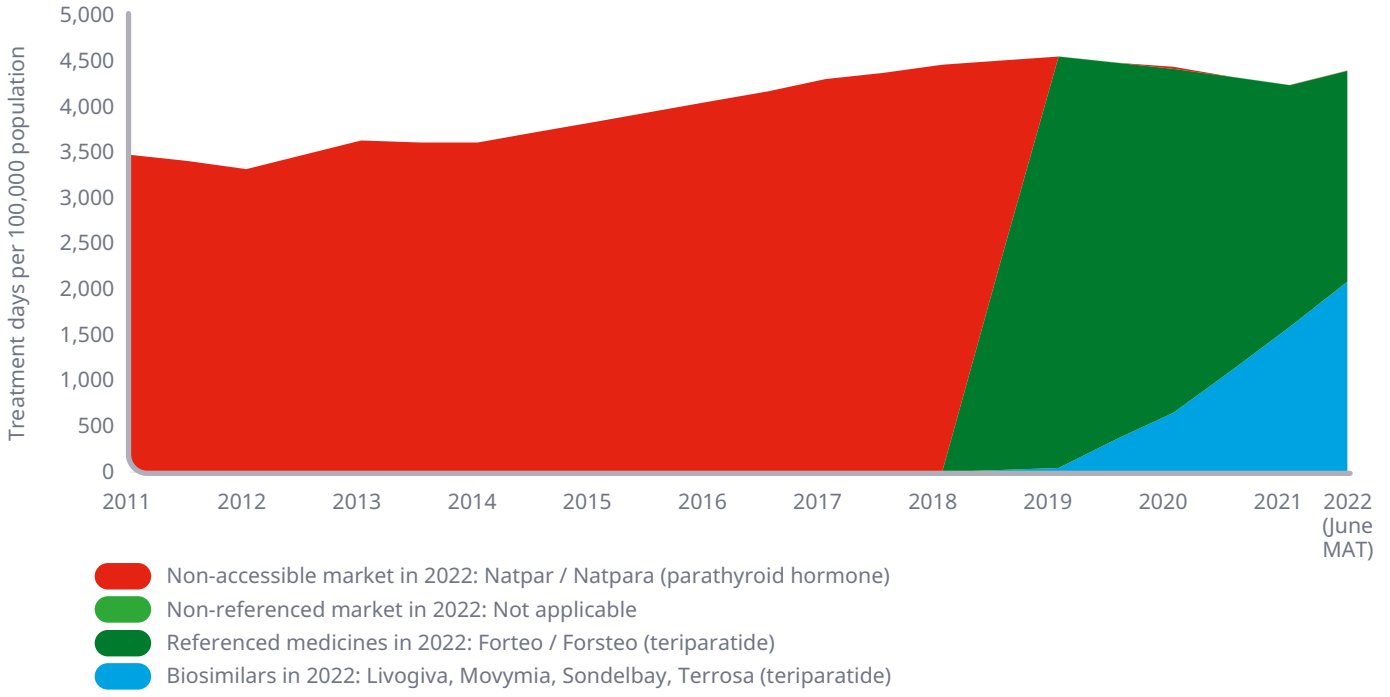
Parathyroid hormones

Parathyroid hormone is an analog of human parathyroid hormone (PTH) used to treat hypocalcemia caused by hypoparathyroidism. Teriparatide is a synthetic form of parathyroid hormone (PTH) used in the treatment of some forms of osteoporosis. According to IQVIA MIDAS and ARK Patent Intelligence insights, protection for recombinant teriparatide (brand name Forsteo) expired in 2019. The first biosimilars for teriparatide had already been centrally approved two years earlier in January 2017 (Movymia and Terrosa), and a third has now been approved in August 2020 (Livogiva). Sales for biosimilar teriparatide are now observed across Europe and this is the first year the market has been included within 'The Impact of Biosimilar Competition' report.

PARATHYROID HORMONES MARKET DEVELOPMENT

Natpar/Natpara and Preotact (parathyroid hormone) have been included in the 2022 report for completeness and classified within the 'non-accessible' market. The total market size has not increased as Natpar/Natpara accounts for <1% market, and Preotact has been withdrawn.

PTH market development



PTH approved indications

NAMING		CLASSIFICATION												INDICATIONS	
MOLECULE	PRODUCT	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022 (JUNE MAT)	OSTEOPEROSIS (IN POST MENOPAUSAL WMOEN AND MEN AT INCREASED RISK OF FRACTURE	HYPOPARATHYROIDISM
TERIPARATIDE*	FORTEO MOVYMIA TERROSA LIVOGIVA SONDELBAY	●	●	●	●	●	●	● ● ●	● ● ●	● ● ●	● ● ● ●	● ● ● ●	● ● ● ● ●	● ● ● ● ●	
PARATHYROID HORMONE	PREOTACT NATPAR/NATPARA	●	●	●				●	●	●	●	●	●	●	●

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

* TETRIDAR has been excluded as it is not approved via EMA biosimilars pathway

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

		AT	BE	BU	CZ	DK	FI	FR	DE	GR*	HU	IE	IT	NL	NO	PL	PT	RO	SK
MARKET SHARE TD (2022, JUNE MAT)	Biosimilar vs Referenced product	69%	0%	76%	77%	14%	8%	29%	42%	0%	93%	13%	61%	81%	49%	0%	34%	69%	100%
	Biosimilar vs Accessible market	69%	0%	76%	77%	14%	8%	29%	42%	0%	93%	13%	61%	81%	49%	0%	34%	69%	100%
	Biosimilar vs Total market	69%	0%	76%	77%	14%	8%	29%	41%	0%	93%	13%	61%	81%	49%	0%	34%	69%	100%
PRICE PER TD (2022 JUNE MAT/YR BEFORE BS ENTRY)	Biosimilar and Referenced product			-56%			-30%			-3%				-36%	-22%		-15%	-33%	
	Biosimilar accessible market			-56%			-30%			-3%				-36%	-22%		-15%	-33%	
	Total market	-59%		-56%	-47%	-65%	-30%	-21%	52%	-2%	-33%	-25%	-28%	-36%	-1%		-15%	-32%	-40%
VOLUME TD (2022, JUNE MAT/YR BEFORE BS ENTRY)	Biosimilar and Referenced product			26%			-18%			0%				7%	24%		4%	-2%	-14%
	Biosimilar accessible market			26%			-18%			0%				7%	24%		4%	-2%	-14%
	Total market	0.72		0.26	0.84	0.60	-0.18	0.04	0.10	0.00	0.18	0.00	-0.28	0.07	0.24		0.04	-0.02	-0.14
	TD per capita	0.10	0.01	0.00	0.02	0.11	0.02	0.05	0.02	0.08	0.04	0.08	0.06	0.04	0.07	0.00	0.02	0.02	0.01
	TD/capita (Yr before BS entrance)	0.06	0.00	0.00	0.01	0.07	0.02	0.05	0.02	0.09	0.03	0.08	0.09	0.03	0.06	0.00	0.02	0.02	0.02
	First recorded sales of biosimilars	2019		2021	2019	2019	2020	2019	2019	2022	2019	2019	2019	2020	2020		2020	2020	2019

* Only retail panel data is available for Greece

Note: Gaps in price and volume per TD are due to there being no 'Non-referenced' or 'Referenced' products in the year before biosimilar entry

Ophthalmology

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

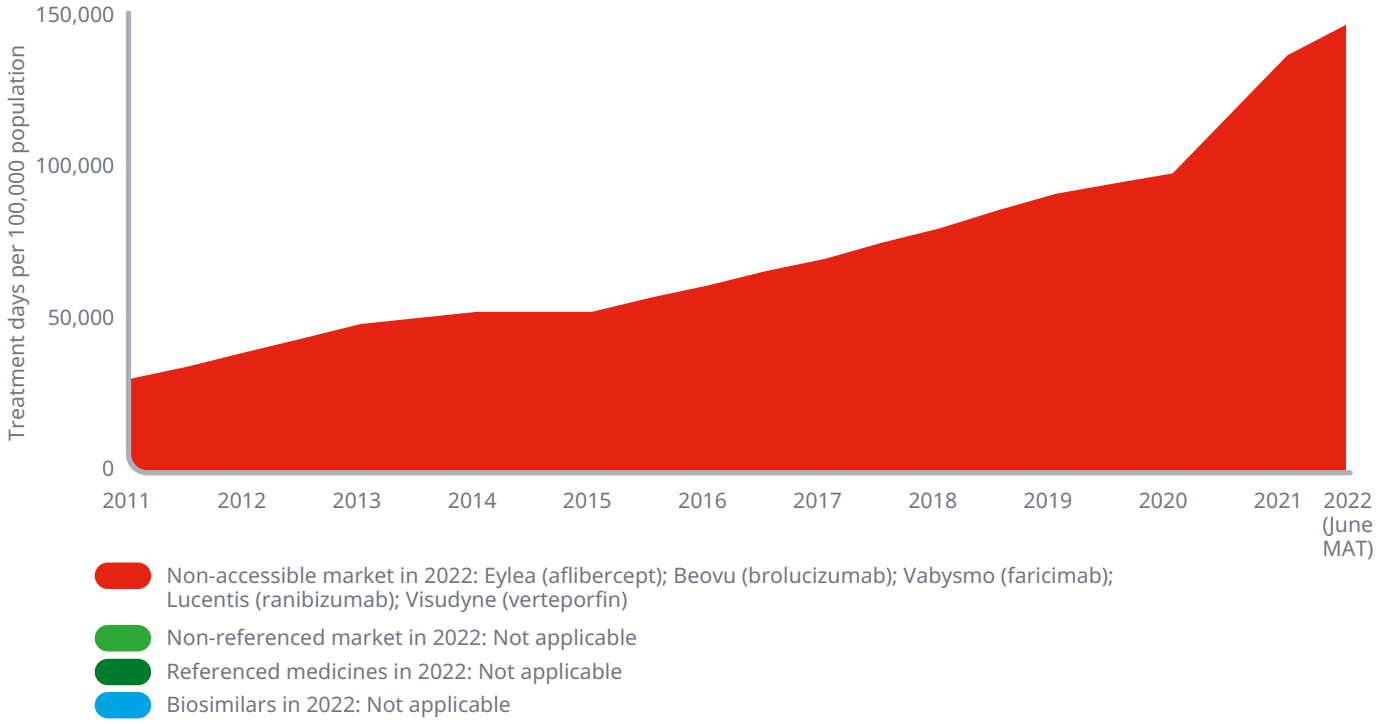
Eylea (aflibercept) and Lucentis (ranibizumab) are anti-VEGF agents used to treat several ocular inflammatory conditions, including wet age-related macular degeneration (AMD), macular edema, and diabetic retinopathy. They work by preventing the growth of abnormal blood vessels in the eye caused by the VEGF protein. Avastin (bevacizumab) is another anti-VEGF agent that is also used to treat inflammatory ocular diseases. However, considering that the primary indications used for bevacizumab biosimilars are in Oncology, and since IQVIA sales and treatment day volume cannot be split by indication, bevacizumab market dynamics are only considered in this separate Oncology section, and not in the Ophthalmology section.

WHO DDD's are not available for products in this class, so the DDD's were calculated using EMA dosing information.

OPHTHALMOLOGY MARKET DEVELOPMENT

Despite biosimilar entry in 2022, Lucentis is classified as 'non-referenced' in the 2022 report as it lost protection after June 2022, according to IQVIA MIDAS and ARK Patent intelligence. This therapy area will be included in subsequent reports to track the impact of biosimilar entry in this newly accessible market.

Ophthalmology market development



Ophthalmology approved indications

NAMING		CLASSIFICATION												INDICATIONS								DOSING	
MOLECULE	PRODUCT	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022 (JUNE MAT)	NEOVASCULAR (WET) AGE-RELATED MACULAR DEGENERATION (AMD)	VISUAL IMPAIRMENT DUE TO MACULAR OEDEMA SECONDARY TO RETINAL VEIN OCCLUSION (BRANCH RVO OR CENTRAL RVO)	VISUAL IMPAIRMENT DUE TO DIABETIC MACULAR OEDEMA (DME)	VISUAL IMPAIRMENT DUE TO MYOPIC CHOROIDAL NEOVASCULARISATION (MYOPIC CNV)	PROLIFERATIVE DIABETIC RETINOPATHY (PDR)	RETINOPATHY OF PREMATURITY (ROP) WITH ZONE I (STAGE 1+, 2+, 3 OR 3+), ZONE II(STAGE 3+) OR AP-ROP (AGGRESSIVE POSTERIOR ROP) DISEASE	EXUDATIVE (WET) AGE-RELATED MACULAR DEGENERATION (AMD) WITH PREDOMINANTLYCLASSIC SUBFOVEAL CHOROIDAL NEOVASCULARISATION (CNV)	SUBFOVEAL CHOROIDAL NEOVASCULARISATION SECONDARY TO PATHOLOGICAL MYOPIA	ROUTE	FREQUENCY
AFLIBERCEPT	EYLEA		●	●	●	●	●	●	●	●	●	●	●	●	●	●	●					Intravitreal	Every 8 wks
BROLUCIZUMAB	BEOVU										●	●	●	●		●						Intravitreal	Every 8 wks
FARICIMAB	VABYSMO												●	●		●						Intravitreal	Every 4 wks
PEGAPTANIB	MACUGEN	●												●								Intravitreal	Every 6 wks
RANIBIZUMAB*	LUCENTIS** BYOOVIZ	●	●	●	●	●	●	●	●	●	●	●	● ●	● ●	● ●	● ●	● ●	● ●	●			Intravitreal	Every 4 wks
VERTEPORFIN	VISUDYNE	●	●	●	●	●	●	●	●	●	●	●	●							●	●	UV + light activation	Every 12 wks

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

* ONGAVIA (ranibizumab) is approved in UK by MHRA but not by EMA;

** Lucentis is not yet considered a referenced product as it lost protection in July 2022

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

		AT	BE	BU	CZ	DK	FI	FR	DE	GR*	HU	IE	IT	NL	NO	PL	PT	RO	SK
MARKET SHARE TD (2022, JUNE MAT)	Biosimilar vs Referenced product	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
	Biosimilar vs Accessible market	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
	Biosimilar vs Total market	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
PRICE PER TD (2022 JUNE MAT/YR BEFORE BS ENTRY)	Biosimilar and Referenced product	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
	Biosimilar accessible market	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
	Total market	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
VOLUME TD (2022, JUNE MAT/YR BEFORE BS ENTRY)	Biosimilar and Referenced product	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
	Biosimilar accessible market	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
	Total market	0%	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	TD per capita	0.36	1.71	0.24	0.87	1.86	0.79	2.12	1.06	0.01	0.16	0.81	0.52	11.60	0.75	0.35	0.48	0.30	0.94
	TD/capita (Yr before BS entrance)	0.36	1.71	0.24	0.87	1.86	0.79	2.12	1.06	0.01	0.16	0.81	0.52	11.60	0.75	0.35	0.48	0.30	0.94
	First recorded sales of biosimilars																		

* Only retail panel data is available for Greece

Appendix

Table 1: EU list of approved biosimilars

MEDICINE NAME	INTERNATIONAL NON-PROPRIETARY NAME (INN) / COMMON NAME	THERAPEUTIC AREA	MARKETING AUTHORISATION DATE (OLD TO NEW)	MARKETING AUTHORISATION HOLDER
OMNITROPE	somatropin	Turner Syndrome; Prader-Willi Syndrome; Dwarfism, Pituitary	12/04/2006	Sandoz GmbH
ABSEAMED	epoetin alfa	Anemia; Kidney Failure, Chronic; Cancer	27/08/2007	Medice Arzneimittel Pütter GmbH Co. KG
EPOETIN ALFA HEXAL	epoetin alfa	Anemia; Kidney Failure, Chronic; Cancer	27/08/2007	Hexal AG
BINOCRIT	epoetin alfa	Anemia; Kidney Failure, Chronic	28/08/2007	Sandoz GmbH
RETACRIT	epoetin zeta	Anemia; Blood Transfusion, Autologous; Kidney Failure, Chronic; Cancer	18/12/2007	Pfizer Europe MA EEIG
SILAPO	epoetin zeta	Anemia; Blood Transfusion, Autologous; Cancer; Kidney Failure, Chronic	18/12/2007	Stada Arzneimittel AG
TEVAGRASTIM	filgrastim	Neutropenia; Hematopoietic Stem Cell Transplantation; Cancer	15/09/2008	Teva GmbH
RATIOGRASTIM	filgrastim	Neutropenia; Hematopoietic Stem Cell Transplantation; Cancer	15/09/2008	Ratiopharm GmbH
FILGRASTIM HEXAL	filgrastim	Neutropenia; Hematopoietic Stem Cell Transplantation; Cancer	6/02/2009	Hexal AG
ZARZIO	filgrastim	Neutropenia; Hematopoietic Stem Cell Transplantation; Cancer	6/02/2009	Sandoz GmbH
NIVESTIM	filgrastim	Neutropenia; Hematopoietic Stem Cell Transplantation; Cancer	7/06/2010	Pfizer Europe MA EEIG
REMSIMA	infliximab	Arthritis, Psoriatic; Spondylitis, Ankylosing; Colitis, Ulcerative; Psoriasis; Crohn Disease; Arthritis, Rheumatoid	10/09/2013	Celltrion Healthcare Hungary Kft.
INFLECTRA	infliximab	Arthritis, Psoriatic; Spondylitis, Ankylosing; Colitis, Ulcerative; Psoriasis; Crohn Disease; Arthritis, Rheumatoid	10/09/2013	Pfizer Europe MA EEIG
OVALEAP	follitropin alfa	Anovulation	27/09/2013	Theramex Ireland Limited
GRASTOFIL	filgrastim	Neutropenia	17/10/2013	Accord Healthcare S.L.U.
BEMFOLA	follitropin alfa	Anovulation	26/03/2014	Gedeon Richter Plc.
ABASAGLAR (PREVIOUSLY ABASRIA)	insulin glargine	Diabetes Mellitus	9/09/2014	Eli Lilly Nederland B.V.
ACCOFIL	filgrastim	Neutropenia	17/09/2014	Accord Healthcare S.L.U.
BENEPALI	etanercept	Arthritis, Psoriatic; Arthritis, Rheumatoid; Psoriasis	13/01/2016	Samsung Bioepis NL B.V.
FLIXABI	infliximab	Arthritis, Psoriatic; Spondylitis, Ankylosing; Colitis, Ulcerative; Arthritis, Rheumatoid; Crohn Disease; Psoriasis	26/05/2016	Samsung Bioepis NL B.V.
INHIXA	enoxaparin sodium	Venous Thromboembolism	15/09/2016	Techdow Pharma Netherlands B.V.
TERROSA	teriparatide	Osteoporosis	4/01/2017	Gedeon Richter Plc.
MOVYMIA	teriparatide	Osteoporosis	11/01/2017	STADA Arzneimittel AG
TRUXIMA	rituximab	Lymphoma, Non-Hodgkin; Arthritis, Rheumatoid; Wegener Granulomatosis; Leukemia, Lymphocytic, Chronic, B-Cell; Microscopic Polyangiitis	17/02/2017	Celltrion Healthcare Hungary Kft.
AMGEVITA	adalimumab	Arthritis, Psoriatic; Colitis, Ulcerative; Arthritis, Juvenile Rheumatoid; Spondylitis, Ankylosing; Psoriasis; Crohn Disease; Arthritis, Rheumatoid	21/03/2017	Amgen Europe B.V.
RIXIMYO	rituximab	Lymphoma, Non-Hodgkin; Arthritis, Rheumatoid; Microscopic Polyangiitis; Wegener Granulomatosis	15/06/2017	Sandoz GmbH
RIXATHON	rituximab	Lymphoma, Non-Hodgkin; Arthritis, Rheumatoid; Leukemia, Lymphocytic, Chronic, B-Cell; Wegener Granulomatosis; Microscopic Polyangiitis; Pemphigus	15/06/2017	Sandoz GmbH

MEDICINE NAME	INTERNATIONAL NON-PROPRIETARY NAME (INN) / COMMON NAME	THERAPEUTIC AREA	MARKETING AUTHORISATION DATE (OLD TO NEW)	MARKETING AUTHORISATION HOLDER
ERELZI	etanercept	Arthritis, Psoriatic; Psoriasis; Arthritis, Juvenile Rheumatoid; Arthritis, Rheumatoid; Spondylitis, Ankylosing	23/06/2017	Sandoz GmbH
BLITZIMA	rituximab	Lymphoma, Non-Hodgkin; Leukemia, Lymphocytic, Chronic, B-Cell	13/07/2017	Celltrion Healthcare Hungary Kft.
INSULIN LISPRO SANOFI	insulin lispro	Diabetes Mellitus	19/07/2017	sanofi-aventis groupe
IMRALDI	adalimumab	Spondylitis, Ankylosing; Arthritis, Rheumatoid; Uveitis; Colitis, Ulcerative; Psoriasis; Arthritis, Psoriatic; Crohn Disease; Hidradenitis Suppurativa; Arthritis	24/08/2017	Samsung Bioepis NL B.V.
ONTRUZANT	trastuzumab	Stomach Neoplasms; Breast Neoplasms	15/11/2017	Samsung Bioepis NL B.V.
MVASI	bevacizumab	Carcinoma, Renal Cell; Peritoneal Neoplasms; Ovarian Neoplasms; Breast Neoplasms; Carcinoma, Non-Small-Cell Lung; Fallopian Tube Neoplasms	15/01/2018	Amgen Technology (Ireland) UC
HERZUMA	trastuzumab	Stomach Neoplasms; Breast Neoplasms	9/02/2018	Celltrion Healthcare Hungary Kft.
SEMGLEE	insulin glargine	Diabetes Mellitus	23/03/2018	Viatris Limited
KANJINTI	trastuzumab	Stomach Neoplasms; Breast Neoplasms	16/05/2018	Amgen Europe BV
ZESSLY	infliximab	Arthritis, Psoriatic; Psoriasis; Crohn Disease; Arthritis, Rheumatoid; Colitis, Ulcerative; Spondylitis, Ankylosing	18/05/2018	Sandoz GmbH
TRAZIMERA	trastuzumab	Stomach Neoplasms; Breast Neoplasms	26/07/2018	Pfizer Europe MA EEIG
HYRIMOZ	adalimumab	Arthritis, Rheumatoid; Arthritis, Psoriatic; Spondylitis, Ankylosing; Uveitis; Hidradenitis Suppurativa; Colitis, Ulcerative; Arthritis, Juvenile Rheumatoid; Crohn Disease; Skin Diseases, Papulosquamous	26/07/2018	Sandoz GmbH
HEFIYA	adalimumab	Spondylitis, Ankylosing; Hidradenitis Suppurativa; Psoriasis; Arthritis, Juvenile Rheumatoid; Uveitis	26/07/2018	Sandoz GmbH
HULIO	adalimumab	Hidradenitis Suppurativa; Psoriasis; Uveitis; Arthritis, Rheumatoid; Spondylitis, Ankylosing; Crohn Disease; Colitis, Ulcerative; Arthritis, Psoriatic	17/09/2018	Viatris Limited
PELGRAZ	pegfilgrastim	Neutropenia	21/09/2018	Accord Healthcare S.L.U.
FULPHILA	pegfilgrastim	Neutropenia	20/11/2018	Viatris Limited
PELMEG	pegfilgrastim	Neutropenia	20/11/2018	Mundipharma Corporation (Ireland) Limited
ZIEXTENZO	pegfilgrastim	Neutropenia	22/11/2018	Sandoz GmbH
OGIVRI	trastuzumab	Stomach Neoplasms; Breast Neoplasms	12/12/2018	Viatris Limited
ZIRABEV	bevacizumab	Colorectal Neoplasms; Breast Neoplasms; Carcinoma, Non-Small-Cell Lung; Carcinoma, Renal Cell; Uterine Cervical Neoplasms	14/02/2019	Pfizer Europe MA EEIG
IDACIO	adalimumab	Arthritis, Rheumatoid; Arthritis, Psoriatic; Psoriasis; Spondylitis, Ankylosing; Uveitis; Hidradenitis Suppurativa; Colitis, Ulcerative; Crohn Disease; Arthritis, Juvenile Rheumatoid	2/04/2019	Fresenius Kabi Deutschland GmbH
GRASUSTEK	pegfilgrastim	Neutropenia	20/06/2019	Juta Pharma GmbH
CEGFILA (PREVIOUSLY PEGFILGRASTIM MUNDIPHARMA)	pegfilgrastim	Neutropenia	19/12/2019	Mundipharma Corporation (Ireland) Limited
AMSPARITY	adalimumab	Arthritis, Rheumatoid; Arthritis, Psoriatic; Psoriasis; Spondylitis, Ankylosing; Uveitis; Hidradenitis Suppurativa; Colitis, Ulcerative; Crohn Disease; Arthritis, Juvenile Rheumatoid	13/02/2020	Pfizer Europe MA EEIG
RUXIENCE	rituximab	Leukemia, Lymphocytic, Chronic, B-Cell; Arthritis, Rheumatoid; Microscopic Polyangiitis; Pemphigus	1/04/2020	Pfizer Europe MA EEIG
NEPEXTO	etanercept	Arthritis, Rheumatoid; Arthritis, Juvenile Rheumatoid; Arthritis, Psoriatic; Spondylarthropathies; Spondylitis, Ankylosing; Psoriasis	20/05/2020	Mylan IRE Healthcare Limited
INSULIN ASPART SANOFI	insulin aspart	Diabetes Mellitus	25/06/2020	sanofi-aventis groupe
ZERCEPAC	trastuzumab	Breast Neoplasms; Stomach Neoplasms	27/07/2020	Accord Healthcare S.L.U.
AYBINTIO	bevacizumab	Colorectal Neoplasms; Breast Neoplasms; Ovarian Neoplasms; Fallopian Tube Neoplasms; Peritoneal Neoplasms; Carcinoma, Non-Small-Cell Lung; Carcinoma, Renal Cell; Uterine Cervical Neoplasms	19/08/2020	Samsung Bioepis NL B.V.

MEDICINE NAME	INTERNATIONAL NON-PROPRIETARY NAME (INN) / COMMON NAME	THERAPEUTIC AREA	MARKETING AUTHORISATION DATE (OLD TO NEW)	MARKETING AUTHORISATION HOLDER
LIVOGIVA	teriparatide	Osteoporosis	27/08/2020	Theramex Ireland Limited
NYVEPRIA	pegfilgrastim	Neutropenia	18/11/2020	Pfizer Europe MA EEIG
ONBEVZI	bevacizumab	Colorectal Neoplasms; Breast Neoplasms; Ovarian Neoplasms; Fallopian Tube Neoplasms; Peritoneal Neoplasms; Carcinoma, Non-Small-Cell Lung; Carcinoma, Renal Cell; Uterine Cervical Neoplasms	11/01/2021	Samsung Bioepis NL B.V.
KIRSTY (PREVIOUSLY KIXELLE)	insulin aspart	Diabetes Mellitus	5/02/2021	Mylan Ireland Limited
YUFLYMA	adalimumab	Arthritis, Rheumatoid; Arthritis, Psoriatic; Psoriasis; Spondylitis, Ankylosing; Uveitis; Hidradenitis Suppurativa; Colitis, Ulcerative; Crohn Disease; Arthritis, Juvenile Rheumatoid	11/02/2021	Celltrion Healthcare Hungary Kft.
ALYMSYS	bevacizumab	Colorectal Neoplasms; Breast Neoplasms; Ovarian Neoplasms; Peritoneal Neoplasms; Carcinoma, Non-Small-Cell Lung; Carcinoma, Renal Cell; Uterine Cervical Neoplasms	26/03/2021	Mabxience Research SL
OYAVAS	bevacizumab	Colorectal Neoplasms; Breast Neoplasms; Ovarian Neoplasms; Fallopian Tube Neoplasms; Peritoneal Neoplasms; Carcinoma, Non-Small-Cell Lung; Carcinoma, Renal Cell; Uterine Cervical Neoplasms	26/03/2021	STADA Arzneimittel AG
ABEVMY	bevacizumab	Colorectal Neoplasms; Breast Neoplasms; Ovarian Neoplasms; Fallopian Tube Neoplasms; Peritoneal Neoplasms; Carcinoma, Non-Small-Cell Lung; Carcinoma, Renal Cell; Uterine Cervical Neoplasms	21/04/2021	Mylan IRE Healthcare Limited
BYOOVIZ	ranibizumab	Wet Macular Degeneration; Macular Edema; Diabetic Retinopathy; Myopia, Degenerative	18/08/2021	Samsung Bioepis NL B.V.
LIBMYRIS	adalimumab	Arthritis, Rheumatoid; Arthritis, Juvenile Rheumatoid; Spondylitis, Ankylosing; Arthritis, Psoriatic; Psoriasis; Hidradenitis Suppurativa; Crohn Disease; Colitis, Ulcerative; Uveitis	12/11/2021	Stada Arzneimittel AG
HUKYNDRA	adalimumab	Arthritis, Psoriatic; Arthritis, Juvenile Rheumatoid; Arthritis, Rheumatoid; Colitis, Ulcerative; Crohn Disease; Hidradenitis Suppurativa; Psoriasis; Spondylitis, Ankylosing; Uveitis	15/11/2021	Stada Arzneimittel AG
SONDELBAY	teriparatide	Osteoporosis	24/03/2022	Accord Healthcare S.L.U.
STIMUFEND	pegfilgrastim	Neutropenia	28/03/2022	Fresenius Kabi Deutschland GmbH
TRUVELOG MIX 30	insulin aspart	Diabetes Mellitus	25/04/2022	sanofi-aventis groupe
INPREMZIA	insulin human (rDNA)	Diabetes Mellitus	25/04/2022	Baxter Holding B.V.
VEGZELMA	bevacizumab	Colorectal Neoplasms; Breast Neoplasms; Ovarian Neoplasms; Fallopian Tube Neoplasms; Peritoneal Neoplasms; Carcinoma, Non-Small-Cell Lung; Carcinoma, Renal Cell; Uterine Cervical Neoplasms	17/08/2022	Celltrion Healthcare Hungary Kft.
RANIVISIO	ranibizumab	Wet Macular Degeneration; Macular Edema; Diabetic Retinopathy; Diabetes Complications	25/08/2022	Midas Pharma GmbH

Source: EMA website, data accessed November 2022.
(https://www.ema.europa.eu/en/medicines/download-medicine-data#european-public-assessment-reports-(epar)-section)

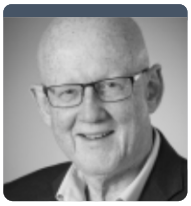
Appendix

Table 2: Most recent list of biosimilars under review by EMA (October 2022)

INTERNATIONAL NON-PROPRIETARY NAME (INN) (SALT, ESTER, DERIVATIVE, ETC.) / COMMON NAME	THERAPEUTIC AREA (ATC LEVEL 2)	ORPHAN PRODUCT	EMA CLASSIFICATION: GENERIC, HYBRID OR BIOSIMILAR	START OF EVALUATION(S)
AFLIBERCEPT	Ophthalmologicals	N	Y	19/05/2022
BEVACIZUMAB	Antineoplastic medicines	N	Y	24/12/2020
ECULIZUMAB	Immunosuppressants	N	Y	24/03/2022 14/07/2022
FILGRASTIM	Immunostimulants	N	Y	24/02/2022
NATALIZUMAB	Immunosuppressants	N	Y	14/07/2022
PEGFILGRASTIM	Immunostimulants	N	Y	30/09/2021 28/10/2021
TERIPARATIDE	Calcium homeostasis	N	Y	01/10/2020
TOCILIZUMAB	Immunosuppressants	N	Y	18/08/2022 29/09/2022
TRASTUZUMAB	Antineoplastic medicines	N	Y	25/02/2021
TRASTUZUMAB	Antineoplastic medicines	N	Y	20/01/2022

"Source: EMA, October 2022: report accessed November 2022 (https://www.ema.europa.eu/documents/report/applications-new-human-medicines-under-evaluation-chmp-October-2022_en.xlsx)"

About the Authors



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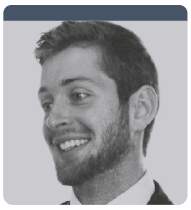

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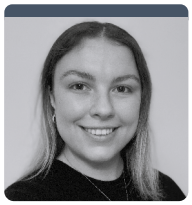

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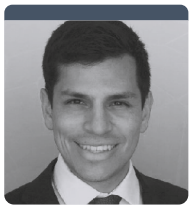

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Aurelio creates topical and forward-looking strategic content relevant to pharma executives worldwide and publishes articles, blogs and white papers on a regular basis. Aurelio's predominant focus is on off-patent markets where he generates evidence-led insights with a view to spark high-level discourse on biosimilars, generics and value added medicines. Moreover, he is involved in numerous projects exploring the interface between healthcare and digital technology.

He is considered a subject matter expert in these areas and speaks at numerous conferences worldwide, presents at board-level meetings and engages in consulting projects. Prior to IQVIA, Aurelio has worked in Discovery R&D and as a strategy consultant in Life Sciences. He holds an MSci in Chemistry from Imperial College London.

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